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Nanotechnology Risk Management: "No Small Risk"

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Introduction

Risk management is an unknown concept to some and a vague or unclear concept to others. But, what is risk management? Risk management is good sound business practice. It's not glamorous, but it's the unseen and often unnoticed foundation on which businesses become successful. It's also a foundation on which businesses fail when there is lack of attention or poor execution.

If there was ever a year to illustrate the need for risk management, it was 2008. Homebuyers took on too much risk making improper assumptions about the value of homes continuing to escalate. When the balloon payment became due, foreclosure resulted. Businesses also took on too much risk putting the balance sheets, stockholders and the entire economy at risk.

Every business faces a multitude of risks. That's the nature of business; if there is no risk there is no reward. How do businesses manage those risks? Fortunately, for most business risks, there are well defined strategies for avoiding, mitigating or transferring risk in order to avoid the catastrophic impact of a negative event.

The risks presented by 20th century manufacturing techniques are well known. But, while there is much continuity between most manufacturing risks of the 20th and 21st centuries, rapid advances in technology present new risks with unknown and unquantified consequences. These new risks challenge both risk managers and environmental health and safety professionals.

Nanotechnology is a new technology that brings previously unknown risks to the workplace, the marketplace and the environment. The risks and rewards must be carefully balanced. The novel nano properties which enhance the features and benefits of products create additional potential risks for employees who make the products and persons who use the products. They also create potential environmental and general liability risks which must be managed.

Some of these new risks are known and quantified. Others remain unknown and unquantified even with a rapidly emerging library of toxicological and environmental impact knowledge. Since nanotechnology is process oriented rather than end product related, it cuts across almost all industry and market boundaries.

What is Nanotechnology?

Nanotechnology refers to man-made, engineered structures between 1 and 100 nanometers in size that are controlled or manipulated at the atomic level. These structures, devices and 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. It is these novel properties, existing only at the nano-scale, that allow physio-chemical interactions that enhance manufacturing processes and product features.

Nano-particles 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 (aka Buckeyballs). Also included are Quantum Dot (i.e., CdSe /ZnS) crystals. There are also repeatedly branched molecules such as dendrimers in the nanoscale. Each structure and its related size and shape, even for the same compound, has potentially different physio-chemical interactions. As a result, each has the potential for different reaction within living tissue or the environment.

For the purposes of this presentation, nano-particles naturally occurring in nature or resulting from byproducts of manufacturing processes or carbon-based fuel engine exhaust are excluded. This presentation concerns engineered nano-particles that result from manipulation at the atomic level in which sizes and shapes are highly controlled.

How Small are Nano-particles?

The size of a nano-particle, a billionth of a meter, is so small that it is difficult to grasp. Relative size comparisons have been made by comparing the size of the Earth to the size of a dime. [1] Mass/ surface area comparisons have been made indicating that one 10 μm particle weighs the same as one billion 10 nm particles, however the surface area of the nanometer sized particles is hundreds of thousands of times larger.[2] It is the massive surface area that allows physio-chemical reactions not possible with macro sized particles.

Concern Is Valid

As with any new technology, there is a risk/reward balance. The rewards are many but the environmental and human risks are not fully quantified. The public has every right to be concerned and educated about potential issues that may arise when they are exposed to products made with nano-particles. It is also important to understand the environmental effects of nano-scale particles throughout their lifecycle. But, hype must be separated from reality.

Nano-particulates 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 nano-particulate to reduce spoilage. Workers have the potential to inhale, ingest or absorb nano-particulate during manufacturing or R & D processes. End-users of some products containing nano-particulate potentially have similar exposures.

There is no easy answer to the question “What happens if I’m exposed, i.e. dosed, to nano-particles?”, since all nano-particles do not have the same toxicology. Likewise, all exposures are

not the same. The emerging library of nano toxicology indicates one thing for sure. The results of interactions of living tissue with particles at the nano-scale are particle specific.

Some organic nano-particles such as carbon Nanotubes clearly have the potential to inflame tissues and potentially cause cancer. For other Nano-particulates, there is little or no indication of the adverse effects. For still others, a different crystalline structure for the same compound determines the potential for increased toxicity. For many, toxicity is unknown since studies on particles and dose responses have not yet been completed. Predictive modeling of toxic potential is in its infancy. The public is looking for valid information that will result in a level of comfort with nano-enabled products and nano-particulate in the workplace.

Risk Management and the Bell Curve

Risk management is about sleeping at night. Does your board of directors sleep at night? Do your investors sleep at night? Do you as an EH&S professional sleep at night knowing that improper treatment of nano risks could adversely affect your employees and your company?

All businesses face risks. How a company handles and mitigates those risks can result in the success or even the continued existence of the firm. In reality, there is a bell curve of risk response in business. It ranges from the very conservative who "always color within the lines" to "high rollers" ready to risk all the stakes. Recent examples of risk taking on losing side of the curve are on Wall St. Improper product risk assumptions and a lack of risk management resulted in numerous financial institutions becoming defunct, acquired or teetering on the edge.

Successful companies assess hazard, characterize risk and determine the likelihood of loss. They stay near the top of the bell curve, examining the probability of events occurring and the results if they do occur. Highest priority is given to those losses most likely to occur.

Risk Treatment

What options do your management and you, as an EH&S professional, have to address these risks? A thorough assessment must be made at all levels so the risk can be identified and prioritized. Once those assessments are made, risk can be treated in a number of different ways. The most common ways are as follows:

- **Risk Avoidance** - Risk avoidance should always be the first option. Companies may choose not to pursue a line of business or in new product offering because the risks associated with those may be so great that they cannot be mitigated. A negative event could have catastrophic effect on the company or in the case of EH&S professionals, on the company's employees. One cosmetic company used risk avoidance by eliminating a line of less profitable face powders which contained nano particulate.

- **Risk Transference** - Usually, the second option is risk transference. Risk transfer is a common method of mitigating risk by either outsourcing or insuring exposures through a third party. Risk transfer can also be done through a non-insurance contract holding a third party liable for specific events. Risk transference is driven by statutory requirements, banking requirements and sound risk management principles. Most EH&S professionals are familiar with risk transference because they deal with workers

compensation issues. Property, general liability and product liability exposures can also be mitigated through risk transfer. Parts of these risks are routinely transferred to an insurance company via insurance contract. However, insurance is only one small piece of the puzzle.

- **Risk Retention** - A third option is risk retention, also known as self-insurance. It's accomplished by a number of financial schemes allowing a company to fund all or part of the potential for its own losses. First the company has to decide how much risk they wish to take and self-insure. Self-insurance operates much as an insurance company does, keeping reserves in place for contingencies. Administration such as loss adjustment and claims handling is often done by third parties called TPAs. While total risk retention is generally reserved for very large companies, it is common for companies to retain some risk via deductibles when transferring risk with an insurance policy.

- **Risk Reduction** - The fourth and most important option to the EH&S professional is risk reduction. Risk reduction is applied to the retained risks not mitigated by the above techniques. However, acceptance of this risk requires that it be mitigated in order to keep potential losses to acceptable levels. EH&S professionals are involved on a daily basis with risk mitigation involving engineering controls, administrative controls, policies and procedures, personal protective equipment etc.

It is key that the EH&S professional broaden his or her horizons concerning how management thinks about risk. Your world is a risk reduction and mitigation. Management has other options. Understanding the way that senior management treats risk through risk avoidance, transference and reduction allows the EH&S professional to better sync with corporate goals and objectives.

Applying Risk Management Techniques to Nanotechnology

Traditional industries having well-known risk parameters, manage risk using a combination of risk management techniques. But, what happens when a new industry evolves having unknown or unquantified risks? What are the long-term risks? How are nanotechnology risks different from any other manufacturing operation?

- **Risk Avoidance** is always the first option to look at. Because nanotechnology spreads horizontally across many manufacturing sectors, it's not uncommon for an idea that works in one sector to be modified for use in another. One nano tech company looking at drug delivery systems came up with an idea to infuse nano-particulate with insecticide for use as an additive in cow feed. The idea was that the insecticide in its nano carrier would pass through the cow to be deposited onto the feedlot ground. The insecticide would then be released, killing the flies on the feedlot. While an interesting idea, it was ripe with all sorts of issues and potential liabilities. In this case, the company chose not to pursue the option, therefore avoiding the risk. However, risk avoidance is rarely an option.

- **Risk Transfer** using insurance contracts is usually an option although some insurers may be wary of unquantified risk. Insurers vary in their approach to and appetite for nanotechnology risk. In general, insurers are conservative in their approach and appetite until a track record is established in the industry.

- **Risk Retention** is almost always done to some extent. Larger companies retain larger amounts of risk. Smaller companies retain lesser amounts of risk. For small startup companies, this is usually less of an option.

Risk avoidance, risk transfer and risk retention are financial options over which senior management has the most control. These are not nano technology specific.

- That leaves **Risk Reduction**, over which EH&S professionals have the greatest control. Although nanotechnology has unknown and unquantified risks, basic risk reduction strategies use a traditional time-tested approach :

    - **Map** processes to identify potentially hazardous scenarios
    - **Prioritize** the scenarios that pose the greatest threat
    - **Devise** mitigation strategies including industry best practices and those mandated by government
    - **Modify** hazardous procedures and emissions
    - **Measure** to validate performance of engineering and administrative controls
    - **Test** to determine risks and management options
    - **Re-validate** protective strategies
    - **Communicate** with all affected corporate departments, business partners and parties affected by your risk management parameters

Personal Risk Management

What risk management techniques will you use to assess and mitigate potential risks associated with nano products that you and your family come into contact with? Most people have not given a lot of thought to this because they do not realize that products containing nano-particulate are increasingly prevalent in the marketplace. Well over 800 currently are available. [3] There is a wide a range of nano products from sporting goods to clothing, to face creams. Manufacturers are more than willing to take advantage of the unique properties that nano-particulates impart to their products. However, they have been reticent to disclose to the public that nano-particulate is contained in the products. This is due to public concern and potential "nano-phobia," fear that nano related products could cause bodily injury.

Nanotechnology Business

Nanotechnology is still in its infancy. Prior to the international financial crisis, markets for nanotechnology products were developing rapidly. Original projections by the U.S. National Science Foundation of a $1 trillion [4] annual market by 2015 may or may not be still valid. Who knows? All of the projections of market size were done before the downturn.

What is certain, however, is that the economic downturn is a speed bump rather than a roadblock to the development of nanotechnology markets. These markets include nano-materials, nano-intermediaries and nano-enabled products. Nanotechnology progress may have been slowed by the downturn, but the promises and profits are too great for research and application to be adversely affected for too long. The speed at which the industry recovers traction will depend on the easing of the economic crisis.

Almost all of the major countries in the world have made significant investments in nanotechnology research. Many of the world's multinational and Fortune 500 corporations have also made significant investments. The surge of interest in green energy products and processes, particularly in the solar arena, is also pushing nano research.

Business Issues for Nano Companies

Nano companies come in all shapes and sizes. A viable idea may be researched in large corporations, small corporations, startups or university laboratories. The nano related risks, whether known, unquantified or unknown are the same for the employees in all of these different sizes of operations. How they are risk managed, however, varies widely due to a function of corporate structure, the availability of capital, nano issue awareness and risk management philosophy, or lack thereof.

Larger corporations have the advantage of having existing Risk Management and EH&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. For smaller companies, particularly startups, risk management is a combination of management experience, business school acumen, corporate governance requirements, scientific knowledge, engineering skill set, insurance broker/ company involvement, local authority having jurisdiction requirements, and industry best practices with hopefully a bit of common sense risk awareness thrown in. In today's world of minimized expenses, some of these functions may be outsourced, particularly as regards startups.

Industry Understanding of Nanotechnology Risk

There has been no new definitive study of nanotechnology industry practices since the 2006 ICON Study "Survey of Current Practices in the Nanotechnology Workspace [5] " queried industry on all phases of nanotechnology. In that study:

- 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.

Pressure on EH&S Professionals

Start-ups are pressure cookers! There is pressure to obtain venture capital, pressure to protect intellectual property, pressure to minimize expense, and pressure to get a product to market start income flow. There is a delicate balance between available funding versus capital expense burn rates.

Once a company accepts nano business risk and realizes that they can make their idea into a viable product, they face a number of hurdles that must be risk managed:

- Can the process be rescaled into a pilot plant?

- Can the pilot be rescaled into a full manufacturing at a reasonable cost of manufacture?
- Do they sell off the intellectual property?
- Do they license intellectual property?
- Do they do a partnership or do manufacturer themselves?
- Do they manufacturer onshore or offshore?

Every one of these milestones has a significant risk mitigation impact on the EH&S professional. Whether a large or small corporation, EH&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 EH&S person(s) will blunt the impact of rapid expansion.

Communication is absolutely critical at all levels. Today's E. H. and S. professional has to be an amazing communicator capable of the following:

- **Business Speak** in business terms in order to obtain proper budget allocations.
- **Tech Speak** in order to communicate with the researchers and scientists.
- **Insurance Speak** the in order to demonstrate control of exposures to insurers.
- **Gov Speak** to work with and negotiate with AHJ's & assorted bureaucrats.
- **Motivation Speak** in order to motivate supervisors, obtain employee compliance, massage egos, and referee virtual fistfights.
- Knowing when to listen and **NOT** to speak.

Nanotechnology Risk

What's different about the risk management approach to nanotechnology? Not much, except that the approach is very conservative because of the unknown and unquantified exposures. The good news is that, per NIOSH, time-tested controls, when used conservatively, should control exposures. These controls include proper engineering and administrative controls such as ventilation, filters, and personal protective equipment. While engineering controls and administrative controls can significantly reduce or mitigate risk and exposure, their limitations vis-à-vis specific nano-particulates are not fully understood. That is why a conservative approach is necessary.

Risk is a function of hazard and exposure. But, before controls can be applied, risks must be quantified, at least as much as possible. The growing body of toxicology studies indicates that some nano-particles have the potential to do harm to the body if inhaled, ingested or absorbed. From a property perspective, nano-particulate has the potential to cause great damage due to explosion potential. In the environment, the effects of particles, such as nano-scale silver and silica, are being explored as to how they interact with soil, air and water.

Assessing and Characterizing Un-quantified Risk

In July of 2008, an expert panel appointed by the Council of Canadian Academies concluded that too little is known to assess the overall human and environmental risks posed by the introduction of nanomaterials and nano-products into society. [6] However, the panel did not identify any evidence that nano-products currently on the market in Canada present risks that cannot be

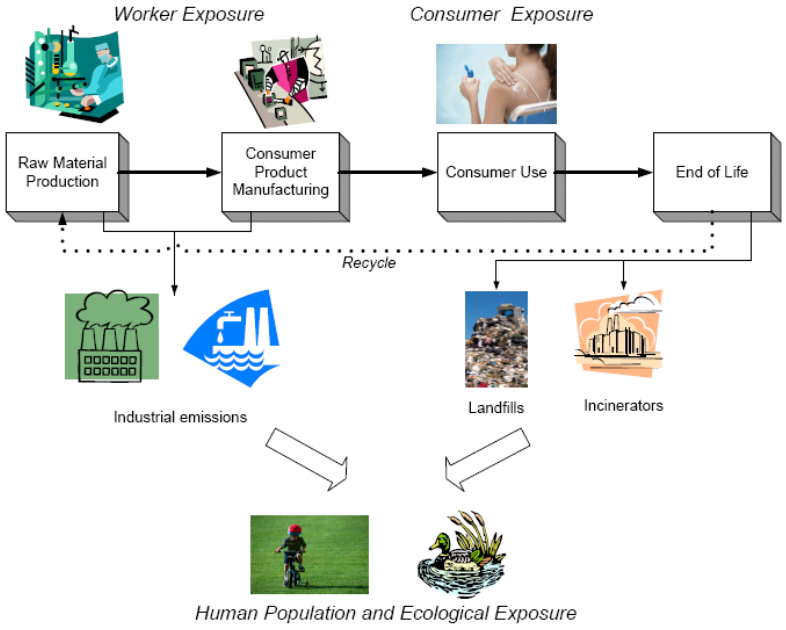
addressed through available risk management strategies. That is the dilemma presented by the introduction of radical new technology. It is known that there are risks but how great are they? It's also good news, however, in that available risk reduction and mitigation strategies are appropriate.

Risk mitigation starts with assessment and characterization of risks and hazards. The more certain the hazard, the more certain are the techniques used to manage them via engineering and administrative controls. When the risks are unknown or not fully characterized, management controls, communication, and precaution need to be greatly increased. Uncertainty requires a conservative approach with extraordinary precautions and controls.

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 .[7]

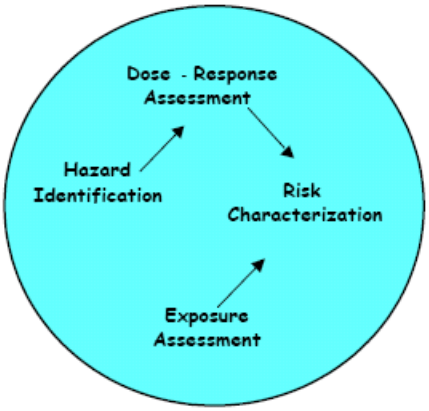
Nano-particulate Exposure Ranking

Environmental Exposure: The EPA assesses nanomaterials from a life cycle perspective. [8]



The EPA's goal is to identify and characterize nano-materials, determine the environmental fate of nano-materials, determine the best way to detect and analyze nano-materials, determine the effect of nano-materials on humans and determine the ecological effects of nano-materials.

The EPA generally follows the risk assessment paradigm described by the National Academy of Sciences (NRC, 1983 and 1994), which at this time EPA anticipates to be appropriate for the assessment of nanomaterials. [9]



Per EPA, the overall risk assessment approach used by EPA for conventional chemicals is thought to be generally applicable to nanomaterials. Larger surface areas per unit of volume, as well as novel electrical properties relative to conventional chemicals create unique materials. Some of the special properties that make nanomaterials useful are also properties that may cause nanomaterials to pose hazards to humans and the environment, under specific conditions. Furthermore, numerous nanomaterial coatings are being developed to enhance performance for intended applications. These coatings may impact the behavior and effects of the materials, and may or may not be retained in the environment. It is necessary to consider these unique properties and issues, and their potential impacts on fate, exposure, and toxicity, in developing risk assessments for nanomaterials. [10]

Human Exposure: Nano-particulate can be divided into two major groups, organic (nanotubes, fullerenes, etc) and inorganic, mostly metal oxides. Nano-scale particles are manufactured, packaged and used in either in solution or dry process, which has the potential for dust and inhalation exposures. 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 risks associated with organic vs. inorganic nano-particulate and wet vs. dry use:

- Inorganic particulate formation in **solution/liquid suspension**
  - Less reactivity
  - Dermal absorption, ingestion but minimal inhalation
- Organic particulate formation in **solution/liquid suspension**
  - More reactivity
  - Dermal absorption, ingestion but minimal inhalation
- Inorganic particulate formation - **dry powder in air or deposition on surface**
  - More reactivity
  - Same modes + inhalation
- Organic particulate formation - **dry powder in air or deposition on surface**
  - More reactivity
  - Same modes + inhalation

Factors that Affect Relative Risk

Aggregated, suspended, embedded or agglomerated nano-particles are factors that decrease risk. Likewise limiting exposure by limiting task duration also decreases risk. Inert atmospheres within enclosures decrease explosion risk. In general, risk of loss is lower in the R&D phase, increasing when companies reach the pilot phase and increasing further, when scaled up to full production.

Nano-particles with high dispersion rates or those less likely to agglomerate, increase risk. Nano-particles made of toxic compounds (i.e. CdSe/ZnS quantum dots) have increased risk in spite of their particle size.

Potential Injury Modes

Up to 50% of inhaled nano-particles may deposit in gas exchange regions of the lung. Because of their greater surface area and reactivity, Nano-particulates, whether metal oxide or organic, cause oxidative stress on living tissue. 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. [11]

Particulate Transfer within the Body

Nano-particulate has the potential to enter the body via the skin, eyes, and the respiratory tract, or the GI tract through absorption, injection, inhalation and ingestion. Interactions may be unpredictable and potentially harmful. Once in the tissue and bloodstream, nano-particulate travel, known as translocation, routes through organs and systems including the central nervous system, the lymphatic system, bone marrow, kidney, spleen, heart, among others. Additional suspected translocation routes are via muscles, placenta and liver. Translocation rates are largely unknown. Some but not all nano-particulate may be excreted through sweat, urine, breast milk, feces, etc. [12]

Particle Specificity

Studies released in mid 2008 confirmed the growing body of knowledge that some lengths of single wall (SWCNT) and multi-wall (MWCNT), carbon nanotubes (CNT's) behave like pathogenic fibers. High aspect ratio CNT's fit the parameters of being long, thin and bio-persistent. In spite of being shorter than other pathenogenic fibers, such as asbestos, CNT's have the unusual ability to stimulate fibrosis in the lungs with the potential for lung cancer if there is sufficient exposure. [13]

Dermal studies show that potential hazard exists as indicated by a biological response by the skin to some specific nano-scale compounds including fullerenes and quantum dots. Skin penetration through stratum corneum is enhanced by cuts, lesions, surface modifications, agitation, and surfactant presence. Studies are on-going to define structure/activity relationships. [14]

The biological response to the physio-chemistries of both organic and inorganic nano-particulate depends on a number of factors. These include: size distribution, agglomeration state, shape & structure, surface area, porosity, surface chemistry and surface charge. Additives such as coatings and impurities to nano-scale compounds have additional potential effects. Because of all of these

variables, it is difficult for toxicological researchers to compare research results unless all of the above parameters are taken into account. Sweeping generalizations such as "All metal oxide nano-scale compounds are safe" or "All carbon nanotubes cause cancer" cannot be made. Toxicity is particle specific, the extent depending on the combinations of factors above.

Risk Reduction and Mitigation Controls

That creates a dilemma for the EH &S professional because definitive data is not available on all the permutations and combinations of the above parameters for most nano-scale particles. Quantified hazards need less conservative controls. However, in the absence of particle specific data, a conservative control approach must be taken.

When developing strategies to mitigate workplace exposures, either quantified or un-quantified, a time tested hierarchy of risk reduction 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. 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, ACGIH best practice compliant exhaust ventilation, HEPA/ULPA filtration and explosion proof electrical fixtures.

Administrative solutions are also an important part of solutions but are less desirable because they introduce the human factor and the human ability to defeat solutions with unsafe acts or lack of follow through. Comprehensive policies and procedures reinforced by frequent training and policy enforcement are essential.

For example, any administrative control whether it be personal protective equipment or particulate sampling, requires total commitment by the EH&S professional, the supervisor and the employee to make sure that the human components are followed, per policy and procedure, on time, every time to provide optimum protection. Human factors can easily defeat even the best sampling or personal protection programs. Distractions, unplanned events, budget issues, changes in management priorities, employee behavior and other negative factors all strive to challenge the successful use of administrative controls.

One model to apply these risk management techniques to an EH& S program is the "Controls for R&D Laboratory Operations" [15] model used by the DOE. It uses the following approach:

- Work planning/hazard assessment

- Control preferences
- Engineer controls
- Administrative controls
- Clothing and personal protective equipment
- Monitoring and characterization
- Worker competency
- Verifying program effectiveness
- Nano particle worker identification
- Workplace characterization and exposure assessments
- Worker health surveillance
- Domestic waste surveys
- Effluent monitoring
- Transferring of nano-materials

Control Banding

Control banding is a technique developed in the high hazard chemical industry to apply control techniques to bands of increasing ranges of exposure and hazard. Because there are no adequate Occupational Exposure Limits (OELs) for nanotechnology, control banding can be very effective.

Per NIOSH, control banding is a technique used to guide the assessment and management of workplace risks. It is a generic and methodical technique that determines a control measure based on a range or "band" of hazards. It is an approach that is based on the fact that:

- There are a limited number of control approaches
- Many problems have been met and solved before (particularly for dangerous chemicals and fumes).

Control Banding uses the solutions that experts have developed previously to control occupational chemical exposures, also known as "potent compounds". These solutions are applied to tasks with similar exposure situations. It is an approach that focuses resources on exposure controls and describes how strictly a risk needs to be managed.

Control Banding is designed to be used in conjunction with health and safety practices such as substitution. Substitution for a less hazardous chemical is still highly recommended to prevent exposure. Control Banding is NOT a replacement for experts in occupational safety and health nor does it eliminate the need to perform exposure monitoring. Control Banding highly recommends the use of professionals to provide recommendations. Control Banding also recommends exposure monitoring ensure the installed controls are working properly.[16]

Control Banding uses a single control technology or strategy matched with a single band, or range of exposures for a particular class of chemicals. Here is an example of four control bands developed for inhalation hazards.[17]

Band	Hazard Group	Exposure Concentration	Control Strategy

no.			
1	Skin and eye irritants	<1-10 mg/m3 dust, or >50 to 500 ppm vapor	General ventilation and good industrial hygiene practices.
2	Harmful on single exposure	>0.1 to 1 mg/m^3 dust or >5 to 550 ppm vapor	Local exhaust ventilation
3	Severely irritating and corrosive	>0.01 to 0.1 mg/m^3 dust or <0.5 to 5 ppm vapor	Process enclosure, an engineering control
4	Very toxic on single exposure, reproductive hazard, sensitizer	<0.01 mg/m^3 dust or <0.5 ppm vapor	Seek expert

Government Regulation

Regulator approach varies. In the EU, regulators have been more proactive in requiring warnings for potential hazards, both for workers and product end users. Government regulation of nanotechnology has been slow and deliberate in the United States for political reasons including a desire not to stifle a new and emerging technology. There has been a significant increase in calls for regulation from public organizations, private organizations and non governmental organizations (NGOs) such as the International Risk Governance Council (IRGC). The U.S. Governmental trend is moving toward more regulation and more warnings. The "hands-off" approach of the previous US administration is now changing with different approaches being taken by NIOSH, the EPA and the FDA.

NIOSH's Approach

NIOSH has taken a slow and deliberate path to analyze exposures and promote best practices. The recent change in administrations is expected to place more emphasis on science and emerging technologies. NIOSH's approach to date is described in two publications which describe the state of industry best practices:

- Approaches to Safe Nanotechnology [18]
  http://www.cdc.gov/niosh/topics/nanotech/safenano/
- Progress toward Safe Nanotechnology in the Workplace [19]
  http://www.cdc.gov/niosh/docs/2007-123/

Last year, as part of its nanotechnology research agenda, NIOSH initiated a study to investigate exposure to fine (0.1µm to 2.5µm diameter) and ultrafine (<0.1µm diameter) metal oxides. The

purpose of the metal oxide study is to measure and characterize workplace exposure to fine and ultrafine metal oxides in both manufacturing and end-user facilities.

In February 2009, NIOSH released "Current Intelligence Bulletin 60: Interim Guidance for Medical Screening and Hazard Surveillance for Workers Potentially Exposed to Engineered Nanoparticles" to provide interim guidance about whether medical screening, including performing medical tests on asymptomatic workers is appropriate.

The executive summary of Current Intelligence Bulletins 60 states: **"Medical** screening is only one part of what should be considered a complete safety and health management program. An ideal safety and health management program follows a hierarchy of controls and involves various occupational health surveillance measures. Since specific medical screening of asymptomatic workers exposed to engineered nano-particles has not been extensively discussed in the scientific literature, this document makes recommendations based upon what is known until more rigorous research can be performed.

Currently there is insufficient scientific and medical evidence to recommend the specific medical screening of workers potentially exposed to engineered nano-particles. Nonetheless, this lack of evidence does not preclude specific medical screening by employers interested in taking precautions beyond existing industrial hygiene measures. If nano-particles are composed of a chemical or bulk material for which medical screening recommendations exist, these same screening recommendations would be applicable for workers exposed to engineered nano-particles as well.

As research into the hazards of engineered nano-particles continues, vigilant reassessment of available data is critical to determine whether specific medical screening is warranted for workers. In the interim, the following recommendations are provided for workplaces where workers may be exposed to engineered nano-particles in the course of their work:

- Take prudent measures to control exposures to engineered nano-particles.
- Conduct hazard surveillance as the basis for implementing controls.
- Continue use of established medical surveillance approaches.

NIOSH will continue to collect and evaluate new research findings and update its recommendations about medical screening programs for workers exposed to nano-particles. NIOSH will also continue to consider the strengths and weaknesses of establishing exposure registries for workers potentially exposed to engineered nano-particles for future health surveillance and epidemiological studies".[20]

There were indications from NIOSH that "Approaches to Safe Nanotechnology" was due for revision, however, the Version 1.1 of 2006 remains on the website as of this writing. MSDS's continue to provide conflicting or inconsistent information where nano-scale materials are involved. MSDS's are not required to address the presence of nanoparticulate. No change is expected in the near future.

OSHA continues to rely on the existing 1910 CFR standards for MSDS, Respiratory Protection, PPE, Lab Chemicals, Medical Records, and HAZCOM to address nano-particulate related exposures. However, these standards are not nano specific. While guidance may start with these standards, they must be integrated with industry best practices as outlined in "Approaches to Safe

Nanotechnology" and elsewhere in order to have a comprehensive NIOSH approach toward nano-scale risk management.

EPA's Approach

The EPA is actively participating in nanotechnology development and evaluation including collaboration, research, funding research, voluntary programs, and risk and hazard review.[21]

The EPA has also been active in stepping up regulatory efforts to regulate nano-scale materials under existing statute authorities. This is a break from previous lack of governmental intervention. Efforts include:

- Issuing a rulemaking petition in process to classify nano-scale silver as a pesticide. The petition requires formal pesticide registration of all products containing nano-scale silver, analysis of potential human health and environmental risks, and regulation under the existing Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).
- Recently determining that carbon nanotubes are chemically distinct and a new compound, requiring additional testing under the toxic substances control act TSCA. [22]
- Promulgated significant new use rules (SNURs) for nano-scale Silica and Alumina.[23]

Examples of potential sources noted in the EPA Nanotechnology White Paper include sunscreens and disposal of sunscreen containers in landfills, metal catalysts in gasoline reducing vehicle exhaust, paintings and coatings and nano impregnated clothing. All of these are potential areas of concern for the EPA.[24]

FDA's Approach

Specific references to the types of products FDA regulates, the FDA "Centers" responsible for their regulation, and guidance on the regulatory processes are found @ (http://www.fda.gov/). Per the FDA, the following list is provided only for illustrative purposes:

- Biological products (vaccines, blood products, tissues)
- Cosmetics
- Devices
- Foods (for humans and animal feed, though generally not meat and poultry)
- Dietary supplements
- Drugs (human and animal)
- Radiation Emitting Electronic Products
- Color additives used in food, drugs, cosmetics, devices
- Combination products (i.e., drug-device, drug-biologic, and device-biologic products)

While the EPA has determined that carbon nanotubes are chemically distinct and a new compound, the FDA has taken a different approach to nano-scale materials. For example, zinc and titanium oxide have been commonly used in sunscreens for many decades. However, in recent years, nano-scale size particles of these oxides have been added to sunscreens. Because no new studies have come forth indicating that nano-scale zinc or titanium oxides are toxic, the FDA

takes the stance that these oxides at the nano-scale are not new compounds which would trigger additional testing since they are still the same compounds.

"For products not subject to pre-market authorization requirements, such as dietary supplements, cosmetics, and food ingredients that are generally recognized as safe (GRAS), manufacturers are generally not required to submit data to FDA prior to marketing, and the agency's oversight capacity is less comprehensive".[25]

"Because the current science does not support a finding that classes of products with nano-scale materials necessarily present greater safety concerns than classes of products without nano-scale materials, the Task Force does not believe there is a basis for saying that, as a general matter, a product containing nano-scale materials must be labeled as such. Therefore the Task Force is not recommending that the agency require such labeling at this time. Instead, the Task Force recommends that the agency take the following action: Address on a case-by-case basis whether labeling must or may contain information on the use of nano-scale materials".[26]

The FDA's position is that until there is research that nano-scale zinc and titanium oxides are toxic, they can be used in sunscreens. Labeling indicating that nano-particulate is present in the product is not required.

This presents a chicken and egg problem. Testing is not required because the compound is not new. But if testing is not required how will there be evidence of safety or a lack of safety? To date, there is no definitive study saying that either zinc or titanium oxide is toxic at the nano-scale. But while the FDA continues to debate the need, there remains no requirement for disclosure. Shouldn't the consumer know that nano-scale particles are in products which are being applied directly to the skin? Without disclosure, an informed choice cannot be made.

The FDA is also under fire from the Washington DC based Project on Emerging Nanotechnologies, based in Washington, DC, whose report "A Hard Pill to Swallow: Barriers to Effective FDA Regulation of Nanotechnology-Based Dietary Supplements", questions whether space in the FDA is equipped to meet the emerging regulatory challenge of dietary supplements that use engineered nanomaterials. The report questions the FDA's capacity to identify nano-based dietary supplements due to a lack of pre-market notification requirements, their regulatory authority over nano-scale diet supplements, and their scientific expertise.[27]

The FDA's response to criticism of their positions is summed up in their website FAQ #6:

"What will be required for nanotech products to receive FDA approval? Should consumer products be regulated any differently because they are made with nanomaterials? Are there any risks associated with these products because of their nanomaterial components?

As noted above, FDA only regulates certain categories of products. Existing requirements may be adequate for most nanotechnology products that we will regulate. These products are in the same size-range as the cells and molecules with which FDA reviewers and scientists associate every day. In particular, every degradable medical device or injectable pharmaceutical generates particulates that pass through this size range during the processes of their absorption and elimination by the body. To date, FDA has no knowledge of reports of adverse reactions related to the "nano" size of resorbable drug or medical device products. If new risks are identified,

arising from new materials or manufacturing techniques for example, new tests or other requirements may be needed".[28]

The same issues exist for food additives, food packaging and other nano-particulate products which have the potential for the end user to inhale, absorb or ingest nano-scale particles. The governmental process is slow due to pressure from both advocates and adversaries of nanotechnology. Eventually, there will be a resolution of the disclosure issue. Until then, lack of disclosure, whether required by the FDA or not, is an area with the potential for future litigation.

It's important to note that there are many products containing nano-scale particles which have the particles embedded in a matrix. Examples include carbon nanotube enhanced tennis rackets and car side panels. Since they are embedded particles, the likelihood of dermal, inhalation or ingestion exposure is very slight. These types of products present much less potential risk to the user. For these products, disclosure is much less of an issue but each must be evaluated on an individual basis.

Other Regulatory Efforts

Regulatory requirements concerning nano production and products are beginning to be put in place.

- Canada plans the first mandatory reporting of quantity, usage and chemical data. The information gathered under the requirement will be used to evaluate the risks of engineered nanomaterials, develop appropriate safety measures to protect human health and the environment, and development of a regulatory framework.
- The EPA issued an interim report on its Nano-scale Materials Stewardship Program. Due to the lack of voluntary data the program garnered, the Agency will consider how best to use the federal Toxic Substances Control Act (TSCA) to gather more risk data.
- The California Department of Toxic Substances Control (DTSC/Department) is requiring information regarding analytical test methods, fate and transport in the environment, and other relevant information from manufacturers of carbon nanotubes. The term "manufacturers" includes persons and businesses that produce in California or import carbon nanotubes into California for sale.
- A Mandatory Nanomaterial Declaration has been proposed by French Government that those who manufacture, import or place on the market nano-particulate substances periodically report to the administrative authorities the identity, quantity and uses of these substances. In addition, information on identity and use of substances should be made available to the public, except if doing so would be potentially damaging to national defense.

Regulators are in a difficult position. They must provide a delicate balance between safe regulation of employee exposures and 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. The trend however is clearly starting to move toward more regulation.

Challenges for the EH&S Professional

Continuing increases in use of nano-scale materials present potential increased exposures to workers, product and users and the environment. The focus on nanotechnology related concerns is increasing. Many longer-term studies concerning the effects of nano-particulate on the body and the environment are underway.

How does the almost a daily deluge of new information affect risk management of nanotechnology? Without up-to-date knowledge, proper strategies cannot be developed. Exposures and controls cannot be properly implemented. Up to date information and a solid a risk management philosophy create a framework for a winning business proposition. It allows the EH&S professional to proactively create and execute his or her role.

It is a significant challenge for the EH&S professional keep up with the changes that affect nano-scale materials. Just sorting the media hype from truly useful information is a challenge. Add to that, the need to keep up with all of the changing EH&S issues that have nothing to do with nanotechnology. A particularly helpful way to stay current is to sign up for free or paid mailing lists that provide summaries of articles on a weekly basis. These are immensely helpful in finding the useful nugget of new risk related information amongst a plethora of text.

Summary

Risk management is one of the most important and most often ignored aspects of company's success or failure. An honest assessment must be made at all layers of management about which risk factors are controllable and the methods used to control them. It is equally important to understand those factors which are out of EH&S professional's control. They can, however, still can be managed using different techniques.

A strong risk management philosophy is important for any company. It is, however, especially important for those companies dealing with the unquantified and unknown risks associated with nanotechnology. The benefits that bring us enhanced products are, at the same time, the very properties that bring unknown exposures into the workplace and the environment.

Having a risk management perspective rather than a pure risk reduction perspective provides the EH&S professional with greater insight into business issues confronted by the company. It results in a balanced risk/reward approach that syncs with company goals and objectives. A comprehensive risk management perspective assists the EH&S professional in developing and providing an effective program which protects the employees, the environment and the business.

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