# BEST PRACTICE#267 UNBOUND ENGINEERED NANOPARTICLES (UNPS) GUIDANCE DOCUMENT

Prepared by:

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## Abstract

This guide provides the basis for establishing a UNP program based on the requirements of Department of Energy (DOE Order 456.1, The Safe Handling of Unbound Engineered) and from recommendations from the National Institute for Occupational Safety and Health (NIOSH). Due to unestablished Occupational Exposure Limits (OELs) and new emerging technology the EFCOG Nano Task Team has developed this guide to provide key concepts, generally accepted methods for conducting qualitative and quantitative exposure assessments from additional resources such as the American Industrial Hygiene Association (AIHA) for establishment of UNP ESH programs that align with DOE Order 456.1.

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## Tables

# Abbreviations

| | |
|---|---|
| $Al_2O_3$ | aluminum oxide |
| Ag | Silver |
| CB | Control Banding |
| CNF | Carbon Nanofiber |
| CNT | Carbon Nanotube |
| Co | Cobalt |
| DOE | U.S. Department of Energy |
| DRI | Direct Read Instruments |
| EC | Elemental Carbon |
| EDS | Energy Dispersive Spectroscopy |
| EFCOG | Energy Facility Contractors Group |
| ENM | Engineered Nanomaterials |
| HEPA | High Efficiency Particulate Air |
| ICP | Inductively Coupled Plasma |
| LLNL | Lawrence Livermore National Laboratory |
| LEV | Local Exhaust Ventilation |
| $MnO_2$ | manganese oxide |
| NEAT | Nanomaterial Exposure Assessment Technique |
| Ni | Nickel |
| NIOSH | National Institute for Occupational Safety and Health |
| OEL | Occupational Exposure Limit |
| OSHA | Occupational Safety and Health Administration |
| PM | Preventative Maintenance |
| PPE | Personal Protective Equipment |
| REL | Recommended Exposure Limit |
| SEM | Scanning Electron Microscopy |
| $TiO_2$ | Titanium Dioxide |
| TEM | Transmission Electron Microscopy |
| UNP | Unbound Engineered Nanoparticle |

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**Commented [AM3]:** Same as above—only used once.

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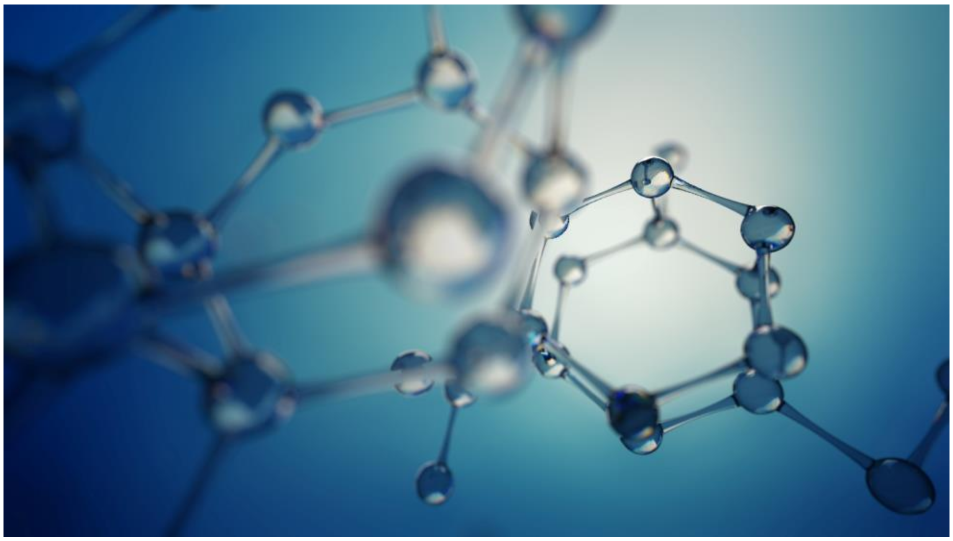

Photo courtesy of Kansas City National Security Campus

## Definitions from DOE Order 456.1

**Engineered nanoparticle**: Intentionally created (in contrast with natural or incidentally formed) material with one or more dimensions greater than 1 nanometer and less than 100 nanometers in size.

**Bound Nanoscale Particles**: 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.”

**Nanoscale particle examples**: Relevant nanoscale particle types include intentionally produced fullerenes, nanotubes, nanowires, nanoropes, nanoribbons, quantum dots, nanoscale metal oxides, nanoplates, nanolayers, and other engineered nanoscale particles.

**Unbound Engineered Nanoscale Particles (UNPs)**: 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.

# Introduction

The U.S. Department of Energy (DOE) provides guidance for assessing worker risk for exposure to nanoparticles as part of an Unbound Engineered Nanoparticles (UNP) program at DOE sites and facilities. This guide provides the basis for establishing a UNP program based on the requirements

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**Commented [JO8]:** Maybe this should read “This Department of Energy (DOE) document…” since we are referring to this document?

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of DOE Order 456.1, “The Safe Handling of Unbound Engineered Nanoparticles,” and recommendations from the National Institute for Occupational Safety and Health (NIOSH).

- Nanoparticles are defined as particles with one or more dimensions greater than 1 nanometer and less than 100 nanometers in size.
- Nanoparticles are classified as bound/unbound, engineered, or natural/incidentally formed.
- Nanoparticles are of concern because of chronic and acute health effects and limited research, guidance, and nano-specific sampling methods and lack of occupational exposure limits (OELs).

Commented [JC11]: I think this should read engineered or natural/incidentally formed. Engineered and Natural nanoparticles are not treated equally.

Commented [JC12]: It is my understanding that initialisms establishes in the abstract should be reestablished in the body of the paper.

Due to the rapid and diverse growth of engineered nanomaterials, more research is needed to understand the health risks associated with nanomaterials exposure in the workplace. This guidance provides clarification of terminology related to nanomaterials (e.g., bound vs. unbound nanoparticles), a brief overview of nanomaterials of concern that are commonly found in use across the DOE complex, methodologies for Industrial Hygiene assessment and control, UNP registry requirements, and medical surveillance.

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## DOE O 456.1A

This directive requires the use of the “best available” hazard information to conduct exposure assessments for activities involving UNPs (2016). Air monitoring programs following recognized exposure assessment guidelines must be established.

Unbound engineered nanoscale particles are 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.” For example, relevant nanoscale particle types include intentionally produced fullerenes, nanotubes, nanowires, nanoropes, nanoribbons, quantum dots, nanoscale metal oxides, nanoplates, nanolayers, and other engineered nanoscale particles.

The following types of UNPs are beyond the scope of this Order:

- Biomolecules (proteins, nucleic acids, and carbohydrates),
- Nanoscale forms of radiological materials,
- Nanoparticles incidentally produced by human activities or natural processes, and
- Ultrafine particles such as those produced by diesel engines and forest fires.

Natural sources of UNPs are those made by nature through (bio)geochemical or mechanical processes, without direct or indirect connection to a human activity or anthropogenic process. Examples include erosion and weathering, natural fires, and volcanos. Incidental nanomaterials are those unintentionally produced by any form of direct or indirect human influence or anthropogenic process.

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Commented [JO15]: Added for clarification and readability

## Differentiation between Bound and Unbound Nanoparticles

Today's consumer and industrial products manufacturers are using more nanomaterials. There are many ways to create engineered nanoparticles including through mechanical-physical processing like milling, as well as through chemical-physical processing like sol-gel, hydrothermal, inert gas condensation, ion sputtering scattering, and others. Understanding which products contain nanomaterials is necessary to the exposure assessment process.

Bonds are the key aspect in the determination of bound vs. unbound. Once a nanomaterial has been identified, determining whether the material is bound or unbound is fundamental to the assessment of its exposure potential. Bound nanoparticles are incapable of becoming airborne under normal conditions. Unbound nanoparticles are easily separated and are potential sources of exposure. The routes of exposure include inhalation, ingestion, and dermal absorption. The next section elaborates on the different types of bound and unbound nanoparticles.

### Unbound Engineered Nanoparticles (UNPs)

#### *Agglomerates*

Agglomeration is when particles are combined loosely and can be broken by simple mechanical forces. Although nanoparticles can agglomerate to a size over 100 nm, they are still considered unbound nanoparticles because they can be easily broken and separated. Agglomerates include particles bound by weaker forces like Van der Waals, electrostatic interaction, or surface tension.

#### *Nanoparticle Suspensions*

Suspensions of nanoparticles in water, oil, or other solvents that have not had a polymerization event are not considered bound. Hydrogen and dipole–dipole bonds are weak and do not constitute bound nanomaterial. Evaporation of nanoparticle suspensions may leave residual nanomaterial that can be easily separated and dispersed as unbound nanoparticles. Misting will also disperse unbound nanoparticles from a liquid suspension. Skin absorption is also a potential risk for UNP suspension.

#### *Nanofibers*

Nanofibers have two alike dimensions (diameter or width or height) in the nanoscale, and a third dimension that is significantly larger (length). Nanofibers, such as in a friable structure, are considered to be UNPs. Not all nanofibers are in the form of a UNP; strong bonds can be formed with nanofibers to form larger bonded structures.

### Bound Nanoparticles

#### *Aggregates*

A strong and dense collection of particles is referred to as an aggregate. Aggregates include nanoscale particles fixed by diffusion, or ionic or covalent bonds in particles over 100 nm in all dimensions.

#### *Solutions*

Typically, solutions are made by forming ions, atoms, or a single compound within the mixture. Nanoparticles that are dissolved into a solution are no longer considered nanoparticles. A true

**Commented [BH16]:** Shane Gillett, INL

**Commented [JO17]:** For consistency with definitions an abbreviations

**Commented [JC18]:** Spaces after periods are inconsistent throughout. I recommend 1 space after a period.

**Commented [JO19]:** The other paragraph titles are nouns so I converted this one to a noun also.

**Commented [JC20]:** Though UNP suspensions are considered unbound, not all UNP post solvent evaporation is considered unbound... as I understand it.

**Commented [JO21]:** This is part of the definition of nanoscale and isn't necessary here.

**Commented [JO22]:** Are all nanofibers considered UNP or only friable ones?  Needs clarification I think.

nanoparticle solution is a homogeneous mixture of two or more substances in which the particle size of the material dissolved (solute) is less than 1 nm.

**Commented [JO23]:** This is a little redundant in this sentence

### *Diffusion-Bonded Metals and Ceramics*

**Commented [JO24]:** Bonded is used consistently in the paragraph so assuming it belongs in the title as well...

Nanoscale metals and ceramic powders that have gone through diffusion bonding are considered bound nanoparticles. Bonded metals and ceramics may have metallic or ionic bonds.

Diffusion bonding is a solid-state process in which similar or dissimilar materials are bonded by atomic diffusion at the interface of the particles. For example, the process of sintering involves applying heat and pressure to bring the surfaces of the materials in contact. This process allows atoms to migrate and form metallurgical bonds. Interdiffusion of atoms across the interface leads to the creation of strong bonds with high integrity.

### *Nanoscale Particles Fixed in a Polymer Matrix*

Nanoscale particles affixed into a matrix of organic polymers are in a bound state. Suspensions of nanoparticles in a solvent containing polymers are considered a bound nanomaterial where polymerization can occur through polymer chains that are cross-linking by covalent and ionic bonds. Properly affixing the nanoparticles into a polymer matrix will prevent particles from becoming mobile and thus removes the exposure potential. Ionic bonds in polymers are less common.

**Commented [JO25]:** I thought this a better closing statement than in the middle of the polymerization discussion.

## Decision Determination of Bound and Unbound Nanoparticles

**Commented [JO26]:** I think capitalization is more consistent here with paragraph titles.

The concept of bound and unbound nanoparticles refers to the ability or inability of particles to be separately mobile. Properly affixing nanoparticles into a polymer matrix or the interdiffusion of atoms across the interface will prevent particles from becoming mobile, thus removing the exposure potential. Exposure assessments that incorporate the classification of bound and unbound will help in the determination of when UNP controls should be implemented.

**Commented [JO27]:** Is this accurate? Or is it just “reducing” exposure potential?

**Commented [SG28R27]:** I believe this will stay “removing”.

# Materials of Concern

**Commented [BH29]:** Cameron Radtke - cameron.radtke@nrel.gov

Engineered nanomaterials are of considerable scientific interest because some material properties change at this scale. These changes challenge the understanding of both the researcher and the safety professional concerning potential associated hazards and their ability to anticipate, recognize, evaluate, and control potential health and safety risks.

**Commented [JO30]:** We should avoid possessive forms in technical writing so I reworded it accordingly.

UNPs can involve a wide range of material sizes, shapes, functionalities, and chemical compositions. The Nanotechnology Products Database lists more than 11,000 nano-enabled products being manufactured across the globe. Due to limited toxicological studies on UNPs, NIOSH has developed recommended exposure limits (RELs) for only three types of UNPs. These include carbon nanotubes (CNTs) and carbon nanofibers (CNFs), nanoscale silver (Ag), and nanoscale titanium dioxide ($TiO_2$).

There are numerous relevant nanoscale particle types with various applications that do not yet have established OELs. Common engineered nanomaterial types in a research setting include intentionally produced fullerenes, nanowires, nanoropes, quantum dots, nanoscale metals and metal oxides, graphite, nanoplates, and polishing solutions containing nanoscale alumina or silica, etc. (Figure 1).

| | Type | Examples |
|---|---|---|
| | Carbon Based | Buckyballs or Fullerenes, Carbon Nanotubes*, Dendrimers<br>*Often includes functional groups like* PEG (polyethylene glycol), Pyrrolidine, N, N-dimethylethylenediamine, imidazole* |
| | Metals and Metal Oxides | Titanium Dioxide (Titania)**, Zinc Oxide, Cerium Oxide (Ceria), Aluminum oxide, Iron Oxide, Silver, Gold, and Zero Valent Iron (ZVI) nanoparticles |
| | Quantum Dots | ZnSe, ZnS, ZnTe, CdS, CdTe, CdSe, GaAs, AlGaAs, PbSe, PbS, InP<br>*Includes crystalline nanoparticle that exhibits size-dependent properties due to quantum confinement effects on the electronic states (ISO/TS 27687:2008).* |

*Figure 1: Common UNPs encountered in the research environment (CNCHE 2012).*

Exposure to these types of engineered nanomaterials may occur through inhalation, dermal contact, accidental injection, or ingestion. The ways that nanomaterials are used as well as their material state can greatly affect the exposure potential (Figure 2).

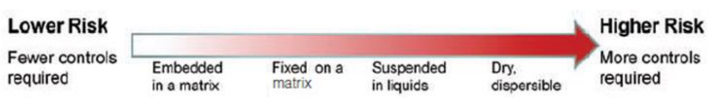


*Figure 2: Risk ranking and controls by material phase (National Research Council 2011).*

For example, if a nanomaterial is embedded or bound within a matrix, the exposure potential is minimal unless it is mechanically disturbed via machining, grinding, cutting, sawing, etc. Handling UNP as a dry, dispersible powder has potential for greater inhalation exposure than working with UNPs suspended in a liquid. It is important to note that UNPs suspended in liquid can dry into a powder and must be handled with care. Sonication, shaking, stirring, pouring, or spraying of a suspended nanomaterial can result in potential exposures. UNP liquid suspensions can also present a significant dermal exposure risk.

Examples of higher-exposure risk scenarios encountered in a research setting may include the following:

- Pouring, heating, or mixing liquid suspensions, or conducting operations with a high degree of agitation involved, such as sonication;
- Weighing or transferring dry powders or pellets;
- Generating or manipulating UNPs in a gas phase or in aerosol form;
- Cleaning reactors potentially contaminated with UNPs;
- Changing filter elements or maintaining dust collection systems used to capture nanomaterials; and
- High speed abrading/grinding of nanocomposite materials.

The toxicity of specific nanoparticles of interest is an emerging field of study and depends on many factors such as chemistry, morphology, surface charges, etc. A growing body of research is

**Commented [CR31]:** Source for Figure 1: California Nanosafety Consortium of Higher Education, Nanotoolkit, Working Safely with Engineered Nanomaterials in Academic Research Settings, April 19, 2012 https://innovation.luskin.ucla.edu/wp-content/uploads/2019/03/Nanotoolkit-Working_Safely_with_Engineered_Nanomaterials_in_Academic_Research_Settings.pdf

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**Commented [JO34]:** This should be all capitalized words or only the first word I think.

**Commented [CR35]:** Source for Figure 2: National Research Council. 2011. *Prudent Practices in the Laboratory: Handling and Management of Chemical Hazards, Updated Version*. Washington, DC: The National Academies Press. https://doi.org/10.17226/12654.

**Commented [BH36]:** Cameron: Please provide your source/citation for this figure.

**Commented [CR37R36]:** National Research Council. 2011. *Prudent Practices in the Laboratory: Handling and Management of Chemical Hazards, Updated Version*. Washington, DC: The National Academies Press. https://doi.org/10.17226/12654.

**Commented [JO38]:** Is gas phase redundant here since aerosols would include particles suspended in gases? Consider deleting gas phase or differentiating between the terms.

**Commented [SG39R38]:** Gas phase and aerosols form are different enough in terms of generating nanoparticles to keep them separate.

**Commented [JO40]:** Punctuation at the end of bulleted items isn't really necessary

**Commented [JC41R40]:** Whichever route we take we should be consistent with previous bulleted lists indicating that exposure to some types of engineered nanomaterials can cause adverse health effects. Based on preliminary toxicological data, a prudent and cautious approach should be followed in the production, use, and disposition of UNPs.

Nanoparticles have been shown to trigger the production of free radicals. The overproduction or chronic production of reactive oxygen species can cause inflammatory reactions; tissue changes; and DNA, protein, and lipid damage. Nanoparticles can also cause mechanical damage within the cells and thus trigger further oxidative stress.

Animal studies involving exposure to engineered nanomaterials indicate that some nanoparticle exposures can result in adverse health effects involving pulmonary and cardiovascular systems and possibly other organ systems.

Carbon nanotubes constitute one particular class of nanomaterials of concern to toxicologists (Table 1). Key physicochemical similarities exist between asbestos fibers and carbon nanotubes, and there is evidence that the "fiber pathogenicity paradigm" can be extended to include some types of carbon nanotubes, as well as other high-aspect-ratio fibrous nanomaterials including metallic nanowires. This paradigm relates properties such as the width, length, and bio-persistence of high-aspect-ratio fibrous nanomaterials to their fate in the body.

*Table 1: Summary of possible health risks for various types of nanomaterials that are commonly used in a research setting (Ray et al., 2009).*

| **Nanomaterials** | **Possible Risks** |
|---|---|
| Carbon nanomaterials, silica nanoparticles | Pulmonary inflammation, granulomas, and fibrosis (Oberdörster et al., 2002; Warheit et al., 2006; Chou et al., 2008; Lam, 2003) |
| Carbon, silver, and gold nanomaterials | Distribution into other organs including the central nervous system (Oberdörster et al., 2002, 2004; Semmler et al., 2004) |
| Quantum dots, carbon, and $TiO_2$ nanoparticles | Skin penetration (Mortensen et al., 2008; Zhang & Monteiro-Riviere, 2008; Baroli et al., 2007; Rouse et al., 2006) |
| $MnO_2$, $TiO_2$, and carbon nanoparticles | May enter brain through nasal epithelium olfactory neurons (Oberdörster et al., 2002, 2004; Hussain et al., 2006; Sharma & Sharma, 2007) |
| $TiO_2$, $Al_2O_3$, carbon black, cobalt (Co), and nickel (Ni) nanoparticles | May be more toxic than micron-sized particles (Warheit et al., 2006; Oberdörster et al., 1994, 2005) |

Health outcomes related to nanoparticle exposure are complex and not yet fully understood. Until clearer understandings emerge, the limited evidence available suggests caution when potential exposures to engineered nanoparticles may occur.



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# NIOSH Sampling Guidance to Determine Exposure

NIOSH's (2022) *Occupational Exposure Sampling for Engineered Nanomaterials* states the following:

> The National Institute for Occupational Safety and Health (NIOSH) developed guidance for workplace sampling for three engineered nanomaterials: carbon nanotubes and nanofibers, silver and titanium dioxide, each of which have an elemental mass-based NIOSH Recommended Exposure Limit (REL).

These RELs are shown in Table 2.

*Table 2: Nanomaterials with their respective RELs (NIOSH 2022).*

| **Nanomaterial** | **NIOSH REL** |
|---|---|
| Carbon nanotubes (CNTs/CNFs) (elemental composition of particles and morphology) | 1 µg/m³, respirable elemental carbon nanomaterials |
| Total silver (Ag) (all three primary particle size dimensions < 100 nm), metal dust, fume, and soluble compounds | 0.9 µg/m³ as a respirable nanomaterial |
| Titanium dioxide ($TiO_2$) | 2.4 mg/m³ for fine nanomaterials (> 100 nm)<br><br>0.3 mg/m³ for ultrafine nanomaterials (nanoscale, 1–100 nm) |

Commented [JO44]: I assume this means (1-100nm) for consistency as a stated range.

## Recommendations

NIOSH NEAT 2.0 recommends establishing an Exposure Monitoring Program with risk ranking based on an assessment. Safety and health professionals should incorporate engineered nanomaterials (ENMs) into the existing exposure monitoring program with appropriate adjustments to ensure that worker exposures to ENMs are maintained below the RELs and to minimize exposures for ENMs without a REL (NIOSH 2011, 2013, 2021). Aspects of the program should include the following:

1. Identification of sources of potential ENM exposures,

2. Establishment of similar worker exposure groups by area or job tasks,

3. Characterization of exposures for all potentially exposed workers, and

4. Assessment of the effectiveness of engineering controls, work practices, personal protective equipment (PPE), training, and other factors used to reduce or eliminate potential exposures.

# Quantitative Assessment

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## Instrumentation and Equipment

NIOSH proposes using a tiered methodology for sampling and using existing analytical methods that utilize both particle concentration determinations and particle classification. An example is NIOSH's nanomaterial exposure assessment technique (NEAT) (AIHA 2018). As one source noted, the NEAT can be implemented as follows:

> Three real-time, field portable DRIs (TSI model 3007 condensation particle counter, TSI Model 3330 optical particle counter, and TSI Dust Trak DRX optical particle counter or other comparable equipment) used together characterize process emissions by determining the number or mass concentration and approximate size range of airborne particles (Eastlake et al. 2016).

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Tables 3 and 4 provide details on the application of these options.

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*Table 3: Summary of NIOSH direct-reading, real-time options (AIHA 2018).*

| **Monitors (Equipment)** | **Particles and Properties of Interest** | **Target Nanoparticle Size** | **Sample Matrix** | **Uses** |
|---|---|---|---|---|
| Condensation particle counter | Detects and quantifies particles | 10 nm to 1 µm | Air | Nanoparticle screening |
| Optical particle counter | Detects and quantifies particles (large agglomerates) | 300 nm to 20 µm | Air | Used in conjunction with condensation particle counters |
| Scanning or differential mobility particle sizer (SMPS or DMPS) | Obtains number concentration by size | 10 nm to 10 µm | Air | Understanding background levels and for analyzing counts related to a task |
| Diffusion charger | Measures active surface area concentration | 30 nm up to a micrometer | Air | Measurement of light-duty vehicle emissions |
| Mass-based aerosol photometer (nephelometer) | Measures particle density | µg/ml | Air, liquids | Measuring the concentration of suspended particulates in a liquid or gas colloid (smoke) |
| Nanoparticle surface area monitor | Measures surface area | $\mu m^2/cm^3$ | Air | Measuring the human lung-deposited surface area of particles |
| Electrical low-pressure impactor (ELPI) | Obtains number concentration by size | 6 nm–10 µm at 10-Hz sampling rate | Air | Understanding background levels and for analyzing counts related to a task. |

Commented [AM48]: Adding verbs in this column to keep them all parallel.

*Table 4: Summary of filter-based, active sampling options (NIOSH 2022, AIHA 2018).*

| **Sampling Method** | **Particles and Properties of Interest** | **Analytical Technique, Elemental Microscopy Method** | **Media** | **Uses** |
|---|---|---|---|---|
| NIOSH 5040 | Respirable elemental carbon nanomaterials, CNTs<br><br>Measures the level of soot in workplace environments | Transmission electron microscopy (TEM), high-resolution scanning electron microscopy (SEM), or scanning transmission electron microscopy (STEM)<br><br>Energy dispersive X-ray spectrometry system attached to the transmission electron microscope | Air | Quartz fiber filter (25 mm size ) in a sampling cassette attached to a respirable cyclone and sampling pump.<br><br>Determines the levels of organic carbon (OC), elemental carbon (EC), and total carbon (TC). The amount of EC can relate to the presence of CNTs. |

Commented [BH49]: Yes. This is acceptable.

| Sampling Method | Particles and Properties of Interest | Analytical Technique, Elemental Microscopy Method | Media | Uses |
|---|---|---|---|---|
| | | Thermo-optical analysis; flame ionization detector (FID) for carbon nanotubes | | |
| | Excellent detail of surface morphology and particle size distribution | SEM | Air, solids, and liquids | Elemental analysis by energy-dispersive spectroscopy (EDS) or wavelength dispersive spectroscopy (WDS) |
| | Elemental analysis on even the smallest individual nanoparticles | TEM | Air, solids, and liquids | Used with EDS |
| NIOSH 7300 and 7303<br><br>OSHA ID-206 | Silver | Inductively coupled plasma (ICP)<br><br>ICP mass spectrometry (ICP-MS) | Air | Single particle count with identification for insoluble particles in suspension |
| | | Dynamic light scattering (DLS) with zeta potential | Bulk as powders, liquids | Used to determine the size distribution profile of small particles in suspension. |
| | | Thermogravimetric analysis (TGA) | Solids, liquids | Used to determine composition purity, including the presence of surface coatings |
| | | Spectroscopy (Fourier transform infrared (FTIR/Raman) | Solids, liquids | Absorption/transmission spectroscopy measures how a sample absorbs light at each wavelength. As light passes through the sample, the resulting spectrum represents the molecular absorption and transmission to create a molecular fingerprint of the sample. |
| NIOSH 0500 | $TiO_2$ | Gravimetric (weight) | Air | Identification and quantitation of total airborne particulate matter not otherwise regulated |

Additional measurement methods (equipment) with descriptions and manufacturers are available in NIOSH's (2022) *Occupational Exposure Sampling for Engineered Nanomaterials* paper.

## Controls

The following information specifies types of controls that laboratories should use to protect workers from exposure. OSHA (2013) also has been providing examples of workplace processes and employer type where nanomaterials can be found.

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### Engineering Controls (NIOSH 2022):

- Fume hood (laboratory chemical hood): must keep hood uncluttered and prevent personnel from walking past the nanoparticle handling process while utilizing the hood. The best practice is to use high efficiency particulate air (HEPA) filters and avoid fugitive emissions.
- Biological safety cabinet (BSC) II: promotes the downward flow of filtered air in cabinet and removes HEPA-filtered exhaust.
- Glove box, negative pressure (if only positive pressure is available, then leak tests need to be performed during routine preventive maintenance).

Please note that secondary UNP exposure may occur during the maintenance of ventilation systems.

### Administrative Controls (NIOSH 2022):

- Labels on containers (for transport and storage) of nanomaterials.
- Hazard awareness signage in designated work areas and entrances, chemical storage areas, and cabinets.
- Detailed housekeeping procedures (HEPA vacuum and/or wet method only) with appropriate disposal methods.
- Work practices (e.g., donning and doffing).
- Sticky mats in front of entry way and exit; replace routinely.
- Chemical-specific training, including routes of exposure and potential contamination migration.
- UNP worker registry/medical surveillance offer.

### Personal Protective Equipment (PPE) (NIOSH 2022):

- Minimum PPE includes safety glasses with side shields or goggles, lab coat (or coveralls), and protective gloves.
- Respiratory protection (APR, P-100, or supplied air) as applicable to the particular nano risk."
- Donning and doffing areas separate from work areas and non-nanomaterial processing areas.

Please note that for low-hazard materials with a low exposure risk, the use of cotton or cotton-polyester lab coats or coveralls may provide sufficient protection. Gloves should be selected for their effectiveness in protecting workers from the nanoparticles and other materials being handled.

## Hazard and Control Banding Examples

### Hazard Banding Example

A graded approach to evaluate and control UNP materials should be developed to include both qualitative and quantitative assessment processes. A graded approach should be used to establish similar exposure groups. Listed below are some examples of this approach.

**Commented [JC52]:** Does NIOSH use language this strong when referring to HEPA use?

**Commented [BH53]:** This is correct.

**Commented [CR54]:** Just a thought; disposable lab coats might not be the only option for every scenario. AIHA has a fact sheet "Personal Protective Equipment for Engineered Nanoparticles." In that fact sheet they discuss several potential options for protective clothing:

"For some situations (low hazard material, low exposure risk), use of cotton or cotton-polyester lab coats or coveralls may provide sufficient protection. For higher risk scenarios (high hazard material or high ENP exposure potential), chemical protective clothing should be made from a low dust-retention/low dust-release fabric. Nonwoven textiles (e.g., high-density/airtight polyethylene) can provide a high level of protection".

**Commented [CR55]:** In case we want to go into more detail regarding glove selection.. Also from the 2018 AIHA Fact Sheet on Personal Protective Equipment for Engineered Nanoparticles: Gloves: "Gloves should be selected for their effectiveness against the characteristics of nanoparticles and other materials being handled, also considering other performance requirements (e.g. mechanical or heat challenges.) If suspended in liquids, take into account the resistance of the glove to both the UNP and the liquid."

**Commented [BH56]:** Shane,

Should it say "Respiratory protection (APR, P-100, or supplied air), as applicable to the particular nano risk."

**Commented [BH57]:** Paterick Thayn, PNNL

NIOSH Publication Number 2018-103, *Controlling Health Hazards When Working with Nanomaterials*, provides the following as a suggested grouping to assess hazard risk:

- Dry powder, which typically presents the highest potential for exposures
- Nanomaterials suspended in liquid
- Physically bound/encapsulated nanomaterials, which typically have the lowest potential for exposure.

The following control banding example is by typical laboratory activities when handling UNPs:

**Commented [AM58]:** Does this section actually belong under the next subheading?

- **UNP-Level 1:** This level is intended for laboratories in which the UNPs used most often have negligible potential for aerosol formation. Example nanomaterials are those that, while not meeting the strict definition of "bound" nanoparticles, are present in a matrix (e.g., colloids, solutions, etc.) where no part of the process is anticipated to generate airborne particle emissions.
- **UNP-Level 2:** This level is intended for laboratory activities in which the UNPs used most often are in a dry powder form and in small amounts (e.g., <10 g). These may have a small potential for airborne UNP dissemination during handling. Example laboratory activities are those involving scooping, weighing, transferring, and/or mounting UNP powders on slides.
- **UNP-Level 3:** This level is intended for laboratory activities in which UNPs are used in a manner that is expected to generate aerosolized nanoparticles. Example laboratory activities are those that involve nebulization, grinding, and aggressive agitation of powders or solutions containing UNPs.

**Commented [PT59]:** I think that I need to focus more on quant analysis but I typed this up so thought that I would leave it for review.

UNP materials that present high risk for exposure require further evaluation to properly identify and assess the risk. This subjective evaluation should include a review of workplace factors to gauge the exposure profiles to the hazard levels of the nanomaterials. A risk-ranking process is used to evaluate the exposure concern for each nanomaterial. This risk-ranking process may include factors such as frequency and duration of use, engineering and environmental factors, hazard level of the agent, quantity and concentration, and health effects and target organs. This subjective assessment becomes the basis for hazard controls, monitoring, and medical surveillance and could drive the need for objective evaluation.

An objective evaluation of nanomaterial work activities results in obtaining representative data on workplace exposure and validates compliance or noncompliance with occupational exposure limits. Sampling that represents each shift, for each job classification, and in each work area should be used to develop the quantitative assessment. Statistical evaluation of sample data sets should be used to provide confidence that exposure limits are not exceeded.

## Control Banding (CB) Example

**Commented [BH60]:** John Cala, LLNL

Such a strategy of grouping or "banding" UNP activities by aerosolization potential is an example of *hazard banding*, which can be a useful technique in performing qualitative exposure analyses. This approach can be further built upon to include additional exposure parameters and assign corresponding countermeasures in what is called *control banding*. Lawrence Livermore National Laboratory (LLNL) utilizes this approach for UNP activities through its novel control banding tool, "CB Nanotool." The CB Nanotool assigns a "score" to each UNP activity by combining the "severity" and "probability" input parameters of the assessment. The criteria include particle size, solubility, and parent material toxicity for the severity score; and dustiness potential, frequency of operation, and amount of material for the probability score. There are also default scores given for “unknown” parameters given that academic and medical research on UNPs is limited. The aggregate score places each activity into a risk level category of 1 to 4, which assigns respective engineering controls of (1) general ventilation, (2) local exhaust ventilation or chemical fume hood, (3) containment, or (4) seek specialist advice, as depicted in Figure 3. Figure 4 shows a representative use of LLNL’s CB Nanotool.

| | | Probability | | | |
|---|---|---|---|---|---|
| | | Extremely Unlikely | Less Likely | Likely | Probable |
| Severity | Very High | RL3 | RL3 | RL4 | RL4 |
| | High | RL2 | RL2 | RL3 | RL4 |
| | Medium | RL1 | RL1 | RL2 | RL3 |
| | Low | RL1 | RL1 | RL1 | RL2 |
| RL1: General Ventilation // RL2: Fume Hood or LEV // RL3: Containment/Glovebox // RL4: Seek Specialist Advice | | | | | |

*Figure 3: The CB nanotool risk matrix and respective engineering controls (NIOSH 2012).*

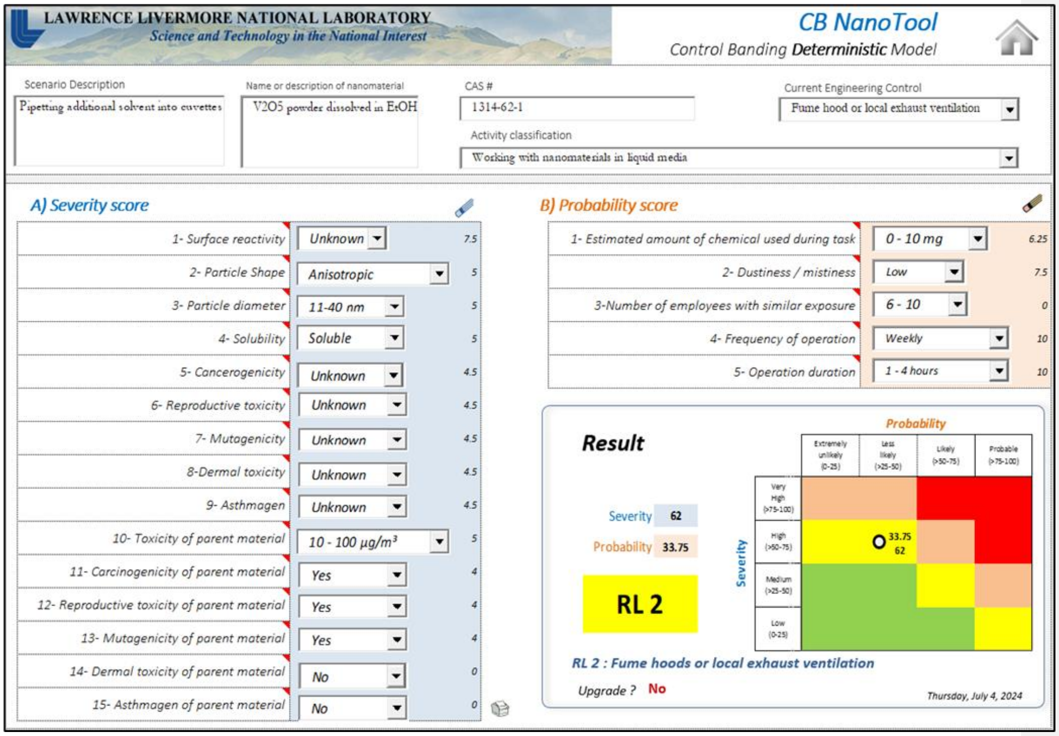


*Figure 4: A completed CB nanotool for a theoretical activity of pipetting dissolved nano vanadium pentoxide. According to the assessment, this activity is RL2 and should take place in a chemical fume hood.*

The LLNL CB Nanotool, along with more detailed descriptions, instructions, and quantitative validation, is available free to the public at https://controlbanding.llnl.gov/.

Both hazard banding and control banding can be helpful strategies for performing exposure analyses of UNP activities, which typically lack existing health information and pose unique challenges to quantitative sampling.

# Order Requirements

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## DOE UNP Registries

It is a requirement within DOE O 456.1 to maintain a UNP worker registry.

The Order requires that sites:

1. Maintain a registry of all personnel who meet the definition of a UNP worker in the order,
2. Use an accessible electronic format,

3. Provide the DOE occupational medicine services provider with a copy of or access to the registry, and
4. Update the registry annually at a minimum.

A UNP worker is defined by the Order as a worker who:

(1) Has the potential for inhalation or dermal exposure to UNPs due to performing work with potential exposure to UNPs; or

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(2) Routinely spends time in an area due to performance of regular duties in which engineered UNPs have the potential to become dispersed in the air or onto surfaces; or

(3) Works on equipment that might contain or bear UNPs that could release UNPs during servicing or maintenance.

The registry entries must include:

1. The UNP worker name,
2. Job title (at the time of being designated a UNP worker),
3. A brief description of the UNP,
4. A brief description of the UNP activity, and
5. The area in which the activity is located.

The use of a registry allows facilities to identify staff who work with UNPs, collect baseline information, describe the health status of UNP workers, and evaluate the effectiveness of health and safety programs as they pertain to UNP work.

UNP worker registries are not centralized or collected at DOE headquarters for analysis. The current number of workers in the registry at each DOE site varies from a few workers (e.g., 10) to many (e.g., 600).

Note: Based on the DOE definition, workers who do not actively use UNPs may still be classified as a UNP worker if there is the potential for exposure based on their job duties. For example, maintenance workers who perform maintenance on equipment contaminated with UNPs would still be classified as UNP workers even though they are not actively using UNPs within the equipment.

**Commented [RC63]:** Trying to address the misconception that an UNP worker is only someone who is actively performing work with the UNP...

If sharing chemical hoods, ventilated enclosures, or other local exhaust ventilation (LEV) with non-UNP workers, a thorough cleaning procedure should be followed to decontaminate shared areas and equipment left in the chemical hood or LEV before they are used by non-UNP workers. Workers potentially exposed to UNPs need to be identified and added to the UNP registry.

## Medical Surveillance

**Commented [BH64]:** Witter, Roxana <Roxana.Witter@nrel.gov>

DOE O 456.1 dictates that UNP workers be offered medical surveillance including the following:

- An occupational and medical history update,
- A physical examination with emphasis on the respiratory system, and
- Specific medical tests (e.g., spirometry, chest X-ray) deemed appropriate by the occupational medicine provider.

**DOE Medical Surveillance Program Examples**

Different DOE sites have taken slightly different approaches to medical surveillance. While the sites each include the required components as outlined in DOE O456.1, the frequency of the exams and additional components vary by site.

**Frequency ranges offered by different sites**:

- Baseline only

OR

- Baseline + annual for all nano workers

OR

- Baseline + every 3 years for all workers

OR

- Baseline + annual for nano workers with high risk (i.e., exposure to CNTs & CNFs)
- Baseline + every 3 years for nano workers not using high-risk materials.

**Components of standard nanoparticle medical surveillance exams offered by all sites:**

- Medical history
- Occupational history
- General physical exam, medical /occupational history review, and work and exposure control review with onsite physician
- Pulmonary function test (spirometry)

**Examples of additional exam components offered by some sites:**

- Chest X-ray at baseline
- Chest X-ray at baseline and repeat chest X-ray if clinically appropriate (e.g., abnormal baseline chest X-ray, abnormal spirometry, symptom development)
- Bloodwork (e.g., CBC [complete blood count], chemistry and metabolic panel, lipid profile)
- Urinalysis

With a few exceptions, the health impacts of nanoparticles are largely unknown (NIOSH 2022). Health impacts could occur due to chemical interactions within biological processes. These chemical interactions could be similar to the health impacts of the bulk materials (e.g., Ni nanoparticles causing allergic reactions similar to bulk nickel) (Tsuchida et al., 2023); or different from the same materials in bulk form due to the special physical characteristics of nanoparticles (e.g., $TiO_2$ induces reactive oxidative species) (Grande & Tucci, 2016).

Nanoparticles may also have different health impacts due to differences in bioavailability (e.g., brain deposition via olfactory nerve; penetration through skin) (Garcia et al., 2015; Nafisi et al., 2018). Nanoparticles may have health impacts that are like materials of similar shape but not related at all chemically (e.g., carbon nanotubes similar to asbestos) (Gupta et al., 2022). To date, biological exposure limits have been recommended for carbon nanotubes and titanium dioxide, but no biological exposure indices (BEIs) have been established for any other nanoparticles (ACGIH 2024). Commercial medical tests are not sensitive enough to detect nanoparticles in the blood or urine.

# Conclusions

This guide provides key aspects for conducting nanoparticle exposure assessments. These include (1) the determination of bound vs. unbound nanoparticles, (2) materials of concern, (3) NIOSH recommendations for sampling, (4) control recommendations, (5) hazard and control banding examples, (6) health effects, (7) UNP worker registry requirements, and (8) medical surveillance practices. Appling these recommendations and practices can provide an in-depth exposure assessment and will help you establish an affective UNP health and safety program at your laboratory that complies with DOE Order 456.1A.

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