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Standard Guide for Handling Unbound Engineered Nanoscale Particles in Occupational Settings[1]

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INTRODUCTION

Nanometre-scale particles are encountered in nature and in industry in a variety of forms and materials. Engineered nanoscale particles as a class comprise a range of materials differing in shape, size, and chemical composition, and represent a broad range of physical and chemical properties. Workers within some nanotechnology-related industries and operations have the potential to be exposed to these engineered nanoscale particles at levels exceeding ambient nanoscale particle concentrations through inhalation, dermal contact and ingestion when not contained on or within a matrix (unbound). Occupational health risks associated with manufacturing, processing and handling unbound nanoscale particles, agglomerates or aggregates of nanoscale particles are not yet clearly understood. Dominant exposure routes, potential exposure levels and any material hazard are expected to vary widely among particular nanoscale particle materials and handling contexts. Additional research is needed to understand the impact of these exposures on employee health and how best to devise appropriate exposure monitoring and control strategies. Until clearer understandings emerge, the limited evidence available suggests caution when potential exposures to unbound engineered nanoscale particles (UNP) may occur.

1. Scope

1.1 This guide describes actions that could be taken by the user to minimize human exposures to unbound, engineered nanoscale particles (UNP) in research, manufacturing, laboratory and other occupational settings where UNP may reasonably be expected to be present. It is intended to provide guidance for controlling such exposures as a cautionary measure where neither relevant exposure standards nor definitive hazard and exposure information exist.

1.2 *General Guidance*—This guide is applicable to occupational settings where UNP may reasonably be expected to be present. Operations across those settings will vary widely in the particular aspects relevant to nanoscale particle exposure control. UNP represent a vast variety of physical and chemical characteristics (for example, morphology, mass, dimension, chemical composition, settling velocities, surface area, surface chemistry) and circumstances of use. Given the range of physical and chemical characteristics presented by the various UNP, the diversity of occupational settings and the uneven empirical knowledge of and experience with handling UNP materials, the purpose of this guide is to offer general guidance on exposure minimization approaches for UNP based upon a consensus of viewpoints, but not to establish a standard practice nor to recommend a definite course of action to follow in all cases.

1.2.1 Accordingly, not all aspects of this guide may be relevant or applicable to all circumstances of UNP handling. The user should apply reasonable judgment in applying this guide including consideration of the characteristics of the particular UNP involved, the user's engineering and other experience with the material, and the particular occupational settings where the user may apply this guide. Users are encouraged to obtain the services of qualified professionals in applying this guide.

1.2.2 *Applicable Where Relevant Exposure Standards Do Not Exist*—This guide assumes that the user is aware of and in compliance with any authoritative occupational exposure standard applicable to the bulk form of the UNP. This guide may be appropriate where such exposure standards do not exist, or where such standards exist, but were not developed with consideration of the nanoscale form of the material.

1.3 *Applicable Where Robust Risk Information Does Not Exist*—This guide assumes the absence of scientifically sound risk assessment information relevant to the particular UNP

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involved. Where sound risk assessment information exists, or comes to exist, any exposure control measures should be designed based on that information, and not premised on this guide. Such measures may be more or less stringent than those suggested by this guide.

1.4 *Materials Within Scope*—This guide pertains to unbound engineered nanoscale particles or their respirable agglomerates or aggregates thereof. Relevant nanoscale particle types include, for example, intentionally produced fullerenes, nanotubes, nanowires, nanoropes, nanoribbons, quantum dots, nanoscale metal oxides, and other engineered nanoscale particles. Respirable particles are those having an aerodynamic equivalent diameter (AED) less than or equal to 10 µm (10 000 nm) or those particles small enough to be collected with a respirable sampler (**1-3**).[2] The AED describes the *behavior* of an airborne particle and is dependent upon the particle density, shape, and size—for instance, a particle with a spherical shape, smooth surface, density of 1.0 g/cc and a physical diameter of 4 µm would have an AED of 4 µm, whereas a particle with a spherical shape, smooth surface, density of 11.35 g/cc and a physical diameter of 4 µm would have an AED of 14 µm and would therefore be of a nonrespirable size. Respirable fibers are those having physical diameters less than or equal to 3 µm (3000 nm) or those fibers small enough to be collected with a thoracic sampler (**4, 5**).

1.5 *Materials Beyond Scope:*

1.5.1 UNP may be present in various forms, such as powders or suspensions, or as agglomerates and aggregates of primary particles, or as particles dispersed in a matrix. This guide does not pertain to UNP incapable, as a practical matter, from becoming airborne or be expected to generate or release UNP in occupational settings under the particular circumstances of use (for example, UNPs dispersed or otherwise fixed within a solid, strongly bonded to a substrate or contained within a liquid matrix such as aggregated primary crystals of pigments in paints). This guide does not pertain to aggregates or agglomerates of UNP that are not of a respirable size.

1.5.2 This guide does not pertain to materials that present nanoscale surface features, but do not contain UNPs (for example, nanoscale lithography products, nanoelectronic structures or materials comprised of nanoscale layers).

1.5.3 This guide does not pertain to UNPs which exist in nature which may be present in normal ambient atmospheres or are unintentionally produced by human activities, such as by combustion processes. Nor does it pertain to materials that have established exposure control programs (for example, safe handling protocols for nanoscale biological agents) or published exposure limits such as occupational exposure limits for welding fumes. See Appendix X1.

1.6 *Handling Considerations Beyond Scope*—The use of this guide is limited to the scope set forth in this section. This guide generally does not address actions related to potential environmental exposures, nor to exposures potentially arising at disposal or other end-uses.

1.7 *Not a Standard of Care*—This guide does not necessarily represent the standard of care by which the adequacy of a set of exposure control measures should be judged; nor should this document be used without consideration of the particular materials and occupational circumstances to which it may be applied. The word "standard" in the title means only that the document has been approved through the ASTM consensus process.

1.8 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.9 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[3]

E2456 Terminology Relating to Nanotechnology

F1461 Practice for Chemical Protective Clothing Program

3. Terminology

3.1 *Definitions*—Refer to Terminology E2456 for definitions of terms used within this guide.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *aerodynamic equivalent diameter (AED), n*—the diameter of a smooth, unit density [ρ_o = 1 gram per cubic centimetre (g/cm^3)] sphere that has the same terminal settling velocity as the actual particle (**6**).

3.2.2 *agglomerate, n—in nanotechnology*, a group of particles held together by relatively weak forces (for example, van der Waals or capillary.) and which may break apart into smaller particles upon processing.

3.2.3 *aggregate, n—in nanotechnology*, a discrete group of particles in which the various individual components are not easily broken apart, such as in the case of primary particles that are strongly bonded together (for example, fused, sintered, or metallically bonded particles).

3.2.4 *control principle, n*—the principle establishes in this guide that, as a cautionary measure, occupational exposures to unbound, engineered nanoscale particles (UNP) should be minimized to levels that are as low as is reasonably practicable.

3.2.5 *nanoscale, adj*—having one or more dimensions on the order of 1 to 100 nanometres.

3.2.6 *particle, n—in nanotechnology*, a small object that behaves as a whole unit in terms of transport and properties.

3.2.7 *program, n*—a management policy to minimize occupational UNP exposures together with the procedures and actions to meet that objective.

[2] The boldface numbers in parentheses refer to the list of references at the end of this standard.

[3] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

3.2.8 *respirable, adj*—airborne particles which are small enough to enter the alveolar (gas-exchange) region of the lung.

3.2.9 *inhalable, adj*—airborne particles which are small enough to enter the head airways through the nose or mouth, or both, during inhalation.

3.2.10 *should, aux., v—as used in this guide*, indicates that a provision is not mandatory but is recommended as a good practice.

3.2.11 *ultrafine particle, n*—a particle smaller than about 0.1 micrometre (100 nanometres) in diameter.

3.2.12 *unbound, adj—with reference to engineered nanoscale particles*, those nanoscale particles that are not contained within a matrix under normal temperature and pressure conditions that would reasonably be expected to prevent the particles from being separately mobile and a potential source of exposure. An engineered primary nanoscale particle dispersed and fixed within a polymer matrix, incapable as a practical matter of becoming airborne, would be "bound," while such a particle suspended as an aerosol would be "unbound."

3.3 *Acronyms:*

3.3.1 *HEPA*—high efficiency particulate air

3.3.2 *MSDS*—material safety data sheet(s)

3.3.3 *PPE*—personal protective equipment

3.3.4 *UNP*—unbound engineered nanoscale particles

4. Summary of Guide

4.1 This guide presents the elements of an UNP handling and exposure minimization program including considerations and guidance, based on a consensus of viewpoints, for establishing such a program. The six principal elements are: *(a)* establishing management commitment to the control principle; *(b)* identifying and communicating potential hazards; *(c)* assessing potential UNP exposures within the worksite; *(d)* identifying and implementing engineering, and administrative controls consistent with the control principle for all relevant operations and activities; *(e)* documentation; and *(f)* periodically reviewing its adequacy.

4.2 *The Control Principle*—Exposure control guidance in this guide is premised on the principle (established in this guide) that, as a cautionary measure, occupational exposures to UNP should be minimized to levels that are as low as is reasonably practicable. This principle does not refer to a specific numerical guideline, but to a management objective, adopted on a cautionary basis, to guide the user when *(a)* assessing the site-specific potential for such exposures; *(b)* establishing and implementing procedures to minimize such exposures; *(c)* designing facilities and manufacturing processes; and *(d)* providing resources to achieve the objective. Additional discussion of the application of the control principle is set forth in Annex A1.

5. Significance and Use

5.1 This guide is intended for use by entities involved in the handling of UNP in occupational settings. This guide covers handling principles and techniques that may be applied, as appropriate, to the variety of UNP materials and handling settings. These settings include research and development activities, material manufacturing, and material use and processing. This guide may also be used by entities that receive materials or articles containing or comprising nanoscale particles fixed upon or within a matrix (that is, bound nanoscale particles), but whose own processes or use may reasonably be expected to cause such particles to become unbound.

6. Establishing a Program to Implement the Control Principle

6.1 *Process for Establishing Program*—To attain the integrated effort needed to minimize UNP exposures consistent with the *control principle*, the user should develop a *program* that addresses the efforts in all management, planning and operational phases of the enterprise to be taken to achieve that objective. The principal topics of this guide outline an iterative process typical of many occupational safety regimes the user of this guide may adopt for the initial establishment and implementation of an effective *program* to minimize occupational UNP exposures.

6.2 *Management Commitment*—A formal, written management policy should be established committing to minimizing potential occupational UNP exposures to levels that are as low as is reasonably practicable. The policy and commitment should be regularly communicated throughout the organization and reflected in *(a)* written administrative procedures, instructions and training materials for operations and contingencies potentially involving occupational UNP exposures, *(b)* facilities design, and *(c)* instructions to designers, vendors and user personnel specifying or reviewing facility design, systems, operations or equipment.

6.3 *Organization of Personnel and Responsibilities*—Responsibility and authority for implementing a minimization program consistent with this guide should be assigned to an individual with organizational freedom to ensure appropriate development and implementation of the *program*. This *program* manager would be responsible for coordinating efforts among the several functional groups (for example, operations, housekeeping, maintenance, engineering, safety, human resources, sales, and shipping) that may be involved or impacted by the *program*, and should have the authority, or direct recourse to an authority, to timely resolve questions related to the conduct of the *program*. The *program* manager should be knowledgeable, or adequately supported by persons who are knowledgeable, concerning the characteristics of the UNP involved, all aspects of the organization's processes and worker activities involving UNP, relevant engineering exposure control methods, and the organization's best information concerning the potential occupational safety and health risks of relevant UNP exposure.

6.3.1 Responsibilities of the *program* manager should include to *(a)* establish and maintain a *program* that implements the management commitment to the control principle, including specific goals and objectives; *(b)* ensure the development of appropriate procedures and practices by which the specific goals and objectives will be met; *(c)* ensure the resources needed to achieve the goals and objectives are made available

as deemed appropriate; *(d)* regularly communicate progress and status information to the user's management.

6.3.2 Responsibilities of all supervisory personnel should include to *(a)* communicate the management commitment to the control principle to user personnel at all levels; *(b)* ensure that the persons within their respective areas of supervisory responsibility have received requisite training in the *program*; *(c)* ensure support from personnel for attaining exposure minimization objectives, including compliance with applicable work rules related to the *program*; *(d)* ensure personnel and facilities are properly equipped consistent with *program* requirements; *(e)* participate in design and process reviews and development of procedures in connection with the *program* to the extent affecting or involving their areas of supervisory responsibility; and *(f)* support the *program* manager in formulating and implementing the *program*.

6.4 *Training and Supervision*—The *program* should include instructing all personnel (including contractor personnel) whose duties may involve potential exposure to UNP, or who direct the activities of others whose duties may involve potential exposure to UNP. Personnel who do not ordinarily enter work areas containing UNP may also require limited instruction in the user's workplace exposure minimization *program* (for example, to respect any access restrictions or personal protective equipment requirements). Personnel should receive initial training and periodic refresher training.

6.4.1 Training should emphasize the importance of UNP exposure minimization as a management objective. The training should be commensurate with duties and responsibilities of those receiving the instruction, as well as the magnitude of the potential exposure that might reasonably be expected. Training should include instruction on relevant hazard information, instruction on the exposure minimization work rules, work practices, operating procedures and emergency response procedures developed and implemented at the facility. Copies of these rules and procedures should be available to those receiving instruction.

6.4.2 Personnel (including contractor personnel) who direct the activities of others should have the authority and responsibility to implement the *program*. During operations in UNP work areas, adequate supervision should be provided to ensure that appropriate procedures are followed, that planned precautions are observed, and that all potential exposure circumstances that develop or are recognized during operations or incidents are addressed in a timely and appropriate manner.

6.5 *Documentation of Program*—The user's *program* should be recorded in a written form and should contain sections that address each of the principal topics presented in this guide.

6.5.1 The objectives for preparing and maintaining such documentation should be to *(a)* record the management commitment to the *control principle*; *(b)* provide an ongoing means to demonstrate to user management that the *control principle* is being applied; *(c)* provide the basis for efficient and informed future periodic evaluations of the potential need to amend the *program* by documenting the practicable engineering and administrative controls adopted and the rationale for their selection among other options; and *(d)* serve as a training and operational reference for the various user personnel responsible for implementing aspects of the *program*.

6.5.2 The extent and form(s) of the documentation should be tailored to the user's individual circumstances consistent with *(a)* meeting the foregoing documentation objectives; *(b)* practical utility; *(c)* updating the documentation over time; and *(d)* the scale and extent of the user's relevant operations. Depending on the user's individual circumstance, documentation to be prepared, maintained and updated (as applicable) may include:

6.5.2.1 Allocation of organizational responsibilities for the *program*;

6.5.2.2 Material characterization and safety information (including underlying basis documentation where the user developed the data or analysis);

6.5.2.3 Documentation of qualitative or quantitative, or both, exposure assessments, risk assessments, and hazard analysis;

6.5.2.4 Relevant engineering and other analyses supporting selection of equipment and operating parameters, including the manufacturer's performance and other specifications for such equipment and alternatives considered;

6.5.2.5 Work rules, work practices, standard operating procedures, policies, and response plans adopted to implement the control principle;

6.5.2.6 Employee training materials and initial and refresher training schedules;

6.5.2.7 Schedules and procedures for periodic substantive review and modification of the program as appropriate, updating program documentation, and reporting results; and

6.5.2.8 Equipment maintenance, certification and calibration schedules.

6.6 *Periodic Review of Program*—At least annually the *program* should be reviewed to ensure that the *program* design, scope and implementation continue to be effective in meeting the management objective of the *control principle*. Amendments to the *program* should be based on the results of any more current empirical research in relevant disciplines (for example, toxicology, epidemiology, exposure measurement, and exposure control and prevention), the development or amendment of relevant and authoritative occupational exposure limits and test methods, changes in workplace processes or personnel, the results of workplace monitoring, lessons learned from any unplanned exposure or potential exposure incidents (for example, accidental spills, releases), the results of any medical surveillance, any worker observations or complaints relevant to the program and the results of any new job hazard or process safety analyses.

6.6.1 Additional program reviews of relevant scope should be conducted in connection with any proposed process changes potentially impacting UNP exposure control, and indicated by the results of incident or accident follow-up investigation such as failure analysis in relation to any unplanned UNP exposure or potential exposure incidents.

6.6.2 The results of *program* reviews should be documented and any amendments to the *program* determined to be warranted should be implemented in a reasonable time frame in view of the circumstances. Any changes to one aspect of the

program should be carried through to other relevant components (for example, training, material safety data sheets or other documentation, and monitoring protocols).

7. Hazard Assessment and Evaluation

NOTE 1—The user should assess the UNP material anticipated to be present in the workplace to identify, to the extent practicable, any physical or health hazards the UNP may present in the event of acute or chronic exposure based upon review of either *(a)* any material safety data sheets provided by the supplier or *(b)* the available, statistically significant, scientific evidence from studies conducted in accordance with established scientific principles and that are otherwise relevant and reliable indicators of hazard. The assessment should evaluate the UNP in the condition or form in which it would be expected to be found in the workplace (for example, dispersed individual particles or as aggregates/agglomerates of primary particles). Where no substance-specific data are available, a qualitative assessment should be made based upon reliable data (as above) and authoritative standards for analogous materials (bulk or nanoscale) as an indication of potential hazards. The method and results of the assessment, even if indeterminate, should be documented.

7.1 *Scientific Uncertainty Concerning Most Significant Characteristics for Assessing Hazard Potential:*

7.1.1 There is little consensus for the relative significance of the physical and chemical characteristics of UNP as an indicator of toxicity. However, current research indicates that particle size, surface area, and surface chemistry (or activity) may be more important metrics than mass and bulk chemistry (**7**).

7.1.2 A number of sources have indicated physical and chemical characteristics that may have important health implications (**8-12**). The toxicity and health risk may be a factor of the following properties, all or some of which may be significant, or not, and whereby some properties may enhance the overall toxicity:

7.1.2.1 Size and size distribution;

7.1.2.2 Shape (for example, fiber diameter, length, and aspect ratios for individual nanotubes and bundles/ropes);

7.1.2.3 Agglomeration state;

7.1.2.4 Biopersistence/durability/solubility;

7.1.2.5 Surface area: "biologically available surface area," "specific surface area," "external (geometric surface area)," and "internal (if material is porous)." Microporous or mesoporous powders exhibit much higher surface areas than nonporous powders;

7.1.2.6 Porosity;

7.1.2.7 Surface chemistry: "surface composition," "surface energy/wettability," "surface charge," "surface reactivity," "adsorbed species," and "surface contamination";

7.1.2.8 Trace impurities/contaminants (for example, metal catalysts, polycyclic aromatic hydrocarbons, etc.);

7.1.2.9 "Chemical composition, including spatially averaged (bulk) and spatially resolved heterogeneous composition";

7.1.2.10 Physical properties (for example, density, conductivity, etc.); and

7.1.2.11 Crystal structure/crystallinity.

7.2 *Occupational Exposure Limits*—Currently, there are no published regulatory occupational exposure limits (OEL) for airborne exposures specific to UNP as a general class of particulates. Occupational exposure limits do exist for nuisance particles (insoluble or poorly soluble) not otherwise classified and may exist for particles of similar physical and chemical composition to the UNP of interest. Refs (**1, 13-17**) identify sources of exposure limits for airborne contaminants that may be considered in selecting target exposure limits for comparative UNP materials. It is essential that the documentation used to derive such values be consulted, since the nanoscale form may have not been considered in its development, and therefore such limits may not be relevant or adequate for poorly-soluble or insoluble nanoscale particles.

7.2.1 *Interim Occupational Exposure Limits*—In the absence of definitive occupational exposure limits, it is prudent to control exposures to "as low as is reasonably practicable." The following are examples of interim occupational exposure limits that one might consider to evaluate the effectiveness of UNP exposure controls. These are provided as examples, only, and professional judgment must be exercised as to the appropriateness of such interim limits for the specific UNP in question.

7.2.1.1 *General:*

(1) ACGIH believes that all particles (insoluble or poorly soluble) not otherwise specified (PNOS) should be kept below 3 mg/m^3, respirable particles, and 10 mg/m^3, inhalable particles, until such time as a TLV is set for a particular substance (**1**). These recommendations apply only to particles that *(a)* Do not have an applicable TLV, *(b)* Are insoluble or poorly soluble in water (or, preferably, in aqueous lung fluid if data are available); and *(c)* Have low toxicity (that is, are not cytotoxic, genotoxic, or otherwise chemically reactive with lung tissue, and do not emit ionizing radiation, cause immune sensitization, or cause toxic effects other than by inflammation or the mechanism of "lung overload." It is important to note that the ACGIH PNOS exposure limits were not based on nanoscale materials and are not likely to be appropriate to apply to nanoscale particles as a general rule.

(2) The U.S. Environmental Protection Agency (EPA) has set National Ambient Air Quality Standards for particle pollution (**18**). Scientific studies have found an association between exposure to particulate matter and significant health problems, including: aggravated asthma; chronic bronchitis; reduced lung function; irregular heartbeat; heart attack; and premature death in people with heart or lung diseases. These outdoor air pollution standards were set to protect public health, including the health of "sensitive" populations such as asthmatics, children, and the elderly. Though not intended for application in occupational environments, such limits may still be useful in assessing exposures in occupational settings. The limitations of using these values include *(1)* the physical-chemical composition of outdoor air pollution is likely to be different than with engineered nanoscale particles, *(2)* those employed in the workplace are generally considered a less sensitive population, *(3)* the averaging times for the EPA standards are based on either 24-hour or annual averaging times, whereas averaging times in the workplace are usually 8-hours per day, 5-days per week. Therefore, even if the physico-chemical composition was similar, an argument could be made that these values should be adjusted for application in an occupational environment. For fine particles, otherwise known as $PM_{2.5}$ (particulate matter of 2.5 μm in aerodynamic diameter and smaller), the EPA standard is 35 $\mu g/m^3$ (0.035 mg/m^3) as a 24-hour average,

and 15.0 µg/m^3 (0.015 mg/m^3) as an annual arithmetic mean. A $PM_{2.5}$ air sampler collects particulate matter that can penetrate into the deep part of the lung referred to as the pulmonary region (alveolar region where gas exchange takes place). Sources of fine particles in outdoor air pollution include forest fires; diesel and gasoline engines; high-temperature industrial processes, such as smelters and steel mills. For PM_{10} (particulate matter of 10 µm in aerodynamic diameter and smaller), the EPA standard is 150 µg/m^3 (0.150 mg/m^3) as a 24-hour average. A PM_{10} air sampler collects particulate matter than could penetrate into either the upper part of the lung referred to as the tracheobronchial region (conducting airways of the lung) or into the deep part of the lung (pulmonary region).

7.2.1.2 *Titanium Dioxide*—There are occupational exposure limits for titanium dioxide, but they do not currently distinguish between nanoscale and larger particles. The 2006 ACGIH 8-hour TWA for titanium dioxide is 10 mg/m^3, as "total" dust. Because nanoscale titanium dioxide is more potent (due to increased surface area) than larger sized titanium dioxide, NIOSH has proposed a 10-hour TWA of 0.1 mg/m^3 for ultrafine titanium dioxide (**19**). However, findings by Warheit et al. on nanoscale titanium dioxide rods and dots run counter to the postulation that, because of increased surface area, nanoscale titanium dioxide will always have increased toxicity compared to larger sized particles of similar composition (**20**). Additionally, crystalline structure may make a difference in toxicity. For instance, anatase nano titanium dioxide was found to be 100-times more cytotoxic than rutile nano titanium dioxide leading Sayes et al. (**21**) to conclude that size as a parameter was far less important than the crystal phase composition of titanium dioxide. Warheit et al. indicates that it remains to be determined whether similar results reported by Sayes et al. will be measured under in vivo conditions (**20**).

7.2.1.3 *Carbon Nanotubes (CNT)*—The 2006 ACGIH 8-hour TLV-TWA for carbon black is 3.5 mg/m^3, as "total' dust. Carbon black is composed of disordered graphite sheets and differs from the continuous graphitic sheet nature of the nanotube surface. The 2006 ACGIH 8-hour TLV-TWA for respirable graphite (all forms except graphite fibers) is 2 mg/m^3. The appropriateness of applying the carbon black or graphite occupational exposure limits for carbon nanotubes has been questioned (**9, 22, 23**). With regard to carbon nanotubes, occupational exposure limits for mass, number, and surface area might be considered. There may also be trace contaminants that may be present and the specific occupational exposure limits for these contaminants may need to be considered, as well.

(1) Mass—Some forms of Single Wall Carbon Nanotubes (SWCNT) have been found to be as toxic as quartz on a mass basis (**22, 23**), which have lead some to recommend applying occupational exposure limits for crystalline silica (for example, quartz), at least in the interim, until SWCNTs are further characterized (**22, 23**); therefore, for at least some forms of SWCNT, the 8-hour time-weighted occupational exposure limit of 25 ug/m^3 (that is, the ACGIH 2006 TLV-TWA for respirable crystalline silica) may be more appropriate than a respirable synthetic graphite OSHA PEL-TWA of 5000 ug/m^3 or 2006 ACGIH TLV-TWA of 2000 ug/m^3. However, applying the quartz exposure limit measure for SWCNT may not necessarily be appropriate in all instances, because the toxicity may vary depending on various factors (for example, agglomeration state, functionalization, trace impurities/contaminants, etc.).

(2) Number—Donaldson et al. cites a study that demonstrated that Multi Walled Carbon NanoTubes (MWCNT)s were highly fibrogenic and inflammogenic, being roughly equivalent to a chrysotile asbestos control and recommended that until better information becomes available, that they should be considered in the same way other biopersistent fibers in workplace risk assessments, using similar assessment approaches (for example, fiber counts) (**9**). However, this approach may be questionable and difficult given that carbon nanotubes agglomerate and mechanically entangle into complex structures/clumps. The 2006 ACGIH 8-hour TLV-TWA for respirable chrysotile fibers is 0.1 fibers per cubic centimetre; 0.2 f/cc for respirable refractory ceramic fibers; and 1 f/cc for glass wool fibers. Some organizations apply an 8-hour TWA occupational exposure limit of 1 f/cc for respirable carbon fibers; however, CNTs are distinct from carbon fibers, which are not single molecules but strands of layered graphite sheets.

(3) Surface Area—Donaldson et al. indicates that CNT number concentration, alone, may not be a suitable metric, and that a surface area metric might be more appropriate (**9**).

(4) Trace Contaminants—Trace contaminants may include organics (such as carbon black and polycyclic hydrocarbons) and metals. Cobalt, iron, nickel, and molybdenum are the most commonly used metals in CNT synthesis (**9**). The ACGIH has established occupational exposure limits for these metals based upon either the inhalable fraction, the respirable fraction, or as "total dust" (**1**). It is conceivable that, in the future, the ACGIH may have exposure limits for some metals that are based upon the thoracic deposition fraction.

8. Exposure Assessment and Exposure Risk Evaluation

NOTE 2—The specific elements of an exposure minimization program (for example, engineering and administrative controls, work practices and any personal protective equipment) should be determined based upon the assessment of the potential UNP physical or health hazards outlined in Section 7, and the assessment of potential occupational exposure outlined in Section 8.

8.1 *Potential UNP Exposure Routes*—As with other particles, workers may potentially be exposed to UNP by way of inhalation, ingestion, injection and dermal contact (including eyes and mucus membranes).

8.1.1 The most common route of exposure to UNP in the workplace is anticipated to be by inhalation.

8.1.2 Ingestion can occur from unintentional hand to mouth transfer of materials; ingestion may also accompany inhalation exposure because particles that are cleared from the respiratory tract may be swallowed.

8.1.3 Some studies suggest that UNP could also enter the body through the skin or eyes during occupational exposure. Research is ongoing to determine whether this is a viable exposure route for UNP (**7**).

8.2 The nature and extent of any UNP exposure will be dependent on the physical characteristics of the material.

8.2.1 *Solids*—Handling of solid materials (for example, nanocomposites) where UNP are bound on or within a solid matrix should pose no risk of exposure during normal handling; however, machining, or combustion of such materials may or may not generate UNP. Like deposition of other types of ultrafine airborne particles, nanoscale particle agglomerates greater than 500 nm in diameter are deposited in the respiratory tract according to their aerodynamic equivalent diameter (AED) **(24)**, which is a function of the particle density, shape, and diameter **(6)**. Diffusion is the predominant deposition mechanism in the respiratory tract for UNP and nanoscale particle agglomerates < 500 nm in diameter and is governed by geometric physical diameter rather than AED **(24)**. The dustier (ability to become airborne) the material, the more it is likely to become aerosolized and become inhaled, inadvertently ingested, or for there to be contact with the skin, eyes, and mucous membranes.

8.2.2 *Liquids*—UNP suspended in liquids may pose potential exposure risks, including inhalation, ingestion or skin absorption if suspensions are either physically contacted (skin, eye, or mucous membrane) or if the suspensions are aerosolized and subsequently inhaled.

8.3 *Inventory of Potential Exposure Locations*—The exposure assessment should begin with assembling a complete inventory of work processes and activities where the potential for exposure to UNP may reasonably be expected to exist. Relevant activities at a facility may include material receipt and unpacking; all manufacturing and finishing processes; lab operations; storage, packaging and shipping; waste management activities; maintenance and housekeeping activities; reasonably foreseeable upset circumstances; and other movements of goods and employees in and out of UNP work areas. Annex A2 provides additional guidance for identifying specific processes and operations that may be a source of UNP and may present a risk of occupational exposure by inhalation, ingestion, or dermal penetration, or a combination thereof.

8.4 *Qualitative Exposure Assessments*—A qualitative assessment of the potential for direct and indirect occupational exposure to UNP should be made for all phases of each activity identified in the inventory. The assessment should include full consideration of the properties of the UNP material at the different process locations, the quantity of material present in each process, the design and performance characteristics of relevant process equipment, any existing engineering controls, and the effect of any existing administrative exposure controls. The method and results of the assessment should be documented. Appendix X2 provides additional guidance for assessing UNP exposure risk.

8.4.1 For new operations, exposure assessments are ideally performed at the pre-design stage so that facilities and process may be designed and constructed to present an inherently low risk of UNP exposure. Assessments should be repeated prior to the start-up of a new task or operation, prior to the re-start of a task or operation following a change, periodically even in the absence of changes in accordance with 6.6, and any other circumstances where the exposure potential needs to be confirmed or reestablished.

8.5 *Quantitative Exposure Assessments:*

8.5.1 Quantitative UNP exposure measurements may be useful for a variety of occupational health and system safety purposes including *(a)* evaluating UNP metrics against standards for analogous materials, *(b)* qualitatively assessing the effectiveness of containment controls, work practices, or the effect of changes to processes or controls; *(c)* identifying sources, patterns and direction of releases, distributions of exposure, *(d)* and estimating exposure levels as a function of process.

8.5.2 *Technical Constraints*—Quantitative and qualitative assessment of potential UNP exposure in occupational setting presents a number of technical challenges. In general there is no consensus regarding: *(a)* the relative importance of the different exposure metrics that might be used; *(b)* the best way to characterize and differentiate exposures against available metrics; or *(c)* the best measurement techniques to monitor exposures in the workplace. Depending on the metric selected, background concentrations of non-target nanoscale particles may significantly interfere with obtaining relevant and meaningful results, and it may not be possible to control for this interference. The direct and indirect sampling and analysis techniques and the commercially available instruments for measuring airborne nanoaerosols vary widely in complexity, accuracy and selectivity depending on the metric to be assessed.

8.5.3 Appendix X2 and Refs **(7, 25-32)** provide additional guidance for employee and workplace UNP aerosol exposure assessments.

8.6 *Exposure Assessment for Materials and Devices Containing Bound Engineered Nanoscale Particles:*

8.6.1 Devices, such as integrated circuits, that contain bound, engineered nanoscale particles or nanoscale features pose a minimal risk of releasing UNP during handling. Likewise, large-scale composite articles which contain nanoscale particles typically do not present significant exposure potential as the nanoscale particles are bound within the matrix of the composite. Absent reason to believe that these materials shed UNP at the exposed surfaces no precautionary measures are warranted.

8.6.2 The risk of UNP exposure from handling or processing materials containing nanoscale particles is greater, however, if the composite matrix is subject to disintegration in the course of foreseeable use or handling (for example, the matrix is brittle or disintegrates), or if the materials or devices are otherwise used or handled in such a manner that that they may generate UNP (for example, machining, saw cutting, drilling, or grinding). The user should evaluate the use of materials containing nanoscale particles for their potential to release UNP in the course of reasonably foreseeable use and handling. This evaluation should be based on information provided by the supplier or manufacturer and the user's circumstances of use or processing of the nanoscale particle containing material. If the result of the assessment indicates a significant risk that UNP may be generated or released, then the user should establish work practices to minimize UNP exposure consistent with the scale of the relevant operations and this guide.

9. Exposure Minimization Methods

9.1 *Generally*—This section of this guide provides information and guidance concerning a variety of exposure control methods potentially available to the user. Not all of the noted control methods will be relevant or necessary to meet control objectives at a given facility. See 1.2. Refs **(7)** and **(29)** provide additional guidance regarding exposure minimization methods.

9.2 *Types of Controls*—Occupational exposure control methods can be generally grouped as one of three types: *(a)* engineering controls (for example, process modification to eliminate toxic material usage, closed manufacturing systems, ventilation systems, and work area enclosures), *(b)* administrative controls (for example, work practices and rules to prevent circumstances of potential exposure) and *(c)* personal protective equipment (for example, gloves, protective clothing and respirators). Engineering controls are the preferred method of control. Personal Protective Equipment should be used when practicable engineering and administrative controls do not sufficiently minimize exposure.

9.3 *Engineering Controls*—For most processes and job tasks, the control of airborne exposure to UNP can be accomplished using a wide variety of engineering control techniques similar to those used in reducing exposures to more common airborne particulates, gases, or vapors, or a combination thereof. Based on what is known of nanoscale particle motion and behavior in air, control techniques such as source enclosure (that is, isolating the generation source from the worker) and local exhaust ventilation systems should be effective for capturing and containing airborne UNP. Engineering controls eliminate or reduce exposure by the use of machinery or equipment. General examples from industry include ventilation systems, process enclosures, sealed process piping, robotic applications of hazardous materials, interlocks and machine guards.

9.3.1 *Isolation*—Employees may be isolated from hazardous operations, processes, equipment, or environments by distance, by physical separation, barriers, control rooms, isolation booths, and by capture ventilation. UNP contained within closed systems or containers present minimal risk of exposure. Most UNP synthesis, product recovery, processing, transfer and other handling activities can be designed to occur within totally enclosed process equipment. All UNP handling systems should be designed to operate in an enclosed manner to the extent reasonably practicable (for example, sealed reactor vessels, closed storage containers or vessels, pumps enclosures, valve isolation, glove boxes **(33, 34)** may be practicable for some operations).

9.3.2 *Fixation Strategies*—Processing UNP in solutions verses handling dry powders may help reduce UNP exposures during handling and processing activities. Processes may be designed to collect nanoscale particles in well-adapted liquids or dust suppression mists to minimize particle releases may be utilized.

9.3.3 *Waste Minimization Strategies*—Processes may be designed and optimized to minimize the quantity of UNP-containing waste generated.

9.3.4 *Ventilation Strategies:*

9.3.4.1 Removing UNP from workplace air by well engineered ventilation systems is an effective and important method for minimizing the potential for inhalation of UNP. Ventilation systems should be designed, tested, and maintained using applicable guidance (for example, Refs **(33-37)**). Current scientific knowledge regarding the generation, transport, and capture of aerosols suggests that capture ventilation control techniques should be effective for controlling airborne exposures to UNP **(7)**.

9.3.4.2 Ventilation control systems that capture emissions at or very near the source (local exhaust ventilation) exist in a variety of designs that are applicable to most occupational circumstances. Local exhaust ventilation systems include *(a)* total enclosures, such as a glovebox; *(b)* partial enclosure hoods, such as laboratory chemical hoods, low-flow vented compounding pharmacist workstations, or low-flow vented balances; *(c)* weigh hoods for dry materials; and *(d)* exterior hoods, which are located adjacent to particle source areas but do not enclose them, such as a receiving hood which catches particles that rise or are thrown into them, and draft hoods, which draw in particles. When using local ventilation to manipulate dry powders, consideration should be given as to avoiding excessive air velocities across the powders that may generate aerosols unintentionally. Preventing inadvertent aerosolization of dry powders may require the use of low-velocity laboratory chemical hoods, cabinets, balance enclosures, gloveboxes, etc. Enclosures and glovebags may also be useful inside higher-velocity hoods in that they will isolate/shield the powder from the high velocities inside the hood.

9.3.4.3 Facility comfort heating, ventilation and air conditioning systems (HVAC) for UNP work areas, including make-up and exhaust air, should be designed, installed and maintained so that UNP do not migrate from production areas to adjacent workspaces. Clean room work areas, if used for UNP containment, should be at a negative pressure differential relative to the surrounding work areas to prevent introduction of UNP in to the surrounding areas.

9.3.4.4 Filters, traps, baffles, and clean-outs, or other containment and control technologies should be used to prevent buildup of UNP within ventilation exhaust systems. HEPA filters are an effective filter medium for nanoscale particulates. Safe change systems (that is, ability to change out exhaust system filters without release of UNP into work environment) may be used where filtration is installed in equipment or ventilation systems.

9.4 *Administrative Controls:*

9.4.1 *General Administrative Controls*—Administrative controls are work practices and operating procedures established to, directly or indirectly, avoid or reduce occupational exposures to substances of concern. Examples from general industry include safety policies, rules, supervision, and training. Administrative controls can form an important supplement to engineering controls. This section of this guide provides information and guidance concerning a variety of administrative control methods available to the user.

9.4.2 *Administrative, Housekeeping Controls to Minimize UNP Aerosolization*—Work practices in all phases of operations should include measures to minimize accumulation of UNP-containing dusts (surface contamination) and to minimize any re-aerosolization of settled UNP or UNP agglomerates through effective housekeeping techniques. Corresponding administrative housekeeping controls may include:

9.4.2.1 Vacuuming in UNP work areas with only HEPA-filtered vacuum equipment and systems. Non-HEPA filtered vacuums may release and aerosolize UNP and increase airborne concentrations of UNP. The use of portable vacuums within UNP work areas should be evaluated to ensure the vacuum exhaust does not aerosolize UNP materials adjacent to the vacuum unit itself.

9.4.2.2 Prohibition of dry mopping, sweeping, dusting and other dry cleaning methods.

9.4.2.3 Prohibition of cleaning using compressed air or blow downs of work areas using portable blowers or fans.

9.4.2.4 Use of surfactants with wet drilling or cutting methods and maintaining good process controls to prevent dust generation.

9.4.2.5 Prohibition of the accumulation of dusts on equipment in UNP work areas and requiring regular and frequent removal of such dusts (for example, daily);

9.4.2.6 Requiring UNP work area surfaces, equipment and furniture to be constructed of smooth, non-porous material that will allow easy cleaning (for example, no fabrics or rough surfaces).

9.4.3 *Administrative Controls to minimize Inadvertent Exposure and Unintended Removal of UNP From Work Areas*—Administrative controls to minimize inadvertent ingestion or removal of UNP may include:

9.4.3.1 Prohibiting eating, drinking, smoking, or applying cosmetics in UNP work areas;

9.4.3.2 Requiring hand washing and other good hygiene practices prior to leaving UNP work areas or the work site; and

9.4.3.3 Limiting access to UNP work areas to those persons with an operational need to be present.

9.4.4 *Administrative Controls To Assure Process Integrity (Process Safety)*—Process safety measures may be important to assure that engineering controls (and associated processes) operate as intended, and do not result in exposures from unanticipated releases of UNP to the worksite. Both experimental (pilot) and production units should reflect proper planning and design. Process flow diagrams, instrument and piping diagrams, even for batch units, should be made. Process safety administrative controls should include:

9.4.4.1 Before start-up, preparing written operating procedures that have been reviewed and approved by all relevant departments;

9.4.4.2 For both pilot and production units, identifying and installing the instrumentation necessary to maintain good process control, including at least a simple control scheme on all independent process variables that can be directly measured, and provide adequate safety condition monitoring and shut down processes to identify and safely shut down systems that may generate release of UNP in the event hazardous/upset operating conditions are detected;

9.4.4.3 Evaluating production and processing practices to identify any flammable or explosive conditions during operations or maintenance activities, and installation of appropriate engineering controls to control any identified fire or explosion risks. Nanoscale combustible material may present a higher risk of explosion or fire than coarser material of similar composition and quantity (**7**). Explosion risk can increase significantly for some metals as particle size decreases (**7**). It is possible that relatively inert materials may become highly combustible when in the nanoscale (**7**).

9.4.4.4 Conducting appropriate pressure testing before pressurized processes are initiated;

9.4.4.5 Conducting regular and timely inspection of process, manufacturing, operational and exposure control equipment and ancillary systems (including ventilation and filtration equipment), and regular and timely preventative and corrective maintenance and repair of such equipment. The frequency and extent of the maintenance program and schedule of service should be greater for those operations with greater potential for physical harm and occupational exposure;

9.4.4.6 Evaluating the effect, if any, on ventilation and other engineering control system performance resulting from each facility or operational change;

9.4.4.7 Establishing equipment lock-out procedures for work on equipment, electrical circuits, or piping that may, directly or indirectly, result in loss of UNP containment or control;

9.4.4.8 Providing sufficient operational training to those personnel who operate systems or perform other operational or maintenance tasks with the potential to result in loss of UNP containment or control if performed improperly;

9.4.4.9 Establishing procedures to assure continuous good process control, such as establishing and testing safe operating envelopes; and

9.4.4.10 Periodically evaluating the ventilation and other engineering controls to ensure they are operating and functioning as designed.

9.4.5 *Medical Surveillance*—For guidance on medical surveillance of UNP workers consult the NIOSH Nanotechnology homepage (**38**).

9.4.5.1 Whether a medical surveillance program is warranted is a management decision to be made in consideration of a number of factors including; whether there is good reason to believe that adverse health effects may occur as a result of the contemplated exposure; the invasiveness of the surveillance procedures, the benefits, risks and costs of the surveillance method; and the utility of the information reasonably expected to be generated by the surveillance program.

9.4.5.2 Any medical surveillance program should be developed and implemented only with medical, industrial hygiene and legal professional consultation, and under the direction of a physician experienced in medical surveillance programs with a high level understanding of the available information concerning the UNP and potential exposure circumstances.

10. Exposure Minimization and Handling in Particular Occupational Settings

NOTE 3—This section describes actions that could be taken by the user to minimize occupational UNP exposures in particular occupational

settings where UNP may reasonably be expected to be present. These actions are intended to supplement the general exposure controls guidance in Section 9. Not all of the noted actions and considerations will be relevant or necessary to meet control objectives at a given facility. See 1.2.

10.1 *Manufacturing*—Gas phase processes have the potential to cause exposure to primary UNP during the synthesis stage of nanomaterials. All process phases (liquid, solid, gas) may give rise to exposure to agglomerated UNP during recovery, handling, and product processing. The probability and potential exposure level will differ according to the specific processes and the stages of the process. The optimum strategy to control employee exposures and the efficacy of the control methods utilized will likewise differ depending on the specific process and phase matrix. Annex A2, Table A2.1 summarizes the potential pathways of exposure in nanoscale particle production and recovery.

10.2 *Laboratory Operations*—The general guidance provided elsewhere in this guide is applicable to laboratory occupational settings. Good laboratory safety practices should be employed when handling UNP in research and development or other laboratories. Appropriate guidance for UNP may be found in or supplemented by a laboratory Chemical Hygiene Plan Refs **(33, 34, 39-42)** are sources of general laboratory safety guidance.

10.2.1 Where there is a potential for exposure to the body, effective protective lab clothing should be worn within the work area if not already addressed by personal protective equipment to minimize street clothing contamination. Care should be exercised during donning and doffing of protective lab clothing to prevent aerosolization of UNP. Outer personal protective clothing when worn for contamination control should not be worn outside the work area.

10.3 *Maintenance, Housekeeping, Commissioning, Decommissioning and Non Routine Activities:*

10.3.1 Housekeeping, maintenance and repair, commissioning, decommissioning, demolition,and non routine activities are likely to present a greater risk of exposure to UNP than normal manufacturing or other routine process operations, and may warrant particular focus and exposure risk evaluation. Based upon this evaluation, operating procedures to minimize UNP exposures during these types of activities should be developed. Personnel who have the responsibilities to perform these types of activities (which may include operations personnel) should be trained in those procedures. Engineering and administrative control strategies to minimize or prevent exposure during these operations may include:

10.3.1.1 HEPA filtration systems with safe-change systems (that is, containment of filters or bags, or both, during removal or replacement);

10.3.1.2 Negative air enclosures designed to minimize dispersal of UNP from UNP worksite areas to other areas, with consideration given for a waste load-out area, such as a two-chamber air lock, to inhibit the release of UNP into other areas;

10.3.1.3 Maintenance and housekeeping activities should be performed in such a manner as to minimize the number of persons potentially exposed during non-routine operations;

10.3.1.4 Decontaminating equipment (instruments, piping, duct work, HVAC units, process units and other miscellaneous facilities) that may have been contaminated with visible or suspected UNP prior to repair or removal from UNP work areas. Use of Clean In Place (CIP) technologies may be used to eliminate the opening of process vessels and reduce the potential for UNP releases during cleaning operations. Marking decontaminated equipment as “clean” (for example, by identification tags or other practicable marking) after decontamination is complete will aid in properly identifying equipment that has been decontaminated. This is especially prudent when UNP contamination may not be visible.

10.3.1.5 Developing written housekeeping procedures that specify cleanliness standards and the frequency and method of cleaning, based on the assessed need to minimize aerosolization and migration of UNP within the worksite.

10.3.1.6 Requiring all surfaces where UNP may have settled to be maintained as free as practicable of any accumulation of visible dust or waste, including prompt collection and containment of all spills, scrap, debris and waste that may contain or be a source of UNP exposure; and

10.3.1.7 Establishing procedures for appropriate design, integrity, and construction of containers potentially containing UNP waste or residuals, to ensure those containers do not react with, deteriorate, or spill UNP waste under normal handling and conditions.

10.3.2 Minimization of maintenance activities by task planning (identification of required tools, replacement parts, etc.) may help reduce exposure time by shortening maintenance times.

10.4 *Transferring Material Between Containers and Processes*—The potential for exposure to UNP exists whenever closed vessels or containers containing UNP are open to the atmosphere, repacked, or UNP are added or removed from the container. Examples of potential UNP release operations during transfer operations include, for example, transfers from enclosed manufacturing equipment to subsequent processing equipment or storage containers or from storage containers to transportation containers or opening of containers containing UNP or product packaging. The extent of UNP release and potential exposures will depend on the properties of the particular UNP-containing material, the transfer method used and the engineering and administrative controls employed. Engineering, work practice, and administrative controls should be developed to minimize any release of UNP to the worksite ambient air for all operations where UNP will be transferred. Established material transfer techniques used in analogous small particle production or processing industries (for example, fumed material or carbon black) may provide useful guidance for safe handling, spill control, and decontamination processes.

10.4.1 Processes should be designed to minimize the number of necessary transfers between containers and other equipment.

10.4.2 Vacuum conveyance is preferred method for transferring UNP from one vessel to another (for example, from a process vessel to a storage vessel). The conveying air moving

through the intermediate vessel should discharge to atmosphere. Sufficient engineering controls (such as exhaust filtration) should be employed to prevent the release of UNP from conveying air discharge.

10.4.3 Where vacuum transfers are not practicable, transfers should be conducted within a fully or partially enclosed exhaust hood or an exterior hood where an enclosed hood is not practicable.

10.4.4 Vessel or container openings should not be larger than is necessary to transfer material from the container, and receiving containers. Openings between the containers should be designed to minimize UNP release locations (that is, mated or sealed when possible).

10.4.5 UNP should be transferred only in designated areas where engineering controls (for example, local exhaust ventilation, chutes, vacuum conveyance) are in place. After a transfer is complete, vessels and containers should be securely resealed.

10.4.6 UNP should be transported (within or from a facility) only in closed containers. Secondary containment may be warranted in some circumstances.

10.4.7 Where there is a potential for UNP to adhere to the exterior of a container, the containers should be wet-wiped, surfaces should be vacuumed with a HEPA collection system, or otherwise safely decontaminated before containers are removed from the designated transfer area, whether UNP are visible or not.

10.5 *Containers and Storage:*

10.5.1 UNP should be stored in containers designed to prevent any release of UNP into the workplace under reasonably foreseeable circumstances. UNP containers should be closed except as necessary to add, remove or inspect the contents.

10.5.2 To preserve containment and support effective cleaning, storage containers should be rigid, non-porous, tightly sealing, leak-tight containers made of compatible materials with smooth surfaces, such as plastic containers, metal drums, or fiber drums coated internally. Containers and seals should be of appropriate strength and construction to maintain integrity during reasonably foreseeable mishandling while full. Examples of such containers include polyethylene tanks fitted with gasket drum lids and locking clamps, and fiber drums closed with gasket lid/locking clamp assemblies. Locking lid seals may be supplemented with tape seals where warranted.

10.5.3 Plastic bag liners should be used when container lids do not create a leak-tight seal. Bag liners may also be used where the container is to be reused or discarded, and would otherwise require cleaning prior to reuse or discard (for example, to prevent contamination of new product). Bag liners should be of appropriate strength and thickness for the particular circumstances of use. Bag liners should be impermeable to the UNP. Plastic bags should only be used to line the inside of a supporting container. Use of anti-static plastic bags should be considered. Once used, plastic liners should not be reused.

10.5.4 Opening and closing bags used as liners may create a risk of exposure and local exhaust ventilation, vacuum techniques or other control measures may be prudent during opening and closing.

10.5.5 *Used Containers and Liners*—Containers intended for reuse should be considered contaminated with UNP. They should be thoroughly washed, wet-wiped, or vacuumed both inside and outside prior to reuse. If similar material is to be placed in used empty containers, thoroughly cleaning the outside only is acceptable. Liners should not be reused and should be properly disposed. Used liners should be placed in leak-tight drums or other containers to contain any residual UNP. Containers not intended for reuse should be sealed where possible and properly disposed.

10.5.6 Where there is a potential for UNP to adhere to the exterior or interior of a reusable container, the inside and outer surfaces of the container should be wet-wiped or vacuumed to remove any loose or adhered UNP prior to reuse, whether or not particle accumulations are visible.

10.5.7 Prior to reuse, UNP filled containers and sealing systems should be inspected to confirm integrity. Worn or fatigued equipment should not be reused and should be discarded.

10.5.8 UNP containers should be stored in one or more designated storage areas. Interim storage outside designated storage areas (for example, day-use containers) should be minimized in quantity and time to the extent practicable.

10.5.9 The exterior of all portable UNP containers of any size should be wiped clean prior to exiting UNP work areas (for example, prior to entering storage areas).

10.5.10 All bulk storage containers should be labeled to identify the contents of the container, including Tare and Net weight, and any appropriate cautionary statements.

10.6 *Waste Handling*—Waste UNP material should be placed into impermeable containers (example 4 mil waste disposal bags) that are marked, labeled, and effectively sealed to minimize release of UNP during normal disposal, handling and storage operations. Sealed waste bags containing UNP should be placed into marked and labeled solid wall containers to minimize deterioration or damage to the waste disposal bags.

10.6.1 Waste containing UNP should be placed in compatible, tightly sealed containers. Waste containers should be labeled to identify the contents of the container and any appropriate cautionary statements or symbols.

10.6.2 Special locations or areas should be designated where waste bags and containers may be temporarily and securely stored before final disposal.

11. Responding to Accidental or Unanticipated Releases of UNP

11.1 Unanticipated releases of UNP present a risk of uncontrolled occupational exposure within and outside of UNP work areas. The potential for accidental releases and emergency responses to UNP releases should be included in the exposure assessment process (Section 8) of this guide, and in the selection and implementation of exposure minimization methods as outlined in Section 9 of this guide. Administrative controls should include a plan describing how the user will reduce the likelihood of accidental releases, and how it will respond to such releases to minimize short and long-term exposure risk should they nevertheless occur.

11.2 An accidental release of UNP should be recovered and cleaned up as soon as reasonably practicable to eliminate the release as a potential continuing source of human exposure, and on a priority commensurate with the health or safety risk it presents in relation to other health and safety risks that may be present in the circumstances of the release.

11.3 When developing procedures for cleaning-up unanticipated releases, consideration should be given to the potential for human exposure during cleanup and the appropriate levels of any personal protective equipment. Inhalation exposure and dermal exposure will likely present the greatest risks. Inhalation exposure in particular will be influenced by the likelihood of material re-aerosolization.

11.4 Response procedures should be developed based upon available information on exposure risks and upon the relative probability of exposure by different routes.

11.5 Response procedures should be developed with consideration of standard approaches to cleaning up powder and liquid spills, and consistent with this guide (for example, HEPA-filtered vacuum cleaners, wetting powders down, using dampened cloths to wipe up powders and applying absorbent materials/liquid traps).

11.6 Procedures to contain, clean-up and recover released UNP will vary depending on the circumstances of the release and the material involved and may include:

11.6.1 Removing personnel from the spill/release area and restricting entry by persons other than those responding to the release;

11.6.2 Modifying the operation of HVAC systems (for example, to minimize distribution of UNP to other areas within a building, or to exhaust released material outdoors);

11.6.3 Procedures to decontaminate or dispose of materials and equipment used in the response;

11.6.4 Providing medical examinations to significantly exposed individuals;

11.6.5 Procedures to recover UNP, UNP-contaminated debris, and cleaning materials and store in appropriate sealed, leak-tight containers;

11.6.6 Procedures to confirm the extent and sufficiency of clean-up activities (for example, confirmatory surface sampling or workplace air monitoring); and

11.6.7 Procedures for handling, storing, and disposing of any waste material.

12. Personal Protective Equipment

12.1 Use of personal protective equipment (PPE) (for example, respirators, protective clothing) by individuals is warranted where practicable engineering and administrative controls do not sufficiently minimize their occupational UNP exposures. The decision to institute use of personal protective equipment should be based on professional judgment and the results of the exposure assessment outlined in Section 8. The user should provide any selected PPE to relevant employees and should ensure it is used as intended. The United States Occupational Safety & Health Administration (OSHA) provides additional guidance on how to perform a PPE hazard assessment which will aid in selection of appropriate PPE for UNP.

12.2 *Respiratory Protection*—Respirators may be warranted where, notwithstanding engineering and administrative controls, the measured or potential airborne UNP concentrations exceed an internal control target or benchmark. Different types of respirators provide varying degrees of protection. If respirators are to be used, they should be selected based on the characteristics of the UNP and the anticipated exposure level. Appendix X3 provides further guidance for the selection of respirators. Some jurisdictions have established obligatory legal standards for the occupational use of respirators to ensure that any respirator use program operates as intended, and does not itself create unwarranted risks for workers. Refs **(43, 44)** identify examples of such standards. These standards may be used as guidance in jurisdictions where no applicable legal standards exist.

12.3 *Protective Clothing*—Where protective clothing (for example, gloves, sleeves, coats, gowns, smocks, uniforms or encapsulating suits) are used to minimize or prevent exposures, the user should select clothing appropriate to the hazard identified and the circumstances of UNP handling. In selecting protective clothing, the user should consult the best available performance data and obtain the clothing manufacturers' recommendations based on the properties of the specific UNP of concern. Refer to Practice F1461 for detailed guidance on the conditions for establishing a protective clothing program and the selection, use and management of protective clothing. Potential for aerosolization of UNP during the removal of contaminated protective clothing should be evaluated. Decontamination processes may be necessary to prevent aerosolization of UNP during clothing removal. Where respiratory protection is required to be used during the routine work operation, the respiratory protection should be left on during the removal of the contaminated clothing.

12.4 *Eye Protection*—Where eye protection equipment (for example, safety glasses, dust goggles, masks, and face shields) will be used to minimize exposures, the user should select such equipment appropriate to the hazard identified. In selecting eye protection equipment, the user should consult the best available performance data and obtain the equipment manufacturers' recommendations based on the properties of the specific UNP of concern. The minimum eye protection should be safety glasses with side shields, with consideration of using dust goggles with seals. Where respiratory protection is used and the respirator provides eye protection (that is, full face piece or hooded/helmeted respirators) no additional eye protection is needed. Ref **(45)** provides additional guidance on eye protection.

13. Communication of Potential Hazards

13.1 Based upon the results of the hazard and exposure assessments, the employer should communicate the following information to all persons within its facilities who may be exposed to UNP under normal conditions of handling or in a reasonably foreseeable emergency:

13.1.1 The identified physical and health hazards (and identified potential hazards and uncertainties) associated with exposure to the UNP;

13.1.2 The operations in their respective work areas where UNP are present;

13.1.3 The methods and observations that may be used, if any, to detect the presence or release of the UNP in work areas (such as monitoring conducted by the user, visual appearance or odor, etc.); and

13.1.4 The specific procedures and other measures to minimize exposures to UNP, such as engineering controls, appropriate work practices and other administrative controls, emergency response procedures, and personal protective equipment to be used.

13.2 The user should evaluate whether hazard warning signs are appropriate at entrances to UNP work areas.

13.3 *Material Safety Data Sheets*—The user should develop or obtain from the supplier material safety data sheets (MSDS) such as those described by Refs **(46-48)**.

13.3.1 The MSDS for the source material of the UNP being handled or produced within the facility should be readably available to affected employees at all times.

13.3.2 The user should provide MSDS for products they produce that may contain UNP to entities to whom the user provides, ships or distributes the material in unbound form. MSDS for the UNP also should be provided to persons to whom the user distributes materials containing nanoscale particles where the user has reason to believe the recipient's use of bound forms may generate UNP. MSDS should be completed in accordance with applicable regulatory requirements for location of operation.

13.4 *User's Containers*—Where a hazard or potential hazard has been identified, the user should ensure that containers of UNP within its facilities are clearly identified as containing UNP and that appropriate hazard warnings are provided and clearly associated with these containers. Container identification and warnings can be provided by a variety of means including labels, tags, signs, placards, process sheets, batch tickets, operating procedures, or other such written materials. UNP identity and hazard information associated with a container may be communicated with words, pictures, symbols, or combinations thereof.

13.4.1 *Containers Leaving the User's Control*—Where a hazard or potential hazard has been identified, the user should ensure that containers of UNP leaving its immediate control are labeled, tagged or marked with the identity of the UNP; any appropriate hazard warnings; and the name and address of the manufacturer or other responsible party.

13.5 *Training*—The training program referred to in this guide should ensure that the user's employees are effectively trained concerning the matters listed in this Section 13. Training should include an explanation of relevant MSDS, any labeling systems, and other information concerning how employees can obtain and use the appropriate hazard information. Such training should be provided prior to an employee's initial assignment to a UNP work area (or other relevant areas).

ANNEXES

(Mandatory Information)

A1. ADDITIONAL GUIDANCE FOR APPLICATION OF THE CONTROL PRINCIPLE

A1.1 As indicated in 4.2, this guide is premised on the principle that, as a cautionary measure, occupational exposures to UNP should be minimized to levels that are as low as is reasonably practicable. Referred to in this guide as the "*Control Principle*," it reflects *(a)* a consensus view that, in the absence of robust risk information, cautionary measures are generally warranted when working with UNP, and *(b)* a consensus concerning the extent of caution generally warranted. This principle does not correlate to any numerical standard of control. Rather, it represents a consensus on the appropriate health and safety management objective for enterprises working with UNP, and a performance-based benchmark against which organizational leaders can gauge their efforts. Neither the control principle nor this guide dictates the means of achieving the objective, which must be determined by the exercise of judgment on a case-by-case basis in consideration of individual circumstances. To assist the user in the exercise of that judgment, this Annex provides further information on the two conceptual components of the Control Principle – cautionary action and reasonably practicable exposure control.

A1.1.1 *Exercising Caution*—Although more commonly discussed in the context of environmental safety and health measures, business leaders have long experience with taking cautionary measures to hedge against the full variety of business risks. Acting cautiously in the face of uncertain business risks through appropriate risk management is central to sound business operations, management and business principles. The exercise of caution does not require forbearance from the potential risk-creating activity until complete information is known. Rather, it suggests acting in a cautious manner, and taking reasonable steps to significantly reduce the potential for harm.

A1.1.2 Properly applied this approach is a positive, proportionate policy tool to encourage technological innovation and sustainable development by helping to engender stakeholder confidence that appropriate risk control measures are in place.

A1.1.3 The determination to act on a cautionary basis does not determine the actions to be taken. For any circumstance, the several options lie along a continuum of measures designed to prevent the possible harm from occurring or to contain or

reduce the possible harm should it occur. A principal focus of this guide is to identify a range of options on the continuum, and to provide information to the user to aid selection.

A1.1.4 Cautionary action is a risk management technique, and risk management principles should be used in selecting particular cautionary measures. This involves making qualitative assessments of risk (that is, the probability of the harm occurring, and the extent of the harm should it materialize) based on credible scenarios of exposure and effect. Exposure minimization options (or possible incremental strengthening or lessening of existing controls) should be evaluated against that model. Consideration should also be given to the following prudential limits generally recognized as appropriate constraints on the selection of analogous precautionary measures:

A1.1.4.1 Measures should be consistent in scope and nature with comparable measures from comparable areas;

A1.1.4.2 Measures should be proportional to the chosen level of protection and the scope of the harm (for example, severity, irreversibility, uniqueness, numbers affected, temporal and spatial extent);

A1.1.4.3 Measures should be chosen with due consideration of costs and benefits (cost effective); and

A1.1.4.4 Measures (and underlying assumptions) should be continuously reviewed in light of new information and understanding.

NOTE A1.1—See for example, Refs (**49-53**).

A1.2 *Reasonable Practicability* —In specifying that efforts to minimize exposures should be completed to the extent "reasonably practicable," this guide roughly defines a benchmark for both the upper and lower bounds of recommended effort. In an environment of scientific uncertainty, this benchmark seeks to balance the goal of sufficiently controlling the indeterminate risk so as to prevent the manifestation of any significant hazards that may subsequently be identified, against being overly cautious and ultimately losing the benefits of the new technologies. On the basis of what is known and good engineering and other professional judgment, the user is advised to develop credible exposure scenarios, and then select and implement practicable controls that can be expected to suitably mitigate risk under those scenarios even if the hazard ultimately is determined to be significant.

A1.2.1 Practicable measures in this context are those that are both feasible, in the sense of being capable of being done in practice at a given location, and practical, in the sense of being demonstrably useful in achieving a particular exposure minimization or other program goal. Reasonable efforts are those that follow from a rational (logical) evaluation and selection process, and excluding both considerations and measures that are extreme or excessive. Thus, this guide does not suggest that the user should take measures that are technically impossible, would provide only speculative benefit, or if the time, trouble or cost of the measures would be disproportionate to the benefit or the risk. This approach largely mirrors the guidelines generally applicable to selecting analogous precautionary actions—proportionality, cost-effectiveness, consistency with actions in similar circumstances, and openness to change with new information or refined analysis.

A1.2.2 Reasonably "practicable" measures should be distinguished from similarly expressed standards from other contexts, such as, "as low as reasonably achievable" (ALARA) or "as low as possible," which may be read to encompass actions that are technically (theoretically) possible, but only by means of such scale, magnitude, complexity or cost as to be disproportionate or infeasible, or actions that provide only insignificant incremental benefit. The assumptions underlying such standards are inapplicable to UNP exposures within the scope of this guide. For example, the ALARA principle (from the ionizing radiation context) is premised on an assumption of a non-threshold, linear (straight-line) dose-effect relationship, independent of dose rate (**54**).

A2. GUIDANCE FOR IDENTIFYING AND ASSESSING POTENTIAL SOURCES OF UNP EXPOSURE

A2.1 Potential Sources of UNP Exposure

A2.1.1 In general, it is likely that processes generating nanomaterials in the gas phase, or using or producing nanomaterials as powders or slurries/suspensions/solutions (that is, in liquid media) pose the greatest risk for releasing UNP. In addition, maintenance on production systems (including cleaning and disposal of materials from dust collection systems) is likely to result in exposure to UNP if it involves disturbing or aerosolizing deposited nanomaterial. Exposures associated with waste streams containing nanomaterials may also occur. The magnitude of exposure to UNP when working with nanopowders depends on the likelihood of particles being released from the powders during handling.

A2.1.2 Both wet precipitation methods and gas-phase processes have the potential to cause exposure to primary UNP during the synthesis stage. All processes may give rise to exposure to agglomerated UNP during recovery, powder handling, and product processing. The nature of the exposure, the likely level and the probability of exposure will differ according to the specific process and the stage of the process. Similarly, the optimum strategy to control employee exposures and the efficacy of the control methods used will differ

depending on the specific process. Table A2.1 summarizes the potential pathways of exposure in nanoscale particle production and recovery.

A2.2 Factors Affecting Exposure To UNP

A2.2.1 Factors affecting exposure to UNP include *(a)* the amount of material being used; *(b)* whether the material can be easily dispersed (in the case of a powder) or from airborne sprays or droplets (in the case of suspensions), or is fixed on or within a matrix (and generally do not present an exposure risk); *(c)* the degree of containment; *(d)* duration of use or presence in exposure areas; and *(e)* state of agglomeration or aggregation (**7**, **56**).

A2.2.2 It is important to understand that a dispersion of UNP in a fluid is thermodynamically unstable. In fact, the challenge in many applications of such structures is to create, at least briefly, unagglomerated nanomaterials. Even in the absence of any bulk flow, Brownian motion causes particles to collide with subsequent coagulation or agglomeration of particles. For monodisperse size distributions, one can calculate concentration as a function of time for various initial particle sizes (**57**, **24**). For ideal systems (monodisperse spherical particles) significant particle lifetimes are calculated only at extreme dilutions of less than 10^6 particles/cc. There is a predicted 50 % reduction in the particle number concentration in 2 milliseconds when the initial number concentration is 10^{12} particles/cc, but at more dilute number concentrations, there is a 50 % reduction in number concentration in 33 minutes and 55 hours when the initial number concentrations are 10^6 and 10^4 particles/cc respectively (**24**, **25**). In "real" systems (that is, polydisperse distributions), non-stagnant fluid and non-spherical particles, these times are significantly reduced. Coagulation can take place more rapidly between dissimilar-sized particles than between same-sized particles. Coagulation between 10 nm and 1000 nm particles is 500-times more rapid than for 1000 nm particles alone and 180 times faster than for 10 nm particles alone (**24**). Thus, an unagglomerated nanoscale particle may exists only fleetingly from the moment of its synthesis until it encounters other, like or unlike particles with which it associates. These agglomerates may quickly grow out of the nanoscale or ultra fine (<0.1 micron) range.

A2.2.3 Some of the workplace factors that can increase the potential for exposure include the following:

A2.2.3.1 Working with UNP in liquid media without adequate protection (for example, gloves) will increase the risk of skin exposure.

A2.2.3.2 Working with UNP in liquid media during pouring or mixing operations, or where a high degree of agitation is involved, will lead to an increased likelihood of inhalable and respirable droplets being formed.

A2.2.3.3 Generating UNP in the gas phase in non enclosed systems will increase the chances of aerosol release to the workplace.

A2.2.3.4 Handling powders that contain UNP can lead to the possibility of aerosolization.

A2.2.3.5 Maintenance on equipment and processes used to produce or fabricate nanomaterials will pose a potential for exposure to workers performing these tasks.

A2.2.3.6 Cleaning of dust collection systems used to capture UNP can pose a potential for both skin and inhalation exposure.

TABLE A2.1 Potential Exposure Pathways in Nanoscale Particle Production Processes and Recovery[A]

Synthesis Processes	Particle Formation	Potential Inhalation	Potential Dermal/Ingestion
Gas phase	In air	Direct leakage from reactor Post-recovery process Post-recovery processing and packing	Airborne contamination of workplace Handling of product Cleaning/maintenance of plant
Vapor phase	On substrate	Product recovery Post-recovery processing and packing	Dry contamination of workplace Handling of product Cleaning/maintenance of plant
Colloidal	Liquid suspension	Drying of product (processing and spillage)	Spillage/contamination of workplace Handling of product Cleaning/maintenance of plant
Attrition	Liquid suspension	Drying of product (processing and spillage)	Spillage/contamination of workplace Handling of product Cleaning/maintenance of plant

[A] Adapted from Ref (**55**).

APPENDIXES

(Nonmandatory Information)

X1. GENERAL INFORMATION CONCERNING NANOSCALE PARTICLES

TABLE X1.1 Classification of Nanoscale Particles Based on Source

NOTE 1—This table was developed based upon information in various sources, including Refs (55, 59-61).

Source		Examples
Natural		Nanoscale particles emitted from plants Ocean spray (sea salt nuclei), forest fire combustion products, volcanic eruptions, alpha particles, asbestos (chrysotile, amosite), fullerenes, etc. Biological molecules—DNA, ferritin, molecular motors (ATP synthase; motors that power cilia in our lungs, bacteria flagella; motors responsible for muscle contraction, transport of vesicles, cell division), glucose, antibodies, proteins, hemoglobin, etc.
Anthropogenic	Incidental, Unintentional	Welding, soldering, thermal cutting and spraying, pyrolysis products, smelting, asphalt fumes, engine combustion products Smog from vehicle exhausts (for example, carbon nanotubes have been found in diesel exhaust), condensed gases from industrial air emissions Food production (for example, grilling, frying), tobacco smoke, material combustion (for example, burning carbon containing materials such as wood, coal, candles etc.), (fullerenes found in the combustion of carbon containing compounds)
	Intentional, Engineered, Unintentional	Dendrimers, fullerenes, nanotubes, quantum dots, nanoshells, nanoscale metal oxides

X1.2 Nanoscale particles exist in nature or can be produced by human activities, intentionally or unintentionally. There are numerous published studies regarding the adverse effects of anthropogenic incidental/unintentional nanoscale particles (environmental air pollution, tobacco smoke, occupational exposure to welding fumes, etc.), but comparatively few on engineered nanoscale particles. Incidental/unintentional nanoscale particles have a complex composition with an ill-defined surface chemistry and wide particle-size distribution. Engineered nanoscale particles are manufactured to meet defined product specifications (for example, specific physical and chemical properties). Typically the particle-size distribution and the chemical composition of manufactured nanoscale particles is defined and controlled by the manufacturing process. Concerns over engineered nanoscale particles are driven by our experiences with anthropogenic incidental/unintentional nanoscale particles, as well as toxicology studies on some engineered nanoscale particles. There is also a concern that some engineered nanoscale particles are in the size range of biological molecules, proteins, and intracellular machinery critical to life, the function which they may react with or interfere (58).

X1.3 Occupational exposures to some incidental nanoscale particles (for example, from welding fumes, manganese, beryllium, asphalt fumes, etc.) have resulted in various diseases when exposures are high and not controlled properly (16).

X2. GUIDANCE FOR EXPOSURE ASSESSMENT AND CHARACTERIZATION

NOTE X2.1—The source of the information contained with in this appendix is primarily from the referenced NIOSH web site (7). It is recommended that the user review the NIOSH web site to obtain the most current information.

X2.1 *Generally*—Until more information is available on the mechanisms underlying any hazards associated with various nanoscale particles, it is uncertain as to what measurement technique should be used to monitor exposures in the workplace. If the qualitative assessment of a process has identified potential exposure points and leads to the decision to measure nanoscale particles, several factors must be kept in mind. Current research indicates that mass and bulk chemistry may be less important than particle size, surface chemistry (or activity) for nanostructured materials (7). Research is still ongoing into the relative importance of these different exposure metrics, and how to best characterize exposures against them. Once the decision has been made to measure exposure, the metric to be used will depend on availability of sampling equipment or instruments and experience with those methods or instruments. Regardless of the metric and method selected, it is critical that measurements be conducted before production or processing of nanoscale particles to obtain background data. Measurements made during production or processing can then be evaluated to determine if there has been an increase in the metric selected. Human exposures should be characterized in terms of the physiochemical nature of the nanoscale particles, the aggregation state and concentration (number, mass, surface area) (8, 26).

X2.2 Sampling Strategy

X2.2.1 Currently there is not one sampling method that can be used to characterize exposure to nanoscale aerosols.

Therefore, any attempt to fully characterize workplace exposure to UNP must involve a multifaceted approach incorporating many of the sampling techniques mentioned herein.. The first step in evaluating the workplace involves identifying the source of nanoscale particle emissions. A condensation particle counter (CPC) instrument will provide acceptable capability for this purpose. It is critical to determine ambient or background particle counts before measuring particle counts during the manufacture or processing of the UNP involved. Limitations of CPCs, including the inability to distinguish between target UNP and ambient UNP, are discussed below. If a specific nanoscale particle is of interest (for example, TiO_2), then area sampling with a filter suitable for analysis by electron microscopy should also be employed. Other analytical techniques such as transmission electron microscopy (TEM) and Micro-XPS can identify specific particles or estimate their size distribution. If a source of emissions is identified, aerosol surface area measurements can be conducted with a portable diffusion charger and aerosol size distributions should be determined with a scanning mobility particle size analyzer (SMPS) or electrical low pressure impactor (ELPI) using static (area) monitoring. A small portable surface area instrument could be adapted to be worn by a worker, although depending on the nature of the work, this may be cumbersome. Further, losses of aerosol with the addition of a sampling tube would need to be calculated. The location of these instruments should be considered carefully. Ideally they would be placed close to the work areas of the workers of interest, but other factors such as size of the instrumentation, power source etc. will need to be considered.

X2.2.2 Personal sampling using filters suitable for analysis by electron microscopy may be employed for measuring exposures to specific UNP. Electron microscopy can be used to identify the particles, and can provide an estimate of the size distribution of the particle of interest. The use of a personal cascade impactor or a respirable cyclone sampler with a filter, though limited, will help to remove larger particles that are not of interest and allowing for a more definitive determination of particle size. In addition, where there are non respirable agglomerates or aggregates, the use of thoracic or inhalable samplers may be used.

X2.2.3 Using a combination of these techniques, an assessment of worker exposure to UNP can be conducted. This approach will allow a determination of the presence and identification of UNP, the characterization of the important aerosol metrics, and will provide a reasonable estimate of exposure. This approach is not without limitations, however, as it largely relies on static or area sampling, which will hamper interpretation and increase the inaccuracy of the exposure estimate.

X2.3 Monitoring Workplace Exposures

X2.3.1 A number of exposure assessment approaches can be instituted to determine worker exposures. These assessments can often be performed using traditional industrial hygiene sampling methods that include the use of samplers placed at static locations (area sampling), samples collected in the breathing zone of the worker (personal sampling), or real-time measurements of exposure that can be personal or static. Personal sampling collected within the employees breathing zone may be more representative of a worker's potential exposure than fixed location area samples if the UNP concentration has a large spatial variation within the work area. General area samples are utilized to augment personal sampling, to help evaluate the overall work environment, to determine the effectiveness of engineering and work practice controls and to aid the making of control decisions. General area samples may provide an adequate measure of an employee's exposure if the UNP concentration is uniform within the work area. The use of area sampling instruments may be required when portable personal sampling methods are not available or infeasible due to size considerations.

X2.3.2 Many of the sampling techniques that are available for measuring airborne nanoaerosols vary in complexity but can provide useful information for evaluating occupational exposures with respect to particle size, mass, surface area, number concentration, composition, and surface chemistry. Unfortunately, relatively few of these techniques are readily applicable to routine exposure monitoring. These measurement techniques are described below along with their applicability for monitoring nanometre aerosols.

X2.3.3 For each measurement technique used, it is vital that the key parameters associated with the technique and sampling methodology be recorded when measuring exposure to nanoaerosols. This should include the response range of the instrumentation, whether personal or static measurements are made, and the location of all potential aerosol sources. Comprehensive documentation will facilitate comparison of exposure measurements and aid the re-interpretation of historic data as further information is developed on appropriate exposure metrics.

X2.3.4 There are various methods to measure different metrics such as particle size and surface area and the results may not always correspond with one another. For instance, there are at least seven methods to measure particle size, and the results may vary as much as 10-fold, but more typically 2-4 fold from each other (**62**): *(1)* aerodynamic diameter, *(2)* vacuum aerodynamic diameter, *(3)* volume equivalent size, *(4)* mobility equivalent size, *(5)* optical equivalent size, *(6)* mass, and *(7)* projected sizes (electron microscopy images). The preferred analytical technique for quantifying employee UNP exposures or for assessing potential impact on health has yet to be determined.

X2.4 *Size-Fractionated Aerosol Sampling—Indirect Methods Requiring Laboratory Analysis*—Studies have indicated that particle size plays an important role in determining the potential effects of UNP in the respiratory system, either by influencing the physical, chemical, and biological nature of the material, affecting the surface area of deposited particles, or enabling deposited particles to move to other parts of the body. Some animal studies indicate that the toxicity of some poorly-soluble nanoscale aerosols (for example, TiO_2, carbon) may be more closely associated with aerosol surface area than the mass concentrations of the aerosol. However,

mass concentration measurements may be applicable for evaluating occupational exposure to nanometre aerosols where a good correlation between the surface area of the aerosol and mass concentration can be determined. NIOSH has proposed a mass based occupational exposure limit for ultra fine TiO_2, as 0.1 mg/m^3, for up to 10 hours/day during a 40-hour work week, and as collected by NIOSH Method 0600 for sampling airborne respirable particles (**19**). NIOSH indicates that NIOSH Method 7300 can be used to assist in differentiating TiO_2 from other aerosols collected on the filter while electron microscopy, equipped with an energy dispersive x-ray analyzer (EDXA), may be needed to identify and measure the fraction of the mass concentration that is attributable to fine and ultra fine TiO_2 particles (**19**).

X2.4.1 Aerosol samples can be collected using inhalable, thoracic, or respirable samplers, depending on the region of the respiratory system most susceptible to the inhaled particles or the potential for the particles to translocate from the site of deposition to another organ system and cause systemic toxicity (**2**). Current information suggests that the gas-exchange region of the lungs is particularly susceptible to nanomaterials (**7**), suggesting the use of respirable samplers. Respirable fraction samplers will also collect a nominal amount of micrometre-diameter particles that can deposit in the upper airways and ultimately cleared or transported to other parts of the body. Thoracic or inhalable samplers may be necessary.

X2.4.2 Respirable fraction samplers allow mass-based exposure measurements to be made using gravimetric or chemical analysis (**7**), or both. However, they do not provide information on aerosol number, size, or surface area concentration, unless the relationship between different exposure metrics for the aerosol (for example, density, particle shape) has been previously characterized. Currently, no commercially available personal samplers are designed to measure the particle number, surface area, or mass concentration of nanometre aerosols. However, several methods are available that can be used to estimate surface area, number, or mass concentration for particles smaller than 100 nm. In the absence of specific exposure limits or guidelines for engineered UNP, exposure data gathered from the use of respirable samplers (**7**) can be used to determine the need for engineering controls, the effectiveness of engineering controls and work practices and for routine exposure monitoring of processes/job tasks. When chemical components of the sample need to be identified, chemical analysis of the filter samples can permit smaller quantities of material to be quantified, with the limits of quantification depending on the technique selected (**7**). The use of conventional impactor designs to assess nanoscale particle exposure is limited, since practical impaction limits are 200 to 300 nm. Low-pressure cascade impactors that can measure particles to 50 nm may be used for static sampling, since their size and complexity preclude their use as personal samplers (**7**). A personal cascade impactor is available with a lower aerosol cut point of 250 nm (**7**), allowing an approximation of nanometre particle mass concentration in the worker's breathing zone. For each method, the detection limits are of the order of a few micrograms of material on a filter or collection substrate (**7**). Cascade impactor exposure data gathered from worksites where nanomaterials are being processed or handled can be used to make assessments as to the efficacy of exposure control measures.

X2.5 Real-Time Particle Size Aerosol Sampling

X2.5.1 The real-time (direct-reading) measurement of nanometre aerosol concentrations is limited by the sensitivity of the instrument to detect small particles, and the inability to distinguish among different particles of the same size. Many real-time aerosol mass monitors used in the workplace rely on light scattering from groups of particles (photometers). This methodology is generally insensitive to particles smaller than 300 nm (**7**). Optical instruments that size individual particles and convert the measured distribution to a mass concentration are similarly limited to particles larger than 100 to 300 nm.

X2.5.2 The Scanning Mobility Particle Size Analyzer (SMPS) is widely used as a research tool for characterizing nanometre aerosols, although its applicability for use in the workplace may be limited because of its size, cost, and the inclusion of a radioactive source. The Electrical Low Pressure Impactor (ELPI) is an alternative instrument that combines a cascade impactor with real-time aerosol charge measurements to measure size distributions (**7**).

X2.6 Surface Area Aerosol Measurements

X2.6.1 Relatively few techniques exist to monitor exposures with respect to aerosol surface area. Isothermal adsorption is a standard off-line technique used to measure the specific surface area of powders that could be adapted to measure the specific surface area of collected aerosol samples. For example, the surface area of particulate material (for example, using either a bulk or an aerosol sample) can be measured in the laboratory using a gas adsorption method (for example, Brunauer, Emmett, and Teller, BET) (**7**). However, the BET method requires relatively large quantities of material, and measurements are influenced by particle porosity and adsorption gas characteristics. BET is often used to estimate the surface area of bulk nanopowders. The use of this method may not correlate to direct reading surface area monitoring results that may be used to evaluate occupational environments.

X2.6.2 The first instrument designed to measure aerosol surface-area was the epiphaniometer (**7**). This device measures the Fuchs or active surface-area of the aerosols by measuring the attachment rate of radioactive ions. For aerosols less than approximately 100 nm in size, measurement of the Fuchs surface area is probably a good indicator of external surface-area (or geometric surface area). However, for aerosols greater than approximately 1 micrometre the relationship with geometric particle surface-area is lost (**7**). Measurements of active surface-area are generally insensitive to particle porosity. The epiphaniometer is not well suited to widespread use in the workplace because of the inclusion of a radioactive source and the lack of effective temporal resolution.

X2.6.3 This same measurement principle can be applied with the use of a portable aerosol diffusion charger. Studies have shown that these devices provide a good estimate of aerosol surface area when the airborne particles are smaller

than 100 nm in diameter. For larger particles, diffusion chargers underestimate aerosol surface area. However, further research is needed to evaluate the degree of underestimation. Extensive field evaluations of commercial instruments are yet to be reported. However, laboratory evaluations with monodisperse silver particles have shown that commercially available diffusion chargers can provide good measurement data on aerosol surface area for particles smaller than 100 nm in diameter but underestimate the aerosol surface area for particles larger than 100 nm in diameter (**7**).

X2.7 *Surface Area Estimation*—Information about the relationship between different measurement metrics can be used for estimating aerosol surface area. If the size distribution of an aerosol remains consistent, the relationship between number, surface area, and mass metrics will be constant. In particular, mass concentration measurements can be used for deriving surface area concentrations, assuming the constant of proportionality is known. This constant is the specific surface area (surface to mass ratio).

X2.7.1 Size distribution measurements obtained through sample analysis by transmission electron microscopy may also be used to estimate aerosol surface area. If the measurements are weighted by particle number, information about particle geometry will be needed to estimate the surface area of particles with a given diameter. If the measurements are weighted by mass, additional information about particle density will be required.

X2.7.2 If the airborne aerosol has a lognormal size distribution, the surface-area concentration can be derived using three independent measurements. An approach has been proposed using three simultaneous measurements of aerosol that included mass concentration, number concentration, and charge (**7**). With knowledge of the response function of each instrument, minimization techniques can be used to estimate the parameters of the lognormal distribution leading to the three measurements used in estimating the aerosol surface area.

X2.7.3 An alternative approach has been proposed whereby independent measurements of aerosol number and mass concentration are made, and the surface area is estimated by assuming the geometric standard deviation of the (assumed) lognormal distribution (**7**). This method has the advantage of simplicity by relying on portable instruments that are finding increasing application in the workplace. Theoretical calculations have shown that estimates may be up to a factor of ten different from the actual aerosol surface-area, particularly when the aerosol has a bimodal distribution. Field measurements indicate that estimates are within a factor of three of the active surface-area, particularly at higher concentrations. In workplace environments, aerosol surface-area concentrations can be expected to span up to 5 orders of magnitude; thus, surface-area estimates may be suited to initial or preliminary appraisals of occupational exposure concentrations.

X2.7.4 Although such estimation methods are unlikely to become a long-term alternative to more accurate methods, they may provide a viable interim approach to estimating the surface area of nanometre aerosols in the absence of precise measurement data. Additional research is needed on comparing methods used for estimating aerosol surface area with a more accurate aerosol surface area measurement method.

X2.8 Particle Number Aerosol Concentration Measurement

X2.8.1 The importance of a particle number concentration as an exposure metric is not clear. In some cases, health end points appear to be more closely related with particle surface area rather than particle number. However, the number of particles depositing in the respiratory tract or other organ systems may play an important role.

X2.8.2 Aerosol particle number concentration can be measured relatively easily using Condensation Particle Counters (CPCs). These are available as hand-held static instruments, and they are generally sensitive to particles greater than 10 to 20 nm in diameter. CPCs designed for the workplace do not have discrete size-selective inputs, and so they are typically sensitive to particles up to micrometres in diameter. Commercial size-selective inlets are not available to restrict CPCs to the nanoscale particle size range; however, the technology exists to construct size-selective inlets based on particle mobility, or possibly inertial pre-separation. An alternative approach to estimating UNP concentrations using a CPC is to use the instrument in parallel with an optical particle counter. The difference in particle count between the instruments will provide an indication of particle number concentration between the lower CPC detectable particle diameter and the lower optical particle diameter detectable (typically 300 to 500 nm).

X2.8.3 A critical issue when characterizing exposure using particle number concentration is selectivity. UNP are ubiquitous in many workplaces, from sources such as combustion, vehicle emissions, and infiltration of outside air. Particle counters are generally insensitive to particle source or composition making it difficult to differentiate between incidental and process-related UNP using number concentration alone. In a study of aerosol exposures while bagging carbon black, Kuhlbusch et al. (**7**) found that peaks in number concentration measurements were associated with emissions from fork lift trucks and gas burners in the vicinity, rather than the process under investigation. Although this issue is not unique to particle number concentration measurements, orders of magnitude difference can exist in aerosol number concentrations depending on concomitant sources of particle emissions.

X2.8.4 Although using nanoscale particle number concentration as an exposure measurement may not be consistent with exposure metrics being used in animal toxicity studies, such measurements may be a useful indicator for identifying UNP emissions and determining the efficacy of control measures. Portable CPCs are capable of measuring localized aerosol concentrations, allowing the assessment of particle releases occurring at various processes and job tasks (**7**).

X2.9 *Particle Size-Selective Air Sampling Conventions for Airborne Particulate Matter*—Occupational exposure limits for airborne particulate matter are increasingly based upon size-selective air sampling conventions such as inhalable, thoracic, and respirable. It is likely that size-selective air

sampling conventions may exist for UNP/ultrafine particles in the future and that there may be corresponding occupational exposure limits for this particle size fraction. In the case of airborne material, the particle size will determine whether the material can enter the respiratory tract and where it is most likely to deposit. Depending upon the nanomaterial and trace chemicals or impurities, one may be concerned about deposition in one or more regions of the respiratory tract, that is, *(a)* the head airways region (nasal passages, mouth, pharynx, and larynx), *(b)* tracheobronchial (includes trachea and ciliated airways), and *(c)* alveolar region (gas-exchange region). Where a substance may cause systemic toxicity or head airway (for example, nasal cavity, throat) irritation, the ACGIH has recommended an inhalable TLV (**2**). The literature points to a potential concern for some types of UNP to translocate once deposited in the respiratory tract. This would constitute potential systemic toxicity. Where the substance may result in head airways disease (for example, nasal cancer), the ACGIH has recommended an inhalable TLV (**2**). Where the substance may result in bronchial disease, they have recommended a thoracic TLV (**2**). Where the substance has resulted in disease to the deep lung, the ACGIH has recommended a respirable TLV (**2**). Depending upon their aerodynamic equivalent diameter (AED) (for agglomerates of UNP > 500 nm in size) or geometric physical diameter (for UNP < 500 nm in size), some inhaled particles will deposit in one or more of these three regions (**2, 3, 24, 63**).

X2.9.1 The inhalable fraction includes those airborne particles which are small enough to enter the head airways through the nose or mouth, or both, during inhalation (**2, 3, 24**). Airborne particles (in the breathing zone of a person) having an AED of 100 µm (1/10 of a mm) have about a 50 % chance of entering the head airways (**1, 2**). Airborne particles > 100 µm AED are likely to have less than a 50 % chance of entering the head airways. Airborne particles < 100 µm AED have a greater chance of entering the head airways, and the smaller they are, the greater the chance (**1, 2**).

X2.9.2 The thoracic particle fraction includes those particles small enough to pass the larynx and enter the lungs, consisting of the tracheobronchial and alveolar regions (**2, 3**). Airborne particles (in the breathing zone of a person) having an AED of 25 µm have about a 2 % chance of entering the lungs (**1**). Airborne particles having an AED of 10 µm (10 000 nm) have about a 50 % chance of entering the lungs, and the smaller they are, the greater the chance (**1**).

X2.9.3 The respirable particle fraction includes those particles that are small enough to enter the alveolar region (**2, 3**). Airborne particles (in the breathing zone of a person) having an AED of 10 µm have about a 1 % chance of entering the lungs (**1**). Airborne particles having an AED of 4 µm have about a 50 % chance of entering the lungs, and the smaller they are, the greater the chance (**1**).

X2.9.4 Diffusion is the predominant deposition mechanism in the respiratory tract for UNP and agglomerates of nanoscale particles < 500 nm in diameter and is governed by geometric physical diameter, rather than AED (**24**). Significant amounts of inhaled UNP will be deposited within the respiratory tract (**59**). Deposition in the head airways increases for particles less than 10 nm due to diffusion, especially in the nose (**24**). For example, during rest, while breathing through the nose, ICRP modeling predicts that 90 % of inhaled 1 nm particles are preferentially deposited in the nasalpharyngeal region, 10 % in the tracheobronchial region, and essentially none in the alveolar region (**59**). A20 nm particle has the highest deposition in the alveolar region (about 50 %), whereas in the tracheobronichial regions this particle size deposits with about 15 % efficiency (**59**). The mass-fraction of nanometre-diameter particles depositing in the alveolar region of the lungs is greater than for larger respirable particles by a factor of about 2-5 (**25**). A3-4 nm particle has the highest deposition in the tracheobronchial region (about 35 %) (**24**).

X2.10 *Respiratory Tract Particle Deposition Models*—Computer programs for predicting respiratory tract deposition of inhaled particles are available (**64-66**). Two models in wide use are as follows. Though reliable and useful for predicting respiratory tract deposition in normal humans, the models below will underestimate local doses delivered to cells in certain areas, such as carinas (which are flow dividers or bifurcation regions) in the tracheobronchial region (**66**).

X2.10.1 International Commission on Radiation Protection (ICRP). The ICRP (1994) provides a computational model for predicting respiratory tract deposition of inhaled particles (**64**). Hinds (1999) provides simplified equations to the ICRP model for monodisperse particles of standard density at standard conditions; the deposition fractions predicted by these equations agree with the ICRP model within ±0.03 over the size range of 0.001 to 100 µm; the equations are for spheres of standard density, but can be applied to other articles by using the AED for particles larger than 500 nm and the physical diameter or equivalent volume diameter for particles less than 500 nm (**24**).

X2.10.2 Centers for Health, Technology Transfer (CIIT). The CIIT Multiple Path Particle Dosimetry (MPPD) Model, is available on-line (free of charge) (**65**). The MPPDI allows the user to input airborne concentrations, specific particle sizes, dispersions and concentrations, breathing characteristics, airway sizes (based on age), and other pertinent information (**66**).

X2.11 *Carbon Nanotube Exposure Monitoring*—Appropriate metrics for measuring exposures to carbon nanotubes may include surface area, mass, and number (**9, 22, 23**). Donaldson et al. (2006) recommended that until better information becomes available, carbon nanotubes should be considered in the same way other biopersistent fibers in workplace risk assessments, using similar assessment approaches (for example, fiber counts) (**9**). Currently, there are no standardized air sampling methods specifically for carbon nanotubes nor are there established occupational exposure limits.

X2.11.1 With regard to particle number, occupational exposures to non-asbestos man-made fibers (for example, carbon fiber, glass fiber, aramid fiber, etc.) are sometimes accomplished by using NIOSH 7400 Method (Phase Contrast Light Microscopy) and counting only respirable fibers according to "B" rules (**4**). The "B" rules include counting only those fibers

that are less than 3 micrometres in physical diameter, longer than 5 micrometres in physical length, and having a length-to-width ratio equal to or greater than 5:1 (**4**). However, though there may be some utility in using the NIOSH 7400 Method for counting carbon nanotube fibers, there are some serious limitations. This method would count nanotube aggregates (bundles/ropes) that meet the physical dimension criteria of a fiber and are from 250 nm to 3000 nm in diameter, however singlet/individual carbon nanotubes and aggregates (bundles/ropes) having a diameter less than 250 nm would not be counted due to the lower limits of particle size detection by the phase contrast microscope method. Donaldson et al. (2006) recommended that electron microscopy should seriously be considered because of the difficulties in applying optical methods such as the NIOSH 7400 Method (**9**).

X2.11.2 The NIOSH 7400 Method is also non-specific and does not identify the type of fiber that is being counted. For asbestos, there is a transmission electron microscopy sampling and analytical method 7402 (Asbestos by TEM) that can provide positive identification, shape, and structure and that was designed to be used with Method 7400 (**67**). However, currently there are no similar standardized TEM sampling and analytical methods for carbon nanotubes. Donaldson et al. (2006) indicates that electron microscopy (for example, TEM) will be necessary to adequately assess levels of carbon nanotubes in the workplace (**9**).

X2.11.3 Thoracic samplers will collect fibers and particles that can penetrate into the lungs (tracheobronchial region and alveolar region). Thoracic samplers are available that match the ACGIH/ISO/CEN thoracic convention (**5**) and may be of use in collecting carbon nanotube air samples for further analysis. Baron (2003) suggests that using a thoracic sampler to collect air samples for analysis has several advantages and that it is likely that thoracic sampling will eventually be in routine use for measurement of asbestos and other fibers (**5**). Baron (2003) showed that sampling fibers with a thoracic sampler was approximately equivalent to counting only mineral fibers with a physical diameter smaller than 3 micrometres (**5**).

X3. GUIDANCE FOR RESPIRATORY PROTECTION

X3.1 Refer to the U.S. National Institute for Occupational Safety and Health (NIOSH) Approaches to Safe Nantechnology for most current guidance on respiratory protection for nanomaterials (**7**).

X3.2 Table X3.1 identifies various types of air-purifying particulate-filtering respirators that can be used along with information on the level of exposure reduction that can be expected from each and the advantages and disadvantages of each respirator type. In order for the respirator to provide the stated level of protection, it must be NIOSH Approved (or non-U.S. country equivalent); the wearer of the respirator must be enrolled in a written respiratory protection program in accordance with OSHA regulation (or non-U.S. country equivalent); and, the respirator must be selected, used, and maintained in accordance with such federal regulations. Respiratory protection factors assume that the filters will remove UNP at efficiency of at least 99.97 %. To assist respirator users, NIOSH has published the document, “NIOSH Respirator Selection Logic (RSL)” (**68**), which provides a process for selecting appropriate respirators for chemicals with exposure limits. Ref (**69**) lists and compares the assigned protection factors of OSHA, NIOSH, and ANSI.

TABLE X3.1 Air-Purifying Particulate-Filtering Respirators

NOTE 1—The assigned protection factors are subject to change. Respirator manufacturers' information and local respiratory protection regulations should be referenced to ensure compliance with allowable protection factors.

Respirator Type and Assigned Protection Factor (APF)		Advantages	Disadvantages
Elastomeric half- face piece with N-100, R-100, or P-100 filters	5 (if qualitatively fit-tested) 10 (if quantitatively fit-tested)	Low maintenance Reusable face-piece and replaceable filters and cartridges No effect on mobility	Provides no eye protection Can add to heat burden Inward leakage at gaps in face seal Communication may be difficult Fit testing required to select proper face-piece size Some eyewear may interfere with the fit
Powered air-purifying respirator with HEPA filter, loose-fitting helmet/hood	25 -1000 (1000 only if the manufacturer, or user, can demonstrate an APF of at least 1000)	Provides eye protection Protection for people with beards, missing dentures or facial scars Low breathing resistance Flowing air creates cooling effect Face seal leakage is generally outward Fit testing is not required Prescription glasses can be worn Communication less difficult than with elastomeric half face-piece or full face-piece respirators Reusable components and replaceable filters	Added weight of battery and blower Awkward for some tasks Battery requires charging Air flow must be tested with flow device before use
Elastomeric full- face piece with N-100,R-100, or P-100 filters	10 (if qualitatively fit-tested) 50 (if quantitatively fit-tested)	Provides eye protection Low maintenance Reusable facepiece and replaceable filters and cartridges No effect on mobility More effective face seal than that of filtering face-piece or Elastomeric half face-piece respirator	Can add to heat burden Diminished field of vision compared to half Facepiece Inward leakage at gaps in face seal Fit testing required to select proper face-piece size Face-piece lens can fog without nose cup or lens treatment Spectacle kit needed for people who wear corrective glasses
Powered air-purifying respirator with HEPA filter, tight-fitting full facepiece,	1000 (if quantitatively fit-tested)	Provides eye protection with full face-piece Low breathing resistance Face seal leakage is generally outward Flowing air creates cooling effect Reusable components and replaceable filter	Added weight of battery and blower Awkward for some tasks No eye protection with half face-piece Fit testing required to select proper face-piece size Battery requires charging Communication may be difficult Spectacle kit needed for people who wear corrective glasses with full face-piece respirators Air flow must be tested with flow device before use

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