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**APPROACHES FOR ASSESSING AND CONTROLLING WORKPLACE
RELEASES AND EXPOSURES TO NEW AND EXISTING NANOMATERIALS**

Chemical Engineering Branch (CEB)
Economics, Exposure and Technology Division
Office of Pollution Prevention and Toxics
Environmental Protection Agency

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PURPOSE

This draft document revises and updates the previous approaches recommended by the Chemical Engineering Branch (CEB) of EPA's Office of Pollution Prevention and Toxics (OPPT) in its draft document dated June 2006, for assessing, monitoring, and controlling releases and exposures to new and existing nanomaterials¹ in the workplace. (See Appendix A for information on the definitions and descriptions of nanomaterials.)

The document focuses primarily on CEB's methodology for evaluating Pre-Manufacture Notice (PMN) nanomaterials within OPPT's New Chemicals Program (NCP). Because of the swiftly changing and challenging nature of nanotechnology, this document represents interim approaches that are based on the best available information to date in the specific areas that it addresses.

The document addresses:

- I. Release and Exposure Assessment.
- II. Inhalation Monitoring.
- III. Engineering Controls
- IV. Personal Protective Equipment (PPE).

The Appendices at the end of this document provide more details for specific topic areas and summarize some issues related to workplace release and exposure assessments for nanomaterials. Some special considerations for nanomaterials, including toxicity, routes of exposure, exposure metrics, and factors affecting exposure are provided in Appendix B.

INTRODUCTION

In the U.S., interim approaches and recommendations for release and exposure assessment as well as control approaches for minimizing workplace exposures to nanomaterials have been developed primarily by the National Institute for Occupational Safety and Health (NIOSH). Several federal agencies with a range of research and regulatory roles and responsibilities are also involved in comprehensive interagency nanotechnology research and development programs like the National Nanotechnology Initiative (NNI). To develop its own internal policies and approaches for nanomaterials, CEB relies, for the most part, on published guidance from NIOSH on nanomaterial assessment and control issues. CEB also incorporates protective requirements from relevant OSHA standards (e.g., respiratory protection in accordance with 29 CFR 1910.134) as well as testing information from standard setting organizations like the ASTM.

¹ In accordance with the convention used by the National Institute for Occupational Safety and Health (NIOSH) in some of its recent guidance, the term "nanomaterials" or "nanoparticles" is used in this document to identify intentionally produced or engineered nanomaterials/nanoparticles and to distinguish between engineered (nanoparticle) and incidental (ultrafine) nanoscale particles; the latter are typically byproducts of processes such as combustion and vaporization. However, this does not imply differences in the properties of these particles as related to hazard assessment, measurement, or control of exposures.

I. Release and Exposure Assessment

CEB's methods, both qualitative and quantitative, for assessing potential workplace releases of and exposure to nanomaterials are currently similar to those used for bulk materials. These estimation approaches have been used for a number of reasons, including limited understanding of the toxicity, worker exposure levels, and associated measurement techniques for nanomaterials. Worker exposure evaluations of nanomaterials to date have been solely for Toxic Substances Control Act (TSCA) section 5 purposes, in which EPA employs screening level approaches for estimating worker exposures to new chemical substances for which data are rarely available. CEB applies its standard methods for bulk-sized materials contained in ChemSTEER, a screening tool, for estimating mass-based releases of and exposures to nanomaterials. Information on EPA's approaches and the primary worker exposure estimation tool (Chemical Screening Tool for Exposures and Environmental Releases, ChemSTEER) is available on EPA's public website at <http://www.epa.gov/oppt/exposure/and> <http://www.epa.gov/oppt/exposure/pubs/chemsteer.htm>.

One limitation of the use of ChemSTEER models is that they generally produce conservative, and in some instances bounding estimates of occupational exposure and environmental releases. At this time, CEB only generates mass-based values for assessment of release (kg/site-day or kg/yr) and exposure (mg/day) to nanomaterials. Current EPA risk evaluations by RAD use mass-based concentrations for inhalation estimates, where the units used are micrograms or milligrams per cubic meter ($\mu\text{g}/\text{m}^3$ or mg/m^3) as an 8-hour time-weighted average (TWA).

Workplace Releases

Although CEB currently applies its standard methods for estimating mass-based releases of bulk-sized materials to nanomaterials, it may choose to deviate from them if submitters provide good quality estimates for site-specific releases of nanomaterials. Sometimes CEB does not assess releases for non-nano materials, either because the release is small (e.g., sampling waste, dust emission from unloading bags, etc.) and is expected to make a relatively insignificant contribution to total releases, and/ or because CEB has no estimation method for a release, and/or because the release is expected to be below a NCP "trigger" amount (i.e., < 5,000 kg/site-yr to land) for which release assessment is not needed for risk assessment. The decision not to assess some releases has been reconsidered for new chemical cases involving nanomaterials, and it is CEB's intent to estimate all releases in nano cases (or alternately, to make note of a release that cannot be quantified).

Workplace Exposures

Workers are likely to have earlier and higher exposures than the general population/consumers during activities involving the manufacturing, processing, and use of nanomaterials. (See Appendix C for processes and operations during which worker exposure to nanoparticles can occur). While dermal absorption and ingestion are potential entry routes for engineered NM, the inhalation route appears to be the most important route for workplace exposure and has also received the most attention (Bergamaschi et al. 2006; Donaldson et al. 2006). (See Appendix B for further information on routes of exposures for nanomaterials.)

EPA prefers to use the following hierarchy to obtain/generate data on worker exposures to chemical substances, which also applies to nanomaterials:

1. Personal monitoring data for exposure to the chemical of interest in the workplace of interest;
2. Personal monitoring data for the chemical of interest in a workplace situation that is similar to the workplace of interest (surrogate workplace situation) OR personal monitoring data for a chemical that is similar to the chemical of interest in the workplace of interest (surrogate chemical);
3. Modeled estimates or concentration assumptions based on regulatory limits.

Several hurdles exist currently to obtaining personal monitoring data which can be used for exposure assessment to all nanomaterials (see discussion under *Inhalation Monitoring Methods*, in Section II, *Inhalation Monitoring* below), including lack of appropriate sampling methods².

Surrogate data has been used for single-walled carbon nanotube material (SWCNT) from a laboratory based study by Maynard et al. (2004) that looked at mechanical agitation, complemented with airborne and dermal exposure while handling unrefined material. Handling resulted in very low airborne concentrations (from 0.7–53 $\mu\text{g}/\text{m}^3$), consistent with the tendency on the SWCNTs to aggregate into larger masses (Maynard et al. 2004). EPA has used the highest concentration determined (53 $\mu\text{g}/\text{m}^3$) in several new chemical cases as tier 2 surrogate data where chemical substances and workplace activities have seemed to match well to those documented in the study.

In most new chemicals cases, the limited amount of applicable literature data leads EPA to employ standard screening methods for estimating particulate exposures. Several of the primary screening methods for estimation dust exposures include the tier 2 “Small Volume Solids Handling Inhalation Model” and tier 3 “OSHA Permissible Exposure Limit (PEL) for Particulate, Not Otherwise Regulated (PNOR), total and respirable particulate” models. Also, several primary screening methods for estimation aerosol exposures in “end-use” scenarios (e.g., liquid spraying or roll coating mist generation) include the tier 2 “UV Roll Coating Inhalation Model (non-volatiles)” and tier 2 “Automobile Spray Coating Inhalation Exposure Model (non-volatile non-polyisocyanates)” models. EPA also uses a suite of standard dermal exposure models to estimate dermal exposures (in mg/day) to nanomaterials. These inhalation and dermal models are documented in the ChemSTEER help system.

Key information and data needed to use these models includes including throughput volumes of materials in kg/day, operating days in days/yr, physical states and concentrations of the nanomaterial of interest at key stages of handling, worker activities with exposure potential, and number of workers for each of these activities. This information is requested in the Premanufacture Notice Form (Form 7710–25).

² For carbon nanotubes (CNTs) and carbon nanofibers (CNFs), recent NIOSH guidance (NIOSH, 2010) recommends use of NIOSH method 5040 with appropriate caveats.

CEB does not typically assess the potential for ingestion. However, it should be noted that although ingestion is likely to be less significant than the inhalation and dermal exposure routes, it can occur in industrial settings. A primary route of ingestion is expected to be unintentional hand to mouth transfer of materials. This occurs with materials other than nanomaterials and it is therefore reasonable to assume it can occur during handling of materials that contain nanoparticles (NIOSH 2009).

Some limited workplace monitoring data are available in the literature for carbon nanotubes, and CEB may examine such 'surrogate' data if the chemicals and workplaces are comparable from an exposure standpoint (e.g., nanomaterials have comparable physical-chemical properties, are handled similarly, processes and throughputs are comparable, etc.).

Engineering Report Assessment Logic for Nanomaterials

The engineering report contains assessments of workplace releases and exposures. For each new chemical case, an Initial Review Engineering Report (IRER) is normally completed prior to the internal OPPT Focus meeting after completing the assessments outlined in the following logic steps for release as well as inhalation and dermal exposure:

Basic Release Assessment Logic

Is a release assessment needed per SAT or NCP policy?

If **Yes**, is there potential for releases of nanomaterials?

If No, then indicate and give rationale in Engineering Report (IRER).

If **Yes**, make a full list of release sources (including disposal of PPE, samples, dusting to air, etc.). Can releases from these sources be estimated in mass-based and other metrics* (e.g., surface area and number of particles) to the media (e.g., air, water, incineration, and land) requested by SAT or by Nano NCP Decision Logic? (Note: SAT or NCP decision logic for metrics and media to assess for nano cases will be followed; if not otherwise specified, CEB assesses mass-based metrics only and all media.)

If No (for a source or metric type), then indicate and explain in IRER (qualitative) either in the introductory notes to the release summary for the operation or in the basis box of the mass-based release estimate.

If **Yes** (for a source and metric type), include estimated releases in mass units and/ or other metrics* in IRER (quantitative); for other metrics, include the estimate in the basis box of the mass-based release estimate.

Basic Inhalation Exposure Assessment Logic

Is an inhalation assessment needed per SAT or NCP policy?

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If **Yes**, is there potential for inhalation of airborne nanomaterials?

If **No**, then indicate and give rationale in Engineering Report (IRER).

If **Yes**, can the potential dose rate (PDR) and other metrics (e.g., surface area and number of particles) requested by SAT or by Nano NCP Decision Logic be estimated? (Note: SAT or NCP decision logic for metrics to assess for nano cases will be followed; if not otherwise specified, CEB assesses mass-based metrics only.)

If **No** (for a metric type), then indicate and explain in IRER (qualitative) either in the introductory notes to the inhalation summary for the operation or in the basis box of the mass-based inhalation exposure estimate.

If **Yes** (for a metric type), include estimated PDR and/ or other metrics* in IRER (quantitative); for other metrics, include the estimate in the basis box of the mass-based inhalation exposure estimate.

* Note: Methods for estimating other metrics (e.g., surface area and number of particles) to include along with PDR do not currently exist. These methods would have to be developed to have a quantitative option for these metrics.

Currently, RAD has requested the percent of the inhaled particulate in the respirable size range and the inhalation concentration in mg/m³ of respirable particles be included, and these data should be included in the Introductory Notes to the Inhalation Summary text box (or in the estimate in the basis box of the mass-based inhalation exposure PDR estimate). Where particle size distribution is not known or not well understood, rules of thumb for estimating percent of particulates in the respirable size range are to assume all particles up to 5 mg/m³ TWA (OSHA's respirable PNOR PEL) may be respirable, and the remainder above 5 mg/m³ is not respirable.

Also, RAD has requested information on whether the nanomaterial being assessed may exist as free particles or agglomerates, whether the nanomaterial is bound in a matrix (e.g., resin dust containing PMN), or both. Such a description should be included in the Introductory Notes to the Inhalation Summary text box.

Basic Inhalation Exposure Assessment Logic for CNT Manufacturing

1. Do worker activities involve 'open-air' handling (e.g., loading/ unloading of containers/ bags) of CNTs at > 54 kg/site-day AND/ OR proximity to unenclosed processes that may create a potentially significant amount of dust (e.g., cutting, grinding, milling)?

If **Yes**, use OSHA Total PNOR PEL-Limiting Model to estimate total particulate exposure, and/ or use OSHA Respirable PNOR PEL-Limiting Model to estimate respirable particulate exposure.

2. If answer to 1. was **No**, do worker activities involve 'open-air' manual transfers of CNTs from one container to another at < 54 kg/site-day?

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If **Yes**, use EPA/OPPT Small Volume Solids Handling Inhalation Model to estimate particulate exposure, where up to the entire exposure may be respirable.

3. If answers to 1. and 2. were **No**, do worker activities involve 'incidental' particulate exposures from activities such as:

- opening glove box where CNTs were handled to move sealed containers of CNTs
- handling CNTs in a fume hood
- sonication of CNTs in a liquid suspension
- other activities not expected to create a significant amount of dust

If **Yes**, use highest value ("53 ug/m³") of Maynard et al 2004 estimates³ of CNTs to estimate particulate exposure, where up to the entire exposure may be respirable.

It is recommended that the Maynard data (53 ug/m³) be used in limited number of "low dust" activities where we think that some small particulate exposures may occur but have no better method to estimate exposures during the activities. Caution is required in applying the limit of 53 ug/m³ as the upper limit of exposure in all cases that fit the logic above for application of the Maynard et al 2004 estimate because the exposure potential would be process and production volume dependant as well as activity specific.⁴ Also, it cannot be assumed that a laboratory-based method of aerosol generation, as used in by Maynard et al. provides a definitive characterization of workplace-related processes.

Some limited data from the most recent NIOSH draft publication on CNTs and CNFs⁵ seems to indicate that higher levels of worker exposure are possible besides the ones estimated by Maynard et al in 2004 during certain settings or activities. CEB in the process of compiling data from these studies and associating estimated worker exposure concentrations with specific production processes or activities. This exercise is aimed at obtaining information from more recent studies than the 2004 Maynard et al. study to evaluate if CEB needs to adjust its decision logic to better reflect current understanding of worker exposure levels during CNT/CNF manufacturing, handling, and other associated activities.

³ Maynard et al studied exposure to carbon nanotube material during handling of SWCNTs during two SWCNT production processes - laser ablation and HiPCO at 4 facilities. About 30 min/ sample (events recorded during period). Fe and Ni were used as surrogates to estimate CNT concentrations, assuming same combined Fe and Ni catalyst fraction (based on 30% Fe catalyst in a HiPCO run immediately prior to one of the monitored activities) and expectation of essentially no variation in catalyst (actual expected variation of within +/- 5% for either production runs or mfg techniques). CNT concentrations estimated are TWA over sample period. Article contains no info on CNT throughputs or specific amounts of CNTs handled.

⁴ Although the metal content of CNTs in the Maynard study were believed to be quite consistent (within +/- 5% -- see footnote above), it is not known whether the same range could potentially apply in other workplaces where a similar extrapolation from metal level to CNT level is used for assessing exposure levels because the amount of Fe and Ni, including other metal content like Co, associated with CNTs varies considerably. Per Maynard et al., "Both the laser ablation material and the HiPCO raw products can contain up to 30% metal catalyst by mass." Also, the 2004 Maynard et al. study focused on harvesting of the product and reactor cleaning and down-stream use activities, e.g. agitation were only monitored for research scale activities.

⁵ NIOSH, 2010. Occupational Exposure to Carbon Nanotubes and Nanofibers. Current Intelligence Bulletin (Draft). November 2010.

If particle size data for the operation is available, we may need to consider deviations from the heuristics. For example, if representative samples of workplace air show a complete absence of particles below 10 um, then respirable inhalation exposures are negligible. Also, it seems that we could extrapolate SWCNT data to apply to all CNT manufacturing and possibly even CNF (carbon nanofiber) manufacturing unless other indicators arise to suggest that such extrapolation is invalid or not advisable.

[Placeholder – additional data/summary results to be added for CNT/CNF exposure assessment using activity-specific surrogate exposure values]

Basic Dermal Exposure Assessment Logic

Is a dermal assessment needed per SAT or NCP policy?

If **Yes**, is there potential for dermal exposure to nanomaterials?

If No, then indicate and give rationale in Engineering Report (IRER).

If **Yes**, can the potential dose rate (PDR) and other metrics* (e.g., surface area and number of particles) requested by SAT or by Nano NCP Decision Logic be estimated? (Note: SAT or NCP decision logic for metrics to assess for nano cases will be followed; if not otherwise specified, CEB assesses mass-based metrics only.)

If No (for a metric type), then indicate and explain in IRER (qualitative) either in the introductory notes to the dermal summary for the operation or in the basis box of the mass-based dermal exposure estimate.

If **Yes** (for a metric type), include estimated PDR and/ or other metrics* in IRER (quantitative); for other metrics, include the estimate in the basis box of the mass-based dermal exposure estimate.

* Note: Methods for estimating other metrics (e.g., surface area and number of particles) to include along with PDR do not currently exist. These methods would have to be developed to have a quantitative option for these metrics.

Additional Information EPA Could Request From Submitters

EPA can request some additional information, generally during the Standard Review process, to supplement the information requested in the PMN form and instructions for New Chemicals submissions. This is done when the additional information is necessary for estimations of releases and exposures to nanomaterials and/or to understand and characterize controls affecting releases and exposures. The evaluation of the information would be noted in the Standard Review Engineering Report (SRER) in the Notes and Key Assumptions section of the report. If new information is requested but not received or not relevant and no other factors impact the original release and exposure assessments, the original IRER is amended to add the contact

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report in which the request was made and a notation is made in the Notes and Key Assumptions section of the report indicating non-receipt or non-relevancy.

Once a case has entered the NCP Standard Review process, some additional information requests could include some or all of the following information:

- Provide a rationale for selecting the protective equipment or engineering controls and note any testing or data (and methods used to generate the data) that were used in making the selection and may help to indicate the effectiveness of the protective equipment or engineering controls.⁶
- Provide information regarding the disposal of used protective equipment (e.g., gloves, respirator filter cartridges) that may have contacted the nanoscale material. Note any procedures or other equipment intended to mitigate exposures to the nanoscale material.
- Provide a summary of any personal or area monitoring data (in mass concentrations, surface area per mass, number of particles, etc.) or associated metrics such as average particle weight and average particle size for the nanoscale material, including the measurement method(s) used to generate the data; provide a copy of the full study containing the data as an appendix. Briefly describe worker training and hazard communication (MSDS, other) specific to the nanoscale material.
- Provide a rationale for selecting the controls, and include a summary of information such as data and methods of waste treatment efficiency studies and associated metrics such as average particle weight and average particle size for the nanoscale material; provide a copy of the full study containing the data as an appendix.⁷

CEB's Current Data Needs for Nanomaterials

Although CEB obtains information and data from PMN forms for a number of key aspects (e.g., particle characteristics, production volume, number of sites) that are essential for assessing releases and exposures to nanomaterials, several outstanding data needs (See Appendix D) related to releases, treatment, occupational exposures, engineering controls, personal protective equipment (PPE), and occupational exposure limits (OELs) still need to be addressed for more accurate estimation of releases and workplace exposure.

CEB is working with other EETD branches to develop a Strategic Plan to document the data gaps and needs and to evaluate how existing tools and programs like PMNs, Test Rules, OECD WPMN, ORD Research etc. can be used to address the data needs.

⁶ For protective equipment and engineering controls included in Part II, Section A.2., column 3 and in Part II, Section B.2., column 6 of the PMN form.

⁷ For control technologies included in Part II, Section A.2., column 5a and in Part II, Section B.2., column 12 of the PMN form.

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II. Inhalation Monitoring

When potential worker inhalation exposures are uncertain but are estimated to be above a threshold of concern (in mg/m³) specified by RAD or CCD, inhalation monitoring may help to reduce uncertainty. In general, PMN submitters subject to a §5(e) Consent Order (or persons subject to a section 5 Significant New Use Rule (SNUR)) have the option to conduct monitoring after manufacture of the PMN substance has commenced and to make a case for removal/adjustment of the PPE requirements based on how site monitoring results compare to the New Chemical Exposure Limits (NCEs) derived by OPPT.

Inhalation Monitoring Methods

There are currently no national or international consensus standards on measurement techniques for nanomaterials in the workplace. NIOSH researchers have developed and used a field assessment strategy by using the Nanoparticle Emission Assessment Technique (NEAT) for determining exposures to engineered nanoparticles that could be used for the evaluation of occupational exposures (Methner, et. al. 2007; Methner, 2008) NEAT allows a semiquantitative evaluation of processes and tasks in the workplace where releases of engineered nanoparticles may occur. NIOSH researchers use several sampling approaches simultaneously with the goal of obtaining key physicochemical particle metrics: number concentration, qualitative size, shape, degree of agglomeration, and mass concentration of elemental constituents of interest. This technique is available in an Appendix titled “Nanoparticle Emission Assessment Technique for Identification of Sources and Releases of Engineered Nanomaterials” in a recent NIOSH guidance document (NIOSH, 2009; at: <http://www.cdc.gov/niosh/docs/2009-125/pdfs/2009-125.pdf>).

Although the NEAT technique presents a framework for semi-quantitative estimation of worker exposure to NPs, communication with a NIOSH industrial hygienist and team leader for NIOSH site visits indicates that the state of instrumentation in terms of their limitations, lack of validated sampling and analytical methods, inability to separate dust/water droplets (as in sonication) from nanomaterials, problems in interpretation of data, as well as availability of consultants who know how/what has to be measured, are all deterrents in asking for monitoring data for nanomaterials from submitters and developing guidelines for such monitoring.⁸ However, use of NIOSH sampling method 5040, with some associated limitations and caveats, has been recommended by NIOSH for estimating personal exposure of workers to CNTs and CNFs in the more recent draft guidance in the form of a Current Intelligence Bulletin⁹ that NIOSH released in November 2010.

CEB is evaluating the 2009 NIOSH guidance and the 2010 NIOSH draft CIB (NIOSH, 2010), to determine whether monitoring protocols outlined by NIOSH can be used by the New Chemicals Program to direct submitters to perform inhalation monitoring to demonstrate lower workplace exposure levels than those estimated by CEB.

⁸ Phone conversation with Mark Methner, PhD, CIH, of NIOSH on March 3, 2010.

⁹ NIOSH, 2010. Occupational Exposure to Carbon Nanotubes and Nanofibers. Current Intelligence Bulletin (Draft). November 2010.

Inhalation Exposure Monitoring Request Logic

The current "standard" decision logic that includes mass-based criteria is shown in the engineering report (IRER), and this logic is completed for each workplace inhalation exposure assessed.

Currently, CEB has no other criteria for nano cases beyond those in the standard decision logic. If it is determined in the future that other criteria are warranted for nano cases, they will be added to the logic.

The initial review engineering report (IRER) containing the release and exposure assessments completed as noted above for the Focus meeting contains the inhalation exposure monitoring request logic results.

If the Logic yields a "Yes" for requesting inhalation monitoring AND NCP determines a need to implement this request in a nano case, the NCP must provide CEB with the metrics (e.g., mass basis, surface area basis, etc.) needed for the monitoring to be requested.

III. Engineering Controls

In the hierarchy of exposure reduction methods, engineering controls are preferred over personal protective equipment (PPE). However, any CEB requirement that submitters use engineering controls for new chemicals, including nanomaterials, has historically been infrequent compared to the CEB requirement for PPE use to control workplace exposures. When assessing Premanufacture Notifications (PMNs) for new chemical substances, PPE is often required to provide an adequate margin of protection to the workers because CEB cannot make a remote assessment of the presence or effectiveness of engineering controls on existing, or potentially new work sites, especially for worksites that are not under the submitters control.

For most processes and job tasks, the control of airborne exposure to nanoaerosols can be accomplished using a wide variety of engineering control techniques similar to those used in reducing exposure to general aerosols. Engineering control techniques such as source enclosure (i.e., isolating the generation source from the worker) and local exhaust ventilation systems should be effective for capturing airborne nanoparticles. Current knowledge indicates that a well-designed exhaust system with a high-efficiency particulate air (HEPA) filter should effectively remove nanoparticles (NIOSH, 2009).

While enclosed environments employed for manufacturing and handling nanomaterials can virtually eliminate potential for exposure during normal operations, one recent study (Tsai et al., 2010) indicates that NP exposures can occur during some workers activities that involve use of some dry powdered NMs in various fume hoods. Potential for exposure still exists during maintenance on equipment used to produce or fabricate nanomaterials, during the cleaning of dust collection systems used to capture nanoparticles in ventilation systems, and the clean-up of spills or waste material.

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If worker exposure to nanoparticles remains a concern after instituting measures to control exposure, the use of respirators and other PPE can further reduce worker exposures.

IV. Personal Protective Equipment (PPE)

Respirators and other PPE may be necessary when engineering and administrative controls do not adequately prevent exposures. Typically, the use of respirators is required if the workplace exposure concentration (in mg/m^3) generated by ChemSTEER exceeds the New Chemical Exposure Limit (NCEL) that has been derived for the chemical substance by OPPT.

Currently, there are no specific regulatory occupational exposure limits (OELs) for airborne exposures to engineered nanoparticles although OELs exist for larger particles of similar chemical composition. However, there is a NIOSH recommend exposure limit (REL) of $1.5 \text{ mg}/\text{m}^3$ for fine particles and a REL of $0.1 \text{ mg}/\text{m}^3$ for ultrafine particles (NIOSH, 2007) for titanium dioxide and NIOSH has also released a REL of $7 \text{ micrograms}/\text{m}^3$ for respirable CNT/CNF in a current intelligence bulletin on which it is seeking comments (NIOSH, 2010). It should be recognized that exposure limits recommended for non-nanoscale particles may not be health protective for nanoparticle exposures (e.g., the OSHA Permissible Exposure Limit (PEL) for graphite may not be a safe exposure limit for carbon nanotubes) (NIOSH, 2009).

Respirators

Preliminary evidence shows that for respirator filtration media there is no deviation from the classical single-fiber theory for particulates as small as 2.5 nm in diameter. The results obtained for filter media have been recently confirmed for NIOSH-approved N95 and P100, and European certified CE-marked FFP2 and FFP3 filtering facepiece respirators which captured nanoparticles as small as 4 nm diameter size more efficiently than larger size particles (Rengasamy et al. 2008; Rengasamy et al. 2009). No evidence for the thermal rebound for particles in the 4 nm diameter was obtained. Nanoparticle leakage through respirator face seal is an important component of respiratory protection. This issue was addressed by measuring the total inward leakage (TIL) for nanoparticles and larger size particles at different breathing flow rates and artificial leak sizes using a manikin (Rengasamy et al. 2011). The results showed that the TIL for 50 nm size particles was ~2-fold higher than the values for larger size (400 nm) particles at smaller leak sizes. This indicates that higher concentration of nanoparticles could occur inside the breathing area of respirators in workplaces where nanoparticles in the most penetrating particle size range are present when leakage is minimal compared to filter penetration. *NIOSH certified respirators are expected to protect workers from nanoparticle inhalation when properly selected and fit tested as a part of a complete respiratory protection program (NIOSH, 2009).*

For new nanomaterial cases that have no NCEL or similar exposure reference value, when respirator use is indicated after evaluation of the exposure data, OPPT typically will require in a §5(e) Consent Order the use of a full facepiece air purifying respirator with P100 (or N100/R100) cartridges. For new nanomaterial cases that have a NCEL or similar exposure reference value, when respirator use is indicated after evaluation of the exposure data, submitters must use respirators that meet the APF requirements assessed to be suitable by the NCP to

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protect workers. These respirators are selected by CEB from the OPPT Respirator Selection Logic which is based on the current OSHA APFs, per 29 CFR 1910.134.

Gloves

Gloves may be required to reduce dermal exposure when the engineering assessment indicates potential for dermal exposure. In general, dermal exposures to chemicals during glove use can occur because of permeation, penetration, and activity-specific conditions. An example of the activity-specific condition component would be dust from the air around the worker floating in between the glove and hand. Another example would be solid or liquid material making its way into gloves in the course of routine activities (e.g., handling material or surfaces contaminated with material) by the worker.

Although specific guidelines exist for the testing and selection of glove materials for dermal protection against bulk chemicals, no guidelines are currently available on the selection of clothing or other apparel (e.g. gloves) for prevention of dermal exposure to nanoaerosols. This is due in part to minimal data being available on the efficacy of existing protective clothing, including gloves.

However, some clothing standards like the ASTM standard F1671–03 (ASTM 2003) and ISO standard 16604 (ISO 2004b) incorporate testing with nanoscale particles and therefore provide some indication of the effectiveness of protective clothing with regard to nanoparticles. NIOSH is currently conducting laboratory research on test methods to determine particle penetration through fabrics used into protective clothing and ensembles (NIOSH, 2009).

Permeation Testing for Gloves

Currently, NCP allows submitters to select gloves but sometimes requires up-front permeation testing. The current CEB draft criteria require the following types of permeation testing for nanomaterials:

For any handling steps where the nanomaterial is in particulate form (e.g., powders, crystals, granules, etc.), or in a suspension with pure water and insoluble in water, gloves must be comprised of material that successfully passes ASTM F-1671. (Note: EPA may consider ASTM F-1671 testing to be adequate for some dilute aqueous suspensions on a case-by-case basis.)

For any handling steps where the nanomaterial is part of a carrier liquid/solvent other than the aqueous suspension noted in the previous paragraph, gloves must be comprised of material that successfully passes ASTM F-739 (continuous liquid contact method). Gloves must be changed before the breakthrough time for the carrier liquid (as determined by the ASTM F-739 testing or by the manufacturer).

Also applicable are general best practices for worker glove use (that would apply to all PMN cases with glove restrictions):

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-Gloves must be discarded and replaced with such frequency as to ensure that they will reliably provide an impervious barrier to the chemical substances under normal and expected conditions of exposure within the work area.

-Damaged or defective gloves must not be used.

-The glove manufacturer's care and maintenance instructions for the gloves must be followed.

LoREx Criteria for PPE Use

Note that the above mentioned requirements for respiratory protection and up-front permeation testing for gloves have been adapted for LoREx cases as follows:

When evaluating Lorex cases with potential nano-sized components, we consider worker exposure criteria to be met if there is no potential for inhalation or dermal exposure to the nanomaterial.

In cases where the potential for inhalation and/or dermal exposure exists during specific activities or handling of the nanomaterial, respiratory and/or dermal protection in accordance with the following draft criteria is required for worker exposure criteria to be met:

1. For worker activities where there is potential for inhalation of particulate/aerosol of the notified nanomaterial, the current draft criteria require use of a full facepiece particulate/aerosol air-purifying respirator with P100 (or N100/ R100) filter cartridges, at a minimum.

2. For worker activities where there is potential for dermal exposure to the notified nanomaterial, gloves that meet the current draft criteria, as applicable, must be used:

- For any handling steps where the nanomaterial is in particulate form (e.g., powders, crystals, granules, etc.), or in a suspension with pure water and insoluble in water, gloves comprised of a material that successfully passes ASTM F-1671 testing must be used. (Note: EPA may consider ASTM F-1671 testing to be adequate for some dilute aqueous suspensions on a case-by-case basis.)

- For any handling steps where the nanomaterial is part of a carrier liquid/solvent other than the aqueous suspension noted in the previous paragraph, gloves comprised of material that successfully passes ASTM F-739 testing (continuous liquid contact method) must be used. Gloves must be changed before the breakthrough time for the carrier liquid (as determined by the ASTM F-739 testing or by the manufacturer).

Also applicable are general best practices for worker glove use (that would apply to all PMN cases with glove restrictions):

-Gloves must be discarded and replaced with such frequency as to ensure that they will reliably provide an impervious barrier to the chemical substances under normal and expected conditions of exposure within the work area.

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- Damaged or defective gloves must not be used.
- The glove manufacturer's care and maintenance instructions for the gloves must be followed.

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APPENDIX A

NANOMATERIAL DEFINITIONS AND DESCRIPTIONS

NIOSH Definitions and Descriptions (NIOSH, 2009)

Engineered Nanoparticles and Ultrafine Particles

Engineered nanoparticles are intentionally produced, whereas ultrafine particles (often referred to as incidental nanoparticles) are typically byproducts of processes such as combustion and vaporization. Engineered nanoparticles are designed with very specific properties or compositions (e.g., shape, size, surface properties, and chemistry). Incidental nanoparticles are generated in a relatively uncontrolled manner and are usually physically and chemically heterogeneous compared with engineered nanoparticles.

The two terms **nanoparticle** and **ultrafine** are sometimes used to differentiate between engineered (*nanoparticle*) and incidental (*ultrafine*) nanoscale particles, however, nanoparticle and ultrafine particle are not rigid definitions.

It is currently unclear whether the use of source-based definitions of nanoparticles and ultrafine particles is justified from a safety and health perspective. This is particularly the case where data on non-engineered, nanometer-diameter particles are of direct relevance to the impact of engineered particles. Also, the use of the term *nanoparticle or ultrafine* does not necessarily imply specific differences in the properties of these particles as related to hazard assessment, measurement, or control of exposures. For example, since the term *ultrafine* has been in existence longer, some intentionally produced particles with primary particle sizes in the nanosize range (e.g., TiO₂) are often called *ultrafine* in the literature.

Agglomerate

An **agglomerate** is a group of nanoparticles held together by relatively weak forces, including van der Waals forces, electrostatic forces, and surface tension (ISO, 2006).

Aggregate

An **aggregate** is a heterogeneous particle in which the various components are held together by relatively strong forces, and thus not easily broken apart (ISO, 2006). Aggregated nanoparticles would be an example of a nanostructured material.

Nanoaerosol

A **nanoaerosol** is a collection of nanoparticles suspended in a gas. The particles may be present as discrete nano-objects, or as aggregates or agglomerates of nano-objects. These agglomerates may have diameters larger than 100 nm. In the case of an aerosol consisting of micrometer-

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diameter particles formed as agglomerates of nano-objects, the definition of nanoaerosol is open to interpretation. It is generally accepted that if the nanostructure associated with the nano-object is accessible (through physical, chemical, or biological interactions), then the aerosol may be considered a nanoaerosol. However, if the nanostructure within individual micrometer-diameter particles does not directly influence particle behavior (for instance, if the nanoparticles were inaccessibly embedded in a solid matrix), the aerosol would not be described as a nanoaerosol.

The National Nanotechnology Initiative Definition

The National Nanotechnology Initiative (NNI, 2010) in the United States defines nanomaterials as follows:

Nanomaterials is a term that includes all nanosized materials, including engineered nanoparticles, incidental nanoparticles and other nano-objects, like those that exist in nature.

When particles are purposefully manufactured with nanoscale dimensions, we call them engineered nanoparticles. There are two other ways nanoparticles are formed. Nanoparticles can occur as a byproduct of combustion, industrial manufacturing, and other human activities; these are known as incidental nanoparticles. Natural processes, such as sea spray and erosion, can also create nanoparticles.

Many important functions of living organisms take place at the nanoscale. The human body uses natural nanoscale materials, such as proteins and other molecules, to control the body's many systems and processes. A typical protein such as hemoglobin, which carries oxygen through the bloodstream, is 5 nms in diameter.

American Chemistry Council Definition

The American Chemistry Council--Nanotechnology Panel (ACC, 2007) has proposed a separate definition for Engineered Nanomaterials. "The ACC Nanotechnology Panel believes that definitions used to describe Engineered Nanomaterials are important because they will be used to guide the public when information requests are made by regulators and NGO's. It is desirable that the definitions be as simple as possible yet not so broad that the collection of meaningless information is encouraged." For this reason, the ACC has proposed the following definition for Engineered Nanomaterials:

An Engineered Nanomaterial is any intentionally produced material that has a size in 1, 2, or 3-dimensions of typically between 1-100 nanometers. It is noted that neither 1 nm nor 100 nm is a "bright line" and data available for materials outside of this range may be valuable. Buckyballs are also included even though they have a size <1 nm.

Exclusions:

1. Materials that do not have properties that are novel/unique/new compared to the non-nanoscale form of a material of the same composition.

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2. Materials that are soluble in water or in biologically relevant solvents. Solubility occurs when the material is surrounded by solvent at the molecular level. The rate of dissolution is sufficiently fast that size is not a factor in determining a toxicological endpoint.

3. For those particles that have a particle distribution such that exceeds the 1-100 nm range (e.g. 50-500 nm) if less than 10% of the distribution falls between 1-100 nm it may be considered as non an Engineered Nanomaterial. The 10% level may be on a mass or surface area basis, whichever is more inclusive.

4. Micelles and single polymer molecules.

International Organization for Standards (ISO) Definitions

In 2008, the International Organization for Standards published the ISO/TS 27687:2008 standard, “Nanotechnologies -- Terminology and definitions for nano-objects -- Nanoparticle, nanofibre and nanoplate”. The standard is intended to facilitate communications between organizations and individuals in industry and those who interact with them.

The ISO/TS 27687:2008 lists the following unambiguous terms and definitions related to particles in the field of nanotechnology (ISO, 2008):

A **nano-object** is defined as material with one, two, or three external dimensions in the size range from approximately 1–100 nm. Nano-objects may be suspended in a gas (as a nanoaerosol), suspended in a liquid (as a colloid or nanohydrosol), or embedded in a matrix (as a nanocomposite). Nano-objects are commonly incorporated in a larger matrix or substrate referred to as a nanomaterial.

Subcategories of nano-object are:

- (1) **nanoplate**: a nano-object with one external dimension at the nanoscale;
- (2) **nanofiber**: a nano-object with two external dimensions at the nanoscale with a nanotube defined as a hollow nanofiber and a nanorod as a solid nanofiber; and
- (3) **nanoparticle**: a nano-object with all three external dimensions at the nanoscale.

Carbon fullerenes represent nano-objects with identical dimensions in all directions (i.e., spherical), whereas single-walled carbon nanotubes (SWCNTs) typically form convoluted, fiber-like nano-objects. Many regular but nonspherical particle morphologies can be engineered at the nanoscale, including flower- and belt-like structures.

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APPENDIX B

Special Considerations for Nanomaterials: Toxicity, Exposure Metrics, Routes of Exposure, and Factors Affecting Worker Exposure

Toxicity and Exposure Metrics

Results of existing studies in animals and humans on exposure and response to ultrafine or other respirable particles provide a basis for preliminary estimates of the possible adverse health effects from exposures to similar engineered materials on a nanoscale. Experimental studies in rodents and cell cultures have shown that the toxicity of ultrafine or nanoparticles is greater than that of the same mass of larger particles of similar chemical composition [Oberdörster et al. 1992, 1994a, b; Lison et al. 1997; Tran et al. 1999, 2000; Brown et al. 2001; Barlow et al. 2005; Duffin et al. 2007].

Various physicochemical parameters of nanoparticles (e.g., composition, size, shape, dimension, surface characteristics, charge, functional groups, crystal structure, solubility, and degree of agglomeration) appear to affect toxicity. It is not known whether size is the overriding parameter, though most studies show that size appears to be the major factor in enhancing the toxicity of engineered nanoparticles compared with the toxicity of larger particles of the same composition. What exposure metrics (e.g., mass, particle count, particle surface area) are most relevant to the most important health concerns is still not known.

Existing toxicity information about a given material of larger particle size can provide a baseline for anticipating the possible adverse health effects that may occur from exposure to a nanoscale material that has some of the same physicochemical properties (e.g., chemistry, density). However, predicting the toxicity of an engineered nanomaterial based on its physicochemical properties may not provide an adequate level of protection. More research is needed on the influence of particle properties on interactions with biological systems and the potential for adverse effects.

Carbon Nanotubes

Carbon nanotubes (CNT) are specialized forms or structures of engineered nanomaterials that have had increasing production and use [Donaldson et al. 2006]. Consequently, a number of toxicologic studies of CNT have been performed in recent years. These studies have shown that the toxicity of CNT may differ from that of other nanomaterials of similar chemical composition. For example, single-walled CNTs (SWCNT) have been shown to produce adverse effects including granulomas in the lungs of mice and rats at mass doses at which ultrafine carbon black did not produce these adverse effects [Shvedova et al. 2005; Lam et al. 2004]. While both SWCNTs and carbon black are carbon-based, SWCNTs have a unique, convoluted, fibrous structure and specific surface chemistry that offers excellent electrical conductive properties. How these characteristics may influence

How these characteristics may influence toxicity is not known. Carbon nanotubes may contain metal catalysts as byproducts of their production, which could contribute to their toxicity, or the CNTs may provide a structure that promotes fibroblast cell growth [Wang et al. 2008].

Although a number of studies have been conducted on CNT toxicity [Li et al. 2007; Sriram et al. 2007; Baron et al. 2008; Shedova et al., 2008; Mercer et al. 2008; Tagaki et al. 2008; Poland et al. 2008] indicate the need for more, there is a need for additional data on exposures of workers to CNTs.

Routes of Exposure and Factors Affecting Exposure

Inhalation

The toxicology of the nanomaterial is likely to change with not only material type, but also with exposure route. Inhalation is the most common route of exposure to airborne particles in the workplace. Discrete nanoparticles are deposited in the lungs to a greater extent than larger respirable particles [ICRP 1994].

The following factors have been observed to affect the deposition of discrete nano-objects in the respiratory tract:

- The particle's aerodynamic or thermodynamic diameter (i.e., the particle shape and size) determines the deposition of nano-objects in the respiratory tract.
- Agglomerates of nano-objects will deposit according to the diameter of the agglomerate, not constituent nano-objects. Evidence indicates that the degree of agglomeration can affect the toxicity of inhaled nano-objects [Shvedova et al. 2007].
- Deposition increases with exercise due to increase in breathing rate and change from nasal to mouth breathing [Jaques and Kim 2000; Daigle et al. 2003] and among persons with existing lung diseases or conditions (e.g., asthma, emphysema) [Brown et al. 2002].
- Discrete nanoparticles may enter the bloodstream from the lungs and translocate to other organs [Takenaka et al. 2001; Nemmar et al. 2002; Oberdörster et al. 2002].

Dermal

Nanomaterials could potentially enter the body through the skin during occupational exposure, as demonstrated by the following studies:

- Tinkle et al. [2003] have shown that particles smaller than 1 μm in diameter may penetrate into mechanically flexed skin samples.
- A more recent study reported that nanoparticles with varying physicochemical properties were able to penetrate the intact skin of pigs [Ryman-Rasmussen et al. 2006]. These nanoparticles were quantum dots of different size, shape, and surface coatings. They were reported to penetrate the stratum corneum barrier by passive diffusion and localize within the epidermal and dermal layers within 8–24 hours. The dosing solutions were 2- to 4-fold dilutions of quantum dots as commercially supplied and thus represent

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occupationally relevant doses. At this time, it is not fully known whether skin penetration of nanoparticles would result in adverse effects in animal models.

- Topical application of raw SWCNT to nude mice has been shown to cause dermal irritation [Murray et al. 2007].
- Studies conducted in vitro using primary or cultured human skin cells have shown that both SWCNT and multi-walled carbon nanotubes (MWCNT) can enter cells and cause release of pro-inflammatory cytokines, oxidative stress, and decreased viability [Monteiro-Riviere et al. 2005; Shvedova et al. 2003].

It remains unclear, however, how these findings may be extrapolated to a potential occupational risk, given that additional data are not yet available for comparing the cell model studies with actual conditions of occupational exposure.

Ingestion

Since traditionally ingestion has been found to occur from unintentional hand to mouth transfer of materials, it is scientifically reasonable to assume that it also could happen during handling of nanomaterials. Ingestion may also accompany inhalation exposure because particles that are cleared from the respiratory tract via the mucociliary escalator may be swallowed [ICRP 1994]. Little is known about possible adverse effects from the ingestion of nanomaterials at this time.

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Appendix C

Processes and Operations with Potential for Occupational Exposure to Engineered Nanoparticles

Four major processes are employed in synthesizing new nanoparticles (Bergamaschi, 2009):

- (i) Gaseous phase condensation processes, which include flame pyrolysis, high-temperature evaporation and synthesis in a plasma, involving nucleation and evaporation phenomena (bottom-up approach);
- (ii) Synthesis by evaporation and vapour deposition (bottom-up approach);
- (iii) Colloid formation by chemical reactions with liquid phase or colloidal solvents, involving controlled precipitation phenomena (bottom-up approach); and
- (iv) Mechanical attrition processes (top-down approach) (for a more complete description of processes, see: Aitken et al. 2004; National Institute for Occupational Safety and Health (NIOSH) 2007; Schneider et al. 2007). In recent years, the limits of each approach, in terms of feature, size and quality that can be achieved, have started to converge. Now the dimensions that can be controlled by either approach are of a similar order, and this is leading to exploitation of new hybrid methods of manufacture.

In all nanoparticle (NP) production processes there is a potential for exposure at both the synthesis and recovery phase of the process (see Table I below). However, emission scenarios (i.e., potential releases, which depends on particle properties), should be distinguished from exposure scenarios (i.e., the potential exposure, which relies on working conditions, exposure routes, environmental conditions).

According to NIOSH (2007), many workplace factors and operations may increase the potential for exposure to nano-aerosols:

- (i) Working with nanomaterials (NM) in liquid media without adequate protection (e.g., gloves) will increase the risk of skin exposure;
- (ii) Working with NM in liquid during pouring or mixing operations, or where a high degree of agitation is involved, will lead to an increase likelihood of inhalable and respirable droplets being formed;
- (iii) Generating nanoparticles in the gas phase in non-enclosed systems will increase the chances of aerosol release to the workplace;
- (iv) Handling nanostructured powders will lead to the possibility of aerosolization;
- (v) Maintaining equipment and processes used to produce or fabricate nanomaterials or the clean-up of spills or waste material will pose a potential for exposure to workers performing these tasks;
- (vi) Cleaning of dust collection systems used to capture nanoparticles can pose a potential for both skin and inhalation exposure; (vii) machining, sanding, drilling, or other mechanical disruptions of materials containing nanoparticles can potentially lead to aerosolization of nanomaterials.

| Table I. Potential risk of exposure in nanoparticle production processes. | | |
|--|--|--|
| Synthesis process | Potential risk of inhalation | Skin contamination |
| Gas phase flame pyrolysis, high temperature evaporation and plasma synthesis | Direct leakage from reactor Product recovery Any further processing or packaging | Touching surfaces contaminated by airborne releases, handling of product during recovery or processing/packing; cleaning or maintenance of the plant |
| Vapour deposition | Product recovery, mechanical removal, processing, packing | Airborne dry powders; handling of product during recovery or packaging; cleaning workplace |
| Colloidal or liquid phase | Recovery by spray drying; Spillage of suspension followed by evaporation | Spillage of the product; dried material handling; recovery, packing; cleaning, maintenance |
| Mechanical attrition grinding, milling and alloying | Product drying; suspension spillage | Spillage of the product; dried material handling; recovery, packing; cleaning, maintenance |

Processes generating NM in the gas phase, or using or producing NM as powders, slurries, suspensions and solutions pose the greatest risk for releasing NP. Maintenance on production systems (including cleaning and disposal of materials from dust collection systems) is likely to result in exposure to NP if it disturbs deposited NM (Aitken et al. 2004; NIOSH 2007). NM-enabled products, such as nanocomposites and surface coatings, and materials comprised of nanostructures such as integrated circuits are unlikely to pose a risk of exposure during their handling and use. However, some of the processes (formulating and applying nanoscale coatings) used in their production may lead to exposure to NP (Aitken et al. 2004; Schneider et al. 2007). Workers could also be exposed to ground CNTs used in polymer composites and other matrices or during cutting, grinding, or polishing of these materials. Given that exposure to SWCNT and MWCNT causes interstitial fibrosis and pulmonary inflammation, respectively, in rodent lungs at relatively low mass doses, NIOSH advises minimizing worker exposure to airborne CNTs (NIOSH, 2009).

As a whole, field surveys have shown that workers from nanotechnology-related industries have the potential to be exposed to nanoaerosols of engineered materials via inhalation as well as through skin contamination.

Exposure to NPs in Workplaces – Air monitoring data

Experimental studies that can mimic the exposure processes reveal the formation of larger agglomerates of NPs after their release. Studies conducted in workplaces confirmed this assumption, however, the data are still very scarce and not easy to compare due to differences in the format of reporting the data (Brouwer D. 2009). A further source of complexity derives from

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the observation that in most environments CNT tend to form larger aggregates or ropes that would lead to the underestimation of their concentration. Moreover, although their toxicity may be also ascribed to their fiber shape, their diameter is too small to be detected with the optical methods used to assess the presence of fibers in the environment (Lam et al. 2006).

Since exposure assessment in new NP processes has begun under the uncertainty about metrology and the lack of internationally recognized occupational standards, few studies have directly investigated exposure. Very active in field measurements are some Institutions, such as the German Federal Institute of Occupational Safety and Health (BAuA). For instance, airborne concentration of TiO₂ detected at the bin filling operation, prior to improve the local exhaust system, revealed that during the normal operation the number concentration were in the order of 10³/cm³ and that particles were mostly airborne aggregates/agglomerates, with primary particles of Ti in the order of 40–50 nm, as confirmed by the subsequent TEM analysis on collected samples. The gravimetric analysis showed low concentrations of TiO₂ (0.18 mg/m³) in inhalable dust fraction (0.232 mg/m³); the corresponding figures for the respirable fraction of collected dusts were 0.019 mg/m³ and 0.10 mg/m³, respectively. However, during leakage at the same plant, concentrations up to 150,000 p/cm³ may occur (Markus Berges: presentation made at 2nd Nanotoxicology Conference, Venice 19–21 April 2007). As compared to the Threshold Limit Values for dusts (10.0 and 3.0 mg/m³, respectively) these data reveal very low exposure levels.

Most studies have focused on the production of nanomaterials, either on bench- or pilot scale or on commercial scale. Many of the activities that were monitored in commercial scale production were related to the end-phase, i.e. packaging of the product, e.g. Kuhlbusch et al. (2004), Kuhlbusch and Fissan (2006), Fujitani et al. (2008), and Peters et al. (2009), whereas others were focused on or included harvesting of the product and reactor cleaning, e.g. Maynard et al. (2004), Han et al. (2008), Bello et al. (2008), Methner (2008), Demou et al. (2008), and Yeganeh et al. (2008). Down-stream use activities, e.g. agitation (Maynard et al., 2004), various activities (Methner et al., 2007), transfer, pouring (Tsai et al., 2008a), and compounding (Tsai et al., 2008b) were only monitored for research scale activities.

Recently, results of some experimental studies focused on the release of nanoparticles due to treatment of ‘end-products’ were published. Bello et al. (2009) focused in their study on the release of nanoparticles during machining (cutting) of CNT composites. Vorbau et al. (2009) quantified the release rate of particles smaller than 100 nm during an abrasion test of a surface coated with a nanoparticles (ZnO) containing coating.

In general, in studies, nanomaterial-related activities could be distinguished from periods with no activities or from background concentration for particle number concentration and mass concentration (if considered). Size distributions and possible influences by nanomaterial-related activities are less unambiguous to interpret. In most cases bimodal distributions were reported, however the modes varied substantially. In some case a mode of the size distribution fell into the nano-sizes (Fujitani et al., 2008; Tsai et al., 2008b), however the authors also reported possible other sources, i.e. a vacuum cleaner and release of polymer fumes, respectively. An enhanced concentration of particles <100nm is most often associated with other sources, e.g. combustion, vacuum cleaning, oil mist or welding/grinding, whereas particle characterization confirmed that larger nanomaterial agglomerates or aggregates were present in the air rather than distinct small

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particles. For carbon nanotubes (CNTs) Han et al., 2008 reported the release of respirable tubes supported by identification of high aspect ratio fibers during off-line analysis (Brouwer D, 2009).

Activities with the end-product during production, e.g. harvesting/ bagging, reactor cleaning, and down-stream use, bag dumping, pouring or transfer, might be mimicked by the dust generation during dustiness testing of nanopowders, with modes of about 200–300nm and 2000–3000 nm. Most field studies showed bimodal-size distributions, with often size modes around 200–400nm and 1000–20,000 nm, whereas elevation of the particle concentration in the smaller size ranges was often associated with other sources than the nanomaterial -related activities or emissions. Off-line analysis confirmed the absence of the primary nanomaterial in the samples. Exceptions are the observations for a CNT production facility reported by Han et al. (2008), who found asbestos-like structures during sample analysis (Brouwer D., 2009).

Details from some of the individual studies mentioned above are summarized below:

Kuhlbusch et al. (2004) found that bag filling in a carbon black producing facility was not a source of ultrafine particles. In the work areas of the reactor and pelletizer of three carbon black production plants Kuhlbusch and Fissan (2006) found that elevated ultrafine particle number concentrations with respect to ambient were related to nearby traffic emissions or to grease and oil fumes from maintenance activities or, in one of the plants, to leaks in the production line, which allowed particulate matter to escape to the surrounding areas. The authors concluded that no carbon black is released in the reactor and pelletizing areas (as ultrafine particles or PM₁₀) from the closed production lines under normal operating conditions.

Maynard et al. (2004) carried out a laboratory based study to evaluate the physical nature of the aerosol formed from single-walled carbon nanotube material (SWCNT) during mechanical agitation, complemented with airborne and dermal exposure while handling unrefined material. Handling resulted in very low airborne concentrations (from 0.7–53 µg/ m³), consistent with the tendency to aggregate into larger masses (Maynard et al. 2004). Air measurements included large airborne clumps of material larger than 1µm or so in diameters that were not respirable. However these particles, together with surface deposits, would pose a dermal exposure risk, as revealed by the material on the individual gloves (from 217–6020 µg), mostly on the parts of the gloves in direct contact with surfaces (inner surfaces of fingers and palms).

Although the actual amount reaching the deep lung seems be negligible for many CNT manufacturing and use settings, other field studies revealed higher airborne concentrations especially in R&D facilities. For instance, in manufacturing multiple-walled carbon nanotubes, researchers from the University of Seoul, showed gravimetric concentrations of total dust before any control measures ranged from 0.21–0.43 mg/m³, then decreased to a non detectable level after implementing the control measures (Han et al. 2008).

Presently, there are only a few published workplace air monitoring studies for production and down-stream use of manufactured nanomaterials. Since a wide range of exposure scenarios and types of manufactured nanomaterials are covered, it is difficult to get a good overall picture of the potential for exposure resulting from activities related to these materials. Moreover, a wide

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variety of the format of presenting the data interferes an overall analysis, however, some general observations can be made (Brouwer D., 2009):

- The likelihood of the presence of primary manufactured nanoobjects in the workplace, both during production and down-stream use, seems to be low.
- There are indications that the type of aerosols is dominated by agglomerates and aggregates, either exclusively consisting of manufactured nano-objects, or in combination with other and 'background' particles, therefore, size fractions up to 400–500nm might be of similar importance as the nano-size range.
- For exposure analysis it would be interesting to know what the contribution of agglomerates for different size fractions would be.
- For risk assessment it would be relevant to know what type of agglomerates and aggregates are present and to what extent these structures will de-agglomerate in body fluids after uptake.

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APPENDIX D

Outstanding Data Needs for Nanomaterial Assessments
(as of February 2011)

Summary of OPPT/CEB Data* Needs for Nanomaterials (NM)

*Data Related to Releases, Treatment, Occupational Exposures, Engineering Controls, Personal Protective Equipment (PPE), and Occupational Exposure Limits (OELs)

| Table 1. Key Release and Treatment Information and Parameters in New NM Cases | | |
|---|---|---|
| Type of Data or Information | Source of Information/ Data | Outstanding Data Needs |
| Models for predicting releases and environmental exposure that are specific to nanomaterials. | Models developed by universities and national and international research organizations. | Not available |
| Production Volume | PMN | None |
| Vapor Pressure (note: negligible for most nano cases) | Chemistry Report | None |
| Molec Weight (note: n/a for most nano cases) | Chemistry Report | None |
| Solubility in H ₂ O | Chemistry Report | None |
| Density (bulk) | Chemistry Report (or PMN) | None |
| Lifecycle steps | PMN or Literature | None |
| PV to each Lifecycle Step | PMN or EPAB | None |
| Process Description | PMN (or past cases or GS) or Literature | None |
| Physical states of NM | PMN (or past cases or GS) or Chemistry Report | None |
| Shipping containers for raw material and/ or product containing NM | PMN (or past cases or GS) or Literature | None |
| List of Release sources for NM | PMN (or past cases or GS) | None |
| # sites | PMN (or past cases or GS) or Literature | None |
| # days/yr (or # batches/yr) | PMN (or past cases or GS) | Generally not available for downstream processing and use |
| Kg/site-day NM produced or used (or kg/batch) | PMN (or past cases or GS) | Generally not available for downstream processing and use |
| NM conc (wt fraction) in raw material | PMN (or past cases or GS) | Generally not available |

Table 1. Key Release and Treatment Information and Parameters in New NM Cases

| Type of Data or Information | Source of Information/ Data | Outstanding Data Needs |
|--|--|---|
| and/ or | | for downstream processing and use |
| Kg/site-day NM Released [or, alternately, Loss fraction (e.g., emission factor per kg/site-day NM production or use rate)] | PMN (or model or GS) | Generally not available for downstream processing and use |
| Days/yr release | PMN (or model or GS) | Generally not available for downstream processing and use |
| Media of release | PMN (or model or GS) | Generally not available for downstream processing and use |
| Particle size | PMN or Chemistry Report | Limited information available |
| Agglomeration characteristics | PMN or Chemistry Report | Limited information available |
| On-site treatment technologies and effectiveness (including treatment related parameters) | A current project being started to gather information treatment technologies in WPMN SG8 | Not available |
| Destruction and removal efficiency in incineration or burning | PMN or OSWER research | Limited laboratory data |

| Table 2. Key Occupational Exposure, Control, Protection, and OEL-related Information and Parameters in New NM Cases | | |
|---|--|-------------------------------|
| Type of Data or Information | Source of Information/ Data | Outstanding Data Needs |
| Models for predicting occupational exposure that are specific to nanomaterials. | Models developed by universities and national and international research organizations | Not available |
| Exposure monitoring | | |
| PBZ monitoring (mass in mg/m ³ / particle numbers) | NIOSH/ Research Articles | Limited information available |
| Area monitoring (mass in mg/m ³ / particle numbers) | NIOSH/ Research Articles | Limited information available |
| Availability of certified consultants/IHs to conduct exposure monitoring | NA | Important for credible data |
| Monitoring Techniques | NIOSH | Limited information available |
| Sampling and Analytical Methods | NIOSH/OSHA | Limited information available |
| Process/Activity specific data for a NM type(data in mg/m ³ / particle numbers) | NIOSH/ Research Articles | Limited information available |
| Data on dermal exposure | NIOSH/ Research Articles | Not available |
| Particle size and distribution in dry state | NIOSH/ Research Articles | Limited information available |
| Agglomeration characteristics in dry state | NIOSH/ Research Articles | Limited information available |
| Engineering Controls | | |
| Presence/Absence of controls (e.g., glove boxes, ventilation) | PMN | Some provided in PMNs |
| Determine effectiveness of controls | NIOSH/ Research Articles | Limited information available |
| Confirm effectiveness of HEPA filters in exhaust ventilation | NIOSH | Not available |
| Effectiveness of Work Practices | NIOSH | Not available |
| Personal Protective Equipment | | |
| Respiratory protection | NIOSH/OSHA | None |
| Respirators | NIOSH | None |
| Dermal protection | NIOSH/OSHA | Limited information |

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| Table 2. Key Occupational Exposure, Control, Protection, and OEL-related Information and Parameters in New NM Cases | | |
|---|-----------------------------|---|
| Type of Data or Information | Source of Information/ Data | Outstanding Data Needs |
| | | available |
| Effectiveness of gloves and other barrier clothing | NIOSH/ASTM | Limited information available |
| Permeation testing for gloves | ASTM | Not available |
| Occupational Exposure Limits (OELs) | OSHA PEL/NIOSH REL | Not available/ Only non-regulatory limits available |
| Carbon nanotubes (CNT)/ Carbon nanofibers (CNF) | NIOSH REL | Only non-regulatory limits available |
| Titanium Dioxide | NIOSH RELs | Only non-regulatory limits available |
| Other NMs | None | Not available |