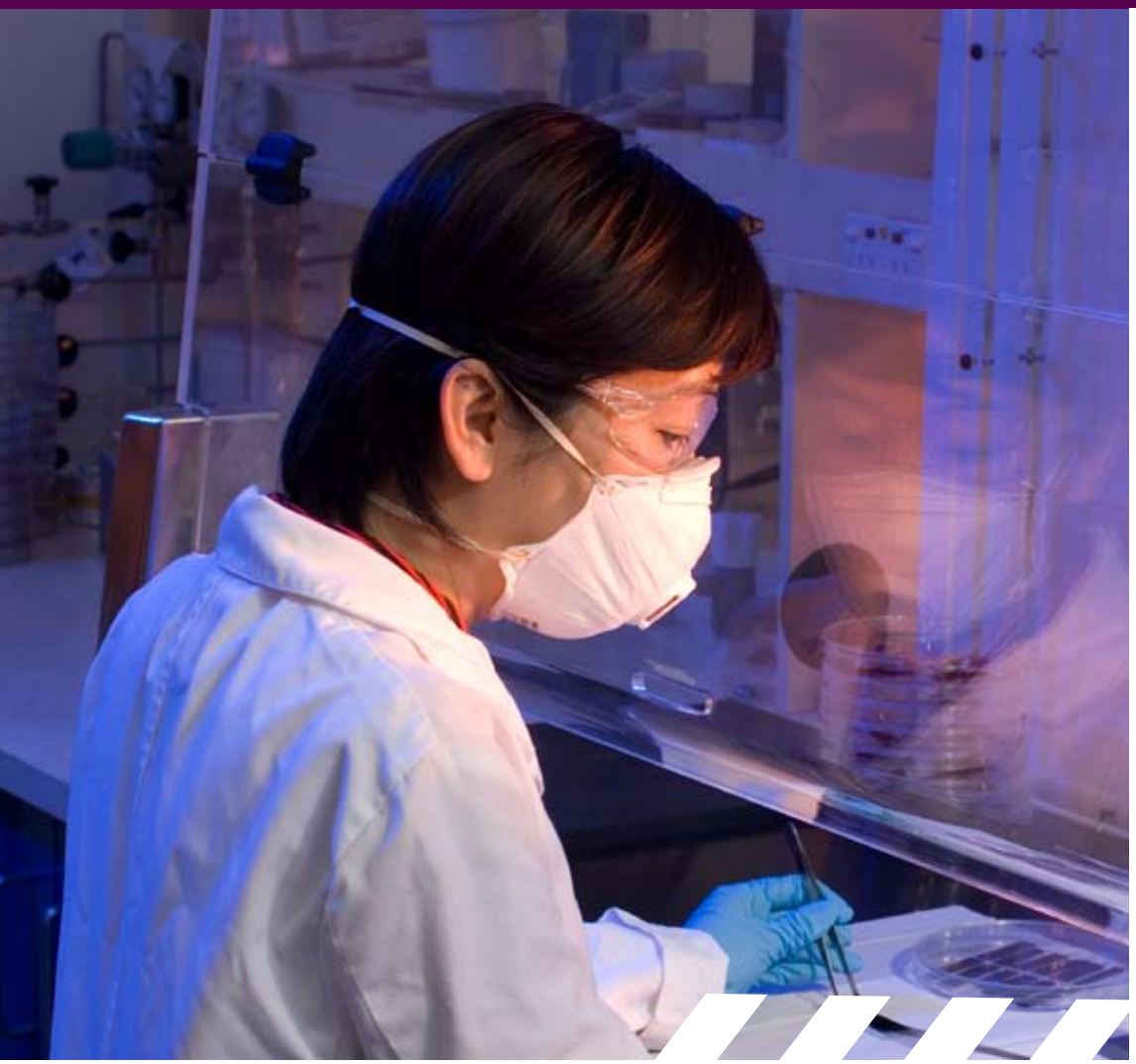
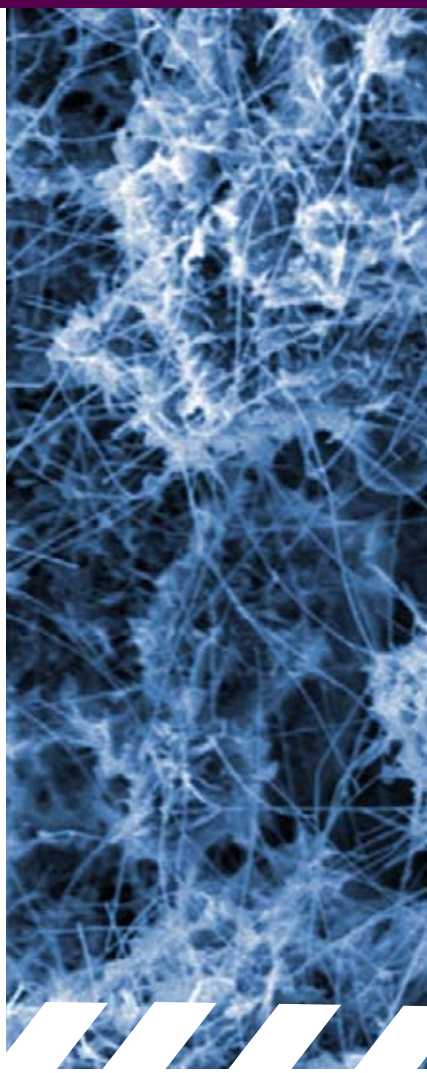
ENGINEERED NANOMATERIALS: EVIDENCE ON THE EFFECTIVENESS OF WORKPLACE CONTROLS TO PREVENT EXPOSURE





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Engineered Nanomaterials: Evidence on the Effectiveness of Workplace Controls to Prevent Exposure

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List of Abbreviations

AC	Alternating Current
ACGIH	American Conference of Governmental Industrial Hygienists
ALARP	As Low As Reasonably Practicable
APS	Aerodynamic Particle Sizer
ASCC	Australian Safety and Compensation Council
ASTM	American Standard Testing Method
BAuA	German Federal Institute for Occupational Safety and Health
BMD	Bench Mark Dose
BSI	British Standards Institute
CMAR	Carcinogenic-Mutagenic-Asthmagenic-Reproductive toxin
CMD	Count Median Diameter
CNTs	Carbon Nanotubes
COSHH	Control of Substances Hazardous to Health
CPC	Condensation Particle Counter
CSIRO	(Australian) Commonwealth Scientific and Industrial Research Organisation
DBD	Dielectric Barrier Discharge
DEEWR	(Australian) Department of Education, Employment and Workplace Relations
DENSRC	(U.S.) Department of Energy Nanoscale Science Research Centers
DMA	Differential Mobility Analyser
DOP	Dioctyl Phthalate
EC	European Community
EDDNP	Environmental Defence Dupont Nano Partnership
EDX	Energy Dispersive X-ray spectroscopy
EHS	Environmental Health and Safety
ELPI	Electrical Low Pressure Impactor
ESP	Electrostatic Precipitators
EU	European Union
FMPS	Fast Mobility Particle Spectrometer
GSD	Geometric Standard Deviation
HEPA	High Efficiency Particulate Air
HIPCO	High Pressure Carbon Monoxide
HOC	Hierarchy of Control
HSE	(Great Britain's) Health and Safety Executive
ICSC	International Chemical Safety Card
ICON	International Council on Nanotechnology
ILO	International Labour Organization
ISO	International Organization for Standardization
JKR	Johnson, Kendall and Roberts (Adhesion Theory)

LEV	Local Exhaust Ventilation
MECH	Fibrous Mechanical Filters
MPPS	Most Penetrating Particle Size
MSDS	Material Safety Data Sheet
MWCNTs	Multi-Walled Carbon Nanotubes
NanoVic	Nanotechnology Victoria Pty Ltd
NIOSH	(U.S.) National Institute for Occupational Safety and Health
NNI	National Nanotechnology Initiative
NNS	(Australian) National Nanotechnology Strategy
NOAEL	No-Observed-Adverse-Effect-Level
NOSH	Nanoparticle Occupational Safety and Health
NRC	National Research Council
OECD	Organisation for Economic Co-operation and Development
OEL	Occupational Exposure Limit
OHS	Occupational Health and Safety
PC	Protective Clothing
PPE	Personal Protective Equipment
PTFE	Polytetrafluoroethylene
QD	Quantum Dot
REACH	Registration, Evaluation, Authorisation and Restriction of Chemical substances
RPE	Respiratory Protective Equipment
SCBA	Self-Contained Breathing Apparatus
SDS	Safety Data Sheet
SEM	Scanning Electron Microscopy
SMPS	Scanning Mobility Particle Sizer
SWCNTs	Single-Walled Carbon Nanotubes
TEM	Transmission Electron Microscopy
TWA	Time Weighted Average
USEPA	United States Environmental Protection Authority
VCI	German Chemical Industry Association

Executive Summary

This literature review has brought together and evaluated evidence on the effectiveness of workplace controls to prevent or minimise exposure to engineered nanomaterials. Only workplace settings such as laboratories, pilot plants and production plants have been considered; environmental safety and consumer product safety were not considered.

The review has determined that there is evidence that control and risk management methodologies which are already known can provide levels of protection for workers from exposure to engineered nanomaterials in the occupational environment. Further testing and data is needed in specific workplace situations to understand the levels of protection afforded, and ensure effectiveness.

This statement however needs to be qualified on the basis of the lack of health effects data that is currently available for many engineered nanomaterials, because without such data, it is not possible to fully inform risk management processes for working with engineered nanomaterials. A further implication of the limited amount of toxicological data available is that a precautionary approach to the prevention and control of workplace exposures should be used.

There are currently two engineered nanomaterials for which Australian National Exposure Standards have previously been established, i.e. fumed silica and carbon black. The fact that these have been established indicates that there is evidence of safe levels of exposure to some engineered nanomaterials, however such evidence is lacking for most engineered nanomaterials.

For nanomaterials, there are issues associated with information provision, relating to labels and the quality of information being provided in some material safety data sheets (MSDS) – which impacts on how well nanomaterials are controlled. This matter is currently being investigated by a Safe Work Australia project.

A number of groups have called for specific regulation of nanomaterials, including for nanomaterials to be assessed as new chemicals. In some cases this would require new safety testing to determine whether a nanomaterial presents a different hazard potential to its bulk counterpart, before being permitted for commercial use.

Workplace controls from each strategy in the hierarchy of control have been examined and the evidence for their effectiveness considered. This evidence, together with the authors' associated recommendations, are as follows:

- **Elimination** – Since the specific properties of engineered nanomaterials are usually required for manufacturing a novel product, it is unlikely that this option will often be feasible, and no examples have been found in this review.

- **Substitution and/or modification** – This control measure is not yet widely used in the workplace for nanomaterials. However, nanomaterial modification has been

shown to reduce the *in vitro* cytotoxicity of various nanomaterials, e.g. of fullerenes, carbon nanotubes (CNT), quantum dots and metal/metal oxide nanoparticles. This review has identified that focus should be placed on potential applications of this approach for the workplace – opportunities to help protect the health of workers should be investigated.

- **Enclosure** – Current evidence indicates that worker exposure is significantly reduced or negated if a process involving engineered nanomaterials, which would otherwise result in the release of airborne particles, is performed in a properly designed enclosure/containment. The method of containment or enclosure is designed for the specific processes, but is usually implemented in combination with other control measures, e.g. administrative controls and/or personal protective equipment (PPE).

- **Extraction** – Evidence indicates that worker exposure is significantly reduced or negated through the use of correctly designed and implemented extraction ventilation and filtration for processes involving engineered nanomaterials that would normally result in the release of airborne particles. This control measure is usually implemented in combination with other control measures, e.g. administrative controls and/or PPE. The better extraction methods have involved the use of high efficiency particulate air (HEPA) filtration and electrostatic precipitation.

- **Administrative controls** – There are a range of administrative controls that may be implemented for workers involved in using engineered nanomaterials. These are usually implemented in combination with other control measures e.g. enclosure, extraction and PPE.

- **PPE** – Evidence indicates that there are a range of PPE which may be used for engineered nanomaterials and can provide some level of protection, including N95, N100 or P100 face mask and filters. N95 and N100 correspond approximately to P2 and P3 Australian type face masks, respectively (see Table B). P100 also approximately corresponds to P3, the difference between P100 and N100 masks being that P100 masks provide oil-proof protection whereas N100 do not. Double-gloving using nitrile type gloves and the use of other garments of non-woven fabrics (e.g. Tyvek polymeric material) can also provide protection.

  The use of PPE should be considered as the last line of defence in the hierarchy of workplace exposure mitigation approaches, after all other available measures have been implemented. PPE should also be worn on a precautionary basis whenever the failure of a single control, including an engineering control, could entail a significant risk of exposure to workers. PPE will also be needed in situations where the use of engineering controls is impractical. PPE is usually implemented in combination with other control measures, e.g. process enclosure, extraction and administrative controls.

The risk management process that is proposed for research and early development activities involving nanomaterials, is that of ‘control banding’, where similar control measures are used within categories of nanomaterials that have been grouped (“banded”) according to their exposure potential and hazardous properties, i.e. grouped according to risk. Control banding

is considered to be an appropriate method because of the current lack of data available for the risk assessment of individual nanomaterials but there is some understanding of hazards posed by different groups of nanomaterials e.g. CNTs.

These control measures include: the engineering controls of enclosure, HEPA filtration and local exhaust ventilation (LEV) for the nanomaterial process; administrative controls; and using P2 or P3 face piece masks or self-contained breathing apparatus (SCBA) as appropriate for respiratory protection, double-gloving and non-woven fabrics for dermal/general protection, and other protective measures as required. The same control measures are expected to be able to protect workers in operations associated with research, e.g. maintenance and cleaning of the work space, and in down-stream operations such as manufacturing or construction activities, however their usage would have to be determined by an appropriate risk management process. However, if nanoscale materials are classified as potential carcinogens on the macroscale (Risk Phrase R45), then specialist advice should be sought when handling these materials.

Then in later development/production activities, and once the toxicological and other relevant properties of the nanomaterial have been determined, the control measures should be reviewed through a thorough process-specific risk assessment and, if warranted, modified accordingly. The authors recommend that a complete life-cycle analysis of the nanomaterial should always be made to identify potential ‘hotspots’ of worker exposure, including construction, packaging, manufacturing, handling, maintenance or cleaning work, and end-of-life and safe disposal issues. There are a whole range of jobs and tasks that need to be considered. Existing ventilation systems that are effective for extracting ultrafine dusts in other industries should also be employed and optimally maintained where appropriate, in order to reduce exposure to engineered nanomaterials.

A specific issue identified is the limited amount of data on the effectiveness of controls for nanomaterial types that are more commonly produced and used by Australian nanotechnology industries, such as silicon, metal/metal oxide and CNT-based nanomaterials. Assessment requires research studies that involve actual workplace measurements taken before/after a nanomaterial process commences, and before/after control measures have been employed, thereby providing accurate comparisons of the levels of both engineered and incidental particulates between each situation. As indicated in the previous paragraph, there are a whole range of jobs and tasks that need to be examined in the assessment process.

Safe Work Australia has established the Nanotechnology OHS Measurement Reference Group to progress the development of nanomaterials emissions and exposure measurement capability in Australian workplaces. Currently, the capability of measuring exposures to engineered nanomaterials is limited. The development of easily operable, transportable, inexpensive and accurate real-time monitoring techniques to determine airborne concentrations of nanomaterials in the workplace is a goal, and would assist in environmental monitoring, detection of airborne nanomaterials and validation of workplace controls.

The uncertainties about health and safety risks, and the possibility of a long latency period before any symptoms of disease develop, suggest a precautionary approach is required to control the manufacture, use, storage, handling and disposal of nanoparticles. Thus, until

accurate and detailed methods are developed to monitor for nanomaterials in the occupational environment, and research has also provided further validated evidence of the effectiveness of workplace controls to protect workers from exposure to specific engineered nanomaterials in the actual workplace, the authors recommend that a precautionary approach guided by reference to the ‘precautionary principle’ be adopted in order to limit workplace exposure. However, once data about the health and safety risks have been determined and defined, the principle of ‘As Low As Reasonably Practicable’ (ALARP) can be adopted.

Background and Scope of this report

There has been an exponential growth in the development of nanomaterials and nanotechnology applications, along with the quantity of related publications. This has been accompanied by an increased awareness of nanosafety issues in government, industry and public groups that has resulted in the expansion of nanosafety and nanotoxicology research.

In July 2006, the Australian Safety and Compensation Council (ASCC) published a report entitled *"A Review of the Potential Occupational Health & Safety Implications from Nanotechnology*" (ASCC 2006). The report reviewed the literature, published until early 2006, with respect to the occupational health and safety (OHS) issues associated with the burgeoning nanotechnology industry. During 2006, Nanotechnology Victoria Pty Ltd (NanoVic) commissioned a position paper from NanoSafe Australia, a research and testing network in nanotoxicology and nanosafety, to provide practical information for the workplace concerning the current OHS best practices for the Australian nanotechnology industry (http://www.rmit.edu.au/nanosafe). The report was subsequently published in the OHS literature (Harford et al. 2007). Between late 2007 and early 2008, NanoSafe Australia members (Paul Wright and Neale Jackson) performed an independent OHS workplace audit of major nanotechnology facilities at the Australian Commonwealth Scientific and Industrial Research Organisation (CSIRO), in support of the newly established Nanosafety Theme of the CSIRO Niche Manufacturing Flagship.

As information on workplace controls was starting to become available, a comprehensive review covering the hierarchy of workplace controls was needed to examine the evidence on the effectiveness of workplace controls for engineered nanomaterials. Consequently, Safe Work Australia commissioned the OHS Research and Education Centre at RMIT University to undertake this review to examine the evidence on the effectiveness of workplace controls to prevent or minimise exposure to engineered nanomaterials during their life-cycle of manufacture, handling, use and disposal.

Methodology employed for this report

The evidence base used in this review for the effectiveness of workplace controls has been developed from previous knowledge, as determined from the literature, and practical experience obtained by the NanoSafe Australia members within the OHS Research and Education Centre at RMIT University. This process has involved input from experts in nanotechnology, nanotoxicology, nanosafety, OHS, occupational hygiene and toxicology, to ensure a relevant and accurate evaluation of current knowledge and technologies.

This review has brought together and evaluated evidence for the effectiveness of workplace controls, and covers the hierarchy of controls, i.e. elimination, substitution, engineering controls, administrative controls and personal protective equipment. Specific workplace evaluations of control effectiveness were not undertaken.

This report considers the following to be evidence of effectiveness:

- Workplace measurements
- Experimental measurements

- Workplace observations
- Recommendations on guidance by organisations (though it is acknowledged that it is not always possible to ascertain from these documents the basis (or evidence) for recommendations)
- How well-structured a risk management process is for managing processes involving engineered nanomaterials

The following review process was undertaken:

a) A list of publications, mainly from the past ten years, was qualitatively examined to determine which publications contained any reference (in either their title or abstract) for content that related to workplace controls of nanomaterials. This list of references was built from a number of databases including (amongst others):

- TOXNET (Toxicology Data Network at http://toxnet.nlm.nih.gov/ that includes "Toxline") and PubMed at U.S. National Library of Medicine (NLM)/National Institutes of Health (NIH)
- U.K. government HSE Nanoalerts (http://www.hse.gov.uk/horizons/nanotech/nanoalert001.pdf)
- International Council on Nanotechnology (ICON) database of published papers on nanotoxicology based at Rice University, Texas, USA (Environmental Health and Safety EHS database at http://icon.rice.edu/research.cfm)
- SAFENANO Publication Database at the U.K. Institute of Occupational Medicine (http://www.safenano.org/)
- Nanoparticle Information Library (NIL, http://www2a.cdc.gov/niosh-nil/) at the U.S. National Institute for Occupational Safety and Health (NIOSH)
- Nanotechnology Risk Resources database of the Nanoscale Science and Engineering Center, University of Wisconsin – Madison, USA (http://www.nsec.wisc.edu/NanoRisks/NS--NanoRisks.php); and their associated weblinks.

b) A total of 56 articles were determined as being relevant by this search for a detailed literature review and evaluation. The review and evaluation was summarised and tabulated to enable easier comparison between specific attributes of the different papers (as shown in Appendix 1, Tables 1 and 2).

Part 1 - Overall Risk Management Approaches

1.1 Nanotechnologies and workplace health and safety laws

Australia's occupational health and safety (OHS) legislation aims to protect the health and safety of researchers and workers developing, manufacturing or using engineered nanomaterials. This is reflected in OHS legal duties which require that:

- manufacturers ensure that, as far as reasonably practicable, substances are manufactured to be safe if they are used as intended
- suppliers ensure that, as far as reasonably practicable, substances supplied to research laboratories and workplaces are safe if they are used as intended
- employers provide and maintain a working environment that is safe, and
- workers follow occupational health and safety requirements to protect their own health and safety, and that of others who may be affected by the work they are doing.

Additionally, there are specific OHS regulations for workplace chemicals, which include engineered nanomaterials. Manufacturers and importers of workplace chemicals, including products which contain engineered nanomaterials, need to determine if their products are hazardous substances and/or dangerous goods before supplying them to workplaces. Employers need to evaluate and manage nanotechnology OHS risks in their workplaces. To evaluate and manage the risks, employers need to understand the:

- hazardous properties of products which contain engineered nanomaterials
- potential for exposure to engineered nanomaterials which may be harmful
- effectiveness of workplace controls to either prevent or minimise exposure.

However, for nanomaterials there are issues associated with information provision, relating to labels and the quality of information being provided in some MSDS – which impacts on how well nanomaterials are controlled. This matter is currently being investigated by a Safe Work Australia project, and this includes identifying any amendments which may be needed to comply with obligations under the relevant regulations (e.g. to the labelling and MSDS Codes of Practice).

This report notes that a number of organisations have expressed concern about the adequacy of regulation of nanotechnology. The Australian Council of Trade Unions (ACTU) published a Fact Sheet on *Nanotechnology – why unions are concerned* in April 2009 (ACTU 2009). In the Fact Sheet, the ACTU makes the following recommendations:

- Nanoscale chemicals must be classified as new chemicals under the National Industrial Chemicals and Notification and Assessment Scheme (NICNAS),
- Government agencies should develop new standards for the handling of nanotechnology,
- A mandatory requirement that all commercial products containing nanomaterials be labelled,

- That a federal registry be established of all companies and organisations manufacturing, importing and supplying products containing nanomaterials,
- A tripartite body to be established to oversee the implementation of this regulatory framework,
- Adoption of the “Precautionary Principle” when dealing with nanomaterials,
- Development and improvement of hazard identification, assessment and control mechanisms for nanomaterials,
- Enforcement of new exposure standards using an active inspectorate, and
- Monitoring of the health impacts on Australian workers involved in nanotechnology and investment in related medical research.

1.2 Potential health effects of engineered nanomaterials

The aim of this section is to provide context for consideration of the effectiveness of workplace controls, not to provide a comprehensive review of the toxicology of engineered nanomaterials. The authors note that Safe Work Australia has commissioned a separate detailed review of the toxicology.

Engineered nanomaterials are being used to develop new and enhanced products and processes that provide significant advances compared to their known alternatives, e.g. semi-conducting materials produced through the development of quantum dots show significantly enhanced conductivity and space-saving potential above previously known semi-conducting materials. There is much interest in using different engineered nanomaterials in these development activities, such as fullerenes, CNTs, metals, metal oxides, quantum dots, nanowires, nanocrystals, dendrimers, graphene sheets and others. Along with these developments, there has also been concern expressed that specific nanomaterial properties may lead to previously unknown health effects.

Specifically, airborne nanoparticles that may enter the respiratory tract and lungs through inhalation are of main concern, and presently we have limited research findings on their potential health effects, although a significant amount of research is underway globally to further investigate their toxicity. There is a large amount of existing data on environmental and occupational aerosols that may be useful in determining the potential health effects associated with engineered nanomaterials. For example, it is known from human studies that the greatest proportion of nanoparticles which are inhaled usually deposit in the alveolar region of the respiratory tract compared to larger particles (ICRP 1995; Kim & Jaques 2004). It is also known that nanoparticles may agglomerate and these may then deposit in other parts of the respiratory tract, or possibly not at all, depending on the agglomerate size and shape. Animal studies have indicated that once exposure has occurred, nanoparticles can be translocated to other organ systems in the body (Takenaka et al. 2001; Kreyling et al. 2002; Oberdörster et al. 2002, 2004; Semmier et al. 2004).

Pathological and epidemiological studies of environmental and occupational exposure to airborne fibres and particles have provided data on known aerosol-related conditions and diseases. Information from ongoing toxicological studies is useful for indicating those particle characteristics, disease mechanisms and dose-response relationships that influence toxicity; these include the particle’s size, shape, solubility, and surface area, chemistry and reactivity.

The health risk potential of engineered nanomaterials will depend on the nature of the nanomaterials, magnitude and period of exposures to airborne nanomaterials, and also on the transformation, release, dispersion and exposure control of nanomaterials in the workplace. Recent key studies showing toxicological effects of well-characterised multi-walled carbon nanotubes (MWCNTs) (Poland et al. 2008; Takagi et al. 2008; Bonner et al. 2009; Hubbs et al. 2009), are discussed in detail in Section 1.6.

Nanoparticles may also exhibit greater gastro-intestinal and dermal uptake compared to larger-sized particles. The ability of substances such as engineered nanomaterials to penetrate the skin depends on its physicochemical properties and size/surface characteristics; also whether the skin barrier is compromised or damaged, in which this absorption may more readily occur (Drexler 2003). To date, some studies have indicated that nanoparticles do not easily cross an intact skin barrier (Cross et al. 2007). Also, the presence of substances such as detergents, surfactants and other 'surface active' chemicals (e.g. dimethylsulfoxide) are known to increase the rate of absorption for some chemicals, and this could also occur with engineered nanomaterials.

Nanotoxicological studies using *in vitro* human and animal and *in vivo* animal systems have suggested that nanoparticle exposure may have the potential to cause cell, tissue and systemic toxicity, and that their very small size and surface characteristics enable nanoparticles to cross cell membranes to interact with sub-cellular structures, such as the nucleus and mitochondria. Oxidative damage and the impairment of several cellular functions of cultured cells have been reported (Geiser et al. 2005; Moller et al. 2005). Animal studies have indicated that some nanoparticles exhibit increased biological activity due to their higher surface area per unit mass, when compared to larger-sized particles with the same chemistry in (mass) dose-response relationships (Oberdörster et al. 1992, 1994a, 1994b; Lison et al. 1997; Tran et al. 2000; Brown et al. 2001). The greater surface area per mass is an important component of the increased chemical reactivity that also leads to greater potential utility for nanoparticles in medical, commercial and industrial applications.

With the main potential exposure routes for engineered nanomaterials being either by the respiratory, dermal or gastrointestinal organ systems, there are several potential disease outcomes. These include: the acute and chronic immune system responses of inflammation, allergy and autoimmunity to viral-sized monodispersed nanoparticles or their bacterial-sized aggregates (Mottram et al. 2007); respiratory, skin and gastrointestinal related disorders (e.g. liver dysfunction following sequestration of circulating particulates); neurological disorders (for nanoparticles taken up and transported via neurons or damage to the blood-brain barrier); and the potential for cancer of several different types due to oxidative damage to DNA, and the tumour promoting events of chronic inflammation and wound repair from ongoing tissue damage. It is important therefore that there are effective risk management systems and exposure control systems in place in order to negate or reduce worker exposure to engineered nanomaterials.

1.3 Risk assessment in the occupational environment

Scope and introduction

The current state of knowledge and practice with respect to risk assessment for the processing and production of engineered nanomaterials is presented in this report. Only workplace settings such as laboratories, pilot plants and production plants have been considered; environmental safety and consumer product safety were not considered.

Risk assessment is currently limited by our limited understanding of the potential for toxicity and the exposure levels for various tasks and situations.

Engineered nanomaterials, or materials comprising engineered nanomaterials, that contain or release unbound or free nanoparticles are of specific concern from a workplace health and safety perspective. Materials such as polymer composites, finishings or coatings, can also result in exposure from processes involving the changing or destruction of materials, such as wet sawing of composites made of polymers that can result in the generation of particulate aerosols (NIOSH 2006). Such aerosols consist of both engineered and incidental nanoparticles. The requirement that these aerosols are well characterised and that methods are developed to ensure that this characterisation is possible, has also been highlighted (Maynard and Aitken 2007).

Physical hazards such as high temperature or voltage are present in many occupational settings, including those involving engineered nanomaterials. Physicochemical hazards may also be associated with the use of engineered nanomaterials, e.g. the risk of explosion. In this review we have concentrated on toxicological hazards rather than physical or physicochemical hazards. It has been reported that the physical and physicochemical hazards associated with handling nanomaterials can be avoided, if they are known, using the basic risk management principles of occupational health and safety (BAuA 1998; EC 1998). Chronic low level exposure can result in health risks and are, by their nature, difficult to evaluate and therefore a challenge to identify the requirements for mitigation (NIOSH 2006).

Safety experts usually conduct risk assessments in collaboration with workplace managers and workers, in order to determine appropriate risk management requirements. Both product and process information is required for this risk assessment analysis. Risk assessment for engineered nanomaterials should be in accord with the existing regulations for individual settings and materials, and does not have its own separate requirements.

1.4 Nanomaterial health risk assessment

The process of health risk assessment is the analysis of possible negative health effects from current or future processes that may be caused by a hazardous material and/or process, taking into account the actions taken to mitigate or control exposure. Risk assessment in the workplace follows a specific process of hazard identification, hazard assessment, exposure assessment and risk characterisation (Herber et al. 2001; NRC 1983, 1994). The goal of risk assessment is to evaluate whether or not the exposure in a specific workplace is above an acceptable level of risk defined by the specific legislation or by

decision-makers, in order to inform decision-makers about the need for the further strengthening of risk management processes. The four components of the process of risk assessment are:

(a) *Hazard Identification* – hazards (intrinsic toxicities) are identified that contribute significantly to risk and exposure;

(b) *Hazard (Dose-Response) Characterisation* – potential adverse health effects that are related to identified hazards are determined;

(c) *Exposure Assessment* – pathways by which individuals can be exposed to the hazard in the workplace, and the level of this exposure, are evaluated;

(d) *Risk Characterisation* – this incorporates the information from a), b) and c) in order to evaluate the potential risk of exposed individuals in the workplace.

This process is sufficiently flexible that it can be adapted to the risk assessment of nanomaterials.

1.5 Quantitative and qualitative risk assessment

Quantitative risk assessment

This is dependent on the availability of exposure data, i.e. exposure levels or probability of exposure, and defined limits for exposure. Limits of exposure are developed from knowledge of the dose-response relationships that indicate exposure levels at which, or above which, adverse health effects may possibly be observed. Examples include Occupational Exposure Limits (OELs) for specific substances, limits of flux on magnetic fields, and decibel limits for noise exposure – below which no adverse health effects will be observed for most people. The ability to measure or estimate exposure in the workplace is required for quantitative risk assessment.

Qualitative risk assessment

If no (or insufficient) data is available that would enable the utilisation of quantitative risk assessment processes for risk evaluation, then estimates of risk can be extrapolated either from existing data or determined by the judgement of experts. For example, safety professionals may be required to express their expert opinions in the evaluation of specific site risk and to recommend options in order to mitigate exposure. NIOSH (2006) has recommended that ‘professional judgement’ should be employed in ‘the decision to use respiratory protection’ with engineered nanomaterials, and that this should be determined by the likelihood and frequency of worker exposure and exposure measurement data.

Expert elicitation is a more formal technique that utilises a systematic process of quantifying and formalising ‘expert judgment’ with respect to uncertain quantities (Morgan & Henrion 1992; Krayer von Krauss et al. 2004). This method could be used for the wide variety of engineered nanomaterials produced, and being developed, while avoiding expensive costs in experimental determinations. In this approach, the nanomaterials could be grouped according to their exposure potential and hazardous properties.

'Control banding' is one such approach that utilises groupings of materials according to their assessed health risk, which is a product of the material type and level of exposure. One example of the application of control banding is the 'risk management toolbox', which has been developed by the International Labour Organization (ILO). The control banding technique has been used most extensively in the development of specific online information packages to help companies comply with the Control of Substances Hazardous to Health (COSHH) Regulations in the U.K. (HSE 1989). This "COSHH Essentials" resource utilises five hazard groups and four risk groups. Similarly, Safe Work Australia has developed the "Essential Chemical Controls for Australian Printers" package, by using and building on the industry-specific "COSHH Essentials for Printers" information package.

An example of how this approach could be utilised for nanomaterials according to their chemical activity, toxicity and bio-persistence is described in Meili et al. (2007).

As the knowledge base expands, re-assessment of available hazard and exposure information is another critical component of qualitative risk assessment in order that the level of assessed risk corresponds to the available knowledge.

1.6 Hazard identification

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 vacuums, strong electromagnetic flux, etc.) and physicochemical hazards. In a comprehensive hazard identification process, all potential occupational hazards, including workplace chemicals should be identified in this step, including hazards that are low-level hazards or of low exposure potential, or hazards already being controlled in the workplace.

In order to identify hazards, information can be obtained generally from many sources including Safety Data Sheets (SDS), MSDS, International Chemical Safety Cards (ICSC), publications from trade associations or government authorities (e.g. NICNAS summaries), test data or proprietary information. For many nanomaterials there is currently a lack of specific knowledge of potential health effects, and exposure limits have not been established. Consequently these sources may not be able to provide sufficient information in order to adequately report the hazards associated with a specific engineered nanomaterial. The quality of information in some MSDS has been reported as an issue, as has the lack of available MSDS for some nanomaterials. If data are not available, then it may be possible to generate data through the testing of specific high-priority nanomaterials.

The characterisation of the physical agent or hazardous material is the next step in the process, and is important in determining the exposure potential. The process of risk assessment involves analysing individual workplaces, the processes and the potential of exposure to engineered nanoparticles. If the initial walk through survey indicates that there is potential for exposure, then further data collection and analysis is required. There are many potential ways in which nanoparticles of concern can be identified (NIOSH 2006). The tools (instruments) that can be employed for this can provide information on characterisation of airborne particle and mass concentrations, and these may be supplemented by data on particle size distribution, chemical characterisation and surface area.

1.7 Assessment of dose-response

Toxicological hazards

In the occupational environment, protection from toxic effects is usually achieved by reducing the exposure to substances of a toxic nature to levels designated as 'safe', which results in an acceptable level of risk. There are two types of toxicological risk – threshold risk, which has a 'No-Observed-Adverse-Effect-Level' (NOAEL), and non-threshold risk, which does not have a NOAEL. For threshold risk, it is possible to identify an exposure level below which there are expected to be no adverse health effects. In the case of non-threshold risk, any exposure will result in a probability greater than zero of adverse effects occurring. In the assessment of threshold effects for quantitative determination of these 'safe levels', the first step involves the determination of human response data if available, e.g. a Bench Mark Dose (BMD) or a NOAEL. The second step (if human response data is not available) is the extrapolation from animal data to human data in which the assumption is made of an equal dose response, but also building in safety factors. Environmental exposure is translated to dose by using models such as human lung dosimetry, which are then used to calculate the exposure concentration over the working lifetime. The third step involves deriving occupational exposure limits taking into account variability, technical feasibility, uncertainties, approximations and the level of acceptable risk.

For nanomaterials there are several potential sources of toxicological effects, including those that relate to the chemical properties of the bulk material and also those that relate specifically to the nanomaterial form. In some cases the bulk toxicological properties are well-defined, whereas the nanomaterial-specific properties are little-known (Nel et al. 2006). Recent toxicological studies have also been performed on relatively new engineered nanomaterials, such as CNTs, that have exhibited toxicity not previously seen in the bulk form of the same chemical (Poland et al. 2008).

Test protocols for nanoparticle toxicological assessment are currently undergoing development in terms of their design, definition and standardisation. The first step involves checking whether currently accepted test guidelines (e.g. from the EU, U.S. Environmental Protection Agency 'USEPA', or the Organisation for Economic Co-operation and Development 'OECD') have applicability to nanomaterials and, if required, improving these guidelines.

One of the major issues in designing experimental (test) protocols is the formation of nanoparticle dispersions. At high concentrations in either gas or liquid phases, nanoparticles have a tendency to form larger agglomerates due to Brownian motion and the relatively strong attractive interactions between nanoparticles. An example of where agglomeration could occur in the workplace would be following an airborne release of nanoparticles during the unloading of nanomaterials off a production line and the packaging of these materials. The extent of agglomeration is typically proportional to the nanoparticle concentration squared and such agglomeration generally stops at a certain size without moving into the supermicron range. Thus, exposure is expected to be to a combination of agglomerated and unagglomerated particles, with the degree of agglomeration increasing with time after release.

Numerous toxicological findings have been reported for nanoparticulates, but at present there is minimal validated hazard data to be derived from toxicological studies that can be related to health-based limits of occupational exposure. A further issue in interpreting findings is that in several cases, the toxicity studies were conducted using test materials which had not been well characterised due to technological limitations.

There are currently two engineered nanomaterials for which Australian National Exposure Standards have previously been established, i.e. the time-weighted average (TWA) for fumed silica and carbon black is 2 and 3 mg/m^3, respectively. The fact that these have been established indicates that there is evidence of safe levels of exposure to some engineered nanomaterials, however for most engineered nanomaterials the evidence is lacking.

There are also few publications of nanomaterial quantitative risk assessments; an example is that of Kuempel et al. (2006) for ultrafine titanium dioxide (TiO_2), ultrafine carbon black and diesel exhaust particulates. The authors concluded that established quantitative risk assessment methods are useful in estimating occupational exposure risk to ultrafine and fine particles and provide a scientific basis for the evaluation of potential risk of exposure to engineered nanomaterials. This study utilised the available data from chronic and subchronic inhalation studies for lung tumour and pulmonary inflammation (Lee et al. 1985; Heinrich et al. 1995; Tran et al. 1999; Cullen et al. 2002). OELs for these nanomaterials were derived from dose-response data using various modelling approaches, in order to provide an estimate of disease risk for workers exposed over a 45 year working lifetime to both ultrafine and fine titanium dioxide. The estimates from rat studies for the working lifetime airborne concentrations associated with 0.1% excess risk of lung cancer are 0.07 to 0.3 mg/m^3 for ultrafine TiO_2 and 0.7 to 1.3 mg/m^3 for fine TiO_2. In another example, mass concentration was used to define OELs for nano-structured carbon black in both aggregated and agglomerated forms which are 1 mg/m^3 for respirable dust and 4 mg/m^3 for total dust (Japan Society for Occupational Health, 2007).

For single-walled carbon nanotubes (SWCNTs), Shvedova et al. (2005) demonstrated that pharyngeal aspiration of SWCNTs elicited unusual pulmonary effects in mice that combined a robust but acute inflammation with early onset yet progressive fibrosis and granulomas, and that these results could potentially be extrapolated to human exposure situations.

Two recent key studies showing toxicological effects of well-characterised MWCNTs are those of Poland et al. (2008) and Takagi et al. (2008). In the first study, the intraperitoneal injection of MWCNTs into the abdominal cavity of mice exhibited similar pathogenic behaviour (pre-mesothelioma events) to asbestos fibres, with mesothelial inflammation and granulomas resulting from fibres that are longer than a macrophage can engulf, e.g. >15 µm (Poland et al. 2008). In the second study, MWCNTs induced mesothelioma when injected at high doses intraperitoneally into a mouse strain with a compromised apoptotic pathway (p53 heterozygous mice) that had previously been reported to be sensitive to asbestos. The cumulative mortality curve from mesothelioma (showing 50% mortality after 180 days) exhibited a similar slope to the crocidolite-injected mice, but with a 25 day longer latency period (Takagi et al. 2008). These two studies may have negative implications for workers who might be exposed to fibrous engineered nanomaterials. However, further consideration of several issues is essential with respect to the relevance of these animal studies to inhalational exposure in workers, including whether the particles penetrate sufficiently into

the alveoli of the lungs, and whether the aggregates are transported to the pleural mesothelium and arrive in a sufficiently stable form that may lead to mesothelioma.

In recent poster presentations at the American Society of Toxicology annual scientific meeting (which have not been peer-reviewed), Bonner et al. (2009) and Hubbs et al. (2009) also reported on mouse studies using MWCNTs. Both studies showed evidence of MWCNTs reaching the pleural mesothelium, after either high dose inhalation or pharyngeal aspiration, respectively, i.e. providing evidence of translocation from mouse lung to pleural mesothelium. An example image of MWCNTs by transmission electron microscopy (TEM) is shown in Figure 1.

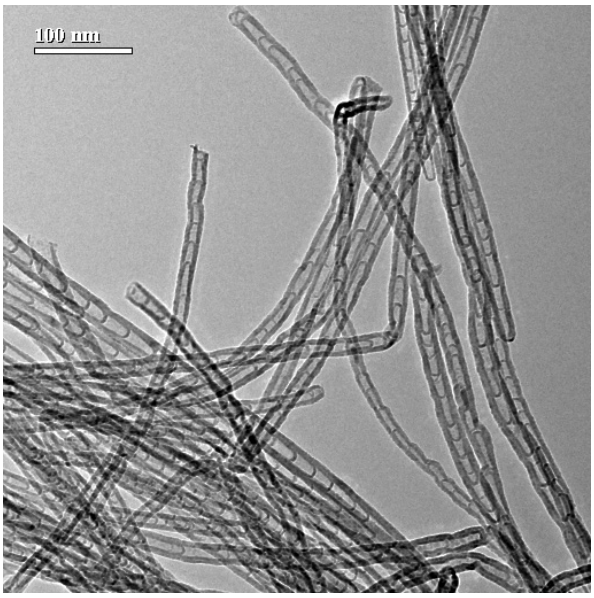

Figure 1: TEM image of MWCNTs with an average diameter of 20 nm (with permission of Dr Bill Li).

In summary, with the present state of knowledge, it is clear that the toxicological properties of most nanomaterials have not yet been fully assessed. Evidence suggests that the toxicological properties of nanomaterials cannot be readily estimated from the known data concerning the bulk form of the material. Due to their nature, particle number and surface area characteristics are more useful parameters for nanoparticle exposure assessment, while mass concentration may not be the most appropriate measure for the characterisation of exposure to many nanomaterials. Consequently, OELs derived from mass concentration and bulk dusty materials are likely to be inadequate for most engineered nanomaterials with a similar composition – exceptions may include some soluble nanoparticles. This matter has been examined by Maynard and Kuempel (2005) and Shvedova et al. (2005).

Physicochemical Hazards

Explosion and fire data have not yet been described for the vast number of different nanomaterials (HSE 2004a). It is possible that due to their increased surface area above bulk forms of the material, that the fire and explosion properties of engineered nanoparticles could

be more pronounced, and therefore additional tests would be required to determine explosivity, flammability and reactivity of nanomaterials. For example, nanoscale aluminium/molybdenum oxide (Al/MoO_3) thermites ignite over 300 times faster than the corresponding micron-sized material (NIOSH 2006). Protocols for the testing for these hazards are available for dusty bulk materials and could readily be applied to engineered nanomaterials; these include self ignition temperature, burning rate and explosive property characterisation. For example, the European Community (1992) Council Directive 92/69/EEC on the 'Approximation of Laws, Regulations and Administrative Provisions Relating to the Classification, Packaging and Labelling of Dangerous Substances' could be used in order to determine nanomaterial flammability, and describes the Fallhammer test for explosive properties of mechanical sensitivity/shock and the Koenen test for thermal sensitivity (EC 1992). Once the physical data on hazards is available, then the risk assessment of explosion and fire hazards can be conducted utilising these techniques.

1.8 Assessment of exposure

Nanomaterial exposure can occur from direct contact to organs such as the lungs or skin. The liberation potential of nanoparticles should be considered in the discussion of possible exposure scenarios. Liberation potential can be related to several physical properties including dusting behaviour, vapour pressure, boiling point and melting point. Process characteristics are also a controlling factor, especially as to whether the material is contained in a liquid or solid format. Mechanical processing of the nanomaterial, e.g. cutting, grating, milling, sawing, drilling, stirring, etc., can also give rise to the release of nanoparticles or nano-structured particulates (BASF 2007; BAuA-VCI 2007). Other processes that may result in exposure to nanoparticles include high energy treatment of nanomaterials, laser drilling, plasma welding and spraying liquid materials, all of which may result in fumed or aerosolised nanomaterials. Engineering processes that range from open-handling to closed-handling processes may lead to a wide range of exposure scenarios. If process equipment does not function optimally or is employed incorrectly, this may also lead to possible exposure scenarios. Furthermore, poor personal hygiene practices, unsafe behaviour of individuals or badly developed work practices could also lead to potential exposure scenarios (BASF 2007; BAuA-VCI 2007).

Exposure assessment needs to be developed from realistic exposure scenarios. Worksites that handle small quantities of materials are expected to have lower exposure potential than sites that handle larger amounts of material. In the workplace, inhalation exposure is the most common exposure route, whilst dermal and oral exposure is considered to be less likely (NIOSH 2006). However, ingestion can result from inhalation exposure via mucocilliary clearance and consequent swallowing of particulates that are inhaled. It is also possible that ingestion may occur from unintended hand to mouth transfer following dermal exposure (BAuA 1998; EC 1998). Needle stick injuries can conceivably result in accidental parenteral exposure. Most studies have reported that intact porcine and human skin cannot be penetrated by nanoparticles (Gamer et al. 2006; Cross et al. 2007; Mavon et al. 2007; Zvyagin et al. 2008). However, studies have found that nanoparticles can penetrate intact skin (Ryman-Rasmussen et al. 2006), especially if skin is flexed (Rouse et al. 2007). With mechanical skin flexing, microparticles have been found to penetrate the stratum corneum reaching both the epidermal and dermal layers of human skin (Tinkle et al. 2003). The issue whether skin flexing permits penetration of nanoparticles is under investigation in Australia (Roberts 2009) and there are indications, as yet unpublished, that dermal penetration does not occur with skin flexing but does occur with damaged skin.

State of the art analytical equipment and methods are usually required to accurately characterise inhalation exposures to nanoparticles, e.g. particle counters and sizers, whereas potential dermal exposures are often characterised by the use of hand-wipe sampling in workplaces followed by scanning or transmission electron microscopy (SEM/TEM) with energy dispersive X-ray (EDX) spectroscopy and/or chemical analysis (Methner et al. 2006, 2007; Han et al. 2008). Assay validation and calibration problems, inadequate consideration of background concentrations (and incidental particulates), humidity affects, and particle agglomeration and aggregation may confound analytical results.

In the absence of exposure data derived from real-time measurements, it is still possible to use qualitative techniques in order to characterise exposure potential. For example, in the control banding approach, three bands are used to characterise exposure potential (i.e. high, medium and low) for the degree of dustiness ("dispersability") for powders containing nanoparticles and for the quantity used in a specific occupational setting (Sullivan 2001).

1.9 Risk characterisation

A review and integration of hazard identification, dose-response assessment and the exposure assessment steps is termed 'risk characterisation'. If quantitative risk assessment has been performed, then this is assessed for its biological or statistical uncertainty. The risk characterisation step assesses the site specific evaluation of both the exposure and hazards, together with whether or not risks for a specific workplace exceed acceptable levels, and whether there are vulnerable populations present. A number of control measures can be considered in order to reduce the risks below acceptable levels, including: elimination or substitution of a nanomaterial that may be hazardous (although this may be difficult because of the unique and desirable properties of nanomaterials); a range of technical processes, such as the implementation of engineering controls and process modifications; organisational measures such as safety procedures and work-based training; and PPE (DENSRC 2007; EDDNP 2007).

1.10 Conclusion

Quantitative and/or qualitative risk assessment methods are used to evaluate the risk of exposure to engineered nanomaterials in the occupational environment. If appropriate data is available (e.g. hazard data and real-time monitoring data), the quantitative risk assessment methods may be used. Currently, this may be applied to two forms of engineered nanomaterials, carbon black and fumed silica.

However, when there is little scientific data available or when a material is unique, then only the qualitative risk assessment method can be used. At present there is a definite lack of toxicological and real-time monitoring data for most nanomaterials. Consequently, occupational health risk evaluation currently is reliant on considerable professional judgement for hazard identification, exposure potential and the determination of appropriate safety measures. Research into the toxicity of a range of engineered nanomaterials is underway in several countries, including Australia, which will inform the risk assessment

process and hence optimise risk evaluation frameworks for nanomaterials. However, further focus and resources are still needed in this area.

Part 2 – Risk Management Methodologies

2.1 Risk management guidance documents

In 2004, the Health and Safety Executive in the U.K. produced a guidance note as a very general overview of risk assessment for nanotechnology, the controls required for handling nanomaterials, exposure protection, and possible health monitoring (HSE 2004b).

In 2006, the U.S. National Institute of Occupational Safety and Health (NIOSH) produced a more detailed guidance document that provided an overview of the potential health and safety effects of working with engineered nanomaterials. This document also discussed in detail the potential scenarios that could lead to exposure to different nanomaterials, and the work practices that can be adopted to reduce the risk of exposure to engineered nanomaterials. This publication cautioned about the problems of working effectively when using filtered respirators while handling engineered nanomaterials. Occupational surveillance was recommended based on the different types of nanomaterials being used and the risk of potential exposure. This document also provides clear advice on the use of different filtered face masks (NIOSH 2006).

The U.S. Department of Energy Nanoscale Science Research Centers (DENSRC) recently developed a document to provide written non-mandatory guidance for the controls required to ensure worker safety while handling engineered nanomaterials (DENSRC 2007). It was written specifically to influence the work practices in the five research centres within the U.S. Department of Energy that handle nanomaterials, however, it would appear to have much broader applicability. Notably, practices developed within this document were adapted from existing work practices i.e. from actual experience in handling nanomaterials. The protocols suggested include (DENSRC 2007):

- a formal review of all risks associated with new processes prior to any work being started, with these to involve subject matter experts,
- a well-defined description of the work,
- life-cycle analysis of the nanomaterials,
- work area design,
- specification of required control measures, with control preferences based on the type of nanomaterial,
- ventilation preferences (including high efficiency particle air “HEPA” filtration),
- defined administrative controls including a chemical hygiene plan, and specified housekeeping methods for laboratories,
- waste disposal practices/management, handling practices, transportation and spills management,
- PPE and clothing requirements,
- labelling and signage,
- worker competency requirements,
- monitoring/characterisation requirements and exposure assessments,
- health surveillance.

The Environmental Defence Dupont Nano Partnership (EDDNP) recently determined that there was a need to develop a risk management framework for use in projects involving engineered nanomaterials (EDDNP 2007). This framework was developed to cover research, development, production, use, disposal/recycling of these materials, to correspond with the nanomaterial's life-cycle stages. The framework offers guidance on the questions and the risk management process that organisations should go through when researching, developing and producing products involving engineered nanomaterials. The framework requires specific inputs in order to generate specific outputs, and has an in-built ability to integrate reasonable assumptions and risk management practices when confronted with unknown situations. A communication strategy was also included within this framework. There are six steps involved within this framework (EDDNP 2007), also described in Medley et al. (2008):

- **Step 1:** describes the material and applications, where a general description of the nanomaterial is developed together with the uses to which it is intended, based on both the literature and other information that is available.
- **Step 2:** involves a life-cycle profile of the material, and requires three sets of information, i.e. material properties, associated hazards and exposures concerned with the life-cycle of the material. Some of this information may be well-defined, but other information may require generation throughout the project itself.
- **Step 3:** involves the evaluation of risks, where information is generated to help identify/characterise the probability, magnitude and nature of the risks posed by the nanomaterial that is to be generated. If information gaps characterise parts of the life-cycle profile, then reasonable 'worst case scenarios' may be used to characterise the risk assigned.
- **Step 4:** involves risk management, where methods of managing the risks that have been identified from step 3 are determined – these are based on the general method of hierarchy of control, in which preference is given to 'safe place' above 'safe person' control options.
- **Step 5:** is to 'decide, document and act'. In this step, a decision is made about whether to continue with the development and production process based on the information generated in the previous step. A worksheet is provided in the package in order to document this process and all decisions taken, in order to ensure transparency of the process to both internal and external stakeholders. If further information is required then this can be timetabled to fit in with the development of the new nanomaterial.
- **Step 6:** involves a review process. Throughout this process there are scheduled regular reviews that may also be event-triggered, in which updates are made to risk evaluation and risk management processes as defined by new information that has been generated. The changes that are to be made are documented and communicated to the required audience/individuals. Case studies involving the application of this process to specific projects are also provided in the framework document (EDDNP 2007).

In December 2007, the British Standards Institute (BSI) published a guide (BSI 2007) designed to specify protocols for the safe handling and disposal of engineered nanomaterials. The document considered the different types of nanomaterials that may need to be handled, defined exposure and risk in the framework of nanomaterial types, and provides a general approach based on previous practice with respect to the handling of

nanomaterials. The competence of people performing risk assessments, and the standard of the required risk assessments was considered in some detail. The application of the hierarchy of control for the handling of nanomaterials was also extensively discussed and included detailed examples. Evaluation methods were defined for specified control measures. Protocols were also defined for the handling of spills and accidental releases, based on the nanomaterial spilt or released. Disposal procedures were discussed based on the types of nanomaterials that were being handled, together with the requirements for preventing fire and explosion concerned with the handling of nanomaterials.

A notable aspect of the BSI document is the suggestion of benchmark exposure levels for proposed classes of nanomaterials based on hazardous properties, and suggested control approaches which are intended to keep potential exposures below the benchmark exposure levels (its control banding scheme). The four categories of nanomaterials are (BSI 2007):

- fibrous,
- carcinogenic/mutagenic/asthmagenic/reproductive toxin (CMAR),
- insoluble or partially soluble, and
- soluble.

For this exercise, the CMAR nanomaterial was assumed to have increased bioavailability and thereby required a 10-fold safety margin over the bulk material, while fibrous nanomaterials received the most rigorous U.K. limit for fibres in the air (0.01 fibres/mL). The insoluble nanomaterial benchmark exposure level was based on the NIOSH TWA proposed limit for ultrafine TiO_2 particulates, which is 15-fold lower compared to fine TiO_2 particulates. Soluble nanomaterials received a minor safety margin of 2-fold over the bulk material, despite indicating that their nanoparticulate forms are unlikely to have greater bioavailability (BSI 2007).

The International Organization for Standardization (ISO) published a document in 2007 on “Workplace Atmospheres – Ultrafine, nanoparticle and nano-structured aerosols – Exposure characterization and assessment” (ISO 2007). This Technical Report provides terms and definitions that can be generally accepted for the measurement of nano aerosols over a range of different parameters. This enables the standardisation of terminology and methods, so that the most relevant experimental measurements can be made to ensure that they are applicable to worker exposure in the occupational environment. This document also reviews the different methods by which nanomaterials may be sampled and characterised in the workplace (ISO 2007).

The American Standard Testing Method (ASTM) E2535-07 was issued in 2007 and describes the actions required in order to minimise human exposure to engineered nanomaterials in the laboratory, research, manufacturing and other occupational settings. This guide recognises that there are a wide range of situations in which engineered nanomaterials may be used, and the practices put forward have been designed with this in mind. The user needs to make judgements with respect to the parts that are the most applicable to their specific situation (ASTM 2007).

Clearly, when minimal toxicological and real-time monitoring data is available for most nanomaterials, an approach to risk management based on the ‘Precautionary Principle’ is warranted. The ‘Precautionary Principle’, as defined by Principle 15 of the United Nations Rio declaration on Environment and Development, states that ‘Where there are threats of serious

or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation' (UNEP 1992). In applying this principle to a precautionary approach for nanomaterials, the present lack of scientific data with respect to the safety and health risks for specific engineered nanomaterials should not prevent the implementation of cost-effective measures to prevent and mitigate potential risks (ISO 2008). Where there is either a lack of exposure standards for workplaces or OHS risk uncertainty, a precautionary approach should be utilised to control the manufacture, handling, storage, use and disposal of nanomaterials, i.e. these materials should be treated as hazardous until there is alternative data to suggest otherwise. As a consequence, airborne release of engineered nanomaterials should be limited by strict prevention measures in the occupational environment via the utilisation of a range of risk management approaches in order to reduce workplace exposures and, wherever possible, eliminate worker exposure (ISO 2008).

As mentioned in the Background section, NanoSafe Australia recently produced a detailed review of OHS best practices for the Australian nanotechnology industry (Harford et al. 2007). The nanotechnology industry and history were reviewed, together with the chemical regulatory regime in Australia. The issues surrounding exposure were detailed, including the types of nanomaterials and their differential toxicity, the different routes of exposure, and the types of instruments available for monitoring nanotechnology workplaces. The use of engineering controls and PPE in protecting workers from exposure to nanomaterials, along with the principle of 'As Low As Reasonably Practicable (ALARP)', were discussed (Harford et al. 2007).

Once data about the health and safety risks have been determined and defined, the principle of ALARP can be adopted. Use of ALARP, as defined in an Australian sense, should reduce the risks to a level that is as low as reasonably practicable. This involves the comparison of the assessment of the risk to be avoided with the assessment of the sacrifice in time, effort and money involved in taking measures to avoid that risk (NOPSA 2009; HSE 2008b; Brouwer et al. 2004). If a measure is practicable and its associated cost is not grossly disproportionate to the benefit gained, then the measure is considered to be reasonably practicable and should be implemented. In terms of ALARP, 'good practice' is any well-defined and established standard practice adopted by an industrial or occupational sector (NOPSA 2009; HSE 2008b; Brouwer et al. 2004). This good practice generally represents a preferred approach, however it is not the only approach that may be taken. The 'good practice' may also change over time due to increased technical innovation or because of increased knowledge and understanding. Evidence to inform ALARP can be provided by: hazard identification/risk assessment; a comparative assessment of risks, costs and benefits; and comparison with codes and standards, technical analysis, performance data, improvement approach and practical tests (NOPSA 2009; HSE 2008b Brouwer et al. 2004).

2.2 Summary of risk management guidance

The guidance materials published to date describe a number of possible methods of risk management for processes that involve engineered nanomaterials. It is likely that different methods will apply for different organisations and the various applications and processes in which they employ engineered nanomaterials. For example, the EDDNP or DENSRC approaches are applicable to the whole product life-cycle and would appear to be practical methods for risk management in the research situation (DENSRC 2007; EDDNP 2007). However, certain principles such as the 'Precautionary Principle' and 'ALARP' can also be

adopted within such a framework, as well as the BSI framework for the control of workplace exposure (BSI 2007). Occupational surveillance has also been suggested as being an important requirement (NIOSH 2006).

This report considers that, in terms of providing workplace control measures that are known to work in order to prevent exposure of workers to engineered nanomaterials, methods such as ‘control banding’ or ‘defined workplace controls’ could be readily applied for the research stage and then a more comprehensive risk assessment employed for the development/production stages. Control banding has on several occasions been mooted as a means of defining or categorising the risks of exposure to engineered nanomaterials (Boenke 2007; BSI 2007). The defined measures within this banding can be determined from scientific evidence from the literature with respect to the different control measures to protect workers from occupational exposure. If this were put in place, then the standard control measures for nanomaterials would be the engineering controls (i.e. enclosure method and local exhaust ventilation) complimented with the required PPE options, e.g. gloves, canister respirators and non-woven fabric garments. However, if nanomaterials are classified as potential carcinogens on the macroscale (Risk Phrase R45), then specialist advice should be sought when handling these materials.

OELs could be grouped for materials, in a manner similar to the grouping of materials for benchmark exposure levels in the BSI guide. This could lead to precautionary exposure limits for some types of nanomaterials, until OELs are defined for specific nanomaterials or groups of similar nanomaterials (Boenke 2007; BSI 2007).

The uncertainties about health and safety risks, and the possibility of a long latency period before any symptoms of disease develop, suggest a precautionary approach is required to control the manufacture, use, storage and handling of nanoparticles. Thus, until accurate and detailed methods are developed to monitor for nanomaterials in the occupational environment, and research has also provided further validated evidence of the effectiveness of workplace controls to protect workers from exposure to specific engineered nanomaterials in the actual workplace, the authors recommend that a precautionary approach guided by reference to the ‘precautionary principle’ be adopted in order to limit workplace exposure (e.g. for nanomaterials such as CNT, fullerenes and quantum dots). However, once data about the health and safety risks have been determined and defined, the principle of ALARP be adopted (e.g. for nanomaterials such as fumed silica, carbon black and titanium dioxide).

Part 3 - Workplace Controls

This section contains the evidence from research and other activities to assess the effectiveness of controls to prevent or minimise exposure to engineered nanomaterials in occupational settings. This evidence was evaluated and compared with predicted effectiveness based on conventional understanding of workplace controls. Summary tables of the evaluation of this evidence are shown in Appendix 1, in which publications have been categorised according to the strength of the evidence of practice, as follows (highest to lowest ranking): references which provide experimental evidence of effective workplace controls (Table 1) and guidance and review documents (Table 2).

3.1 Workplace controls used for engineered nanomaterials

A detailed survey of controls used in nanotechnology workplaces was undertaken by the International Council on Nanotechnology (ICON 2006). The survey found that organisations generally used conventional chemical safety methods when working with engineered nanomaterials, with some taking measures beyond those of conventional chemical hygiene. Control measures for engineered nanomaterials are also based on the toxicity and physicochemical properties of other materials being handled in the laboratory, e.g. most respondents indicated that their choice of gloves was based on which solvents were being used.

3.2 Review articles

The Health and Safety Executive (HSE) in Great Britain has provided detailed reviews of issues concerned with nanomaterials. The first of these 'Nanoalerts' provides a summary of the literature from 2000 to 2006, including measuring and monitoring of exposure to nanomaterials, exposure data, control measures, and characterisation of nanomaterials (HSE 2006). Human health effects are also included, specifically covering human studies and epidemiology, animal *in vivo* studies, computational models evaluating nanoparticles, studies on CNTs and *in vitro* studies. Over 49,935 references were initially considered by the HSE, which was narrowed down to a total of 1800 references considered for their review. Three further updates were made during 2007 and one during 2008 (HSE 2007b, c, d; HSE 2008a).

A presentation available online by Boenke (2007) provides access to much information either not in the public domain, or not readily accessible. It provides an overview of how the European Union (EU) is developing a nanomaterials strategy within the European Community legislative framework on "Registration, Evaluation, Authorisation and Restriction of Chemical substances" (REACH, Regulation EC 1907/2006), and thus developing OHS guidelines for the use of nanomaterials in the occupational environment. This involves a process of risk assessment that includes toxicological evaluation of the material. It also discusses possible monitoring methods for different nanomaterials, the types of filters to be used in facemasks, methods of deposition of ultrafine particles, PPE options and specific work techniques that need to be undertaken in order to control worker exposure to nanomaterials. The use of control banding as a risk management tool is also discussed (Boenke 2007).

A detailed review of the occupational hygiene science that underpins the OHS requirements for engineered nanomaterials has also been provided by Aitken et al. (2004). Details were provided with respect to physical characteristics and properties of nanomaterials, routes of exposure, possible methods of control of nanomaterials, and predictions of populations that will be exposed to nanomaterials. Notably, this paper provided a scientific understanding of the use of engineering controls and filtration mechanisms for engineered nanomaterials, including the rationale behind the use of HEPA filters, Brownian diffusion as a mechanism of particle entrapment in filters, and the science behind thermal rebounds that may result in particles escaping from filters - although nanoparticles generally exhibit a low rebound effect (Aitken et al. 2004).

3.3 Work practice guidance documents

A number of publications provide guidance on general control measures for engineered nanomaterials that can be employed in work practice. The company BASF has provided comprehensive and specific guidance for their employees when handling nanoparticles in different work processes (BASF 2007). The document discerns the need for enclosing processes that involve nanomaterials, provides advice on the type of gloves, filtration masks/SCBA and protective garments that should be used when handling nanomaterials in the workplace and discusses the problems of monitoring for the concentration of nanoparticles in the occupational environment.

The European Union's Nanosafe2 program has very recently provided a summation of the use of conventional PPE and RPE, and their applicability in terms of protecting workers from nanoparticles and nanoaerosols (Nanosafe2 2008). Some significant conclusions were reached, based on studies using graphite nanoparticles, including:

- that normal fibre filters are very efficient at removing nanoparticles as small particles get trapped in fibres through a combination of Brownian motion and Van de Waals forces.
- that masks made with fibrous filters, respirator cartridges and HEPA filters are efficient at trapping nanoparticles, the major issue with the PPE being the lack of tightness obtained between face and mask through poor fit testing.
- that non-woven air-tight materials are far more efficient against nanoparticle penetration than woven fabrics, such as cotton. Consequently, woven fabric lab coats are not the best option for workers to prevent contact with nanoparticles in laboratories or other workplaces.
- that there are a range of commercially available gloves through which nanoparticles may penetrate. Therefore, it is recommended that at least two layers of gloves are used (Nanosafe2 2008).

A recent joint review by the Germany's Federal Institute for Occupational Safety and Health (BAuA) and the German Chemical Industry Association (VCI) discussed the different types of processes used to manufacture nanomaterials and the OHS requirements for workers that need to be determined through the process of information gathering, hazard assessment, determination of effective measures and review of implemented work practices. A flow chart titled 'hazard assessment for nanoparticles in the workplace' provided a detailed guide with respect to how this process should be followed. This document provided advice on glove

selection methods, including the requirement to consider permeation time, and details were also given with respect to the types of filters to be used in filter masks, as well as other possible PPE that could be of use in protecting the worker from engineered nanomaterials. Substitution of nano-sized particles for materials that are less finely divided (i.e. of higher dimension size) was discussed as a possible control measure where feasible (BAuA-VCI 2007).

The exposure issues for workers handling fine particulate material, such as SWCNTs, have been considered for NIOSH by Baron et al. (2003), and a number of recommendations were made. These issues, and recommendations for addressing them, are:

- that unrefined low density SWCNTs readily become airborne during handling despite their agglomeration. Therefore a sealed system should be used during production.
- when a container of SWCNTs is vigorously agitated, large numbers of particles that are respirable may be released. There may be single fibres (nanotubes), or fibrous agglomerates and tangles released through this agitation. Therefore precautions should be taken in order to prevent unnecessary release and exposure to these respirable particles.
- that dermal exposure may be significant. Thus potentially-exposed skin should be suitably covered during the handling of such materials.
- that PPE should consist of gloves and a full face HEPA-filtered respirator, while the use of a full body suit may be required in certain circumstances.
- that vacuum cleaners with HEPA filters should be used to clean up the material rather than standard vacuum cleaners.
- as it was not clear what percentage of the SWCNTs released are inspirable and what percentage are respirable, that further research should investigate this.
- that more stringent precautions may be required for more toxic CNT- materials (Baron et al. 2003).

In a follow-up publication, Maynard et al. (2004) discussed the problems of SWCNTs production in terms of worker exposure. Gentle agitation from a laser ablation process of SWCNTs did not lead to significant aerosol generation, however more vigorous agitation led to particle generation <100 nm in diameter, which were found to be small clumps of nano-ropes. However, vigorous agitation of SWCNTs (from a high pressure continuous stream of carbon monoxide “HIPCO” process containing up to 30% metal) generated particles below 10 nm in diameter that were stable over a 15 minute period. Estimates of airborne particles released during handling suggested that concentrations <53 $\mu g/m^3$ and lower were generated. Glove deposits were determined to be between 0.2-6 mg per hand. Measurements indicated higher concentrations for the HIPCO process than the laser ablation process (Maynard et al. 2004).

Tsai and Hallock (2007) undertook an in-depth study of the efficacy of control measures to a range of engineered nanomaterials during processing including: CNTs synthesis, fullerenes during reactions, electrospinning processes, use of a torque rheometer, twin screw extrusion, and handling of silica and carbon black. In this study, a fast mobility particle spectrometer (FMPS) was the main instrument used to monitor for airborne concentrations of engineered nanoparticles. Results of their studies are presented in later sections.

In relation to work practices for nanomaterials in laboratories, Tsai and Hallock (2007) had several recommendations, including that nanoparticles should be synthesised in closed systems (e.g. fume cupboards, glove boxes, and furnaces or reactors should be handled in closed systems), and that all other nanomaterial handling should be performed in ventilated enclosures. If nanomaterials are to be transferred, then this should be performed within enclosures and secondary containers. When reaction vessels or furnaces are opened, then adequate atmospheric purging should be made. The use of disposable bench liners should be considered for fume cupboards or other work surfaces, and work surfaces should be cleaned at the end of the experiment, or at least daily, using HEPA vacuum or wet wiping techniques. With respect to spills of nanomaterials in the laboratory, the authors recommended that spills of dry nanomaterials should be HEPA vacuumed or be wet wiped, a sorbent suitable for a liquid should be used for liquids containing nanoparticles, and that exposure should be minimised during cleanup by the use of a respirator with HEPA cartridges when spills are made outside the normal process containment area.

Overall the authors concluded that if engineering controls are well designed they will be effective in limiting nanoparticle exposure, and that elimination of nanoparticle release at the source is the primary solution. However engineering controls need to be supplemented by good work practices and the use of appropriate RPE and PPE (Tsai & Hallock 2007).

3.4 Elimination

Since the specific properties of engineered nanomaterials are usually required for manufacturing a novel product, it is unlikely that this option will often be feasible or practicable, and no examples have been found in this review.

3.5 Substitution & modification of engineered nanomaterials

Regarding the potential substitution or modification of nanomaterials to reduce the hazard, there is the associated issue of maintaining required functionality. The authors have identified little evidence for the substitution or modification of nanomaterials being undertaken for the purposes of OHS management. However, in regard to medical applications of engineered nanomaterials, reducing the toxicology of nanomaterials by modifying the particles has received significant focus. There is mounting evidence that certain nanomaterial characteristics (e.g. surface chemistry and shape/form) are very important in exerting their biological effects and that several intracellular organelles are potentially involved (particularly mitochondrial dysfunction), with many reports coming from Prof. Vicki Colvin's research group at the Center for Biological and Environmental Nanotechnology (CBEN), Rice University, Texas, USA (Sayes et al. 2004, 2006a, b; Chang et al. 2006).

The most likely situation for a nanomaterial to have novel toxic potential that is different from its bulk material, is in the case of an insoluble nanoparticle that penetrates biological membranes and can persist in the body (and can be termed a "nanomaterial of concern" NMOC, or "nanoparticle of concern", NPOC). The insolubility and penetrance characteristics impart an increased bioavailability compared to the bulk material, while persistence within the body may be due to either extensive tissue distribution and binding, or sequestration and slow remobilisation from such tissue deposition sites within the body.

Modifying the surface properties of certain engineered nanomaterials has been found to reduce their toxicity – especially where the polarity, which gives rise to hydrophilicity, can influence the toxicity or where different forms can differ in toxicity despite having the same chemical composition. Examples of this include:

- **Fullerenes:** The simplest C_{60} fullerene (i.e. the non-polar "buckyball"), when made progressively polar by carboxylation and hydroxylation, also became progressively less cytotoxic to human dermal fibroblasts exposed for 48 hr (Sayes et al. 2004). Comparative molecular dynamics studies of the relative translocation of C_{60} and its $C_{60}(OH)_{20}$ derivative across a model cell membrane (dipalmitoylphosphatidylcholine bilayer) are providing a mechanistic explanation for the reduced acute toxicity of functionalized fullerenes (Qiao et al. 2007). These simulations show that the pristine C_{60} molecule can readily 'jump' into the bilayer and translocate across the membrane within a few milliseconds, while the $C_{60}(OH)_{20}$ molecule barely penetrated the bilayer. These different fullerenes also differentially affected the membrane structure when adsorbed into/onto the phospholipid bilayer.

- **Carbon nanotubes:** several reports have highlighted the potential adverse health effects from exposure to unmodified CNTs. The potential for mesothelioma formation in mice exposed to CNTs was dependent on a physical Structure Activity Relationship (SAR) that was similar to 'long' fibre asbestos, as short fibre asbestos and tangled CNTs did not cause pre-mesothelioma effects (Poland et al. 2008). However, it is also reported that CNTs functionalised by chemical modification have significantly reduced toxicity for some cytotoxicity endpoints. Although CNTs and fullerenes all consist of pure carbon, their cytotoxicity varies widely, i.e. their order of potency when alveolar macrophages are exposed *in vitro* is: SWCNT > MWCNT > C_{60} (Jia et al. 2005). The cytotoxicity of SWCNT can be reduced more effectively by sidewall functionalisation than surfactant-stabilisation (Sayes et al. 2006a). This covalent functionalisation therefore offers significant improvements in the toxicity profile of CNTs, both *in vitro* and *in vivo*, potentially enabling them to be employed as drug-delivery vehicles for the treatment of cancer and other diseases, and for use in nuclear medicine (Reilly 2007; Srinivasan 2008).

- **Quantum dots (QD):** The cytotoxicity of QD, which can contain Cd/Se cores, is progressively reduced by polymer coatings of increasing thickness that prevent QD from being internalized into the cell and trafficked to the highly acidic (~pH5) and oxidative environments of lysosomes and peroxisomes for degradation – resulting in leaching of toxic Cd (Chang et al. 2006). Surface chemistry also affects the interaction of nanomaterials with serum proteins and ultimately clearance from the body, e.g. recent studies involving intravenously-administered QD in rodents have indicated some nanoparticle requirements for renal filtration and urinary excretion, i.e. Zwitterionic or neutral organic coatings of QD prevent adsorption of serum proteins that otherwise increased hydrodynamic diameter by >15 nm and prevented renal excretion, while a final hydrodynamic diameter <5.5 nm resulted in rapid and efficient urinary excretion and elimination of quantum dots from the body (Choi et al. 2007).

- **Metal/metal oxides:** different crystalline forms of TiO_2 nanoparticles have different reactivities and can differ in their toxicity despite having the same chemical composition. Anatase crystals of TiO_2 are more UV-active than the rutile crystals of TiO_2, resulting in the cytotoxic potency of anatase crystals being far greater than the

rutile form (Sayes et al. 2006b). The UV photoactivity of metal oxide nanoparticles can be altered by adding 'dopants' into their crystalline structure. Also different particle sizes and surface modification of metal and metal oxide nanomaterials like silver and gold nanoparticles, can alter their internalisation after binding to cells, and the subsequent *in vitro* cytotoxicity (Jiang et al. 2008). For example, Uboldi et al. (2008) recently found that surface modification of gold nanoparticles (5-25 nm) with sodium citrate impaired cell viability and proliferation greater than unmodified nanoparticles, in human alveolar type-II cell lines exposed *in vitro*.

In light of this evidence, there is the potential for nanomaterial modification or substitution to be used to reduce potential toxicity and hence workplace hazards in certain cases. Options of changing the nanomaterial form to reduce potential exposure may also be considered. Consequently, for engineered nanomaterials there is a need to further investigate substitution and modification options that reduce the hazards associated with exposure to these materials.

3.6 Enclosure of process

Two research reports which report on the measured effectiveness of process enclosure for engineered nanomaterials, and demonstrate the effectiveness of this control option when equipment is well-designed, are those by Han et al. (2008) and Tsai and Hallock (2007).

Levels of airborne MWCNTs in a Korean research facility have recently been measured and reported by Han et al. (2008). Monitoring occurred before and after the implementation of control measures. These researchers found that the potential exposure to MWCNTs was greatly reduced in terms of the number of MWCNTs after enclosing and ventilating the furnace, and placing the chiller outside. This reduced the total airborne particle concentration and number of airborne MWCNTs in personal and area samples to non-detectable, or almost non-detectable levels, e.g. from 193.6 to 0.018 CNTs/mL (Han et al. 2008). An increase in airborne particle concentration was also observed when enclosed blending equipment was opened.

Tsai and Hallock (2007) undertook a study of the efficacy of control measures in university research centres to a range of engineered nanomaterials. Synthesis of CNTs within a ventilated fume hood resulted in a very low concentration of particles in the worker's breathing zone. However, electrospinning of a continuous fibre in a researcher-designed exhausting enclosure did not prevent release of particles effectively.

3.7 Use of ventilation controls to remove nanoparticles

The practice of controlling ultrafine particles in the household situation with central fans and in-duct filters to reduce the concentration of nanoparticles in the air was examined by Wallace et al. (2004). Some improvement was observed through use of the central fan, but greater improvement came from application of either fibrous mechanical filters or electrostatic precipitators in the duct.

Regarding general ventilation, recently, Han et al. (2008) reported that the installation of a simple fan in laboratories did not have much impact on reducing the potential exposure to MWCNTs.

The reduction of nanoparticle aerosol exposure by the modification of flow patterns in ventilation booths used for welding operations has been reported by Lee et al. (2007). An 88% reduction of particle concentration in the breathing zone of welders was demonstrated, in addition to a more rapid nanoparticle clearance rate (i.e. 6 minutes, down from 11 minutes). This article is useful because it indicates the actual practice of controls and reports the efficiency to reduce exposure to nanoparticles, i.e. the actual efficiency of a fume cupboard capture process during an actual workplace welding process. Nonetheless, the authors indicated that potentially high levels of exposure may still exist and that detailed studies mapping out flow patterns would be essential for designing systems to minimize airborne concentrations (Lee et al. 2007).

Lu and co-workers designed a method for the evaluation of Local Exhaust Ventilation (LEV) and the retention of airborne contaminants contained within the system (Lu et al. 2007). In this study, a spray-drying aerosol generator was used to produce nanoparticles with diameters between 4-100 nm. There was found to be no significant difference between the capture efficiencies of tracer sulfur hexafluoride gas and the generated nanoparticles, see Figure 2 (Lu et al. 2007).

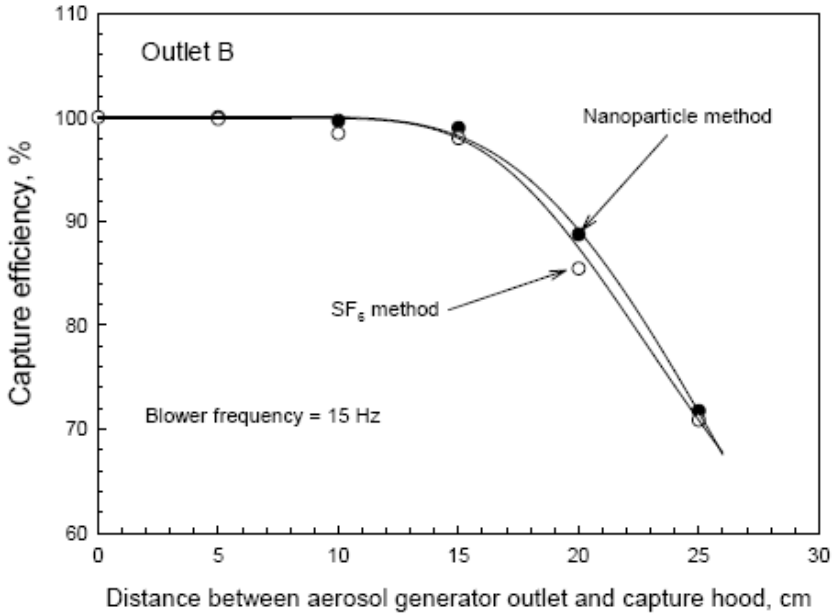

Figure 2. Capture efficiency measured using nanoparticle and SF6 methods (adapted from Lu et al. 2007).

Tsai and Hallock (2007) examined a nanocomposite compounding process where the materials used were polymer and nanoalumina, and found that a poorly designed local hood did not prevent release of particles.

Geraci (2008) has presented a number of important points about process enclosure and LEV. The relationship between the effectiveness of LEV in the capture of particles of different

sizes is detailed in Figure 3. Geraci indicated that nanosilver particles up to 500 nm are easily captured by LEV, whereas particles above this size show a lower capture efficiency, i.e. a reduction to 96% and 93% for particles 1 and 10 µm in size, respectively. In an example of a reactor cleanout operation, Geraci (2008) indicated that a reduction of 74-96% in air particulate mass concentration can result, if efficient and well-maintained LEV is effectively utilised.

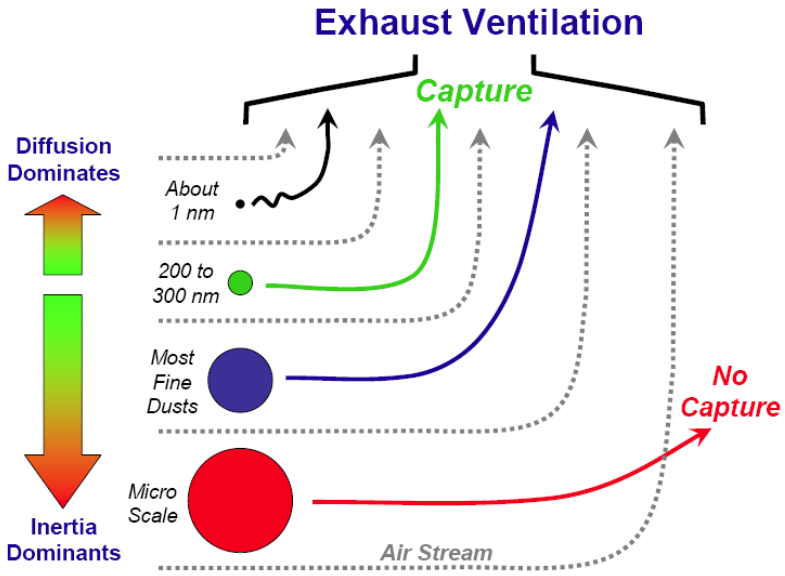

Figure 3. The impact of particle size on exhaust ventilation effectiveness – indicating that conventional controls should work (from Geraci, 2008).

3.8 Use of electrostatic filter media and electrostatic precipitators

Evidence regarding the potential effectiveness of filtration processes has been found and is described in this section.

However, information has not been found relating to issues associated with managing parameters such as lifetime (how often to change), preventing nanomaterial release at changeover and safe disposal.

A process called ‘triboelectrification’ can produce an electrostatic filter that can remove particles between 1 µm and 100 nm (Sullivan 2001). This process has been used for over 20 years in order to produce filters that have been patented as “Technostat”. However, its efficient ability to remove small particles, including nanoparticles of 100 nm and smaller, has only recently been recognised. Due to the potential range of particle sizes present it is recommended to use a high charging level for electrostatic filters. Notably, this article also provides a method of capturing both positive and negatively charged particles through the specific method of filter construction (Sullivan 2001).

Martin and Moyer (2000) studied the penetration through electrostatic respirator filters, commonly referred to as Electrotect filters (N95, N99, R95 and P100), by sodium chloride and dioctyl phthalate (DOP) nanoparticles. The NaCl aerosol had a count median diameter

(CMD) of 75 ± 20 nm and a geometric standard deviation (GSD) not exceeding 1.86, whereas the DOP aerosol had a CMD of 185 ± 20 nm and a GSD not exceeding 1.60. The test protocol included deliberate filter charge reduction by dipping in isopropanol and used a TSI8160 filter tester to determine the most penetrating particle type. In all six filter models tested, the particle penetration increased with decreased electrostatic charge, and the more penetrating particles were found to be of larger sizes (Martin and Moyer 2000). All N95 filter pieces tested were below 5% penetration for NaCl solid nanoparticles, whereas >5% penetration was observed for DOP oil nanoparticles, a range of maximum penetration of 19.4 % to 36.2 % penetration was observed. This difference was attributed to two alternate deposition mechanisms for solids versus oils. This work indicated the characteristics of Electrotect filters and their practicability for filtering nanoparticles, but more research is needed to elucidate this applicability (Martin & Moyer 2000).

Electrostatic precipitators are used as a means of remediating ultrafine dust present in incineration plants for sewage sludge (Ferge et al. 2004). The efficiency of the electrostatic precipitator in operating over a number of different “rapping cycles” was studied by comparing upstream particle concentrations with downstream particle concentrations using an electrical low pressure impactor and an aerodynamic particle sizer. This study provides a method by which conditions of operation for an electrostatic precipitator can be manipulated in order to reduce the re-entrainment of captured ultrafine particles back into the atmosphere. The study concluded that nanoparticles can be effectively precipitated electrostatically, however the efficiency is dependent on a number of operating conditions, including charge and “rapping cycles” (Ferge et al. 2004). For differential mobility analyzer (DMA) classifiers (also electrostatic precipitators), a high charging level is recommended (Sullivan 2001).

Collection efficiency for particles less than 20 nm has been reviewed by Heim et al. (2005), both experimentally and theoretically. Theoretically, thermal rebound effects are associated with decreasing nanoparticle size, resulting in decreased collection efficiency. Heim et al. (2005) generated nanoparticles by atomisation of a salt through condensation/evaporation (with or without charge) using a DMA classifier. Polypropylene, nickel or stainless steel test filters were used and the efficiency of small particle size detection was determined in a number of condensation particle counters (CPCs). After extensive testing, the range of nanoparticles (2.5 to 20 nm in size) showed no indication of thermal rebound/bounce, and accordingly there was no reduction in particle collection efficiency. Charged filter fibres were found to enhance particle collection. This paper discussed and examined filter processes and their effect upon capture efficiency and provides strong evidence of the ability of filtration systems to be used as a control for nanoparticles in the lower end of the size classification range (Heim et al. 2005).

The size distributions of submicron bi-modal aerosol particulates have also been determined, and their collection efficiency estimated, by Byeon et al. (2006) using a hybrid (2-stage) electrostatic precipitator. In this study, a dielectric barrier discharge (DBD) particle charger was coupled with an ESP charged particle collector, and the flow conditions and electrical charge applied by the DBD charger were varied. Particle collection efficiency was found to increase with increasing voltage (AC) at a constant frequency/flow rate. However particle collection efficiency decreased if the frequency and flow rate were increased at a fixed AC power/voltage. This article reports a laboratory-based evaluation of the capture efficiency of an electrostatic precipitator, in addition to an evaluation of thermal effects with selected particle sizes. However, no workplace application of the theoretical model is provided as a component of actual workplace evaluation (Byeon et al. 2006).

In a preliminary report, Alonso and Alguacil (2007) modified an electrostatic precipitator to simultaneously capture nanoparticles by both diffusional and electrostatic deposition. This was achieved by setting the wire screens of the electrostatic precipitator perpendicular to the gas flow to capture the larger particles, whereas diffusional deposition was used to capture the smaller particles. Particles of a few nanometres in size were reported captured at a rate of 99% by this method.

3.9 Filtration and facemask filters for nanomaterials

Efficiency of filter materials

A significant amount of evidence has been found on the efficiency of filter materials in capturing nanoparticles, and this is presented in this section.

The majority of reports reviewed in this section mention the US NIOSH certified filter face pieces - refer to Table B for a comparison of Australian filter types and their equivalence to US filter types.

Filtration is a major control method applied in both respiratory protective equipment and air cleaning. Particle penetration through a filter is usually measured as ‘filter capture efficiency (otherwise known as filter collection efficiency or filter efficiency)’, which is an important quantity to determine for aerosols made from nanoparticles. The fractional capture efficiency for different particle sizes can be explained by the different capture mechanisms of diffusion, inertial impaction and interception, as indicated in Figure 4. The most penetrating particle size (MPPS) is considered to be around 300 nm for some types of filters (e.g. HEPA filters), but this can vary based on the type of filter media employed and flow rate (as shown in the evidence presented later, where the MPPS can be <100 nm), and the condition of the respirator. These factors will also impact on the overall capture efficiency of the filter material. ‘Flow rate’, usually measured in L/min is also an important factor in determining filter capture efficiency, generally the lower the flow rate the higher the capture efficiency.

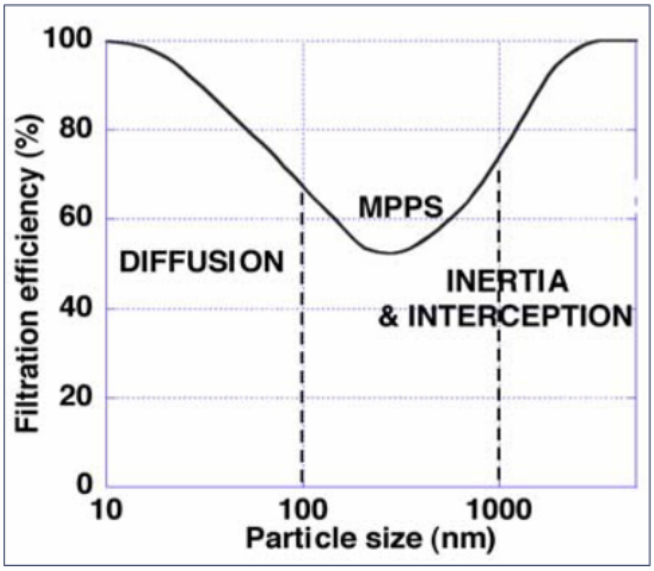

Figure 4: Primary mechanism of capture for various particle diameters. The lowest filtration efficiency is the maximum penetrating particle size (MPPS) (from Nanosafe2 2008).

In an earlier theoretical paper, Wang and Kasper (1991) described the development of a model of filter efficiency for nano-sized particles, incorporating the particle rebound effect from filter surfaces due to thermally related velocity. The Johnson, Kendall and Roberts (JKR) adhesion theory and Boltzmann velocity distribution were used to calculate thermal rebound. Diffusion and impaction/interception are the two classical particle filtration methods, but below 10 nm thermal rebound was identified by the model as being a significant phenomenon. The exact particle size below which there is marked deterioration in filter efficiency due to thermal rebound can be predicted by determining the following parameters; temperature, particle-surface adhesion energy and other filter-related parameters (Wang and Kasper 1991).

Richardson et al. (2005) were sponsored by the U.S. government as a result of an antiterrorism initiative, to test respirator filter efficiency against particulate and biological aerosols under medium to high flow rates. Normally NIOSH certifies respirators based on flow rates of 85 L/min, however with certain activities for a short duration, a flow rate of 300-400 L/min is more realistic. The respirators tested were all N95 or P100 face piece/cartridges. The inert testing demonstrated that penetration of submicron particles tends to increase with filtration velocity or flow rate. This report also provided guidance on the most useful filter types and which particle sizes are capable of the most penetration. Specifically, Richardson and co-workers determined that the maximum penetrating particle size (MPPS) for P100 cartridges was usually between 100 to 200 nm and shifted toward the lower end of the range with increased flow. The MPPS for N95 cartridges were found to be 50 to 100 nm under all flow conditions, while the MPPS for both N95 and P100 filtering face pieces was 30 to 100 nm. Penetration through N95 and P100 were less than 5% and 0.03%, respectively, at low flow rates and met NIOSH requirements but for high flow rates the maximum for N95 was above 5% and for P100 above 0.03%. Figure 5 shows an example of high penetration for N95 cartridges.

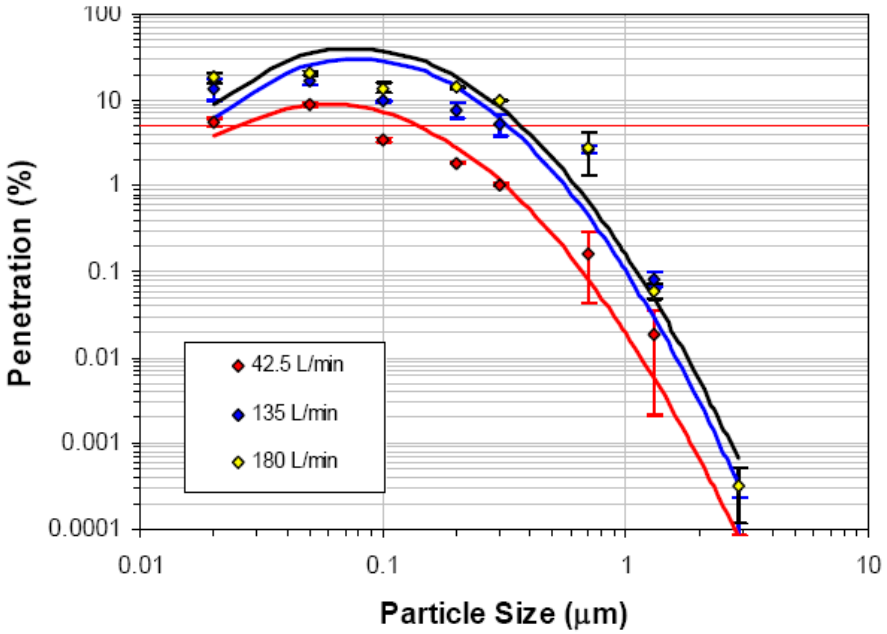

Figure 5. Effect of particle size and constant flow rate on measured penetration through the North 7506 N95 Cartridge (from Richardson et al. 2005).

The filtration efficiency of N95 face-piece filters has been examined by Balazy et al. (2006). These authors used two models of N95 filters with electrostatic filter material in their face-pieces that were sealed onto manikin heads and subjected separately to constantly-maintained flow rates at 30 and 85 L/min. A particle range between 10 nm-10 µm was generated by salt solution atomisation. The most penetrable particle size was from 40-50 nm, and there was no increase in penetration at lower particle sizes. If the flow rate was increased then the peak penetration was also found to increase. The maximum particle penetration is normally set at 5% for N95 filters, but this reached up to 5-6% for both respirator models with the most penetrable particle size of 30-80 nm, when a flow rate of 85 L/min was used. The maximum penetration was less than 5% at 30 L/min for the same respirator models. Penetration of charged particles was reduced compared to uncharged particles, a three fold reduction not being unusual. This study appeared to be very practically-oriented and very broadly-based and has potential for transferability to a workplace control program (Balazy et al. 2006).

The collection efficiency of commercially-available polytetrafluoroethylene (PTFE), gelatine and polycarbonate filters for collecting viruses, airborne bacteria and a range of other non-biological particles between 10-900 nm, was studied by Clark-Burton et al. (2007). The collection efficiency for PTFE was 100% and for polycarbonate was 20-90% for particles less than 100 nm (Clark-Burton et al. 2007).

A device has been developed by Iwashita et al. (2007) to trap airborne nanoparticles in plasmas at low pressure. This device employs two stainless steel plates (0.8 mm thick with 20 slits that are 3 mm in length) that capture particles by collision and attachment. It is reported that this device has a trapping efficiency of at least 98% with particles ≥2 nm. This paper discussed the laboratory efficiency and conditions for this device, but no transfer to a workplace application was reported (Iwashita et al. 2007).

Japuntich and co-workers (2007) used two different test methodologies for filters challenged by a very narrow size distribution of sodium chloride and dioctyl phthalate particles (ranging between 10-400 nm, determined by DMA). This study used an automated filter tester (TSI8160), which included a particle analyser and an electrically-neutralised aerosol. Particle concentrations before and after the filter were measured by a scanning mobility particle sizer (SMPS) and condensation particle counter (CPC) respectively, to derive penetration values. Fibreglass filter papers known to be of good efficiency were used at a flow rate of volume of 32 L/min (face velocity of 5.3 cm/s). In two tests performed, penetration versus particle size curves for the different filters studied indicated decreasing penetration with decreasing particle diameter for particles <100 nm – which is in-line with the 'Brownian capture theory' that applies to particles as small as 10 nm. This paper is a useful description of a laboratory-based filter collection efficiency study, using emerging commercial measurement equipment for pre- and post-filtration measurement (Japuntich et al. 2007).

The ability of several commercially available filters (four fibreglass, one nanofiber, four Electret filters) to capture nanoparticles was investigated by Kim et al. (2007). Silver nanoparticles between 3-20 nm were used at face velocities between 5.3 and 15 cm/s. Both upstream and downstream nanoparticle concentrations were determined for the neutralised silver aerosol using a nano-DMA, while upstream and downstream particle concentrations were determined using a CPC. The major finding was that penetration of particles decreased with decreasing particle size, to as low as 3 nm. The authors indicated that they did not believe that any thermal rebound occurred for these nanoparticles. This paper reports practical filter efficiency measurements that are laboratory-based, and although no transfer to a workplace application is shown, a high particle capture efficiency of up to 99.99% has been demonstrated (Kim et al. 2007; Pui & Kim 2006).

The effectiveness of approved respiratory protective devices against ultrafine particulates was recently assessed by Mohlmann et al. (2007), using 30 nm nanoparticles of sodium chloride and welding fumes. They measured the nanoparticle number concentration following passage through the filters using an SMPS at air flows of 95 and 47.5 L/min. Standard glass fibre P2 filters showed a decrease in capture efficiency at around 200 nm or higher, whereas electrostatic pad P2 filters showed decreased efficiency around 60 nm. In general, an increase in filter efficiency is observed for smaller particles down to 14 nm, due to higher levels of diffusion. The researchers concluded that if the correct filter class is selected, it is possible to stop over 99% of ultrafine particles; however they consider the proper leakage-free fit of the breathing apparatus to be the main problem in the use of RPE (Mohlmann et al. 2007).

In a simulation, Maze et al. (2007) studied unsteady state filtration in nano-fibre media, with reduced operating pressure. Nanoparticles between 50-500 nm were examined and it was concluded that collection efficiency increased with decreasing nanofibre media diameter, and the diameter of the most penetrating particles consequently decreases (see Figure 6). The collection efficiency was also found to increase by increasing the flow temperature. It should be noted that this was a theoretical study that completed a large series of simulation studies upon filtration efficiency, under a variety of conditions, which may or may not be available in the workplace. In this study constant fibre volume was maintained with the different fibre size samples that were simulated.

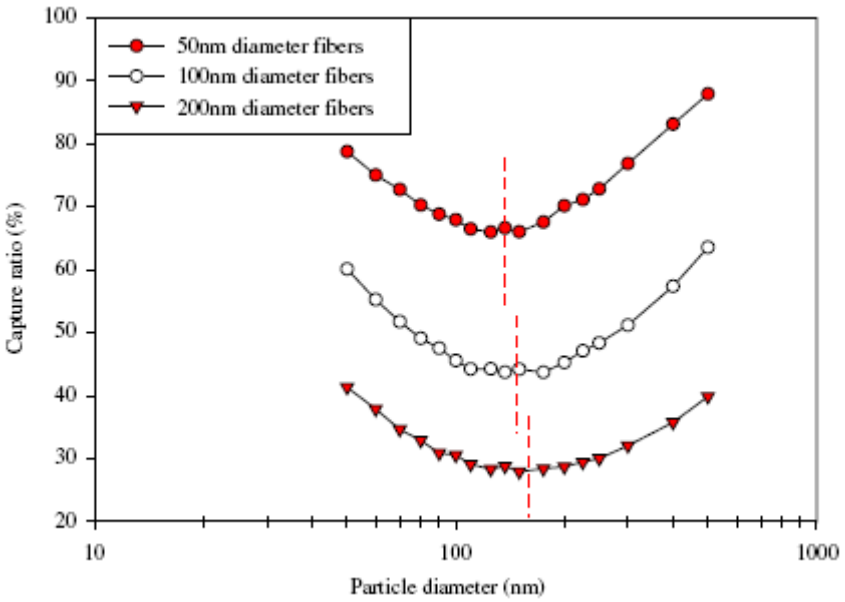

Figure 6. Collection efficiency of filter media made of fibres of 50, 100 and 200 nm diameters. All the three webs have identical thickness and pressure drops but different solid volume fractions. It can be seen that the collection efficacy increases by decreasing the fibre diameter. The diameter associated to the most penetrating particles decreases when fibres are smaller (from Maze et al. 2007).

A recent HSE summary (HSE 2007a) reported on a number of projects that were sponsored by the Nanoparticle Occupational Safety and Health (NOSH) in order to determine specific information required to assess and protect workers from exposure to nanoparticles. These projects commenced in January 2006 and were completed by October 2007.

There were three major deliverables, i.e.: synthesis of aerosol nanoparticles of various chemistries, including aerosol characterisation instrumentation and examination of aerosol behaviour over time; the development of a portable aerosol monitor; and the development of a test method to measure filtration efficiency, and measurement of nanoparticles filtration efficiency of commercially available filters. With respect to filter media efficiency, several important conclusions were reached (HSE 2007a):

- that manufacturer's materials differ in terms of filter efficiency,
- that N100 filter media has higher filter efficiency for nanoscale aerosols than do N95 filters,
- that uncharged and charged aerosol particles had different filtration efficiency in the filter media tested,
- that charged particle filtration efficiency decreased with time and the manufacturer's recommendations on the lifetime of filter media should be strictly adhered to,
- that the P100 and N100 filter efficiency was at least 99.97% upon exposure to NaCl, citric acid, silicon dioxide or titanium dioxide,
- that increasing humidity enhanced particle capture, with the exception of electrostatic filter material.

The EU Nanosafe2 program recently reported that HEPA filters and fibrous respirator and mask filters are efficient in clearing nanoparticulates, thus confirming the conventional filtration theory and disproving the 'skimmer model' that only particles larger than the pore size should be stopped (Nanosafe2 2008). Consequently, MPPS of fibrous filters is 150 -

300 nm, as larger particles are blocked by interception and inertia, while smaller particles are trapped by diffusion and collision enhanced by Brownian motion (Figure 4). Nanosafe2 also highlighted that the main risk for RPE comes from a lack of tightness between the face and mask (Nanosafe2 2008).

Filtration results are summarised in Table A below. Results show that the capture efficiency of filter materials varies with filter type and flow rate. Data shows that under some conditions filter material meets or exceeds certified levels (e.g. less than 5% penetration for N95), but in some cases filter material performance does not meet it, e.g. at high flow rates.

Respirator Fit

An additional critical factor is the effectiveness of respirator fit.

The U.S. NIOSH assigned protection factor (APF) is defined as the minimum anticipated protection provided by a properly functioning respirator or class of respirators to a given percentage of properly fitted and trained users (NIOSH, 2009). The APF values developed by U.S. NIOSH take into consideration a number of factors, including leakage around the face seal of the respirator, penetration through the filter by inward leakage and, importantly, are based on laboratory studies. The relative contributions of these two sources of inward leakage are critical, because for many applications the predominant source of exposure to the respirator wearer results from leakage around the face seal (due to a poor fit) and not penetration directly through the filter media.

Four N95 filtering facepieces (certified by NIOSH) each with an APF of 10 had their protection factors towards inward leakage measured while being used by human test subjects exposed to particles of between 40 nm to 1.3 μm. It was found that minimum protection factors were observed for particles between 80 and 200 nm. A wide variation was observed between the four filtering facepiece models, however the mean of all the protection factors across the range of particle sizes tested was 21.5 (Rengasamy et al. 2007, 2008).

Lifetime of respirator

The report of Rengasamy et al. (2007) also indicated potential limits to the useful lifetime of a respirator, in that the FPP3 electrostatic filter penetration by nanoparticles increased when used – this was likely to have resulted from the moisture introduced in human perspiration.

3.10 Personal protective equipment – clothing and gloves

The two primary routes of exposure to particulates for workers using protective clothing are direct penetration through the materials and leakage through gaps, seams, defects, and the interface and closure areas. The relative contributions from these two inward leakage sources are not well-understood (NIOSH 2009).

The lack of available data is further complicated by the limitations and difficulties of current test methods which fall into two basic categories: penetration tests on material swatches to determine barrier efficiency; and system level aerosol testing to determine product ensemble integrity. Huang et al. (2007) reported on work where a homemade atomiser (model 8700-

120, Sonotek Inc) with an ultrasonic atomising nozzle was used to generate polydispersed aerosols of nanometer, submicrometer and micrometer sized NaCl particles. The output of aerosol was neutralised to Boltzmann charge equilibrium using a radioactive source before introduction into a mixing and test chamber. Two different aerosol size spectrometers were used to measure the upstream and downstream concentrations and size distributions of the aerosol, i.e. SMPS equipped for nanosizes or a long-DMA equipped for the correct particle size. The results indicated that the MPPS was 100-500 nm, which is similar to penetration of filter media. Protective clothing 5 (PC5) exhibited a penetration of about 17% at 100 nm whereas protective clothing 2 (PC2) was found to have a penetration of about 80% at 500 nm. PC5 and PC2 showed a penetration of about 0% and 30% respectively at 4 nm and of about 17% and 75% at 100 nm. The data about airflow rate used in this study is unclear (Huang et al. 2007).

Nanosafe2 recently reported that non-woven (air-tight) fabrics are efficient in reducing nanoparticle penetration, and that the use of cotton fabrics in PPE, as used for standard laboratory coats, should be avoided. Using graphite nanoparticles of 30 and 80 nm without airflow, which is closer to normal conditions than the imposed airflow employed by Huang et al. (2007), they showed that polyethylene textiles (e.g. Tyvek) performed better than paper or cotton PPE (Nanosafe2 2008). Glove material was also examined and showed that the same nanoparticles could penetrate almost equally through commercially available gloves made of vinyl, nitrile, neoprene or latex materials. The glove material, elaboration (fabrication) process and thickness are major issues in determining diffusion of nanoparticles (penetration of 80 nm nanoparticles was found to be higher than 30 nm nanoparticles), and therefore at least 2 layers of gloves are recommended to be worn while handling nanomaterials (Nanosafe2 2008).

Note should be made that although there is a general lack of quantitative data in the open literature that relates to the penetration of engineered nanomaterials to specific glove types, there appears to be a wealth of information that provides workplace practice guidelines for the use of gloves when working with engineered nanomaterials (Baron et al. 2003; Maynard et al. 2004; HSE 2004b; Maynard & Kuempel 2005; NIOSH 2006; BASF 2007; BAuA-VCI 2007; BSI 2007; DENSRC 2007; EDDNP 2007; Harford et al. 2007; Huang et al. 2007; Methner et al. 2007; Mohlmann et al. 2007; Tsai & Hallock 2007; Nanosafe2 2008). Therefore, without such data it is not possible in this document to provide application guidelines for glove material types (e.g. Nitrile or latex) related to specific nanomaterials (e.g. MWCNTs).

This report has found that the extent of practical issues associated with the use of impermeable, non-woven, materials (e.g. Tyvek) as fabrics for protection from engineered nanomaterials has not been studied in detail. Similarly, information relating to the extent of issues associated with taking off, handling and storing protective clothing used with engineered nanomaterials has not been identified.

A challenge to making appropriate recommendations for dermal protection against nanoparticles is the need to strike a balance between comfort and protection. Garments that provide the highest level of protection (e.g. an impermeable suit) are also the least comfortable to wear for long periods of time, while garments that are probably the least protective (e.g. thin cotton lab coat) are the most breathable and comfortable for employees to wear (NIOSH 2009). However, PPE made from impermeable materials are used effectively for other work.

Eye Protection

Eye protection, e.g. (spectacle type) safety glasses, face shields, chemical hazard splash goggle, or other safety eyewear that is appropriate to the type and level of hazard, is recommended by U.S. DOE (2007). It is not considered that face shields or safety glasses provide sufficient protection against unbound, dry materials that could become airborne.

Handling liquids containing engineered nanomaterials

The U.S. DOE (2007) guidance specifically considers the handling of liquids containing nanomaterials, and recommends:

- wearing polymer (e.g. nitrile rubber) gauntlet-type gloves or nitrile gloves with extended sleeves when handling engineered nanomaterials and particulates in liquids. Gloves should be chosen only after considering the resistance of the glove to the chemical attack by both the nanomaterial and, if suspended in liquids, the liquid;

- wearing eye protection i.e. safety eyewear appropriate to the level and type of hazard such as chemical hazard splash goggles, face shields or spectacle type safety glasses.

The presence of substances such as detergents, surfactants and other ‘surface active’ chemicals (e.g. dimethylsulfoxide) are known to increase the rate of absorption for some chemicals e.g. carbon tetrachloride (Jackson 1989). In a workplace that uses both engineered nanomaterials and surfactants/surface active chemicals, the possibility of increased exposure by transdermal absorption must be considered. The ability of substances such as engineered nanomaterials to penetrate the skin depends on its physicochemical properties and size/surface characteristics, also whether the skin barrier is compromised or damaged, in which this absorption may more readily occur (Drexler 2003).

Table A. Summary of particle type, size ranged analysed, flow rate, filter material type, filter certification and filter efficiency for the different filtration efficiency studies of nanoparticles*.

Reference	Particle type	Size range analysed	Flow rate & face velocity	Filter material type	Filter certification	Filtration efficiency for particles <100 nm
Martin & Moyer (2000)	NaCl	Mean 75 nm	Flow rates of 42.5 & 82 L/min	N95	<5% penetration	<5% penetration
Alonso & Alguacil (2007)	Not stated	Few nm	Not stated	Electrostatic precipitator, wire screens	Not stated	<1% penetration
Richardson et al. (2005)	Particulate	Range below & above 100 nm	Range of flow rates From 20 to 400 L/min	N95	<5% penetration	<5% for low flow rate Max >5% for high flow rate
Richardson et al. (2005)	Particulate	Range below & above 100 nm	Range of flow rates 85 L/min & 300-400 L/min	P100	<0.03% penetration	<0.03% for low flow rate Max >0.03% for high flow rate
Balazy et al. (2006)	Salt	10nm-10 µm	Flow rates of 30 & 85 L/min	N95	<5% penetration	<5% for 30 L/min Max 5-6% for 30-80 nm at 85 L/min
Clark-Burton et al. (2007)	Number of types	10-900 nm	Not stated	PTFE, Gelatine, Polycarbonate (PC)	Not stated	Collection efficiency PTFE: ~100%. PC: 20-90%
Kim et al. (2007)	Ag	3-20 nm	Face velocity: 5.3-15 cm/s	Fibreglass, Nanofiber, Electret	Not stated	Penetration 0.01-30%
Mohlmann et al. (2007)	NaCl Welding fumes	14-100 nm	Flow rates: 47.5 & 95 L/min	P1, P2, P3 Glass fibre P2 Electrostatic pad P1 & P2	P1: penetration <20% P2: penetration <6% P3: penetration <0.05%	Integrated penetration values for 14-100 nm: P1: 2.1% P2 (fibre): 1.4% P2 (pad): 0.5% P3: 0.018%
HSE (2007a)	NaCl Citric acid SiO_2, TiO_2	<100 nm	Not stated	P100 N100	<0.03% penetration	Penetration < 0.03%

*N95 and N100 filter type face pieces correspond approximately to Australian P2 and P3 filter type face pieces (see Table B).

Table B. Comparison Australian filter types and their equivalence to US filter types.
(Refer to AS/NZS (2003) for Australian filter types and NIOSH (1996) for US filter types)

Australian Filter class	Recommended uses of filter	Allowed penetration	US Filter class	Recommended uses of filter	Allowed penetration
P2	Intended for use against both mechanically and thermally generated particulates	Not >6%	N95	Fine particulate when no oil or solvent is in the air	Not >5%
P3	Intended for use against all particulates including highly toxic materials	Not >0.05%	N100	Extremely fine and very toxic particulate when no oil or solvent is in the air	Not >0.03%
			P100	Extremely fine and very toxic particulate when oil or solvent is also in the air	Not >0.03%

3.11 Workplace monitoring

Nanoparticles or ultrafine particles are particles which have an aerodynamic diameter <100 nm, tend to have low solubility and are usually formed via evaporation, gas to particle reactions or nucleation. Most engineered nanomaterials are produced by a nucleation route e.g. saturated vapours arising from a laser ablation or the HIPCO process (Maynard et al., 2004; Maynard & Aitken, 2007; ISO 2007; Wake et al., 2002). Mechanical processes such as polishing, cutting or grinding may also be used to generate engineered nanomaterials (Zimmer & Maynard, 2002). With the increasing number of possible applications of nanoparticles identified, the potential number of workers who may be exposed has also increased.

The effective monitoring for engineered nanomaterials in the workplace is problematic at present, and much work is being focused on this topic globally. Safe Work Australia has commissioned a number of projects to progress workplace emissions and exposure assessment. In order to be relevant for risk evaluation, the assessment of exposure for workers needs to be aimed at determining the measures that are biologically relevant. A number of different measures may be relevant, e.g. chemical composition, particle morphology, surface area, mass concentration and number concentration. The technologies that are required to measure these metrics have been identified, unfortunately these are not available in the form required for the measurement of personal exposure on an ongoing basis. Some of the instrumentation which is capable of detecting these metrics is both large and cumbersome, which limits their use to static monitoring. Table C provides a list of instrumentation and techniques that are available to characterise engineered nanomaterials and ultrafines.

The factors which have been found to make the monitoring of nanomaterials difficult include:

- Differentiating engineered nanomaterials from background concentrations of other materials, especially when the background concentration level of other contaminants is high, e.g. a ratio of 1:250,000 of engineered nanoparticles to background concentration is possible.
- Trying to account for the variation in background levels of contaminants can be very disruptive if the relative concentrations are similar to those in the dot point above.
- The same nanoparticle may have different shapes and sizes and there may be several different types of nanoparticles present in the same sample.
- Nanoparticles tend to agglomerate, aggregate and stick to larger particles which makes estimating their concentration level difficult even when an actual airborne concentration has been determined.

Table C. Readily available instruments and techniques for the characterisation of engineered nanomaterials (adapted from Brouwer et al. 2004).

Metric	Device	Remarks
Mass	Size-selective personal sampler	No specific separation in UF size range
		Off-line gravimetric detection
		Results of other (static) size-selective devices (impactors) could be used to establish the relation between different size ranges
Number	CPC	Real-time number concentration not specified for UF size range
	SMPS	Real-time size distribution (mobility diameter) detection of number concentration
	ELPI	Real-time size distribution (aerodynamic diameter) detection of number concentration
		Size-selective sampling for other (off-line) analysis
Surface area	Series of SMPS and CPC	Estimates based on projected area equivalent diameter
	Series of SMPS and ELPI	Estimates based on fractal dimensions (differences in immobility and aerodynamic diameters)
Identification	SEM off-line analysis	Off-line microscopic analysis of morphology
	TEM off-line analysis	Samples may be collected by personal sampling or size-selective static samples (e.g. ELPI, impactors)
	X-ray microanalysis	Off-line analysis following SEM/TEM element identification
	XRF/XRD	Off-line analysis
		Samples may be collected by personal sampling or size-selective static samples (e.g. ELPI, impactors)

The first relevant detailed workplace monitoring report in the literature resulted from a request received by NIOSH in July 2005 to perform a health hazard evaluation at the University of Dayton Research Institute in Dayton, Ohio, USA (Methner et al. 2006). This request involved an evaluation of the sources of potential emissions from CNTs research processes. The team observed work practices, monitored the workplace by obtaining surface and air samples for CNTs, measured air concentrations of CNTs using real-time instruments (by CPC, diffusion charger, aerosol photometer and an electrical low pressure impactor, ELPI), evaluated the laboratory ventilation system and considered the PPE that was being used by the workers. Methner et al. (2006) found that many of the handling processes did not release CNTs, but some processes did raise the airborne concentration compared to background, i.e. wet sawing of composited material and transferring processes. It was also found that CNTs could be tracked out of the laboratory and into the office area, probably by transfer from footwear. The researchers recommended: the use of LEV during the transfer and wet sawing of CNTs; training of laboratory staff in the correct handling techniques was required; and sticky mats should be installed in order to prevent transfer of material outside the laboratory. It was suggested also that HEPA filtration was appropriate in order to clean

up any spilled CNTs and that nitrile gloves should used rather than latex gloves (Methner et al. 2006).

An occupational hygiene survey performed in a QD workplace by Methner et al. (2007), also resulted in recommending a series of workplace controls to protect workers, including: using a class 10,000 clean room with sticky mats at entrances, in which disposable cotton lab coats or Tyvek coats were used, single-pass laboratory hoods, controlled air pressure glove box, a partially-enclosed weighing station connected to a HEPA-filtered exhaust system, nitrile gloves and safety glasses. In this survey, surface Ghost Wipe™ samples were collected from several areas of the facility, including the office areas, and CadmiumCheck™ surface sampling kits were used to evaluate the presence of cadmium on surfaces throughout the laboratory and office area. A total of 84 air samples were also collected in the laboratory from four locations in the process, to measure for the presence of QD or other cadmium-containing materials. They also provided an in-depth workplace characterisation of sources that could possibly emit QDs, by using direct reading real-time instruments (Methner et al. 2007). There was no evidence of contamination of cadmium or QDs or other associated materials in any of the air or surface samples collected. Very low quantities of cadmium were detected on a few surfaces (<1 µg) that were most likely due to surface contact with a contaminated glove, and therefore regular discarding of gloves after specific operations would prevent such contamination (Methner et al. 2007).

Emissions of ultrafine lithium titanate particles in a workplace were examined by Singh et al. (2007) using a DustTrak aerosol monitor, an AeroTrak nanoparticle aerosol monitor (TSI Inc., MN, USA), a handheld CPC, and an SMPS. The concentrations of particles in the vicinity of a large furnace were measured and a gap in the exhaust system was found to be leaking a large number of nanoparticles. This nanoparticle leakage ceased once minor changes were made in the exhaust system (Singh et al. 2007).

The air retention characteristics of standard laboratory fume cupboards when handling nanoalumina has been tested using an FMPS (5 - 560 nm in 32 channels) (Tsai et al. 2007). Polycarbonate filters were used for particle collection and were analysed using SEM. Samples were taken in the workers' breathing zone, as background room measurements and around the handling location. Different handling operations were made during manipulations, including spatula handling and pouring of the nanomaterials. Variables studied included different hood designs, face velocity/sash location and the height of the breathing zone. Results were very specific for the two fume hoods examined in this study, preventing generalised conclusions, and indicated that more nanoparticles are carried out of the hood during handling at the higher velocity of 1 m/s, when the sash was lowered to the researchers low chest height. Elevated particle concentrations were also measured in the researchers' breathing zone as well as 1 m from the hood. When handling operations were carried out in a particular hood, the nanoparticle concentration in the lab was found to increase greatly. These researchers concluded that fume cupboards must only be used as LEV for worker protection when handling ultrafine and nanoparticles with the appropriate work practices in place (Tsai et al. 2007).

The concentration, size, shape and number of airborne MWCNTs in a Korean research facility has recently been measured and reported by Han et al. (2008). This facility produced MWCNTs by thermal chemical vapour deposition and subsequent processes involved ball milling, weighing, spraying and blending. General air sampling and personal sampling was conducted, together with real-time aerosol monitoring instrumentation, in order to determine

the degree of personal exposure and ensure that the implemented control measures were working correctly. Monitoring occurred before and after the implementation of control measures using an SMPS and aerodynamic particle sizer (APS) to determine particle size distribution, whilst an aethalometer was employed to determine mass concentration of particles in the air. The MWCNTs in workplace samples were on average ~58 nm in diameter and 1.5 µm in length. These researchers found that the implemented engineering control measures to be very effective, i.e. enclosing the blending stage and using extraction fans to ventilate the source of MWCNTs production, while general ventilation was not effective. These controls reduced the total airborne particle concentration and number of airborne MWCNTs in personal and area samples to non-detectable, or almost non-detectable levels, e.g. from 193.6 to ~0.018 CNTs/mL (Han et al. 2008).

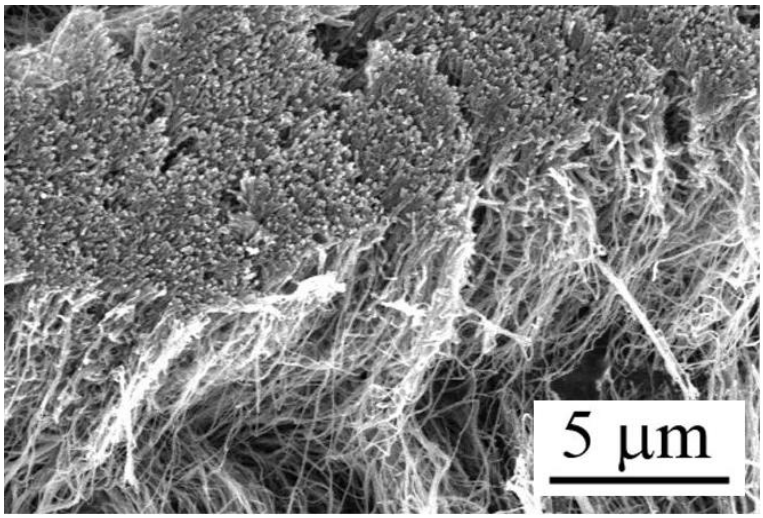

Figure 7. SEM image of MWCNTs with an average length of 15 µm (with permission of Dr Bill Li).

3.12 Medical surveillance

The recent NIOSH report of “Interim Guidance for the Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles” indicated that there is insufficient medical and scientific evidence to recommend ‘specific medical screening’ for workers who are exposed to engineered nanoparticles (NIOSH 2007). However the authors also concluded that if there are known methods for monitoring the specific nanomaterial, then it may be possible to employ these, as well as known occupational hygiene methods, as standard exposure measurement methods. The authors also recommend that medical surveillance methods are established in order to help assess whether or not implemented control measures are effective and to identify new or unrecognised problems and health effects (NIOSH 2007).

The published scientific literature concerning health effects that may result from exposure of workers to engineered nanomaterials was reviewed Schulte et al. (2008), in order to determine possible options for the health surveillance of workers. They identified options of specific surveillance that could be required if the toxicological properties of a nanomaterial were known or could be derived from the known properties of the bulk material, and options for general health surveillance, which could be used if the toxicological properties of the

material were not known and there was general concern for the health of workers through exposure. The major barrier to specific health surveillance for workers is reported to be the lack of actual epidemiological data for worker exposure (Schulte et al. 2008), but that is arguably a very good situation. Also, the authors believed that this data would not be generated quickly because the growing concern in using engineered nanomaterials has resulted in effective workplace controls being implemented in order to negate worker exposure (Schulte et al. 2008).

A useful method of biological monitoring for nanomaterial exposure, which may be linked to future medical surveillance methods, is achievable through the production of special formulations of engineered nanomaterials that have been enriched with rare stable isotopes (Casey & Gulson, 2008). This has been successfully employed using stable zinc isotopes to determine the dermal absorption of zinc oxide nanoparticles, following the topical application of sunscreens in human subjects (Casey & Gulson, 2008).

The ideal biomarker of exposure would employ dual-labelling techniques (i.e. using ZnO containing enriched rare stable isotopes for both zinc and oxygen) in order to exclude dissolved material from the measurement and thereby accurately determine the persistence of intact nanoparticles in the body. Although dual-label formulations of stable isotopes are potentially cost-prohibitive, they avoid the ethical issue of using tracer radioisotopes in human subjects. Dual-labelling biomarker studies would be easier to conduct in situations where the nanomaterial contains elements that are not usually present in the body's tissues and fluids (e.g. with minimal interference from background levels). However the alternative method of adducting fluorescent markers to nanoparticles can result in a new nanomaterial with greatly modified physico-chemical and biological characteristics.

3.13 Summary of evidence for the effectiveness of workplace controls following the 'hierarchy of control'

The control of worker exposure is paramount in the workplace, and is achieved using the widely-recognised 'hierarchy of controls', i.e. elimination, substitution, engineering controls, administrative controls and personal protective equipment.

The following section:

- Summarises evidence of effectiveness
- Lists key references where the controls have been examined and
- Proposes control measures for nanomaterials, based on the evidence obtained and evaluated for this report.

a) Elimination

Since the specific properties of engineered nanomaterials are usually required for manufacturing a novel product, it is unlikely that this option will often be feasible or practicable, and no examples have been found in this review.

b) Substitution

Regarding the potential substitution or modification of nanomaterials to reduce the hazard, there is the associated issue of maintaining required functionality. The authors have not

identified much evidence for nanomaterials substitution or nanomaterials modification being undertaken for the purposes of OHS management. However in regard to medical applications of engineered nanomaterials, reducing the toxicology of nanomaterials by modifying the particles has received significant focus. Modifying properties by adding functional groups to nanomaterials has been shown to reduce toxicity (Srinivasen 2008; Reilly 2007; Sayes et al. 2006a; Qiao et al. 2007; Uboldi et al. 2008). Thus, there is the potential for nanomaterial modification or substitution to be used to reduce workplace hazards.

Consideration should also be given with respect to whether the process or nanomaterial can be changed or substituted to achieve a lower risk of exposure. For example, using a material with a larger particle size may still provide the necessary improved properties in the product, but with less potential for exposure of workers to engineered nanomaterials. If it is technically feasible, a pelletised, paste or dispersion form of a material could be used rather than its nanopowder form. This option is discussed in the BAuA-VCI review (2007), the possibility of substitution /modification of the nanomaterial should always be a control option for consideration.

c) Engineering controls

i) Enclosure

Current evidence indicates that worker exposure is significantly reduced or negated if a process involving engineered nanomaterials, which would otherwise result in the release of airborne particles, is enclosed or contained. Evidence also indicates that enclosure must be well designed. It is also possible to isolate personnel in a cabin/compartment to protect them from a specific process. This may easily be applied to processes such as spray drying or gas phase nanomaterial processes, and may also be applied to processes that involve the use of dry nanomaterials. The method of containment or enclosure is designed for the specific processes, but is usually implemented in combination with other control measures, e.g. administrative controls and/or PPE.

Information about the application (or the suggested application) of this control method is provided in several reviewed articles (Baron et al. 2003; HSE 2004b; Maynard & Kuempel 2005; NIOSH 2006; BASF 2007; BAuA-VCI 2007; Boenke 2007; BSI 2007; DENSRC 2007; EDDNP 2007; Harford et al. 2007; Methner et al. 2006, 2007; Han et al. 2008; Tsai & Hallock 2007). The method of enclosure chosen in practice should depend upon the individual production and application processes for each nanomaterial.

ii) Extraction ventilation and filtration

Evidence indicates that worker exposure can be significantly reduced or negated through the use of correctly designed and implemented extraction ventilation and filtration for processes involving engineered nanomaterials that would normally result in the release of airborne particles. This control measure is usually implemented in combination with other control measures, e.g. administrative controls and/or PPE. The better extraction methods have involved the use of HEPA filtration and electrostatic precipitation. However, information has not been found relating to issues associated with managing parameters such as lifetime (how often to change), preventing nanomaterial release at changeover and safe disposal.

In the absence of enclosure the use of extraction ventilation should be considered for all nanomaterial processes that involve or might produce airborne particulates, e.g. in dusts, fumes or aerosols. There are a wide range of methods by which dust can be extracted using

a ventilation system, including dust extractors, fume hoods and fume cabinets. The selection of the most appropriate method will depend on the process being performed and the level of risk that it entails. As a rule, extracted air should undergo exhaust air purification before it is expelled or recirculated. If there are concerns about the efficiency of the purification system, then the exhaust air should not be recirculated into the workers' environment. It is important that performance and maintenance testing of such extraction systems is undertaken on a regular basis.

Information about the application (or the suggested application) of this control measure is provided from a number of sources, including specific mention of filtration methods that may also involve the use of electrostatic precipitators (Sullivan 2001; Baron et al. 2003; HSE 2004b; Balazy et al. 2006; Maynard & Kuempel 2005; Byeon et al. 2006; NIOSH 2006; BASF 2007; BAuA-VCI 2007; Boenke 2007; BSI 2007; Clark-Burton et al. 2007; DENSRC 2007; EDDNP 2007; Harford et al. 2007; Iwashita et al. 2007; Japuntich et al. 2007; Maze et al. 2007; Tsai & Hallock 2007; Nanosafe2 2008).

Evidence and information for ventilation or LEV is provided from a number of sources (Baron, et al. 2003; Wallace et al. 2004; NIOSH 2006; BAuA-VCI 2007; BSI 2007; DENSRC 2007; EDDNP 2007; Lee et al. 2007; Lu et al. 2007; Singh et al. 2007; Tsai & Hallock 2007; Tsai et al. 2007; Geraci 2008). The method of exhaust ventilation and/or filtration chosen in practice should depend upon the individual production and application processes for each nanomaterial.

Engineering control options can also be implemented to reduce the possibility of dermal exposure by the re-engineering of work processes to avoid immersion, splashes or spillage.

d) Administrative controls

There are a range of administrative controls that may be implemented for workers involved in using engineered nanomaterials. These types of procedural controls should be used in conjunction with engineering controls and/or PPE, however their application should be based on a risk assessment of a specific process or situation and may in certain cases, but not usually, be sufficient on their own (e.g. for nanomaterials embedded in matrices that do not shed nanoparticles during specific processes).

These methods include: limiting the process to specified areas; limiting access to areas; reducing time spent in possible exposure areas (e.g. hot areas); and reducing the number of personnel that may be potentially exposed. There must be an element of personnel training, and information provision (if available) about special measures for handling engineered nanomaterials, and the possibility of negative health effects from exposure to engineered nanomaterial dust. Information in operating instructions must be provided and routine medical and health surveillance, together with routine monitoring (if a method is available), should be carried out where practicable – particularly for nanomaterials for which such surveillance is a requirement for the corresponding macro-sized compounds. PPE and other work wear should be provided and cleaned by the employer, and stored away from private clothing. Thorough cleaning of the workplace should be performed on a regular basis using vacuum cleaners fitted with HEPA filters, or wet wipes if the use of vacuum cleaners is not possible.

Information about the application (or suggested application) of administrative control measures is provided in numerous sources (HSE 2004b; Maynard & Kuempel 2005; NIOSH 2006; BASF 2007; BAuA-VCI 2007; BSI 2007; Boenke 2007; DENSRC 2007; EDDNP 2007; Harford et al. 2007; Tsai & Hallock 2007). Information about the suggested application of medical surveillance is provided in two reports (NIOSH 2007; Schulte et al. 2008). The method of administrative controls and/or medical surveillance chosen in practice should depend upon the individual production and application processes for each nanomaterial.

e) Personal protective equipment (PPE)

Evidence indicates that there are a range of PPE that can provide some level of protection when used with engineered nanomaterials, including N95 or P100 face mask and filter types, double-gloving using nitrile type gloves and the use of other garments of non-woven fabrics (e.g. Tyvek polymeric material). Further testing and data is need in workplace situations to ensure effectiveness.

The use of PPE should be considered as the last line of defence in the hierarchy of workplace exposure mitigation approaches, after all other available measures have been implemented. PPE should also be worn on a precautionary basis whenever the failure of a single control, including an engineering control, could entail a significant risk of exposure to workers (DENSRC 2007). PPE is usually implemented in combination with other control measures, e.g. process enclosure, extraction and administrative controls.

i) Respiratory protective equipment (RPE)

Filtration results are summarised in Table A earlier. Results show that the capture efficiency of filter materials varies with filter type and flow rate. Data shows that under some conditions filter material meets or exceeds certified levels (e.g. less than 5% penetration for N95), but in some cases filter material performance does not meet it, e.g. at high flow rates. Filter materials never completely prevent exposure. An additional factor which is critical, and for which there is only limited evidence to date, is the effectiveness of respirator fit.

There are a number of sources from which information on the appropriate use and selection of respirators can be obtained, e.g. the specific HSE document for correct use within Great Britain (HSE 2003) and Australia (AS/NZS 1994). There are many different types of RPE, including disposable filter face pieces and full or half face masks, together with a range of air-supplied hoods, helmets, suits and blouses. P2, P3 and FFP3 high efficiency filters should always be used where RPE is determined to be required by risk assessment, and fit testing is required to ensure proper wearing. The use of airline respirators may be possible depending on the specific workplace arrangements and fit requirements. There is also a significant commitment in resources for maintenance, supervision and training to ensure that the RPE provides the required degree of protection. It is likely that the RPE will not protect the worker effectively if it is incorrectly selected or fitted, and would also give a false sense of security.

Evidence and information about the application (or the suggested application) of RPE for use with engineered nanomaterials is provided in a number of sources (Wang & Kasper 1991; Martin & Moyer 2000; Baron et al. 2003; Ferge et al. 2004; HSE 2004b; Balazy et al. 2006; Heim et al. 2005; Maynard & Kuempel 2005; Richardson et al. 2005; NIOSH 2006; BASF 2007; BAuA-VCI 2007; Boenke et al. 2007; BSI 2007; DENSRC 2007; EDDNP 2007; Harford et al. 2007; HSE 2007a; Iwashita et al. 2007; Japuntich et al. 2007; Kim et al. 2007; Maze et

al. 2007; Methner et al. 2007; Mohlmann et al. 2007; Tsai & Hallock 2007; Nanosafe2 2008). There are useful guidelines in these documents concerning the use of RPE, notably Nanosafe2 (2008), BASF (2007) and BAuA-VCI (2007).

ii) Protection from dermal exposure

When handling engineered nanomaterials, it is likely that dermal protection can be provided by a number of measures, including a double layer of protective gloves, garments made from non-woven fabrics and protective goggles that also have side protection (Nanosafe2 2008).

There are four basic criteria for protective glove selection: (1) they need to be appropriate for the conditions and risks where they are to be used; (2) they should be suitable for both the state of health of the worker and ergonomic requirements; (3) they should fit the intended worker correctly; and (4) they should be effective at exposure prevention without an overall increase in risk (Packham 2006). Correct maintenance and wearing procedures are required, and a glove management system needs to be introduced that reinforces and emphasises factors which need to be addressed and considered, to ensure that adequate protection is maintained. The key elements of this system include maintenance, storage, removal, disposal, training, ergonomics, material selection and the exposure/task scenario (Packham 2006).

Information about the application (or the suggested application) of gloves in handling engineered nanomaterials is provided by several sources (Baron et al. 2003; Maynard et al. 2004; HSE 2004b; Maynard & Kuempel 2005; NIOSH 2006; BASF 2007; BAuA-VCI 2007; BSI 2007; DENSRC 2007; EDDNP 2007; Harford et al. 2007; Huang et al. 2007; Methner et al. 2007; Mohlmann et al. 2007; Tsai & Hallock 2007; Nanosafe2 2008). The type and use of gloves chosen should depend upon the individual production and application processes for each nanomaterial. However there are some useful guidelines in these documents, notably by Nanosafe2 (2008), BASF (2007) and BAuA-VCI (2007).

Non-woven fabrics have been recommended to be used as the material for other PPE garments used to protect workers from engineered nanomaterials, e.g. lab coats, overalls, and trousers (Nanosafe2 2008). Specifically, garments made from air-tight high density polyethylene textiles (e.g. Tyvek) have been recommended to be used rather than garments of cotton or paper construction (Nanosafe2 2008).

For handling liquids containing engineered nanomaterials, the U.S. DOE (2007) recommends wearing polymer (e.g. nitrile rubber) gauntlet-type gloves or nitrile gloves with extended sleeves when handling engineered nanomaterials and particulates in liquids. Gloves should be chosen only after considering the resistance of the glove to the chemical attack by both the nanomaterial and, if suspended in liquids, the liquid. The use of eye protection is also recommended.

Part 4 – Implications for protection of workers to exposure from engineered nanomaterials

4.1 Potential risk to workers

There is a wide range of nanomaterials currently being researched, developed, manufactured and used by Australian businesses and research institutions and organisations. At present, the silicon, metal/metal oxide and carbon nanotube-based nanomaterials are the most common types produced and used in Australia. The proportions of various types of nanomaterials may differ in Australia compared to other countries, but overall there is likely to be a similar range of nanomaterial types being used.

There is a potential risk for the exposure of Australian workers and researchers while handling engineered nanomaterials. This exposure risk may increase as the Australian nanotechnology industry expands and the range of applications for engineered nanomaterials broadens. It is therefore imperative that appropriate and effective workplace controls for minimising worker exposure to engineered nanomaterials are implemented in a practicable and timely manner.

4.2 Health and safety practices

There is evidence that a number of conventional controls may be effective in preventing exposure to engineered nanomaterials (see Section 3.5-3.9.). Most of the evidence provided in this literature review is derived from basic experimental knowledge and work practices, taking into account the regulatory requirements. From this literature an understanding about what constitutes effective workplace controls is derived which is then applied to consider effective control methods to prevent exposure towards engineered nanomaterials.

The majority of technical papers that address the handling of nanoparticles have looked at situations that either simulate particle performance/movement through a filter substrate, or the effect of LEV re-configuration to minimise particles in the potential worker breathing zone and skin exposure, for as yet undefined industrial processes. These provide very valuable evidence.

However, there is only limited evidence from research in the workplace for the effectiveness of these controls. Recent key reports (Tsai & Hallock, 2007; Han et al. 2008; Methner et al 2006; Geraci 2008) provide some data in this regard, however these studies need to be expanded upon and generalised to a wider range of exposure scenarios of workers handling engineered nanomaterials.

4.3 Risk control approaches

Ideally, an occupational hygienist would follow these steps to prevent or minimise nanoparticle exposure in process design:

Step 1. Theoretical consideration of the nanoparticle size range and potential control mechanism(s), in simulation mode – if this yielded a potentially acceptable exposure, then go to step 2 (if not, then consider additional potential control mechanisms until a potentially acceptable exposure is achieved theoretically).

Step 2. Laboratory-scale prototype controls applied to the process – with apparent confirmation of outcomes from the theoretical models, go to step 3.

Step 3. Actual workplace measurements of the worker exposure, which may be particle monitoring and subsequent concentration measurement, and qualitative analysis for toxicological consideration, and biological monitoring of the worker's system for actual body burden of candidate materials. If the level/concentration of nanomaterial is determined to be higher than a determined exposure standard then action will need to be taken to reduce this exposure level.

However given the current levels of knowledge and understanding of risk, in terms of the implementation of possible workplace control measures the authors recommend that the following is a reasonable and appropriate strategy to employ:

For the research and early development scenario: the control banding approach should be used. It is noted that the toxic potential is currently not fully understood for nanomaterials, and the eventual scale-up and manufacture of a product containing the nanomaterial may be uncertain. As the specific toxicology knowledge for a nanomaterial develops, it may be allocated to a different risk group that would require different (or more specific) control measures to be taken. A complete life-cycle analysis of the nanomaterial should always be made to identify potential 'hotspots' of worker exposure. That is, every process involved in this early phase should implement the most stringent controls indicated by the risk assessment/risk management process, as determined from the worst-case scenario. This would involve the following (although additional measures may also be necessary in specific circumstances): the engineering controls of enclosure, local exhaust ventilation and ventilation/filtration using HEPA filters, if required; possible administrative control options to reduce the potential for workplace exposure; and, as a last line of defence, appropriate PPE, including N95 or P100 face-piece mask, the use of double-gloves of a suitable material that does not allow penetration, and also non-woven fabrics for other protective garments (See Table B for a comparison Australian filter types and their equivalence to US filter types).

For the pilot/full production scenario: a more comprehensive toxicological testing profile, i.e. a sufficient range of tests that cover the breadth of potential toxicological effects possible, needs to be made for nanomaterials in this scenario. This will give more definition to the risk assessment process and allow the assignment of the appropriate workplace controls during production for this specific raw material.

Due to the lack of hazard data for individual nanomaterials, they could be grouped according to a presumed hazard level. The approach of control banding of substances as used in the UK's COSHH Essentials package identifies five different hazard groupings. Such an approach could be used for the wide variety of nanomaterials produced, and being developed, while avoiding expensive costs involved in the experimental determinations. The

BSI (2007) document, which includes the control banding approach, is a suitable model for use in this manner, but further analysis needs to be made of this system. In addition to this, there are several other documents with useful guidance materials as listed in Part 3.9, notably those provided by Nanosafe2 (2008), BASF (2007) and BAuA-VCI (2007).

4.4 Recommendations for workplace controls

The authors recommend that workplace controls for reducing exposure to engineered nanomaterials should involve a combination of engineering controls, administrative controls and as a last line of defence, PPE, if the higher order options of elimination and substitution are not appropriate for the specific engineered nanomaterials in question (see section 3.3-3.9). Further focus should be placed on examining opportunities for modification of nanomaterials to reduce toxicity.

The engineering controls should initially involve the highest order control measure of enclosing the process, coupled with extraction ventilation/LEV and suitable filtration of exhaust air before it enters the external environment. Generally exhaust air should be HEPA-filtered to ensure that nanoparticles are removed. Existing ventilation systems that are effective for extracting ultrafine dusts in other industries should also be employed where appropriate. These should be installed, tested and maintained in accordance with American Conference of Governmental Industrial Ventilation guidelines (ACGIH 2001) to maintain optimal efficiency in removing nanoparticulates. Less engineering control measures would be required for specific processes involving nanomaterials embedded in matrices that do not result in shedding of nanoparticles. A limitation on the use of engineering controls is that there are a number of workplace scenarios where their use is impractical. Protection for workers then relies on administrative controls and, as a last line of defence, PPE.

Administrative controls are always options that can be used in order to further reduce the potential for worker exposure. These have been discussed previously (in Section 3.12), and there are several standard OHS methods by which these measures can be implemented, e.g. job rotation, and processes occurring when workers are not present.

The PPE should consist of a filter-based facemask respirator N95 (corresponding to P2 Australian type, see Table B), efficiency or above, or SCBA if required, double gloving using glove materials that are resistant to penetration by engineered nanomaterials, together with other protective garments that are made of non-woven fibre (e.g. not cotton). One of the main concerns is to ensure that facemasks and SCBA items go through a proper fitting regime for each worker to ensure integrity of the protection during their operation. Further issues with PPE lies in worker comfort with prolonged use, and identifying how frequently to change PPE.

Taken together, all of these controls should provide a robust regime through which nanomaterials exposure to workers will be reduced to very low levels.

The workplace controls that have been defined in this report are expected to be able to be used across a number of operations involving engineered nanomaterials including research, development, maintenance, construction, packaging, cleaning and other downstream operations (BSI 2007; BAuA-VCI 2007; ICON 2007; BASF 2007). However their use in

specific workplaces needs to be determined by an appropriate and rigorous risk management processes that determines the need for their use (NIOSH 2006; NIOSH 2007; ISO 2007; ICON 2007).

4.5 Issues identified

Relevant research is taking place internationally on an ongoing basis in the area of effective workplace controls to prevent exposure of workers to different nanomaterials. An indication of the current trends in international research themes addressing aspects of nanotechnology environmental health and safety (EHS) in order to better understand the risks associated use of nanomaterials, was recently described for the USA in their National Nanotechnology Initiative document issued in February 2008 (NNI 2008). The Australian government's National Nanotechnology Strategy (NNS) is being supported in this area by the Safe Work Australia Nanotechnology OHS Program, which covers: OHS support for Australian nanotechnology businesses and research organisations; research coordination for Australian research projects and international collaborations; evaluation and development of workplace controls; and consideration of the OHS Regulatory Framework in relation to Nanotechnology, and includes identifying the specific information and knowledge requirements to ensure the framework operates effectively (DEEWR 2008).

Overall, there is limited data on actual workplace measurements taken before/after a nanomaterial process commences, and before/after control measures have been employed, that would provide accurate comparisons of the levels of both engineered and incidental particulates between each situation. There is an absence of data on controlling and detecting nanomaterial types that are more commonly produced by Australian nanotechnology industries, such as silicon, metal/metal oxide and carbon nanotube-based nanomaterials.

Other issues identified are as follows:

(a) Determining any detail that needs to be added to the OHS regulatory framework for working with engineered nanomaterials in the workplace.

(b) Determining what are effective workplace risk management strategies for different types of workplaces, whereby their effective implementation will decrease or negate the exposure of workers to engineered nanomaterials in the Australian workplace.

(c) Determining the applicability of the control strategy of 'control banding'/ 'risk management toolbox' approach towards defining control measures in Australian workplaces for engineered nanomaterials. Furthermore, to determine the minimum toxicological (and other) characterisation required for an individual nanomaterial to provide a sufficient risk profile to modify 'control banding' measures.

(d) For engineering controls in Australian workplaces: confirming the predicted effectiveness of the use of HEPA filters and electrostatic precipitators as means of removal of engineered nanomaterials when used in workplace.

(e) For PPE in actual Australian workplaces: determining which types of gloves, glove combinations and glove materials provide effective barriers to dermal exposure of workers; determining the effectiveness of different filter types in face masks/pieces to provide removal of engineered nanomaterials from the air inhaled by workers; determining the effectiveness and issues associated with using different types of non-woven and other fabrics in garments used to protect workers from exposure to engineered nanomaterials.

(f) Gain a deeper understanding of the potential health risks posed by the exposure of workers to engineered materials.

(g) Determining the effects of the presence of surfactants and other surface active materials in mixtures with engineered nanomaterials and their ability to enhance transdermal absorption of engineered nanomaterials.

(h) Developing accurate, reliable and practicable methods for monitoring air and surface concentrations of engineered nanomaterials in the Australian workplace.

This report considers that the development of commercially-available robust instrumentation to accurately measure airborne concentrations of nanoparticles in the occupational environment, either as a nuisance dust or a process-specific toxicant, is trailing nanotechnology industry applications and developments. It is recognised that real-time particle monitors are optimised for (and calibrated with) spherical particles and consequently may not accurately measure irregularly-shaped particles with large aspects ratios (i.e. length divided by diameter, which is >10,000 for many CNTs). Direct comparisons are required for particle number concentration (e.g. CPC) and size distribution (e.g. SMPS), with confirmation of particle morphology (e.g. TEM). Determining the extent of this inaccuracy and verifying the most appropriate real-time particle monitors for irregular nanoparticles, will facilitate prospective studies in Australian workplaces.

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Appendix 1: Evaluation summary of literature for evidence of effective workplace controls

The following tables summarise the evaluation of the reviewed literature concerning the evidence of effective workplace controls. The publications are categorised into two groups, and include the authors' opinions regarding the applicability of information contained, i.e.:

1. Experimental evidence, or
2. Guidance and review documents.

Table 1. References which provide experimental evidence of effective workplace controls

Reference	Laboratory or Workplace setting?	Nanoparticle Type	Mention made of Bio-monitoring	Which elements of Hierarchy of Control were examined	Relevance to Australian Setting	Authors opinion of Robustness / Practicality of guidance	Authors opinion of whether principles are applicable
Han et al. (2008)	Workplace	MWCNTs	No	[a] Enclosure, ventilation, filtration	Yes	Yes, provides strict monitoring method for MWCNTs	Yes
Nanosafe2 (2008)	Both	Several NM types	No	[a] Filtration, [c] PPE gloves, face filter masks, non-woven fabrics	Yes, widely applicable	Yes, scientific principles very robust and can be applied practically	Yes, principles look highly applicable
Lee et al. (2007)	Workplace	Welding fumes	No	[a] Ventilation	Yes	Yes, applicable to specific welding situations, with possible broader applicability	Yes
Methner et al. (2007)	Workplace	Quantum dots	No	[a] Enclosure, filtration, [c] PPE gloves, other PPE as required	Yes	Robust application, results can very practically be applied	Workplace application
Singh et al. (2007)	Workplace	Lithium titanate	No	[a] Ventilation	Yes	Robust and practical application of real time monitoring methods	Workplace application
Tsai & Hallock (2007)	Both	Several NM types	No	[a] Enclosure filtration, [b] Admin (various), [c] PPE gloves, face filter masks, other PPE as required	Yes	Yes, scientific principles very robust and can be applied practically	Yes

Tsai et al. (2007)	Workplace	Nano alumina	No	[a] Ventilation	Yes	Robust and practical conclusions	Workplace application
Methner et al. (2006)	Both	MWCNTs	No	[a] Enclosure filtration, [b] Admin (various), [c] PPE gloves, face filter masks, other PPE as required	Yes, widely applicable	Yes, robust and practical framework for handling NM	Yes
Baron et al. (2003)	Laboratory	SWCNTs (1.5 nm diam. ~1 mm length)	No	[a] Enclosure Filtration, [c] PPE gloves, face filter masks, other PPE as required	Yes, applicable for SWCNTs	No, more information required than just this study	No, but may be applicable to specific situations
Casey & Gulson (2008)	Practical Application	ZnO	Rare stable isotopes	Not used	Yes	Useful biomonitoring technique where a rare isotope is both applicable and available	No but principles can be applied
Clark-Burton et al. (2007)	Laboratory	Biological (10-80; 900 nm) & non-biological (10-600 nm) test aerosols	No	[a] Filters	Yes	Yes. robust and practically applicable	No, but may be applicable to specific situations
HSE (2007a)	Laboratory	NaCl, SiO_2, TiO_2 and citric acid	No	[c] Face filters	Yes, underlying principles are applicable	Yes, scientific principles very robust and can be applied practically	No, but principles look highly applicable
Iwashita et al. (2007)	Laboratory	Produced H_2 & silicon hydride (2-100 nm)	No	[a] Filtration (particle entrapment)	Yes	Yes. robust and practically applicable	No, but may be applicable to specific situations
Japuntich et al. (2007)	Laboratory	NaCl & DOP (10-400 nm)	No	[a] Filtration	Yes	Yes. robust and practically applicable	No, but may be applicable to specific

							situations
Kim et al. (2007)	Laboratory	Silver (3-20 nm)	No	[c] PPE filter masks	Yes	Yes, robust and practically applicable	No, but may be applicable to specific situations
Maze et al. (2007)	Laboratory	Simulation	No	[a] Filtration	Yes	Yes, useful general principles	No, but may be applicable to specific situations
Mohlmann et al. (2007)	Laboratory	NaCl and welding fumes	No	[c] Filter face masks	Yes	Robust application, results can very practically be applied	No but principles can be applied
Byeon et al. (2006)	Laboratory	NaCl (20-100nm) and DOP (50-800 nm	No	[a] Filtration	Yes	Yes, good study design	No, but may be applicable to specific situations
Balazy et al. (2006)	Laboratory	NaCl (10-600 nm)	No	[a] Filtration, [c] efficiency of PPE respirators	Yes, data can be applied	Yes, robust data set	No, but may be applicable to specific situations
Richardson et al. (2005)	Laboratory	Aerosolised bacterial & solid particulates (DOP, NaCl)	No	[c] Face filters	Yes, underlying principles are applicable	Yes, scientific principles very robust and can be applied practically	No, but principles look highly applicable
Ferge et al. (2004)	Workplace	Combustion aerosol from incineration	No	[a] Filtration	Yes	Yes, electrostatic precipitation method is robust and can be applied practically	No, but may be applicable to specific situations
Maynard et al. (2004)	Laboratory	SWCNTs	No	[c] PPE gloves	Yes, for SWCNTs production	Limited, depends on production method	No

Wallace et al. (2004)	Domestic application	Indoor ultrafines (candle fumes, kitty litter fines)	No	[a] Ventilation – with precipitator addition	Yes, for general guidance on filtration type	Yes, electrostatic precipitation method is robust and can be applied practically	No, but may be applicable to specific situations
Sullivan (2001)	Practical application	Not enough detail given	No	[a] Filtration	Yes	Robust and practical application	No, but principles have good practical application
Martin & Moyer (2000)	Laboratory	NaCl and DOP	No	[c] Face filters	Yes, underlying principles are applicable	Yes, scientific principles very robust and can be applied practically	No, but principles look highly applicable
Lu et al. (2007)	Practical application	Not stated	[a] Ventilation	Yes	Robustness and practicality cannot be judged from data provided	No but principles can be applied	No but principles can be applied
Heim et al. (2005)	Laboratory	Uncharged NaCl (2.5-20 nm diam.)	[a] Filtration	Possible, as a means of engineering filtration	Yes, method has general applicability	No, but may be applicable to specific situations	No, but may be applicable to specific situations
Wang & Kasper (1991)	Theoretical	Theoretical paper	[a] Filtration, [c] PPE Filter face masks	Yes, principles applicable to numerous scenarios	Yes; scientific principles very robust	No, but principles have good practical application	No, but principles have good practical application
Huang et al. (2007)	Practical application	NaCl	[c] Protective clothing	Yes	Results are robust and can be practically applied	No but principles can be practically applied	No but principles can be practically applied

Hierarchy of Control (HoC): assuming the higher order options of elimination and substitution are generally excluded, i.e. [a] Engineering – Enclosure, Ventilation, Filtration/Filters; [b] Administrative controls; [c] Personal Protective Equipment (PPE).

Table 2. Guidance & review documents

Reference	Application	Nanoparticle Type	Mention made of Bio-monitoring	Which elements of Hierarchy of Control were examined	Relevance to Australian Setting	Authors opinion of Robustness / Practicality of guidance	Authors opinion of whether principles are applicable
Nanosafe2 (2008)	Practical Application	Several NM types	No	[a] Filtration, [c] PPE gloves, face filter masks, non-woven fabrics	Yes, widely applicable	Yes, scientific principles very robust and can be applied practically	Yes
ASTM (2007) E2535-07	Theoretical; principles are applicable	N/A	N/A	N/A	Yes	Document provides important definitions	No
BASF (2007)	Workplace	Not specified, but generally applicable	No	[a] Enclosure, filtration, [b] Admin (various), [c] PPE gloves, face filter masks, other PPE as required	Yes	Yes, robust and practical framework for handling NM	No, but guidelines are practical and applicable to specific situations
BAuA-VCI (2007)	Workplace	Not specified, but generally applicable	No	Substitution (larger particles) [a] Enclosure, filtration, [b] Admin (various), [c] PPE gloves, face filter masks, other PPE (not specified)	Yes	Yes, robust and practical framework for handling NM	No, but guidelines are practical and applicable to specific situations

BSI (2007)	Theoretical and practical guidelines	Not experimental	Yes, depending on NM type	[a] Enclosure, filtration, [b] Admin (various), [c] PPE gloves, face filter masks, non-woven fabrics	Yes	Yes, robust and practical framework for handling NM	No, but method generally applicable across a range of scenarios
EDDNP (2007)	Theoretical	Not experimental	Yes, as required by risk management process	[a] Enclosure, filtration, [b] Admin (various), [c] PPE gloves, face filter masks, other PPE (not specified)	Yes, generally adaptable	Yes, robust but practicality of use of this risk management framework needs to be assessed	No, but method generally applicable across a range of scenarios
DENSRC (2007)	Theoretical/ Industry Philosophy	Not experimental	Yes, implicit health surveillance	[a] Enclosure, filtration, [b] Admin (various), [c] PPE gloves, face filter masks, non-woven fabrics	Yes	Yes, very robust and practical framework for handling NM	No, but method generally applicable across a range of scenarios
NIOSH (2006)	Theoretical and practical guidelines	Not experimental	Yes, depending on NM exposure type	[a] Enclosure filtration, [b] Admin (various), [c] PPE gloves, face filter masks, other PPE as required	Yes	Yes, robust and practical framework for handling NM	No, but method generally applicable across a range of scenarios
Schulte et al. (2008)	Not specified	Not specified	Yes	Not used	Yes, possible applicability of biological	No firm conclusions reached	No

					monitoring		
Boenke (2007)	Laboratory	Lists most possible types	No	[a] Enclosure, filtration, [b] Admin (various), [c] PPE face filter masks	Yes, underlying principles are applicable	Yes, scientific principles very robust and can be applied practically	No, but principles look highly applicable
Harford et al. (2007)	Laboratory and Workplace	Not experimental	Yes, details not specified	[a] Enclosure, filtration, [b] Admin (various), [c] PPE gloves, face filter masks, other PPE as required	Yes	Yes, very robust principles and widely-applicable	No, but principles have good practical application
Maynard & Kuempel (2005)	Theoretical and practical guidelines	Not experimental	No	[a] Enclosure, filtration, [b] Admin (various), [c] PPE gloves, face filter masks, other PPE as required	Yes, but not specific	Does not provide a robust risk control framework, work is practical but lacks specifics	No, but method generally applicable across a range of scenarios
Aitken et al. (2004)	Theoretical/ Discussion	Not experimental	No	Detailed discussion of Philosophy of Controls	Yes	Yes, very robust principles and widely-applicable	No, but principles have good practical application
HSE (2004b)	Theoretical/ Industry Philosophy	Not experimental	Yes, details not specified	[a] Enclosure, filtration, [b] Admin (various), [c] PPE gloves,	Yes	Yes, is based around general principles which can be practically applied	No, but method generally applicable across a range of scenarios

				face filter masks, other PPE as required			
Tutungi et al. (2008)	Theoretical / guideline discussion	Not experimental	Theoretical discussion of controls	Yes	Theoretical guidelines and recommendations on monitoring	No but principles can be applied	No but principles can be applied
ISO (2007)	Laboratory	Several NM types	[a] Enclosure, filtration	Yes, widely applicable	Document provides important definitions	Yes, but provides general rather then specific information	Yes, but provides general rather then specific information

Hierarchy of Control (HoC): assuming the higher order options of elimination and substitution are generally excluded, i.e. [a] Engineering – Enclosure, Ventilation, Filtration/Filters; [b] Administrative controls; [c] Personal Protective Equipment (PPE)