A White Paper on NANO-SAFETY

Executive Summary:

Nanotechnology is becoming ubiquitous in consumer products. As its use continues to grow, so do concerns about its impact on both humans and the environment. Therefore, products are undergoing increased scrutiny, as in a recent case in which the incorporation of nanoparticles caused a German cleaning product to be removed from the market, or as another example, the concerns about the titanium oxide nanoparticles in sunscreen and the unknown effect on people. Also unknown are the effects of beneficial applications. While the potential benefits of the application of nanomaterials to treat and cure cancer offers hope to many seriously ill people, the long-term impact of nanomaterials on the human body is not completely known. Employing silver nanoparticles in wound dressings, promotes healing while reducing potential infections; but, these same nanoparticles could also destroy helpful bacteria in the environment if the particles are not properly handled.

Concerns like these frequently result in media reports that portray nanotechnology as a future curse rather than the beneficial technology that it has the potential to be. Because insufficient scientific information is not available to the public, reports like those mentioned above become the source of information. Since nanotechnology is relatively new, it is understandable that information is not widespread. Another reason for this lack of information is that the fundamental properties of nanomaterials are generally unknown. Investigations of the properties need to be accomplished in a systematic manner and disseminated to as wide an audience as possible. However, a problem with determining the material properties is that there is a lack of equipment that can accurately investigate the material properties in the nano realm. Complicating the matter is a lack of standardized procedures for handling and employing the nanomaterials. The approach to developing the understanding of the behavior of materials in the nano requires a systematic plan to address the various elements of nanotechnology.

This lack of knowledge about nanomaterials inhibits their application. The semiconductor industry at the July 2007 ITRS meeting indicated that one of the issues with future improvements in devices is the lack of knowledge about the properties of nanomaterials. The lack of knowledge also raises the specter of danger to people. The fundamental question is about safety to the people who handle it, to the people who use the products, and to the environment. This issue, NANO-SAFETY, needs to be addressed in a systematic approach to provide information needed to develop advanced applications employing nanomaterials in a safe and sure manner.

This white paper addresses four key areas for developing a NANO-SAFETY effort and identifies the key areas as: 1) nanomaterial properties; 2) the effect on humans and the environment; 3) the means of handling the materials correctly; and, 4) the procedures that must be in place to minimize risk in applications. The scope of this effort is larger than any one organization is capable of handling. Therefore, the approach presented herein employs a collaborative effort that includes universities, medical facilities, and industry. This collaboration in conjunction with various US governmental organizations can provide a leadership role in developing new applications employing nanomaterials that will improve the overall quality of life for people and develop new jobs for the production of these products.

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Background:

Nanotechnology has captured the imagination of writers, entrepreneurs, venture capitalists, and even politicians. Nanotechnology is postulated as the solution to many of the world's problems, ranging from energy storage to curing cancer. At the same time that many applications have been developed, and many more are being envisioned, a new concern has arisen: the issue of nanotechnology safety. Articles have been written about the need for investigation on the impact on safety. Numerous reports of anticipated dangers from nanotechnology-based products have been published (the July 2007 issue of *Consumer Reports* is only one example). Other specific concerns, such as those below, have been appearing in various media.

1) Silver particles are instrumental in expediting the healing of wounds. A study done by the Italians in 2006 indicates that 12nm silver particles will cure infections as well. Employing the 12nm silver particles prevents the bacteria from developing a resistance to the treatment, unlike what happens with drug-based approaches. Nevertheless, the Environmental Protection Agency has put a restriction on any application of silver nano particles because of the perceived potential of its also destroying good bacteria if released into the environment.

2) DuPont published a report in 2004 that concluded that carbon black nanoparticles are unhealthy and can cause damage in a person's lungs. While containing factual information, the article is misleading people to think that only carbon black nanoparticles are dangerous. People who work in coal mines have been aware of the dangers of coal dust, regardless of size quantification, for over 100 years. [Fact: There is research that has shown particles under 10μm have the ability to be absorbed by passing through human tissue. The application of the "nano" characterization is misleading at best, and quite possibly disingenuous.]

3) The city of Berkeley, California, has passed an ordinance that requires Material Safety Data Sheets (MSDS) on any Nanomaterials that will be brought into or manufactured in the city. Unfortunately, data sheets that would cover all aspects of the materials do not exist, and actually can not exist, because there is no overall understanding of the properties that need to be evaluated. Existing MSDS are based on the physical properties that can be readily measured, the bulk material properties. These properties, which include the melting and boiling points irrespective of size, are known and the values are published. This is not the situation in nanomaterials since the material properties change as the size becomes smaller. The ability to quantify the properties at the nanoscale needs additional development. Without the tools to quantify properties, the development of specifications is misleading.

Expressing these and other concerns without a means of evaluating the issues and identifying where the actual concerns should be does not promote good science. What is missing is a comprehensive effort that addresses the issues, identifies the problems, and works toward solutions. The crucial question is what needs to be done, and how quickly can the issues be addressed and resolved. Unfortunately, nanotechnology ushers in a new realm of science that retains almost none of the existing knowledge of bulk material properties. The old, established "truths" no longer can be relied on in the nano realm as fundamental properties of materials. For exam-

ple, consider only one of the properties that are "known." The melting point of a metal is a constant at a given pressure. Gold, for example, melts at 1064.18^{o}C at standard pressure. This property, the melting point, has been employed for hundreds of years to process gold into various products. However, nanoparticle gold has a reduced melting point as compared with the bulk property. As the size of the particle drops below 12nm, the melting point starts to decrease and eventually drops below 500^{o}C. This decrease in melting point is only one of the properties of nanoparticles; unfortunately, exact data do not exist on all the properties of nanoparticles. One of the reasons for this lack of data is the lack of metrology equipment that can provide accurate measurements for all properties. Another reason is the lack of a coordinated program to determine these "new" properties. Until the material properties are determined, each specific issue raised will need to be addressed individually. This situation of constantly needing to determine the specific properties of interest will cause many problems and the wasted effort of repeated determination of values. The systematic approach addresses the resolution of properties in the nano realm as a coordinated effort to determine the actual values only once.

There are three issues that summarize the concerns: 1) The knowledge of the nanoparticle properties and consequently their behavior is unknown and needs to be determined. The task of protecting people from the consequences of interaction with nanoparticles that could be harmful is challenging based on existing knowledge. 2) Nevertheless, people and the environment need to be protected, a fact that requires an effort to evaluate what exists today, what is missing and needs to be developed, and how to initiate safety procedures based on today's knowledge. Improvements to the procedures will be made as new information becomes available. 3) Efforts are needed to create an environment where both people and the environment are protected.

These three issues create a fundamental problem addressed by NANO-SAFETY: How does one ensure that both people and the environment will be protected from materials employed in nanotechnology products when the actual properties of materials change based on the size, and the capability of measuring the materials to the required accuracy is not available? Another part of the concern is the lack of definition on what properties need to be identified, quantified, and reported on. Statements are being made, as indicated earlier, regarding specific concerns about nano, which are based on some facts but, in reality, based more on conjecture and speculation. This conjuncture—based on limited information, postulated as facts in published and broadcast media—gives a misleading impression to the general public. This fear-based approach is good for increasing revenue based on viewers or readers, but has the potential to inhibit the insertion of truly beneficial products.

A number of medical investigations are underway that promise novel methods for fighting cancer, but the societal impact of the development has not been addressed. For example, what will happen when a procedure or material is developed for eliminating a certain type of cancer and then someone discovers that it is detrimental to the environment?

While many researchers are working on various issues regarding the effects of nanomaterials, a scientifically neutral, comprehensive effort is not being made to identify, quantify, and collect <u>all</u> the pertinent information as it becomes available. Focused, published research that develops facts will provide some counter to claimed danger from nanotechnology if the effort is part of an overall investigation to determine the fundamental properties of the nanomaterials and how they interact with people and the environment.

Introduction

Safety – paramount in the workplace and the environment—is especially important for developments in nanotechnology, in which case material properties may be completely unknown. NANO-SAFETY requires many things: knowledge of effects, understanding of particle behavior, toxic effects depending on the application, residual impact on the environment, etc. The areas of understanding can be characterized in a number of categories, which include: 1) Material Properties; 2) Impact on People and the Environment; 3) Handling of Nanomaterials; and 4) Business Focus.

1) *Material Properties:* Obviously, one aspect is the development of an understanding of the properties of all the materials, a situation complicated by the lack of availability of metrology tools. A more fundamental question is what properties should be investigated. If the starting point is to ensure an understanding of the impact of the nanomaterials on people and the environment, then investigations can be focused on material properties within the expected operational parameters, like room temperature, atmospheric pressures, etc. Understanding the properties is necessary before it is possible to understand their impact.

2) *Impact on People and the Environment:* Another aspect is a greater understanding of the impact of nanomaterials on the human body. For instance, significant advances are being made in the treatment of cancer by employing customized molecules that incorporate nanoparticles and deliver them to cancerous sites. These specialized molecules either deliver specific chemicals or other material like gold or carbon nanotubes to the site requiring treatment. The chemicals will react with the cancer and begin destroying it. The other materials can be heated by many different methods and destroy the cancerous cells through the elevated temperatures. These approaches promise significant advances in treatment of diseases; however, the long-term impact on the body is under investigation and no definitive answers exist.

3) *Handling of Nanomaterials:* The question of handling and storing Nanomaterials is important from both the implications for the people involved and the impact on the environment. Yet, without any knowledge of the basic properties, the extent of the precautions required is unknown. One always wants to err on the side of safety, but potentially onerous procedures, based on worst-case scenarios, will diminish the progress being made in applying nanotechnology to everyday problems. Procedures are required based on fundamental evaluations and historical efforts.

4) *Business Focus:* The business aspect is important. Given the fact that businesses need to protect their workers as well as their corporate liability, they need to operate according to established guidelines. These guidelines do not exist! Consequently, there is the potential for significant corporate liability.

NANO-SAFETY is not something that will come into place before there is a need, since the need is today. The application of nanomaterials has been happening for some time. Unlike earlier times in history when people simply proceeded and ignored the consequences, today's environment requires that people and organizations be responsible for their actions. Action is required now!

Actions Required

NANO-SAFETY is not a simple solution or a quick fix, but must be a methodical approach that evaluates the risks and develops reasonable actions to ensure the safety of both people and the environment. Efforts must be initiated so that information can be developed and analyzed so that people can make informed decisions. The following actions must occur:

1) The lack of a comprehensive program to identify the material characteristics provides a significant void in what materials can have what impact. This void needs to be remedied.

2) Many researchers are working on employing nanotechnology to deliver medicines to specific sites. This research, including benefits and issues, is being reported in various journals. There is a need to develop a comprehensive source of the information with a methodology of evaluating the information.

3) Without knowledge of nanomaterial properties, it is difficult to provide a completely risk-free method of handling the properties. Procedures that provide adequate safety for the people involved in the efforts need to be established, documented, and distributed. Programs need to be developed to disseminate the information to all parties involved in nanotechnology.

4) The business aspect is the most important for the development and commercialization of nanotechnology. The benefits of avoiding litigation provide businesses the incentive to implement the best practices for their workers' safety. Establishing practices that minimize risk, creating training, developing controls, and ensuring worker safety require an established methodology based on the knowledge of the science and technology on nanomaterials.

Eventually, all four of these areas should be addressed as nanotechnology is developed and becomes part of the everyday environment. However, if it is allowed to develop in a random manner the development process will be long. Moving forward with an aggressive plan will provide the total concept of NANO-SAFETY much more quickly. With the importance of nanotechnology to future products, time is of the essence.

Actions Planned

The ability to address the various issues is much larger than a single organization, even at the Federal government level, can accomplish. The planned actions described below indicate only the proposed alliances for the beginning of the effort. As the development of NANO-SAFETY occurs, organizations throughout the world will likely participate in the activities to establish a worldwide standard. It is critical that the organizations involved include all stakeholders. Consequently, multiple organizations need to participate: from academia to health institutions, governmental organizations, independent research institutions, and independent for-profit companies. To a lesser degree, organizations/companies with definite stake-holding in nanotechnology should participate but not be a driving force. Key elements of the proposed program follow:

1. The identification of the properties to be investigated and the development of the actual properties of nanomaterials are absolutely critical to understanding whether or not the material may have in any interactions with people or the environment. One of the first tasks is the establishment of the size at which

the properties of each of the materials begin to change. The realm of properties between bulk and atomistic are unknown or ill defined. This region of mesomaterial properties (between bulk and quantum) must be addressed and quantified. This task is not unlike developing a new Handbook of Physics and Chemistry with the onerous job of describing historically single value constants as multi-dimensional parameters. The scope of the effort is enormous and beyond the capability of any single organization to accomplish. While the overall effort to determine the nano properties belongs within an organization like the National Institute of Standards and Technology (NIST), the effort needs to begin with an agreement on what will be pursued. Although preliminary discussions with NIST have taken place over the last two years, there has not been a strong incentive to address the total issue. Now, NANO-SAFETY is one driving force. In July 2007, the International Technology Roadmap for Semiconductors (ITRS) committee held meetings on the revision of the ITRS. Lack of having fundamental properties for materials in the nanoscale range was identified as a critical item that needs to be addressed to enable continued semiconductor technology progress. This requirement from a key manufacturing industry becomes an additional driving force. ***Recommendation:*** Establish a partnership with NIST, key universities, and industry. By Spring 2008, hold a defining meeting to determine the needs and the direction required to move forward. The initial meeting, led by the *Nanomaterials Application Center* (NAC) at Texas State University-San Marcos, would involve a limited number of key researchers to discuss issues, evaluate progress, identify concerns, and develop a list of critical issues to be investigated. A second meeting within nine months would focus on the research results and the direction of the investigations. Based on these results, a nanomaterials investigative roadmap would be developed for dissemination worldwide. These results would provide guidance for researchers to address the critical issues. [Note: Dr. Walt Trybula, Director of NAC, led the successful investigation of immersion lithography for the semiconductor industry. From the initial planning to resolution of identified issues, the evaluation was completed in less than 15 months.]

2. The development of a comprehensive source of information requires two steps. The first involves developing the methodologies for collecting data and developing it into an effective database. The second involves the maintenance of the database and the dissemination of the information. The first needs to involve academic and medical organizations as well as commercial suppliers. ***Recommendation:*** Involve industry and academic institutions, like Rice University, UT Health Sciences Center–Houston, Texas State University-San Marcos, Lamar University, NanoTox, Inc., and others in an initial meeting to define the needs and means of proceeding. Other organizations will need to be added as the program develops. The source of funding should include National Institutes of Health, Environmental Protection Agency, and NIST. The development of the eventual information repository will be identified during the course of the initial phase.

3. The development of a program to address NANO-SAFETY requires the consideration and evaluation of all the potential known issues and the ability to include other issues as they arise. The program also will require that training programs be put in place to develop the expertise required for handling any nanotechnology issues that arise. ***Recommendations:*** Numerous steps will be required to develop this effort. The first is the considerations of the work accomplished at major institutions, like Rice University Center for Biological and Environmental Nanotechnology (CBEN). Additional health aspects can be incorpo-

rated based on inputs from major organizations, like UT Health Sciences Center–Houston. The business aspect from both risk and business controls will be administered by Texas State and its Environmental Risk Management program in consultation with businesses and other organizations. The first activity is to have the interested parties come together to discuss the focus of each of the segments and to identify the steps required for accomplishing the tasks. This step needs to be accomplished by early Spring 2008 at the latest. Once this effort is focused at the university and research institute level, schools focusing on technician level training, like Austin Community College (with a nano scholar program) and Texas State Technical College (with a nano technician program) will participate in the planning for the development of NANO-SAFETY technicians.

4. The business aspect of the manufacture and application of nanotechnology requires an evaluation of the responsibility of the organization for the safety of its workers and products. Businesses must have procedures and plans for NANO-SAFETY. Some existing programs can be expanded and developed to provide the basis for this focus. ***Recommendation:*** NANO-SAFETY needs to be available on at least two levels. At the corporate level, Risk Management is critical to understand the issues and concerns. The Environmental Risk Management Institute at Texas State is currently expanding its program to encompass the issues of nanotechnology. The second level is the development of a program for NANO-SAFETY reviews at companies, laboratories, and medical institutions. This program needs to build on the existing efforts at major universities, Rice University, Texas State, and corporate entities, like NanoTox, Inc. Rice University CBEN, under the efforts of Dr. Vicki Colvin, evaluates safety in laboratories. NanoTox, along with Texas State University, has conducted an initial industrial NANO-SAFETY pilot program visit. These efforts could become the prototype for a program that could be offered to organizations. Key people from these organizations will meet in the Spring 2008 to determine how to proceed in the development of a program that addresses the concerns of both businesses and institutes to ensure NANO-SAFETY for both people and the environment.

The NANO-SAFETY effort will be coordinated through the Nanomaterials Application Center, which has a record of being able to coordinate industry-academic activities and provide guidance in expediting the commercialization of products.

Benefits

The benefits of expediting the NANO-SAFETY program to an early arrival are enormous. First, the general public will benefit with the knowledge that an effort is in place to ensure their safety. In addition, this program will show worldwide leadership by the United States and Texas institutions in addressing emerging technology issues. Also, by creating a resource for nanotechnology safety issues, we will become a focus of these efforts and obtain worldwide recognition for the effort. Additionally, all participating schools and scientists will receive recognition for their research efforts and nano educational programs. For the companies involved, the recognition of their efforts, as well as the interest in their products and offerings will increase their value. In addition, significant funding should become available to the institutions. Every organization that participates should receive a substantial increase in public awareness.