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Nanotechnology: Health & Safety Exposures in a Shrinking World

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Introduction

Will nanotechnology cause the earth to be overrun with a "Gray Goo" of replicating nano-robots creating an environmental catastrophe of Biblical proportions? Or, will nanotechnology slip unseen into products providing features and enhancements that will increase the quality of your life? Your car may already have a stronger lighter bumper because of nanotechnology. You may already be wearing a sunscreen that has enhanced UV protection. Your nano-enabled shirt repels coffee stains, all because of unique properties of nanoparticulates.

Because the chemical properties of materials change at the nano level, manufacturers are able to provide products with enhanced or novel features and benefits. These property changes apply to compounds including metal oxides and carbon, commonly used in manufacturing today. Since nanotechnology is process oriented rather than an end product related, it cuts across almost all industry and market boundaries.

At the same time, the very properties that allow these enhancements bring unknowns into the workplace. Concern and caution are appropriate since there are many unanswered questions as to how nanoparticulate interacts with the human body and the environment. Most of these exposures are as yet un-quantified. The small but growing body of research is just now beginning to yield indications of answers to these questions.

What is Nanotechnology?

Nanotechnology refers to man made, engineered structures between 1 and100 nanometers in size that are controlled or manipulated at the atomic level. These structures, devices & systems have novel properties different from larger particles of the same compound. Changes in properties include color, electrical conductivity, catalytic interaction, strength to weight ratios and melting points, among others. One 10 micron particle has the same mass as 1 billion particles that are one nanometer in size. However, the surface area is, for the nano sized particles, 5 orders of magnitude higher for the same mass leading to significantly increased chemical reactivity. These may be familiar materials such as metal oxides (Ag, Zn, Si, Ti, Au) or new, discrete, carbon structures such as carbon nanotubes and C60 Fullerenes. Also included are Quantum Dot (i.e., CdSe /ZnS) crystals.

Nanoparticulate Sources

Nanoparticles have been in nature since the beginning of the Planet, resulting from volcanic eruptions and forest fires. The industrial revolution created more by product nanoparticulate from cooking, manufacturing processes, welding, diesel and jet engines. These are man made particles referred to as fine (micron sized) and ultra-fine (nano range). Industrial exhausts are man made but are not engineered.

Today's nanotechnology refers to engineered nanoparticles that result from manipulation at the atomic level. Size and shape are highly controlled. The results are metal oxide, polymer and organic particles (nano-spheres, -wires, needles, -tubes, -shells, -rings, etc.) each of which have different sizes and properties. Manufacturing involves positional assembly, i.e., moving molecular pieces into their proper relational places to make a compound. Self-replication techniques, i.e., multiplying positional arrangements in some automatic way are being investigated. R & D includes the building of self replicating manufacturing devices and self assembly using atomic forces. These self-replicating nanoparticles barely exist in R & D and are a long way from the "Gray Goo" scenario.

How Small are Nanoparticles?

The size of a nanoparticle is so small that it is difficult to grasp. It is helpful to compare particles in the 1-100 nm range to familiar objects such as those found in the bloodstream. The following table provides relative sizes:

Object	**Nanometers**
White blood cell	~10,000
Bacteria	1,000 – 10,000
Materials internalized by a cell	<100
Viruses	75 – 100
Nanoparticle Range	**1 – 100**
Protein	5 – 50
Quantum Dots	**8**
DNA (width)	2
Fullerenes	**1**
Single atom	0.1

Table 1. Nanoparticles Size vs. Cells[1]

Many nanoparticles are only orders of magnitude larger than a single atom. Other useful information on relative sizes can be found on a chart “The Scale of Things- Nanometers and More” provided by the US DOE. [2]

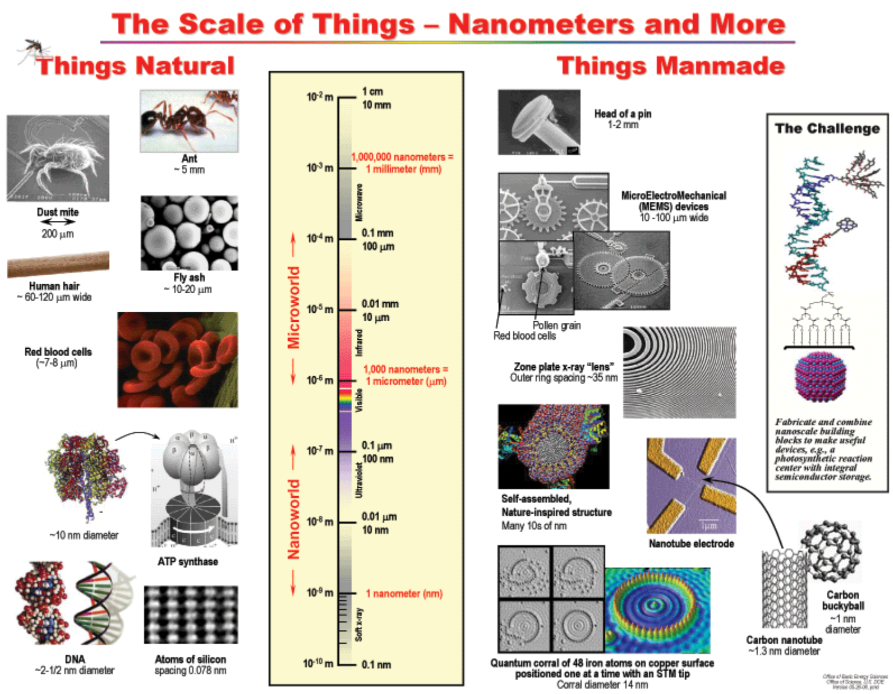


Exhibit 1.

Public Concern: Perception versus Scientific Problem

It is important to separate hype from reality. When trying to quantify nanotechnology exposures to humans and the environment, all possibilities must be explored. There are those who fear that runaway replicating nanobots, or "Gray Goo” will take over the earth. While possible, the scenario is not probable.

“Gray Goo” self replicating nanobots, if ever developed, would face a much harder task than merely replicating themselves. They would have to survive in an environment prone to agglomeration and aggregation of nano-sized particles. In addition, they would have to move around to find raw materials and an energy source. While research is being done in replication techniques, the unlikely “Gray Goo” scenario is preceded by other valid and immediate concerns. “Gray Goo” is more of a public perception issue fueled by science fiction writing, rather than a scientific problem.

Public Concern is Valid

The introduction of any new technology must weigh the benefits versus the potential hazards. Nanoparticulates are already in products that are ingested or dermally applied. These include: pills, dietary supplements, foods, cosmetics, sunscreens, antibacterial and antiviral applications. Food packaging uses nanoparticulate to reduce spoilage. Workers have the potential to inhale, ingest or absorb nanoparticulate during manufacturing or R & D processes.

Interactions may be unpredictable and potentially harmful. Do these particles enter the bloodstream or tissues? Where do they go after that? Are they retained in or excreted from the body? How long do they exist in the body or the environment? All are valid questions which need to be answered.

Toxicity databases, while growing, are limited. Hazards are not fully quantified; testing data is in process or yet to be done. There is a fine balance between protecting the public's interest and inhibiting commerce. The public is looking for valid risk and benefit information that will result in workplace safety and a level of comfort with nano-enabled products.

Nanotechnology Business

Nanotechnology is in its infancy. Markets are rapidly developing and expanding with well over 600 products on sale world wide by year end 2007. The number of products is roughly doubling every year. There is potential usage in almost all industries & markets. There will be a market in excess of a US $1 Trillion [3] for nano materials, nano-intermediates and nano-enabled products by 2015.

Nanotechnology requires an integrated approach to diverse sciences in order to obtain desired electronic, optical, physical & chemical properties. Technologies include: Biology, Physics, Chemistry, Materials science, Computer science, Mechanical and Electrical engineering. Markets for nano-enabled products include health and fitness, home & garden, electronics, biotech, cleantech, food & beverage, coatings, automotive, appliances and children's goods.

Business Issues for Nano Companies

Many multi-national and Fortune 500 companies are involved in nanotechnology research and/or manufacturing. Therefore their employees are potentially at risk. Larger corporations have the advantage of having existing E H & S structures and personnel in place. However much of the R & D in nanotechnology is being done by start-ups who have to develop those structures and programs.

Start-ups have many taskmasters! There is always a race to market for competing intellectual property & patents. Venture capital firms place pressure on startups to get products to market to increase their ROI through public offerings. There is a delicate balance between available funding versus capital expense burn rates.

Whether a large or small corporation, E H & S professionals have to be diligent about obtaining an adequate budget to provide a safe working environment. In a start-up environment, nanotechnology companies often quickly reach the point of rapid expansion where they outstrip their management procedures and capabilities. Awareness of nanotechnology risk issues, a strong corporate risk management commitment and implementation of industry best practices by the E H & S person(s) will blunt the impact of rapid expansion.

Processes Used in Nanotechnology

Almost all nanotechnology related facilities have R & D labs doing wet chemistry in glove boxes, fully enclosed or partially enclosed hoods. Reactor vessels for R & D or pilot operations are common. They also have dry labs containing metrology equipment such as scanning electron, e-beam or atomic force microscopes, HPLCs and other high valued equipment. Metrology equipment is often housed in clean rooms.

Some R & D or pilot facilities have arc furnaces or chemical vapor deposition equipment (CVD) to make small runs of carbon nanotubes. Others use photolithography, thin film and other semiconductor related processes for layering and doping. These may require the use of toxic and/or flammable dopant gases which must be stored and used in accordance with NFPA 318 and industry best practices such as the Santa Clara, CA Toxic Gas Ordinance.[4] Along with these processes come the concern for toxic gas exposure and smoke and fire related exposures from wet benches and wet bench processes.

Bulk Manufacturing

Bulk manufacturing facilities also may have arc furnaces or CVD equipment to manufacture carbon nanotubes Bulk manufacturing of wet, suspended nanoparticulate is done in contained liquid suspension reactors. Unless the suspension is flammable, there are fewer fire exposures due to the lack of a fire and explosion hazard. Inhalation exposure is also non existent or very limited due to the containment of particles in suspension.

Dry particulate manufacturing is often done in liquid or plasma reactors and spray on deposition equipment. Heat treating, milling and surface treatment operations may follow. Closed, dry powder transfer equipment is used to take the nanoparticulate to the shipping container. Commercial off the shelf equipment is available to provide vacuum transfer of powders. To reduce dust exposure and explosion potential, options may include putting powder into a slurry.

Packaging and transfer equipment for bulk dry product creates the greatest dust exposure, both for explosion and inhalation. Work practices will have a significant effect on exposure during material transfer, particularly when filling drums without proper enclosure and ventilation. Leaks also present explosion and inhalation potential. Frequent clean up and housekeeping are essential. Best practice spill procedures should be in place.

Nanotechnology Risk

In spite of the many benefits of nanotechnology, nanoparticulate has the potential to do harm to the body if inhaled, ingested or absorbed. As with most dusts, nanoparticulate has the potential for explosion when suspended in air. In the environment, little is known about how long nanoparticulates will stay in the nano size range, as they interact with soil, air and water.

Some risks, exposures and controls concerning nanotechnology particulate are known and quantified, but they are few. Many are known or suspected but remain un-quantified. Still others are unknown. It is known that:

- Some potential hazards exist
- Some exposure occurs
- Some unknown risks may exist
- Nanoparticles can be measured
- Nanoparticles can be controlled
- Proper engineering and administrative controls such as ventilation, filters and respirators should protect workers

Among the risks, exposures and controls that remain unknown or un-quantified are:

- Nature and extent of hazard?
- Nature and extent of exposure?
- Nature and extent of risk?
- Specific exposure limits?
- Limitations of controls & protection?
- What physiochemical data to gather (mass, size distribution, agglomeration state, exact shape, crystal structure, chemical composition, impurities, surface chemistry, surface charge & coatings, porosity)? [5]
- What to compare sample results against?

Industry Acceptance of Nanotechnology Risk

In order to risk manage exposures presented by the introduction of nanotechnology processes, industry must first except that there are indeed new and un-quantified exposures that must be addressed. The 2006 ICON Study "Survey of Current Practices in the Nanotechnology Workspace" [6] queried industry on all phases of nanotechnology. Concerning reported belief in nanotechnology risk:

- 40% were aware of the potential special risks that needed to be addressed
- 22% reported "Don't know- need more information"
- 38% indicated that there were no special risks

Clearly there is additional education and motivation needed in some parts of industry regarding the potential health hazards and appropriate workplace controls for nanotechnology.

Assessing and Characterizing Un-quantified Risk

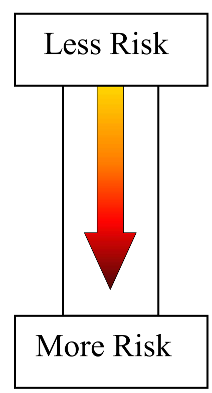
How do you assess and characterize risks and hazards? The more certain the hazard, the more defined the management, communication and precautions. When the amount of risk is unknown or uncharacterized, management, communication, and precaution need to be greatly increased. Uncertainty requires extraordinary precautions and controls.

Extraordinary precaution and control is the approach that should be taken when there is exposure to nanoparticulate. NIOSH believes, based on available information to date, that a comprehensive risk management program including minimizing employee exposure to airborne contaminants via existing engineering techniques while further controlling exposure through administrative controls (duration , PPE, etc,) will contain and control potential exposures if properly applied in a conservative fashion.[7] These familiar engineering and administrative controls have been used for many years and are codified in OSHA 1910.

Ranking Nanoparticulate Exposure

Nanoparticulate can be divided into two major groups, organic (nanotubes, fullerenes, etc) and inorganic, mostly metal oxides. Likewise, nanoparticulate is manufactured, packaged and used in either in solution or dry process. In general, there is more risk with organics than inorganics because they are more reactive. Also in general, there is more risk with dry powders than solutions because of the potential inhalation and explosion exposures. Therefore it is possible to rank relative increasing risk associated with group and wet or dry use:

- Inorganic particulate in solution
  - Less reactivity
  - Absorption, ingestion but minimal inhalation
- Organic particulate in **solution**
  - More reactivity
  - Absorption, ingestion but minimal inhalation
- Inorganic particulate **- dry powder**
  - More reactivity
  - Same modes + inhalation
- Organic particulate **- dry powder**
  - More reactivity
  - Same modes + inhalation



Solid or agglomerated nanoparticles are factors that decrease risk. Likewise limiting exposure by limiting task duration also decreases risk.

Nanoparticles that do not readily agglomerate and have high dispersion rates, increase risk. Nanoparticles made of toxic compounds (i.e. CdSe/ZnS quantum dots) have increased risk in spite of their particle size. These factors, along with increased reactivity and inhalation exposure are the factors that most greatly increase risk and subsequent injury potential..

Potential Toxicity Vectors

Up to 50% of inhaled nanoparticles may deposit in gas exchange regions of the lung. Because of their greater surface area and reactivity, nanoparticulate, whether metal oxide or organic, cause oxidative stress when inside the body. Oxidative stress leads to inflammation. Long term inflammation leads to other potential outcomes such as changes to DNA, the lymphatic and the central nervous systems. Fibrosis, COPD, metal fume fever and cancer may result. [8]

Potential movement through the Body

Nanoparticulate has the potential to enter the body via the skin, the respiratory tract, or the GI tract through absorption, injection, inhalation and ingestion. Once in the tissue and bloodstream, nanoparticulate may migrate or translocate to the central nervous system, the lymphatic system, bone marrow, kidney, spleen, heart, among others. Translocation rates are largely unknown. Some but not all nanoparticulate may be excreted through sweat, urine, breast milk, feces, etc. [9]

Carbon Nanotube Toxicity

In order to behave like other pathogenic fibers, single wall (SWCNT) and multi-wall (MWCNT), carbon nanotubes (CNT's) should to be long, thin and bio-persistent. CNT's are thin (SWCNT ~5nm; MWNT ~200nm) and bio-persistent (graphite stays in the lungs) but not as long as other pathenogenic fibers, such as asbestos. These are generally longer than about 20μm in length. CNT's are significantly smaller, however, in spite of their short length, CNT's have the unusual ability to stimulate fibrosis in the lungs with the potential for lung cancer if there is sufficient exposure. [10]

Results of Early Animal Toxicity Studies

Among the results of early lung studies:

- MWCNT exposure to mouse stem cells caused cell death and DNA Modification [11]
- Lung cancer has been found in rats exposed to ultra fine (nm) particles of Ti02.
- Rodent lung inflammation and fibrosis has resulted from exposure to nanoparticles at workplace levels.
- Small doses of SWCNT have caused fibrosis in mice.
- Cardiovascular results show an air pollution epidemiology resulting in asthma
- Inflammatory effects, thrombosis and platelet aggregation in animals.
- Brain/Central nervous system results show that inhalation results in direct transfer of metal particulate to the brain via olfactory pathways. Graphite rods also accumulate in olfactory lobe of brain. [12]

Dermal studies show that hazard exists as indicated by a biological response by the skin. Exposure is evidenced by the ability of fullerenes and quantum dots to penetrate through stratum corneum. Surface modifications, agitation, surfactant presence and dosing conditions are crucial. Studies are on-going to define structure/activity relationships. [13]

Controls for the Hazards of Working with Nanoparticulate

When developing solutions to mitigate workplace exposures, either quantified or un-quantified, a time tested hierarchy of controls exists:

- CHANGE the design so hazard no longer exists
  - Substitute with less hazardous materials
  - Replace a high hazard with a lower hazard
- ENGINEER
  - Isolation
  - Ventilation
  - Guard
- ADMINISTRATE
  - Procedures, Policies, Shift Design
  - Personal Protective Equipment
  - Industrial Hygiene and Hygiene testing

Change and engineering solutions are always best because they tend to stay corrected for a long period of time. Administrative solutions are an important part of solutions but are less desirable because they introduce the human factor and the ability to defeat solutions with unsafe acts or lack of follow through.

When dealing with nanoparticulate, particularly in R & D, change and substitution are less of an option. There is heavy reliance on engineering controls such as enclosure, limited access, local exhaust ventilation, HEPA/ULPA filtration and explosive atmosphere electrical fixtures. Care must be taken to design ventilation scrubber systems to capture nanoparticulate because of low particle mass. Electrostatic scrubbers are more effective than cyclone for this reason. General and local exhaust systems should be designed in accordance with the ACGIH Industrial Ventilation Manual.

Human factors cannot be ignored. It is important to administrate good work practices manufacturing and spill clean up. These include:

- Reducing periods of exposure
- Particle sampling including background sampling
- Using proper PPE and respirators
- Uniform usage and laundering procedures
- Enforcing personal hygiene rules
- Minimizing dust accumulation
- Regular cleaning to avoid dust re-suspension
- Immediate spill clean up
- Medical monitoring (if indicated)
- Transport in closed containers

- Dispose of waste as hazardous material
- Comprehensive training of effected employees

Sampling for Nanoparticulate

When dealing with nanoparticulate, what do you measure and how do you measure? The percentage of the same sample differs when measured by particle count, surface area or mass. Significant exposures also exist outside measurable respirable dust concentrations. Gravimetric pumps may be used for total dust samples results but are misleading.

There are currently no national or international consensus standards on measurement techniques for nanoparticles in the workplace. However, information and guidance for monitoring nanoparticle exposures in workplace atmospheres has recently been developed by the International Organization for Standardization and is in press [ISO 2006]. [14]

Until more information becomes available on the mechanisms underlying nanoparticle toxicity, it is uncertain as to what measurement technique should be used to monitor exposures in the workplace. Current research indicates that mass and bulk chemistry may be less important than particle size and shape, surface area, and surface chemistry (or activity) for nanostructured materials. [15]

Many of the sampling techniques that are available for measuring airborne nanoaerosols vary in complexity but can provide useful information for evaluating occupational exposures with respect to particle size, mass, surface area, number concentration, composition, and surface. Unfortunately, relatively few of these techniques are readily applicable to routine exposure monitoring. Regardless of the metric or measurement method used for evaluating nanoaerosol exposures, it is critical that background nanoaerosol measurements be conducted before the production, processing or handling of the nanomaterial/nanoparticle.

When feasible, personal sampling is preferred to ensure an accurate representation of the worker's exposure, whereas area sampling (e.g., size-fractionated aerosol samples) and real-time (direct reading) exposure measurements may be more useful for evaluating the need for improvement of engineering controls and work practices. [16]

Care must be taken when selecting the type of equipment to be used for nanoparticulate measurement. Optical Particle Counters (OPC) measure particles within the 100 nm to 10 µm range. Condensation Particle Counters (CPC) measure particles in the 4 nm to 1 µm range. A Scanning Mobility Particle Sizer spectrometer (SMPS) is also useful. OPC & CPC measurements are just a starting point. Additional sample evaluation by microscopy may be warranted.

Respirator Usage

Any respiratory protection program must meet OSHA's Respiratory Protection Standard 1910.34.134 including all required key elements. Care must be taken in selecting the appropriate respirator for the exposure to be sure that it has an appropriate APF (Assigned Protection Factor).

When choosing a NIOSH approved respirator, the N95 series is for oil free particulate and the R & P series are for all particulates. These respirators stop 95% of particulate averaging 300nm in size. Fit testing, as with any respirator is crucial. Surgical masks have no certification, no fit testing, low efficiency and are not appropriate for use with nanoparticulate.

Exposure to Maintenance Workers

Engineering and administrative controls, if properly implemented, do an excellent job of protecting workers. However don't forget that the greatest exposures are often to maintenance staff. Some of the highest exposures in industry have traditionally been seen among maintenance workers. Administrative controls and where applicable, engineering controls should be strictly enforced with the maintenance staff.

Regulation

Another delicate balance is taking place to provide safe regulation of employee exposures without under or over regulating the nanotech industry. Policy experts and consumer advocates want to toughen oversight to insure the public health is protected. Commercial interests are concerned about regulatory delays and stifling of breakthroughs. They want reliance on existing standards and procedures.

NIOSH has taken a slow and deliberate path to analyze exposures and promote best practices. NIOSH's approach is described in two publications which describe the state of industry best practices:

- Approaches to Safe Nanotechnology [17]
  http://www.cdc.gov/niosh/topics/nanotech/safenano/
- Progress toward Safe Nanotechnology in the Workplace [18]
  http://www.cdc.gov/niosh/docs/2007-123/

OSHA currently relies on the following existing standards to address nanoparticulate related exposures:

- MSDS 1910.1200.
- Respiratory protection 1910.134.
- Personal protective Equipment 1910.132
- Lab chemicals 1910.1450
- Medical records 1910.1020
- HAZCOM 1910.1200

- Certain substance specific standards

However, these standards are not nano specific. In the interim, until nano specific regulations are implemented, issues remain in limbo. For instance, MSDS's provide conflicting or inconsistent information where nanoparticulate is involved. They are not required to address the presence of nanoparticulate. Contrasting examples of excerpts from two MSDS's include:

- Carbon Fullerenes – CAS # 7782-42-5 (Graphite)
  - The PEL provided is for Synthetic Graphite
  - Effects – No Known Toxicological Effects (In spite of research that showed at current Graphite PEL exposure levels workers exposed to nanoparticulate receive an equivalent harmful dose in just 20 days.) [19]
- Carbon nanotubes – Multiwall
  - No CAS # or PEL/TLV is noted
  - Effects - Irritant to the eyes and respiratory system

Contrast these MSDS's with the EU equivalent of the MSDS which includes language such as: "Several reports suggest that carbon nanotubes are potentially toxic for humans if inhaled. These reports are based on studies on rates being instilled with severe doses of materials...." EU labels also include hazard symbols such as the Saint Andrew's Cross (a black diagonal cross on an orange background to denote a harmful or irritant substance).

Resolution of the MSDS issue is not imminent nor is nano specific regulation. Until then, E H & S professionals will have to rely on the OSHA standards and the best practices provided in the NIOSH documents noted above and those emerging from the EU.

National Strategic Nanotechnology Initiative: NNI

Until recently Federal Government nano related research efforts have been somewhat fragmented between individual departments. The recently updated National Nanotechnology Initiative (NNI) is a Federal R&D program established to coordinate the multi-agency efforts in nanoscale science, engineering, and technology. It calls for increased emphasis on the responsible development of nanotechnology. [20]

Concurrently, a diverse group of nanotechnology interested parties, including non-governmental organizations, large and small companies and research organizations, have applauded a Consolidated Appropriations Act for Fiscal Year 2008 measure that will aid in the development and implementation of a comprehensive Federal nanotechnology E H & S research strategy. The Environmental Protection Agency (EPA) is to contract with the National Academy of Sciences' (NAS) Board on Environmental Studies and Toxicology (BEST) to develop and monitor implementation of a comprehensive, prioritized research roadmap for all Federal agencies on E H & S issues for nanotechnology. This effort is independent of the NNI to address the E H &S implications of nanotechnology.

Challenges for the Future

Many studies concerning the effects of nanoparticulate on the body and the environment are underway. The amount of available toxicological data is increasing almost daily. As data, government funding and regulatory efforts increase, there will be fewer un-quantified exposures associated with nanotechnology. In the interim, it is a challenge for the EH & S professional to keep current with new information. This is essential to maximize the effectiveness of existing standards and best practices.

Summary

Nanotechnology is here to stay. The benefits will bring us enhanced products that will increase our quality of life. At the same time, the very properties that allow these enhancements bring unknown exposures into the workplace. While some exposures are known or anticipated, unknown toxicity exposures remain a wild card. However, extraordinary precaution and control will contain exposures to nanoparticulate. Existing engineering and administrative controls will contain and control potential exposures if properly applied in a conservative fashion. Regulation will be slow in coming. Using proven policy and best practice control strategies will mitigate nanotechnology exposures.

Endnotes

1. P. A. Schulte, PhD CDC/NIOSH: Presented at the International Conference on Nanotechnology Occupational & Environmental Health & Safety; Research to Practice, Dec 2006 Slide10

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3. National Science Foundation SOCIETAL IMPLICATIONS OF NANOSCIENCE AND NANOTECHNOLOGY March 2001 P.11

4. Santa Clara Toxic Gas Ordinance http://www.unidocs.org/hazmat/gases/un-027.pdf

5. P. A. Schulte, PhD CDC/NIOSH: Presented at the International Conference on Nanotechnology Occupational & Environmental Health & Safety; Research to Practice, Dec 2006 Slide 20

6. ICON: "Review of Safety Practices in the Nanotechnology Industry, Phase One Report: Current Knowledge and Practices Regarding Environmental Health and Safety in the Nanotechnology Workplace" Rice University, October 18, 2006 P.41

7. NIOSH: Approaches to Safe Nanotechnology http://www.cdc.gov/niosh/topics/nanotech/safenano/ p.xii

8. Lang Tran & Ken Donaldson, University of Edinburgh: Presented at the Toxicological and Health Effects International Conference on Nanotechnology Occupational & Environmental Health & Safety Research to Practice; Dec 2006; Slide 7

9. Günter Oberdörster, University of Rochester: Nanoparticles (NP) and the Brain: Nanoparticles (NP) and the Brain: Pathways of Translocation and Pathways of Translocation and Effects - Presented at the Toxicological and Health Effects International Conference on Nanotechnology Occupational & Environmental Health & Safety: Research to Practice Slide 2

10. Lang Tran and Ken Donaldson, University of Edinburgh- Toxicological and Health Effects International Conference on Nanotechnology Occupational & Environmental Health & Safety: Research to Practice Dec 2006; Slide 15

11. Zhu et al.2007 DNA damage induced by MWCNTs in mouse embryonic stem cells. Nano Letters 7(12): 3592-3597

12. LCDR Mark M. Methner, Ph.D., NIOSH: Nanotechnology Exposure, The NIOSH Nanotechnology Exposure Assessment Field Research Program - Presented at the Toxicological and Health Effects International Conference on Nanotechnology Occupational & Environmental Health & Safety Research to Practice; Dec 2006 Slide 4

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14. NIOSH Safety and Health Topic: Nanotechnology Approaches to Safe Nanotechnology: An Information Exchange with NIOSH http://www.cdc.gov/niosh/topics/nanotech/safenano/assessment.html

15. Oberdörster et al. 1992, 1994 a,b; Duffin et al. 2002

16. NIOSH Safety and Health Topic: Nanotechnology Approaches to Safe Nanotechnology: An Information Exchange with NIOSH http://www.cdc.gov/niosh/topics/nanotech/safenano/assessment.html

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19. A.A. Shvedova NIOSH- Presented at the Toxicological and Health Effects International Conference on Nanotechnology Occupational & Environmental Health & Safety Research to Practice; Dec 2006 Slide 5

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