Minnesota Nanotechnology

A Report to the Minnesota Legislature

February 1, 2011

Preface

In response to a directive from the Minnesota legislature, the University of Minnesota and MNSCU have drafted the following report on nanotechnology within the state. In keeping with the language of the request, the areas of emphasis for this report are a basic understanding what constitutes nanotechnology, how it is likely to impact our state's economic climate, public safety concerns about applications of nanotechnology, social and ethical concerns related to nanotechnology, and the impact of nano on our educational institutions. The report concludes with a brief section outlining the needs of these institutions for further state investments in nanotechnology-related facilities. A small sample of Minnesota-produced products and academic research are included throughout the report to familiarize the reader with the breadth of applications that are being developed under this technology. The captions use the following departmental acronyms: CEMS – Chemical Engineering and Materials Science; Chem – Chemistry; ECE – Electrical and Computer Engineering; ME - Mechanical Engineering; and Neuro - Neurology.

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1.0 Introduction
1.1 What is nanotechnology?

The term nanotechnology refers to the manipulation of matter at the scale of tens or hundreds of atoms in each direction, that is, length scales between one and one hundred nanometers (http://nano.gov). A partner discipline, nanoscience, refers to the study of the behavior of materials at this length scale. In some cases, applications of nanotechnology are interesting simply due to the scaling. This may represent structures that are better by some metric (smaller, denser, cheaper, and faster) or have higher surface area per unit weight to increase the rate of chemical reaction. Material behavior at the nanoscale, however, can be significantly different than the behavior of the same material at larger dimensions. This can be mechanical properties like strength or facture toughness, electrical properties like conductivity, optical properties such as absorption and emission, magnetic properties like remnant magnetization, or chemical properties such as reactivity. These differences often arise because this length scale is the transition between atom-like behavior and bulk material behavior. As a result, one can change the properties of a material by simply changing the length scale. This can provide an unprecedented avenue to tune material properties to meet the needs of the application of interest.

One can reasonably say that nanotechnology is not new. Since proteins are nano-scale structures, nanotechnology has existed in nature for at least a billion years. Eric Drexler's 1986 book, Engines of Creation[1] laid the foundation for the modern field, articulating both the amazing possibilities and the concerns associated with engineering structures at the molecular scale. A great deal of work has demonstrated that chemical processes can be exploited for a variety of applications if the proper reaction conditions exist. This type of approach is referred to as bottom-up nano. Bottom-up nano processes are often adapted to be able to economically manufacture large quantities of nanostructures. Examples include the formation of gold nanoparticles in solution and various types of self assembly processes.

One can also look at leading manufacturers of high technology including such Minnesota employers such as 3M, Cypress Semiconductor, Honeywell, and Seagate, and make a persuasive argument that they have been depositing films whose thickness is squarely in the nanoscale regime for years. Work in which nano structures are made by direct interventions such a film deposition and patterning in application-driven designs is called top-down nano. Computer chips and recording heads in disk drives are good examples of top-down nano.

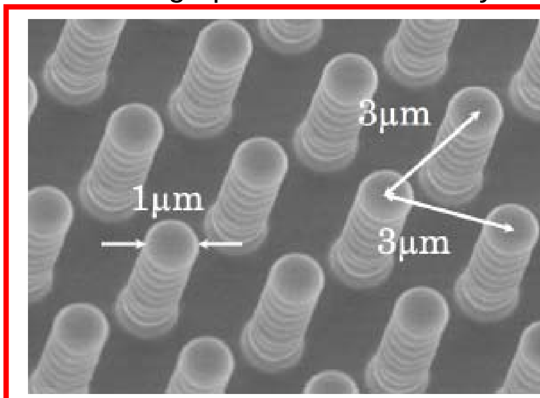
Recent years have seen dramatic improvements in our ability to design and fabricate nano structures (top-down nano), particularly structures on the nanoscale in two and three dimensions, and our ability to easily visualize, characterize, and controllably make both bottom-up and top-down nano structures. These capabilities provide the feedback necessary to discover and exploit nanostructured material properties in a reproducible manner. As a result, the application of nanostructured materials and various nanoscale devices is rapidly moving out of the research lab and into a wide variety of products. At the same time, research is continuing into new application areas.

1.2 Why is it Important?

Nanotechnology is often described as an enabling technology, rather than an independent field. Advances in this area typically begin with work in nano structured materials – the development of new materials, material structures, and material synthesis techniques. These material advances are then applied to a very wide variety of disciplines. The list of application areas is expanding rapidly, with more than 1000 consumer products in 2009.[2] However the majority of nano products are not on this list since they are embedded in larger systems such as computers and cell phones. This rapid expansion initially led to some initial unrealistic expectations such as space elevators and autonomous therapeutic robots. While many of these have fallen by the wayside, practical commercial applications of the principles of nanotechnology have expanded rapidly. The National Nano Initiative estimates that the worldwide market for nano-enabled products will be approximately one trillion dollars per year by 2015. This will require 2 million jobs directly in the field, of which 800,000 will be in the U.S. With the necessary supporting jobs, this figure could reach 2.8 million jobs in the U.S.[3] By 2020 there will be about three trillion dollars per year in products that incorporate nano."[4] This impact on jobs is already being seen.[5]

Similarly, European groups have estimated that, by 2014, 15% of all goods manufactured globally will involve nanotechnology.[6] According to a recent five-year study, "Few industries will escape the influence of nanotechnology. Faster computers, advanced pharmaceuticals, controlled drug delivery, biocompatible materials, nerve and tissue repair, surface coatings, better skin care and protection, catalysts, sensors, telecommunications, magnetic materials and devices – to name but a few of the areas where nanotechnology will have a major impact. In effect, nanotechnology is a radically new approach to manufacturing. It will affect so many sectors that failure to respond to the challenge will threaten the future competitiveness of a large part of the economy."[7]

Not only does nano represent an enormous economic potential, it also has the potential for significant improvements in quality of life. For both of these reasons it is vitally important that Minnesota be engaged in this area of technology. At this writing the most common broadly defined application areas for applications of nano are materials, medicine and biology, information systems, energy. As such, most of the field is inherently multidisciplinary and involves groups of researchers working as a team. Facilities that support the responsible development of these materials and their exploitation in a flexible multidisciplinary environment are crucial to the



Professor Kevin Dorfman (CEMS) is investigating microfabricated post arrays for DNA separation that can reduce genotyping time from hours to minutes.

Nanomedicine Research

success of a nanotechnology project.

Hysitron (Eden Prairie) is the world leader in developing nanomechanical test instruments.

Materials Products

Materials: The field of nanotechnology largely leverages advances in materials. In some cases, these materials are used directly because of their improved the mechanical, electrical, or optical properties. 3M (St. Paul) has many existing or emerging products that fall into this area. For example, they have developed a new line of dental restoratives based on the improved mechanical properties of nanoparticles. Similarly, Rushford Hypersonic has licensed a technology from the University to create super hard nanoparticle coatings which could ultimately be used to reduce wear on mechanical components such as drill bits, turbine blades, and medical prostheses. Carbon nanotubes are another example of a new material that has an enormous strength to weight ratio. In Winona, RTP has begun putting these materials in plastics to increase the mechanical strength of the material. Of particular interest are the applications of these materials for high-value weight sensitive areas such as aerospace and defense. Companies such as Aveka (Minneapolis) have put nanoparticles in cosmetics and sunscreens. Cima Nanotech (St. Paul) makes nanoscale metal particles for printed circuits that are also useful for touch screens, displays, solar energy, and other applications.

Medicine: The application of nanotechnology to a wide variety of problems in health care is very early, but shows tremendous promise. According to the National Institutes of Health: "scientists lack the technological innovations to turn promising molecular discoveries into benefits for cancer patients. It is here that nanotechnology can play a pivotal role, providing the technological power and tools that will enable those developing new diagnostics, therapeutics, and preventives to keep pace with today's explosion in knowledge."[8] A great deal of work is currently underway in the use of nanoparticles to target the delivery of therapeutic agents that have toxicity concerns when delivered systemically. Targeting can be accomplished by particle size, by chemically treating the particles with the appropriate receptors, or using magnetic fields. While this work is just beginning to emerge from the laboratory with phase one human trials currently in progress, it is one of the most promising areas of cancer treatment.

While cancer treatment is a very active area of research, it occupies only a small fraction of the total nanomedicine umbrella. Other areas of intense interest include microfluidic devices for disposable diagnostics (lab on a chip), implantable drug reservoirs that incorporate both medical devices and pharmaceutics in a single platform, embedded sensors and other types of enhanced detection schemes, quantum dots and magnetic nanoparticles for both *in-vivo* and *ex-vivo* diagnostics, neural-inorganic interfaces for prosthesis control, devices for glaucoma detection and control, and scaffold substrates for tissue regrowth and repair. Given the massive medical device industry in the Minnesota area, nanomedicine is expected to be a major impact area for the local economy. A recent study by the Bio Business Alliance, Destination 2025, has prominently discussed the importance of nanotechnology to this industry,[9]

Information Systems: This is a large section of the nanotechnology application portfolio that once again impacts strongly on the Minnesota economy. Disk drive heads as manufactured by Seagate have long been in the nano regime, with critical layer thicknesses of only about 1 nm. Integrated circuits, such as those manufactured by Cypress Semiconductor (Bloomington), Honeywell (Minneapolis), and Polar Fab (Bloomington), have scaled into the nano regime. Sensors such as those made by Goodrich (Burnsville), Honeywell, Nonvolatile Electronics (Eden Prairie), and many small companies are key components to a wide variety of industries such as aerospace, electronics, control systems, and construction. This type of application typically involves both micro and nano scale components. 3M is active in this area as well, with new products in data storage and display that rely on nanotechnology. Each of these applications also involves ancillary markets such as precision machining and packaging, which are predicted to begin to adopt nanotechnology approaches. Furthermore, the reduced size and cost of these information systems is driving them into nontraditional markets.

Energy and Green Manufacturing: One of the most recent applications for nanotechnology is green manufacturing. While reducing the size and improving the wear resistance of conventional products is inherently green, this category refers to products that can provide carbon-free energy, remediate or prevent environmental pollution, and reduce energy requirements for broad swaths of the economy. Nano is playing a key role in the development of improved efficiency solar cells. This includes the use of thin film absorbs to reduce cost and the use of quantum dots and nanowires to improve energy conversion efficiency. Another area of interest is the incorporation of window coatings, either to collect solar energy that is not needed for illumination, or to control noise transmission through the glass. Energy storage is a second very important area for a green economy. Cymbet (Elk River) has been developing thin film batteries for several years. Many organizations are investigating the enormous surface area of nano structures such as carbon nanotubes, graphene, nanowires, and nanoporous carbon aerogels to make extremely high energy density batteries and capacitors. Unlike conventional batteries, such capacitors would never wear out, would be unaffected by temperature, and would be easy to charge. Several nanotechnologies can be used to reduce energy consumption. Light emitting diodes (LEDs) consume about eight times less energy than conventional bulbs without the mercury concerns of compact fluorescents. In another approach, nanostructured membranes are being

Cypress Semiconductor (Bloomington) produces high-performance, mixed-signal, programmable integrated circuits as well as memories and programmable timing devices.

Information Systems Products

developed by 3M for use in advanced fuel cells. Nanoscale holes in various types of membranes have been applied by companies such as Donaldson (Bloomington) and TSI (Shoreview) to a host of monitoring and filtration applications ranging from DNA size selection to removal of pollutants or even water from air, or the removal of contaminants from water. One commercial product of this variety is capable of removing salt from sea water by nano filtration.

1.3 Research and Facilities at the University of Minnesota and MNSCU

In addition to its impact on the commercial sector, nanotechnology is vitally important to research universities such as the University of Minnesota. The federal government invested 1.78 B$ in nano in fiscal 2010, making it one of the most heavily funded areas of research. Major federal funding agencies include the National Science Foundation, the Department of Defense, the Environmental Protection Agency, the National Aeronautics and Space Administration, the National Institute for Occupational Safety and Health, the U.S. Department of Agriculture and the Department of Justice. As a result, the University currently has more than a hundred faculty that are active in some aspect of nanotechnology research. Faculty are working on nanoscience and nanotechnology to improve solar cells, make better renewable fuels, improve medical diagnostics, and target medicines to tumors. They are also working on biological assays to test the toxicity of nanomaterials, on better nanoparticle detectors, and on exposure assessment in the workplace (Section 2). They are also highly involved in defining policies and ethical standards for this new area (Section 3) and, along with MNSCU, have developed leading edge technical degree programs (Section 4). With a mission statement to become one of the top public research universities in the world, the University of Minnesota cannot afford to ignore this area.

While a great deal of work in the area is conducted by small groups, the capital equipment costs and the need to involve experts in multiple disciplines is often a significant barrier. This is true both in the research area and in commercialization, especially for small companies. University-based core labs, where equipment is not only shared among many researchers but is also widely available to the public, provide an attractive avenue to resolving this problem. These labs provide access to equipment on a “fee-for-service” basis with no long-term commitment. This has multiple positive aspects:

- Small companies can develop key concepts without capital equipment acquisition
- Companies have access to technology experts for consultation
- Students and faculty can interact with private sector researchers to develop an understanding of commercially relevant problems
- Capital expenses and maintenance costs can be spread across many users

The University has several such facilities. While they are supported and administered through the College of Science and Engineering, additional support is received from the Office of the Vice President for Research, and in the case of the Characterization Facility, the Medical School, and the School of Dentistry.

NFC: The Nanofabrication Center (www.nfc.umn.edu) operates a 7000 square foot facility, including 3000 square feet of class 10 clean room. The Lab contains all of the major pieces of processing equipment for making thin film electronics, sensors, micro and nano mechanical systems, light emitting diodes, solar cells, microfluidics, and many other types of devices. A new three million dollar direct write electron beam system, won through a competitive grant process from the National Science Foundation, was installed in November 2010. NFC not only maintains these systems, it also provides online scheduling through the Coral lab operating software, maintains safe operating procedures, and trains students in the operation of the equipment. The clean room and most of the equipment are available twenty four hours per day, seven days per week. Rates for equipment usage are posted online. NFC receives partial support in its mission from the National Science Foundation through the National Nano Infrastructure Network (www.nnin.org) program.

The NFC clean room contains a wide variety of equipment for building micro and nano scale devices.

The number of NFC users has dramatically increased from a few dozen when it was first opened in 1990 to about 400 today. In addition to overcrowding, the lab is not designed to handle new nano research areas such as energy and medicine. The University is currently pursuing a new Experimental Physics and Applied Nanotechnology building which will house the necessary space to support these emerging areas.

CharFac: The Characterization Facility ("CharFac") is a multi-user, shared instrumentation facility for materials research spanning from nanotechnology to biology and medicine. Analytical capabilities include microscopy via electron beams, force probes and visible light; elemental and chemical imaging including depth profiling; elemental, chemical and mass spectroscopy; atomic and molecular structure analysis via X-ray, ion or electron scattering; nanomechanical and nanotribological probes; and other tools for surface and thin-film metrology.

Well over 100 faculty research programs use these capabilities. These researchers originate from dozens of University of Minnesota departments under several colleges. The lab also works with some 50 industrial companies in a typical year, ranging from small start-ups to multinational corporations; these interactions include analytical service, training for independent use, and research collaboration. CharFac is supported by the National Science Foundation as a key node in the Materials Research Facilities Network (via the MRSEC program) to work with external academic institutions including research universities, 4-year colleges, technical colleges, and K-12 schools.

Various MNSCU institutions have equipment similar to the University of Minnesota although in smaller concentrations level of capability as the labs described above. MNSCU equipment is predominantly used in lab courses as part of nanoscience, electronics or biology programs. In such use the activities are controlled, instructor directed and standardized. Local industry has access and uses the equipment and in some cases students will perform assessment of industry provided materials. Students also use this equipment to participate in student/faculty research. This research is unique in two year nanoscience programs and Dakota County Technical College is the pioneer in this area and acknowledged as such by the National Science Foundation

The Characterization Facility houses state of the art tools for visualizing and characterizing a wide range of nanostructures. Pictured is an extremely high resolution electron microscope.

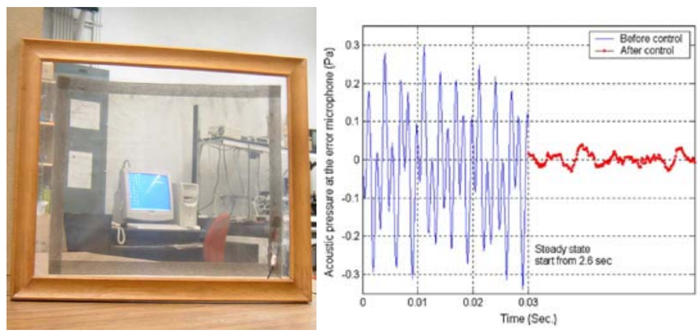
1.4 Nanotechnology Impacts on the Individual

The last section listed some of the economic impacts of nanotechnology. While the role of nano in driving the economy and job creation is impressive, one must also assess other aspects of the adoption of nanotechnology. Nano is an inherently green technology. One of the previous sections summarized some of the potential impacts of nano on alternative energy and environmental remediation. More generally, however, as new nanostructured materials are developed that are more wear resistant, are lighter weight, and require fewer resources to manufacture, nano will reduce the impact of the industrial society on the environment.

Nano carries with it, however, several important concerns that cannot be overlooked. Initial worries about self-replicating machines (the so called 'grey goo' scenario) are now widely discredited. A more legitimate concern relates to health effects. Materials at the nano scale have very large surface to volume ratios. For processes like chemical reactions that are surface area mediated, nanostructures can behave differently than bulk materials.

The impact of nano on the environment is a serious concern and the subject of a great deal of active research. The National Science Foundation (NSF) and the Environmental Protection Agency (EPA) created two centers in 2008 to study the environmental impact of nanotechnology. NSF and the EPA granted the two centers $38 million over five years; EPA's $5-million contribution is the biggest it has ever given to the field. The Center for Environmental Implications of Nanotechnology (CEiN) is a collaboration between the Los Angeles and Santa Barbara campuses of the University of California. CEiN has about 75 researchers, including 30 postdoctoral fellows and graduate students. Duke is headquarters for the second center, the Center for the Environmental Implications of NanoTechnology (CEiNt), which includes five other universities. CEiNt employs 36 faculty members and 76 undergraduate and graduate students.

It is important, however, to keep the magnitude of the problem in perspective. It is estimated that 2.5 billion tons of nanoparticles are released into the air every year. Approximately 60% of these occur naturally including salt particles (1 billion tons), soil particles (0.5 billion tons) and pollen. Common human-produced particles include soot from diesel engines and volatile organic compounds which are a byproduct of combustion[10] are another concern. Nanoparticles that have been engineered for their unique properties are being produced at far lower volumes than these incidental nanoparticles. As a result, "It is very unlikely that new manufactured nanoparticles could be introduced in doses sufficient to cause the health effects associated with nanoparticles in polluted air. However, some may be inhaled in certain workplaces in significant amounts."[11] For that reason, control of freestanding nanostructures in workplace environments where such products are manufactured is the most immediate concern.[12] Examples of this would be particles, wires, and tubes, in powder form that would be added to other materials to alter the properties of that material.



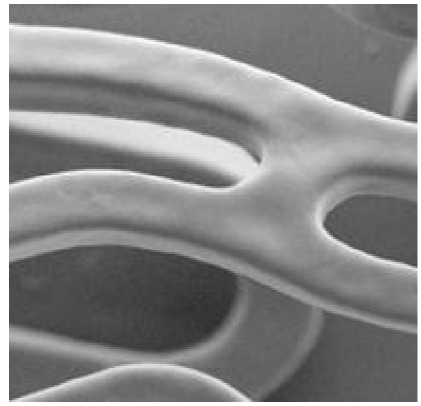
Profs. Rajesh Rajamani and Tianhong Cui (ME) have developed a process for coating windows with a thin layer of carbon nanotubes. By applying an electrical signal the coating can cancel sound transmission through the window.

Energy & Environment Research

The next few sections will detail some of the concerns raised by nanotechnology. These sections will cover nano health and safety, as well as societal impacts and ethical concerns. The University is at the forefront in several of these areas, helping to set national guidelines and policy.

2.0 Health and Safety Implications of Nano

2.1 Overview: why engineered nanostructures carry EHS implications



SurModics (Eden Prairie) develops surface modification and drug delivery technologies in the cardiovascular, ophthalmology, pharmaceuticals, and biotechnology markets

Nanomedicine Products

While a significant proportion of the population will use or come into contact with products containing nanomaterials, the most significant exposures and risks will likely be in the occupational arena. According to a recent Royal Society report,[13] "We expect the likelihood of nanoparticles or nanotubes being released from products in which they have been fixed or embedded (such as composites) to be low". There are several industry sectors and processes where worker exposures to nanomaterials have the potential to be significant if not properly contained, including chemical and pharmaceutical companies, construction and manufacturing (e.g., powder handling processes and cement manufacture), and electronics and communications. Potential exposure to engineered nanomaterials can be broad and it is important to consider both volume and diversity of nanostructures in each environment. At an industrial scale, production of nanomaterials along with subsequent formulation and application in products can produce high volumes of materials, but their composition and characteristics are likely to be refined and uniform. However, at research scales, including research and development activities in universities and nanotech start-up companies (HSE, 2004), exploratory activities generally utilizes smaller volumes of materials but with more diverse compositions and characteristics. In both settings, traditional ultrafine particle sources such as welding, diesel exhaust, and other combustion processes may be present, and relevant safety measures may already be in place.

Despite the large investments in nanotechnology, corresponding investments in environmental, health, and safety aspects of this technology and its processes and products have lagged (Maynard 2006). Much is still unknown or poorly known regarding the health risks of nanomaterials. Additionally, key mechanisms for exposure processes and toxicity effects of manufactured and incidental nanomaterials on humans remain poorly understood. Mechanistic uncertainties include those related to such general questions as: (a) how long do manufactured nanomaterials persist in the atmosphere; (b) how stable are nanomaterials over time given specific occupational conditions; (c) what is the effect of particle shape, size, and surface chemistry on their fate and transport; (d) what are likely routes of exposure (e.g., inhalation, dermal, ingestion, and ocular); (e) what are the metrics by which exposure should be measured (e.g., particle mass or number or surface area concentration); (f) what are key mechanisms of translocation to different parts of the body after nanomaterials enter the body; (g) what are possible mechanisms of toxicity, including oxidative stress due to surface reactivity, presence of transition metals leading to intracellular calcium and gene activation, and intracellular transport of nanomaterials to the mitochondria (Kandlikar et al., 2007); (h) what are the degradation mechanisms and excretion routes for internalized nanostructures. Classic tools for characterizing and categorizing materials do not necessarily capture the chemical and physical properties of nanostructures (based on the emergent materials- and size-dependent properties). In addition, traditional measures of exposure and toxicity assessment are not always appropriate in the case of nanostructures. In assessing overall risk, both the exposure and hazard aspects of risk are poorly understood. Studies in both aspects are ongoing within laboratories worldwide; however, the studies are often not systematic across laboratories, making it difficult to compile the data to achieve synergistic conclusions. Some efforts are being made, especially within the nanotoxicology community, to form international collaborations and overcome this deficit.

2.2 Assessing and managing exposure to nanomaterials

The uncertainties described above have led to the use of control banding approaches to assessing risk levels and guidance for controls for nanomaterials in workplaces (Maynard and Kuempel, 2005; Paik et al., 2008). While control banding is useful as an interim approach, there is currently sufficient information available to facilitate the development of an exposure assessment strategy using monitoring data for many nanomaterials. A generic and highly tailorable exposure assessment strategy for nanomaterials that enables effective and efficient exposure management, (i.e., a strategy that can identify jobs or tasks that have clearly unacceptable exposures) while simultaneously requiring only a modest level of resources to conduct is feasible at this time. The strategy is based on the strategy of the American Industrial Hygiene Association (AIHA), a generic framework that can be adapted for nanomaterials and that seeks to ensure that the risks to workers handling nanomaterials are being managed properly (Ignacio and Bullock, 2006). The strategy is focused on arriving at decisions based upon collecting and interpreting the available information. In that sense, this strategy parallels the control banding approach.

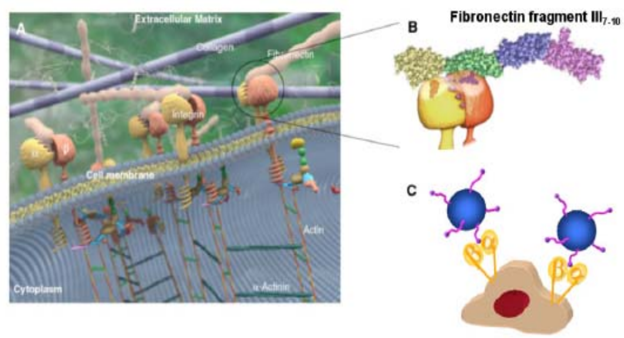
Basic characterization of the workplace consists of collecting and organizing information needed to make accurate exposure assessments, including the collection of information on the workplace, workforce, and environmental agents. Processes leading to direct airborne nanomaterial releases could include vapor-phase synthesis reactors, heavy conveying or bagging operations, and shaping and grinding steps. Even for processes that are closed systems, these may require high levels of emission controls. In closed systems, unless there are unintentional leaks, the probability for exposure may be low. Exposure potential can be higher when products are being conveyed or being dried, during reactor maintenance and cleaning operations, and other material handling tasks when nanomaterials can become resuspended. In research laboratory settings, the quantities of nanomaterials handled may be smaller than in a

3M (Maplewood) has many nano related products. Pictured above is a privacy filter for display applications.

Materials Products

manufacturing or production environment, but the numerous processing conditions as well as the subtle variations in nanomaterial characteristics can make a proper assessment of exposure potential challenging, time intensive, and costly. The presence of functionalized nanoparticles, the type of process, and the surfactants used may also affect the potential to become airborne. In order to understand nanomaterial characteristics, there must be good communication between the scientists and engineers who manufacture, process, and handle the nanomaterials and the industrial hygienists.

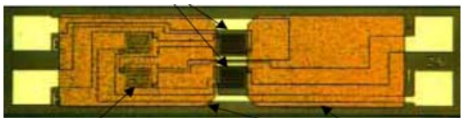
Background Aerosol: While identifying the sources, it becomes necessary to distinguish between engineered and incidental nanomaterials on one hand and background aerosols on the other. Background nanomaterials can be either naturally occurring nanomaterials or incidental nanomaterials not caused as a result of any occupational activity i.e. diesel exhaust from cars driving down a nearby road. Incidental nanoparticles that are caused by occupational processes must be included in any assessment of occupational environments. This needs an understanding of both the location and generation of nano and non-nano particles in the workplace, material handling tasks which can produce incidental nanomaterials, work practices and procedures, material transfer, PPE and other controls. Investigation of other potential co-contaminant particle sources is also required and professional judgment may also be needed to determine if these are causes for concern with respect to subsequent measurements. Combustion and high temperature sources whether process or non-process related should be particularly noteworthy. The incidental nanomaterials typically are not the focus of the exposure assessment. However in sufficiently high concentrations these incidental particles may also be considered a mixed exposure, since these particles may not be without their own adverse health risks. While these particles may be in the same size range as the engineered particles of interest, they are difficult to distinguish definitively using only commonly used real-time. Accounting for the background and incidental nanomaterials can be done in several ways and is situation-specific. Options include measuring nanomaterial concentrations before or after the process, measuring outdoor ambient concentrations, and measuring at the intake of some processes. Measurements can be made simultaneously with process-related monitoring or pre- and post-process.



Profs. John Bischof (ME) and Efie Kokkoli (CEMS) work on molecular adjuvants that can improve cancer treatment control and efficacy. Integrins hold a cell in place by binding to proteins of the extracellular matrix by recognizing specific motifs within adhesion domains. Specially prepared nanoparticles are recognized by integrins and so can be delivered only to cells that over express the integrins of interest.

Nanomedicine Research

Construction of Similarly Exposed Groups (SEGs): The exposure assessment process first begins with a definition of similarly exposed groups (SEGs). There are several methods for classifying workers into SEGs. Most commonly, this is done on the basis of an *a priori* understanding of the processes and tasks that each group of workers are engaged in and the likelihood of exposure to the contaminants of interest. The creation of SEGs for engineered nanomaterials is a combination of subjective professional judgment and measurements.



Nonvolatile Electronics (Eden Prairie) develops and manufactures practical spintronics devices. Products including sensors and couplers that are used in industrial, scientific, and medical applications.

Information Systems Products

Concentration Mapping: Concentration mapping is a technique to illustrate spatial and temporal variability of the aerosol concentration distribution in a workplace as a function of work processes. This technique can be applied to identify contaminant sources or as a pre-survey tool to determine sampling locations for aerosol concentration measurements. Mapping can be utilized to help determine similar aerosol concentration areas within a workplace. Such areas with similar aerosol concentrations utilizing the same aerosol characterization metric can loosely correspond to SEGs, or more precisely, similar aerosol concentration areas. Workplaces may be categorized into two types from the perspective of the need for mapping measurements: production and laboratory. Workplaces in the production category often have regular work, materials handling, and processing schedules and minimal changes in nanomaterial characteristics. Laboratory type workplaces feature irregular and less predictable work schedules, very broad and frequent changes in nanomaterial characteristics, and procedures, typically batch type processes and small scale operations. Different strategies are required for characterizing airborne levels of engineered nanomaterials in these two types of workplaces. For production type workplaces, mapping measurement can be useful and is recommended. In these facilities, longer sampling times are feasible and enable better aerosol concentration estimates and study of spatial and temporal variation. Mapping can provide useful information for basic characterization of the workplace in such instances. However, mapping may not be appropriate in lab type workplaces because of infrequent and irregular task occurrences involving engineered nanomaterials that may have very different characteristics. Most labs are small and processes are often sequential. Therefore, aerosol monitoring can be focused on the aerosol-generating task. Despite relatively short sampling times for each task, task-based sampling can be used to cover the whole process in each lab. Pilot plant facilities typically have characteristics of both laboratories and production operations and the best strategy for these work settings must be considered on a case-by-case basis. If the process is sufficiently long and stable, particle measurements at several locations would be helpful to understand how particles are distributed spatially. Otherwise, task-based monitoring may be more feasible. In this situation, simple line plots for all metrics can be constructed that show the concentration metrics by process, thus providing an intermediate version of concentration mapping.

Job Task Related Measurements: Similar to concentration mapping, job task related measurements can help identify spatial and temporal variability of the aerosol concentration during specific job tasks initially identified as potential exposure sources. Here, breathing zone measurements are made during specific tasks and relative particle measurements are used to identify potential sources or work methods that release higher levels of nanomaterials. This technique can be applied to identify short duration contaminant sources and compare the relative effectiveness of work process control techniques in reducing exposure potential. They are also very effective in identifying processes in need of exposure control activities based upon comparative readings.

Exposure Metrics: While mass concentration has traditionally been used as the metric for exposure assessment of airborne particles and the basis for regulation, it may not always be appropriate for nanomaterials. Number and surface area concentrations have been proposed as alternate exposure metrics for nanomaterials. The choice of the most appropriate exposure metric is critical both for risk assessment and risk management. If exposure concentration by a less relevant exposure metric is used to determine exposure categories, workers could be misclassified into incorrect categories resulting in weaker exposure-response associations or inappropriate and incorrect exposure control and management decisions. Since the question of the correct exposure metric is still a matter of debate, as an interim strategy for measuring airborne engineered nanomaterials, it is advisable, if possible, to obtain area or job task related measurements of all these metrics and to understand the relationships among mass, number, and surface area concentrations in workplaces. This will lead to better understanding of workplace factors that affect engineered nanomaterial emissions.

Professors Uwe Kortshagen (ME) and Steve Campbell (ECE) have developed silicon dots that luminesce. This could lead to efficient and environmentally benign lighting technologies.

Energy & Environment Research

Instrumentation: It is recommended that measurements of airborne particle mass, surface area, and number concentrations be conducted using real-time instruments. There is value in maintaining both the time averaged results and the real-time data points for these metrics to enable future evaluations of the information. Portable aerosol photometers (e.g., DustTrak, Model 8520, TSI Inc., Shoreview, MN, PDM-3 Miniram, Mie Inc.) can be used for monitoring mass concentration using light scattering. Condensation particle counters (e.g., CPC Model 3007 or P-Trak Model 8525, TSI Inc., Shoreview, MN) are real-time, single-particle counting instruments that measure particle number concentrations of particle sizes from 0.01 µm to greater than 1.0 µm, with a concentration range of 0 to 100,000 particles/cm^3. Diffusion chargers (e.g., Nanoparticle surface area monitor, NSAM model 3550 or AeroTrak 9000, TSI Inc., Shoreview, MN or the DC2000CE from EcoChem Analytics) are used to measure the surface area concentration of positively charged nanoparticles with sizes from 10 to 1000 nm. Time-integrated and size-classified measurements can be obtained using a Nano-MOUDI (Model 125A, MSI Inc., Minneapolis, MN). The Nano-MOUDI impactor can be used to measure particle size distribution by mass or number and to obtain samples for chemical analysis or electron microscopy. This model collects particles ranging from >18 µm to 0.010 µm on thirteen stages.

Cymbet (Elk River) leader in solid state energy storage and energy harvesting power management solutions.

Energy & Environment Products

Laboratory analysis of longer term samples, such as with Scanning Electron Microscopy (SEM) or Transmission Electron Microscopy (TEM), are also valuable to help interpret the real-time instrument data, particularly to help make judgments on the meaning of the real-time measurement particle size and source of the nanomaterials being measured. When employing electron microscopy methods, representative specimens of bulk source materials of the engineered nanoparticles or source area air samples in close proximity to areas can be obtained to use for reference purposes. The source particulates can be analyzed to identify unique characteristics that can be used to establish material-specific analysis protocols.

Multiple sampling methods can be used to yield a specimen suitable for TEM or SEM analysis. Open-faced filter sampling is arguably the easiest and most straightforward method. Polycarbonate (often preferred especially for SEM studies) or mixed cellulose ester filters can be used to perform an initial sampling study. In addition to open-faced filter sampling, samples can also be obtained using size-selective sampling devices (for example, cyclones, elutriators, and cascade impactors) to deposit particulate on impaction substrates. Sampling techniques such as electrostatic or thermal precipitators are also available to collect particles for TEM or SEM evaluation. Size-selective sampling may be desirable for separating airborne particles based on aerodynamic mass to evaluate different size fractions of materials in the air.

2.3 UMN/MNSCU research on health and safety implications

The Division of Environmental Health Sciences in the School of Public Health has been carrying out research on the health and safety of nanoparticles, the proper occupational exposure assessment strategies, techniques for using available instrumentation to measure all relevant exposure metrics, and risk assessment. The publications listed in Appendix EHS1 have appeared in peer-reviewed journals and illustrate the range of issues that have been dealt with by UMN investigators.

In addition, research focused on developing new assays to study nanotoxicity and explore mechanisms of nanoparticle interaction with biological cells and tissues has been ongoing in the Department of Chemistry in the College of Science and Engineering. The publications in Appendix EHS2 are from peer-reviewed journals that illustrate recent University results in this area.

2.4 Recommended EHS standards and guidelines for UMN and MNSCU in nano

The selection of an appropriate Occupational Exposure Limit (OEL) for the exposure assessment is the key criterion for making distinctions between exposures that are excessive and those that are not expected to result in adverse health effects.

There are well-developed methodologies by which formal OELs can be established (Schulte et al., 2010). Before an OEL can be established, several conditions need to be met:

1) the criteria for exposure assessment need to be established (e.g., what aerosol fraction and what exposure metric is most health-relevant);
2) the exposure assessment strategy should specify if one needs to measure short-term or long-term exposures;
3) the instrumentation and analytical methods for measuring these metrics should be available;
4) and a dose-response relationship should be established by means of toxicity data and quantitative risk assessment.

Only once these conditions are met can an exposure limit be set. Of these four needs, only the instrumentation and analytical methods (condition 3) are generally available for most nanomaterials. Because none of the other conditions are met for broad types of nanomaterials, very few nanomaterials have specific OELs. Exceptions include amorphous silicon dioxide with an OEL in Germany (TRGS 900, 2007) and titanium dioxide with a proposed draft OEL from NIOSH of 1.5 mg/m^3 for fine and 0.1 mg/m^3 for ultrafine as time weighted average concentrations for up to 10 hr/day during a 40-hours work week (NIOSH, 2005). Schulte et al. (2010) suggest that there may be value in considering titanium dioxide to be representative of a whole class of poorly soluble low toxicity dusts. Bayer Material Science derived an in-house OEL of 0.05 mg/m^3 for its MWCNT product (Baytubes) based on subchronic inhalation studies on MWCNTs (Bayer, 2010). Another company, Nanocyl, utilizes an OEL of 0.0025 mg/m^3 for MWCNTs for an 8-h/day exposure (Nanocyl, 2009). The German Federal Institute for Occupational Safety and Health (BAuA) published risk-associated exposure limit for respirable biopersistent particles of toner containing a large fraction of nanoscale particles equal to 0.06 mg/m^3 (BauA, 2008). Besides these exceptions, most nanomaterials have no OELs.

Rushford Hypersonic (Rushford) manufactures equipment to apply superhard nanoparticle coatings to reduce wear.

Materials Products

One way forward is to adopt a very conservative approach to “benchmark levels” that have been developed for four classes of nanomaterials by the British Standard Institute (2007). For insoluble nanomaterials a general benchmark level of 0.066 ×OEL of the corresponding microsized bulk material (expressed as mass concentration) is proposed. This factor of 0.066 is in line with the potency difference of microscale and nanoscale titanium dioxide as described by NIOSH (NIOSH, 2005). For fibrous nanomaterials a benchmark level of 0.01 fibers/ml is proposed. This level is derived from the current limit value in asbestos removal activities in the UK. For highly soluble nanomaterials a benchmark of 0.5 × OEL is proposed. For CMAR (carcinogenetic, mutagenic, asthmagenic or reproductive) nanomaterials a benchmark level of 0.1 × OEL of the corresponding microsized bulk material (expressed as mass concentration) is suggested.

The Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA, 2009) recommended benchmark limits for an 8-h work shift and to be used for monitoring the effectiveness of protective measures in the workplace. They were careful in stating that these were not health-based exposure limits but rather were aimed at minimizing exposure. The benchmarks proposed were 20,000 $\#/cm^3$ for biopersistent granular materials (metal oxides, others) with a density greater than 6000 kg/m^3, 40,000 $\#/cm^3$ for biopersistent granular materials with a density less than 6000 kg/m^3, and 0.01 $fibers/cm^3$ for CNTs.

Clearly, the research necessary to establish OELs is underway, and the relevant EHS professionals must stay abreast of the research, dynamically updating university recommendations. In all cases, researchers and workers with potential exposure to nanoscale materials should wear standard personal protective equipment (though there are many ongoing studies investigating the effectiveness of standard personal protective equipment such as respirators and masks against nanoscale materials) and handle potentially airborne nanoscale materials within a fume hood whenever possible.

Research at the University is carried out in diverse locations and can involve a range of hazardous materials and activities. Federal, state and local regulatory constraints on the conduct of research are extensive and are expanding. The Research Safety Program provides the University with a course of action to supervise and maintain safe, compliant, and responsible research. The University's Research Safety Program is described in its institutional Lab Safety Plan or LSP, which is a requirement of the OSHA Standard on Occupational Exposure to Hazardous Chemicals in Laboratories. Each research department customizes the institutional lab safety plan according to the research needs.

The University of Minnesota Research Safety Program assures that research is carried out in a way that:

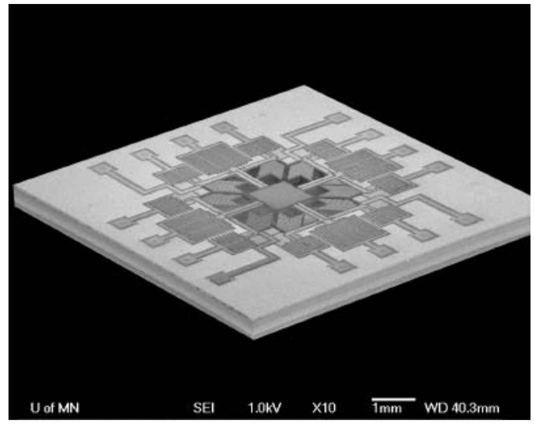
- prevents accidents;
- minimizes exposure to hazardous agents and conditions;
- prevents degradation of the environment through responsible waste management and active waste reduction;
- conserves resources and minimizes losses;
- achieves regulatory compliance.

The University's Research Safety Program consisting of the following elements:

- Research safety responsibilities are defined for all members of the research community.

- A cadre of well-trained and empowered Research Safety Officers (RSO) is established within colleges and departments.
- Central research safety support and oversight is provided through the Department of Environmental Health and Safety and the Office of the Vice President for Research.
- Safe physical research environments are provided; and
- Relevant environment, health and safety regulations are followed.

Implementation of the Research Safety Program at the University is a shared responsibility. PIs, lab staff, Research Safety Officers, department heads, deans, and DEHS staff all have roles to play.



Professor Rajesh Rajamani (ME) designed and built a novel micro electro mechanical system (MEMS) angle sensor that measures inertial angle directly instead of angular rate. It can be used for a variety of positioning and navigation applications.

Information Systems Research

The Research Safety Program provides procedures to follow to ensure regulatory compliance; based on the Office of Vice President for Research: Sponsored Projects' Regulatory Compliance model.

- Research Safety Officers (RSOs) identify instances of non-compliance with environmental health and safety regulations and policies and report them directly to the appropriate principal investigator. Cases of continued non-compliance are reported to the unit head and to the Department of Environmental Health and Safety (DEHS). The RSO, in conjunction with the DEHS and the unit head, have the authority to halt research activities that present an imminent hazard.
- DEHS conducts inspections and reviews records of RSOs. Reports are made to principal investigators and, if necessary, unit heads.
- The Department of Audits reviews compliance with environmental health and safety regulations as part of general audits. Audit Reports are sent to the unit head and to DEHS.

Steps Required for Implementing a Nanotechnology Research Safety Program

A. Amend the Laboratory Safety Plan (Appendix F) to include specific safety requirements for work with Nanotechnology

This Laboratory Safety Plan (LSP) describes policies, procedures, equipment, personal protective equipment and work practices that are capable of protecting employees from the health hazards in laboratories. The LSP is intended to safely limit laboratory workers' exposure to hazardous substances.

- Evaluate workplaces for the presence of hazardous substances, harmful physical agents, and infectious agents.

- Monitor workplace exposure if there is reason to believe that the exposure will exceed an action level, PEL or cause adverse health effects.
- If exposures to any regulated substance routinely exceed an action level or permissible exposure level there must also be employee medical exposure surveillance.
- Provide training to employees concerning those substances or agents to which employees may be exposed.
- Written information on agents must be readily accessible to employees or their representatives.
- Labeling requirements for containers of hazardous substances and equipment or work areas that generate harmful physical agents.

B. Establish a review process for nanotechnology research

Departments are required to establish a review process for research involving particularly hazardous materials. 'High hazard' research is that which due to the nature of the hazard, or the quantity of the material, or the potential for exposure poses higher than usual risk to the worker. Work with nanoparticles must be classified as high hazard research.

In addition, certain laboratory operations, procedures or activities may warrant prior approval from a designated supervisor before each use. Principal Investigators (PI) must consider the toxicity of the chemicals used, the hazards of each procedure, and the knowledge and experience of the laboratory workers to decide which will require pre-approval.

- The RSO must work with the PI to develop a prior approval procedure. This procedure should be described in the departmental LSP.
- Research may require formal review and approval by a researcher's departmental safety committee, perhaps with involvement of DEHS personnel.
- RSOs should consult with Principal Investigators to identify research programs which may fall into this 'high hazard' category.
- PIs whose research is identified as 'high hazard' should provide copies of their SOPs to the RSO and their department's safety committee for review and approval.

C. Surveillance and risk assessment

In order to determine the extent and types of research using nanotechnology across the University, a surveillance effort will be necessary. The RSOs will be asked to report on nanotechnology research in their respective departments. With this information we can categorize the range of hazards presented, and whether existing controls in laboratories are sufficient to eliminate exposure to nanoparticles.

Laboratories are built with engineering controls such as easily cleanable surfaces, ventilated chemical storage, good general ventilation, and are equipped with chemical fume hoods and biological safety cabinets that can eliminate or reduce exposures. Nanotechnology research may require additional engineering, administrative and personal controls. When prevention of exposure is not possible, exposure will be assessed by hazard control banding and appropriate administrative controls and personal protective equipment will be selected. Basic standards for administrative control and personal protective equipment are described in the University's LSP.

- Initially, the Laboratory Safety Listserve will be used to survey for nanotechnology research activities. DEHS will then inspect every laboratory which is identified in the survey.
- RSOs will inspect PI labs at least once per year.
- DEHS will review RSO inspection findings and periodically conduct independent inspections.
- DEHS will conduct work place exposure monitoring when there is a potential for worker exposure.
- Recommendations will be made to prevent exposure to research staff as a result of an assessment of the research process or as a result of exposure monitoring.
- When requested by the RSO, DEHS will review proposed research involving nanotechnology. DEHS will also review any protocols involving nanotechnology, which are submitted to Institutional Animal Care and Use Committee (IACUC) for use of research animals.

D. Conduct incident investigation

Conduct an incident investigation whenever there is a laboratory fire, explosion or unintended hazardous material release. Incidents suggest a safety system failure. When incidents occur, information about causation will be used to improve procedures, processes or engineering controls. The investigation may be conducted by the PI, RSO and DEHS staff. The departmental safety committee will review reports and comment to involved parties.

- Use an incident investigation checklist.
- Document findings in the laboratory safety plan.
- Recommend corrective action including training, improved controls or changes to SOPs.

E. Convene a University Committee on Chemical and Physical Hazards

The University intends to create a committee on chemical and physical hazards to provide technical advice and oversight of high hazard research. The committee could function in a manner similar to the Institutional Biosafety Committee which reviews and approves protocols involving use of biohazardous agents in research.

The responsibilities of this committee with respect to nanotechnology research would include:

- Establish basic safety standards for nanotechnology and other high hazard research.
- Publish generic SOPs to use as templates from which to develop process specific procedures.
- Review and approve individual nanotechnology and other high hazard research protocols.
- Set exposure guidelines and approve control methodologies.

- Identify research programs which may fall into the 'high hazard' category.
- Communicate with RSOs and departmental safety committees.

In addition to the establishment of safety standards at the University, DCTC faculty are working with the National Science Foundation and educational institutions (Rice University, University of California San Diego, University of California Santa Barbara, State University of New York, etc.) to create a consortium of educational institutions to develop uniform standards, procedures and best practices for handling nanoscience materials. This consortium will work with industry and government agencies to build from what already exists and expand where needed. This consortium would create the initial set of standards and guidelines for working with novel and new nano materials.

3.0 Social and Ethical Implications of Nano

3.1 Overview of the field and ethical, legal, and social implications (ELSI) research

Nanotechnology is developed within a societal context. It is derived from human efforts and affected by social, cultural, and political climates. However, generally, R&D for emerging technologies does not start with upstream attention to the ethical, legal, and social implications (ELSI). These issues tend to be raised after technological development and deployment. Regulatory or policy action is usually sparked only after controversies. In contrast, with the U.S. National Nanotechnology Initiative (NNI), resources have been directed towards the study of societal issues from the outset.

The NNI was formed in 2000 as a U.S. national funding program for nano-scale science and engineering and its use in nanotechnology for product research and development. It brings together multiple federal agencies in the funding of nanoscience, and nanotechnology research. Approximately 4% of NNI funding has been directed to the social, educational, and ethical implications of nanotechnology.[14] However, there has been criticism that not much of the money is going specifically to risk assessment research or ELSI, but rather to education and environmental applications of nanotechnology. Maynard estimates that less than 1% of NNI funding has gone to highly relevant studies for assessing risk.[15] In light of this, the attention to Environmental Health and Safety (EHS) and ELSI increased in the second strategic plan for the NNI (Table 3.1), and more efforts in EHS research related to EHS implications and ELSI are suggested in a draft 2009 Senate Bill (S 1482) to reauthorize the NNI. This bill proposed better coordination of EHS and ELSI programs in the Office of Science and Technology Policy (OSTP) in the White House through the National Nanotechnology Coordination Office (NNCO).[16] The bill has not been acted upon in the past year, however.

NNI Strategic Plan II (2004) for FY 2006–2010

Goal: Support responsible development of nanotechnology (with a focus on EHS research; education; and ethical, legal, and social implications)

Program component on societal dimensions:

1. Research directed at EHS impacts of nanotechnology development and risk assessment of such impacts
2. Education-related activities, such as development of materials for schools, undergraduate programs, technical training, and public outreach
3. Research directed at identifying and quantifying the broad implications of nanotechnology for society, including social, economic, workforce, educational, ethical, and legal implications

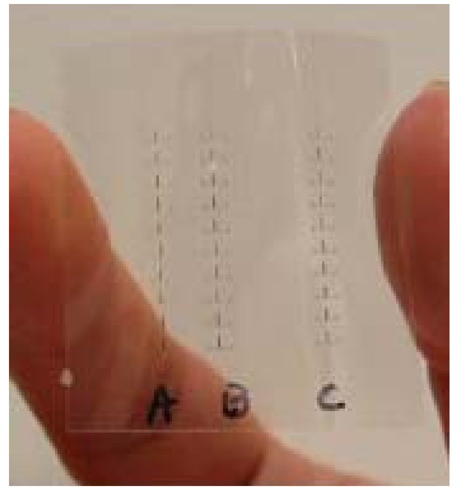
Crosscutting areas of application: Environmental improvement

1. Improved understanding of molecular processes that take place in the environment
2. Reduced pollution through the development of new "green" technologies that minimize manufacturing and transportation of waste products
3. Better environmental remediation through more efficient removal of contaminants, especially ultrafine particles, from air and water supplies, and by continuous measurement and mitigation of pollution in large geographical areas

(Roco, Mihail C. 2005. Environmentally responsible development of Nanotechnoogy. Environmental Science & Technology 39 (5) (3): 106A-12A,)

The National Science Foundation (NSF) has funded most ELSI work on nanotechnology, including a Center for Nanotechnology and Society at Arizona State University (ASU) and the University of California at Santa Barbara (UCSB) and significant (over $1 Million) projects at the

University of Minnesota and elsewhere (see below, Section 3.4). Negative societal experiences with past technologies, such as nuclear power, stem cell research, and genetic engineering, were largely the impetus for dealing with the contextual issues associated with nanotechnology early and often.



Printed transistors on plastic using high capacitance, nanostructured gate dielectrics by Professors C. Dan Frisbie, (CEMS), and Tim Lodge, (Chem). Printed transistors show low-voltage operation and high on-current.

Information Systems Research

ELSI issues and research fall into many categories, including environmental risk, human health protection, regulatory policy, privacy protection, equity and access, informed consent and product use, funding structures and decisions, intellectual property and transparency, laboratory oversight, and human enhancement. Nanotechnology seems to pose the same fundamental ELSI issues as other emerging technologies.[17,18] However, some issues could be considered unique to nanotechnology. For risk assessment and regulatory review, there has been much discussion in the literature about the special properties of engineered nanoparticles and whether special attention might be needed to assess their potential increased reactivity, penetrability, and biological persistence. These may lead to increased toxicity at lower concentrations in comparison to larger particles. Some nanoparticles have been found to move more readily within organisms, for example through the blood-brain barrier.[19]

Other ELSI issues might be more pronounced for nanotechnology, but are not necessarily new ones. Nanotechnology can have great benefits to the environment, for cheaper solar cells, remediating water pollution, and greener manufacturing methods. Nanomedicines are expected to be more effective at lower doses and more targeted with reduced side effects. The University of Minnesota is doing significant work in this area, as well as nanocomposites in solar film. ELSI issues include appropriate incentives for developing nanotechnologies for social good and making sure the poor have access to them (e.g. developing countries or U.S. low income). These issues are likely similar for other products and technologies, like vaccines or water filters.

Other applications are generating concern. Engineered nanomaterials are being used to develop very small detection devices, ones that would be invisible to the eye. Their deployment without the consent or knowledge of those being monitored generates concern about privacy. Nanotechnology for human enhancement poses another set of ELSI issues exaggerated with nanotechnology. The NSF has published reports about the promising capabilities of nanotechnology for human enhancement using the convergence of nanotechnology, biotechnology, information technology, and cognitive science.[20] This endorsement of government funding for such purposes has concerned some ethical scholars. Nanotechnology brings increased abilities to engineer particles that can be introduced in the brain to improve memory, cognition, and emotion, although these applications are not currently in the marketplace.

Seagate (Bloomington) manufactures a wide variety of data storage solutions including the portable FreeAgent™ platform.

Information Systems Products

A lot of ELSI work has focused on understanding public perception of and public engagement in discussions about the implications of nanotechnology. It is clear that most people are unaware of what nanotechnology is and where it is being used. Despite the 1000+ products on the market, people generally do not know that many of the ones that they are using contain engineered nanomaterials. When given information, however, they seem to form temperate attitudes. Generally, people are excited about the promise of nanotechnology, but they want mandatory regulatory systems, transparency about products, their risks, and benefits, and opportunities for input into how nanotechnology is used and overseen.[21] Without proper consideration of public values in technology development, "public failures" are likely to occur.[22]

The literature suggests that public attitudes are still forming and that positive and negative viewpoints could be easily swayed by future events.[23] Public trust is hard earned and easily lost, and maintaining such trust while not restricting the development of nanotechnology is a task that requires considerable effort.[24] The use of citizen consensus conferences can act as a method of both allowing citizens to actively participate and influence the formation of policies which control the development of nanotechnology. It is also a way to inform the citizenry of its risks and benefits, thereby cultivating a deeper understanding and appreciation of nanotechnology. In addition, the response of participants can help to gauge the level of understanding present in the society. [25,26]

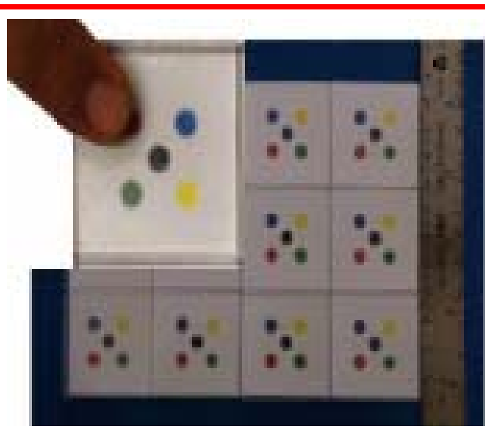
Fortunately nanotechnology ELSI research has been able to draw from many past lessons of other technologies.[27] [28] In addition to the broad vision communicated through the NNI, there is room for individual states to propose and implement their own governance frameworks for nanotechnology.[29]

3.2 Development of OHS best practices as an ethical issue

Discussions of oversight frameworks for nanotechnology have largely focused on occupational health issues associated with engineered nanoparticles, such as buckyballs and carbon nanotubes (CNTs). CNTs have been a focus of human health implications given their asbestos-like effects in the lung in animal studies.[30] Less attention has been paid to oversight for widespread applications in medicine, food and agriculture, and the environment, for which consumers, patients, ecosystems, farmers, or the general public may bear the risks and benefits.[31] For example, some studies suggest that under some conditions, there will be only very limited exposure to nanomaterials migrating out of packaging materials, but these studies are largely based on modeling not product testing during use.[32]

An example of an area with broad risk but limited research is, in nanoparticles used in environmental applications. Products with nanotechnology use will release nanoparticles into the environment as they wear down with use and are discarded. The potential data gaps and complexity of nanoparticle breakdown and accumulation in the environment or in life-forms (human and non-human) pose a unique challenge for researchers and regulatory bodies.[33] Scholars have pointed out the need to look at the whole product life-cycle when considering risk and regulation.

A key point of EHS concern is the frontline: the exposure of workers to nanoparticles in laboratory or manufacturing settings. However, Occupational Health and Safety (OHS) is not just a scientific issue. The interpretation of quantitative or qualitative risk information and standard setting must include some subjective judgments.[34] For example, science can help determine what the exposure in the workplace is, what potential effects there might be, and what the chance of those effects is, but it cannot determine what is "safe". People think differently about what is safe to them and set their own levels of risk-taking or precaution based on values and perception factors. For example, if the risk is voluntary and known, providing benefits to them (e.g. driving a car), people might be more willing to accept it. However, if the risk is involuntary, unknown, and provides little direct benefit to them, they are less likely to accept it. Ethical issues come into play in the right for people working with materials to know whether they are hazardous and how to protect themselves. Having a choice (autonomy) to expose themselves and bear the risk, no matter how small, is considered an important ethical principle.



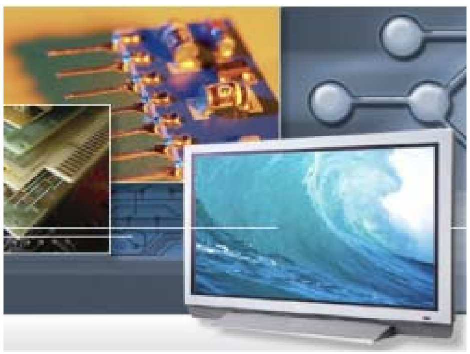
Dr. William Kennedy (Neuro) method to rapidly test tactile sensitivity on the finger pads. Nanoscale bumps detects the first signs of nerve pathology in cancer patients receiving chemotherapy and screens for diabetic neuropathy.

Nanomedicine Research

Oversight policy has been a focal point for the UMN ELSI research, and scholars here are leaders in this area (see below, section 3.4). Oversight includes not only formal laws and regulations that may apply to nanoproducts, but also informal policies, programs, and efforts to minimize the downsides and maximize the benefits in responsible ways. Appropriate oversight of nanotechnology will continue to be important for ensuring the health and environmental safety of products and instilling public confidence. It includes more than just risk and safety, but also rights to know and choose, transparency in product development and review, and opportunities for democratic input into technological development. Adverse events in the absence of public inclusion can preclude future support, use, and development of nanotechnology.

3.3 Developing ethical awareness in nano researchers and connections between UMN and MNSCU ELSI work and engineers/natural scientists

The National Science Foundation has been active in ensuring that engineers and natural scientists working in the laboratory with nanotechnology research and development are aware of social and ethical implications (SEI) of nanotechnology. The University of MN has been a part of this effort. NSF has required the National Nanotechnology Infrastructure Network (NNIN) sites to expose researchers and facility users to SEI issues. Cornell University has been coordination point for SEI "training" and discussion between ELSI researchers and engineers and scientists. Since 2008, Jennifer Kuzma has served as the UMN point person for SEI in the NNIN. Kuzma and her graduate student, Jonathan Brown, have been participating in meetings to improve SEI training and dialogue for the past year. They have developed new materials and a format for SEI training at the UMN. The revised training events will take place in Winter 2010. They have also led ELSI seminars for the UMN's undergraduate research program (REU) for Materials Research, Science, and Engineering Centers in summer 2009 and 2010. Materials for these events are available upon request.



Cima Nanotech (St. Paul) has developed an economical process for generating silver nanoparticles that can be used in printed electronics, plasma displays, touch screens, LEDs,

Information Systems Products

For the past three academic years, the UMN has offered a course on "Nanotechnology and Society" (PA 8790/Law 6037/BHTX 8000—cross listed in public affairs, law, and bioethics). Jordan Paradise and Kuzma developed this course for Fall 2008, and it was also offered in 2009 and 2010. This was one of the first national courses of its kind. It has been somewhat successful in attracting scientists and engineers at the UMN. Out of 65 total students who have taken this course (17, 25, and 23 for the three years), about 10 have or are working toward Ph.D.s in the natural sciences or engineering. These students have reported positive experiences in the class. More needs to be done to attract these students to this course or other ELSI courses (e.g. their research Ph.D. advisers could encourage their participation).

Another way that the UMN has been connecting ELSI researchers with natural scientists and engineers at the UMN is by including faculty from those departments on NSF-funded ELSI projects. For the NSF grant *Evaluating Oversight Systems for Nanobiotechnology, Assessing Oversight Mechanisms for Active Nanostructures and Nanosystems: Learning from Past Technologies in a Social Context* (*NIRT Award SES-0608791, 2006-2010) (Susan Wolf (PI) , Jennifer Kuzma, Jordan Paradise, Effie Kokkoli, Gurumurthy Ramachandran (co-PIs))*, one of the co-PIs is a UMN chemical engineer and another is from the school of public health. Three working group members come from natural science, medical, and engineering departments (A. Taton, Chemistry, D. Pui, Mechanical Engineering, and Stephen Ekker, Mayo Clinic, College of Medicine). Several other working group members are natural scientists and engineers from outside the UMN. Bi-directional learning and collaboration took place between them and social scientists, ethicists, policy scientists, law scholars, and environmental scientists in this interdisciplinary project (see also below, Section 3.4).

In a recently funded *National Institutes of Health (NIH) project on Nanodiagnostics and Nanotherapeutics: Building Research Ethics and Oversight (1RC1HG005338-01, 2009-2011, Wolf, McCullough, Hall, and Kahn co-PIs)* these inter-departmental collaborations between ethicists and lawyers and natural scientists are continuing.

3.4 UMN research and outreach in ELSI

Engagement through research: The UMN was an early leader in oversight policy for nanotechnology and continues to have national and international prominence in this area. The UMN, through the Humphrey Institute, hosted the 1st national conference on nanotechnology oversight, producing both a public report and peer-reviewed publication from this workshop. The conference brought together over 100 scholars and practitioners from the White House NNCO, federal agencies, industry, academe, and non-governmental organizations, resulting in two key publications[35].

A key NSF funded project arose out of this workshop *Evaluating Oversight Systems for Nanobiotechnology, Assessing Oversight Mechanisms for Active Nanostructures and Nanosystems: Learning from Past Technologies in a Social Context* (see also section 3.3). This project was the first to look specifically at oversight systems for nanotechnology applied to or derived from biological systems. It developed a new methodology to evaluate historical or contemporary oversight systems from multiple perspectives (ethical, legal, policy, risk, and social science criteria) and apply lessons to the future. It has brought together key stakeholders from the local and national industries, NGO community, academe, and state and national government through its working group, as mentioned above. Numerous publications resulted from this work, including a special symposium of the Journal of Law, Medicine, and Ethics. Through this grant, another national workshop was hosted at the UMN by the Consortium on Law and Values in the Health, Environmental, and Life Sciences (the Consortium). Leaders from the Occupational Health and Safety Administration, Environmental Protection Agency, Dupont, International Center for Technology Assessment (a NGO promoting strict regulation), Nanocopeia (local nanotech company), MN Pollution Control Agency, and scholars from around the country participated.

Donaldson (Minneapolis), a leading worldwide provider of filtration systems in the industrial and engine markets, uses micro and nanoscale fibers to trap particles.

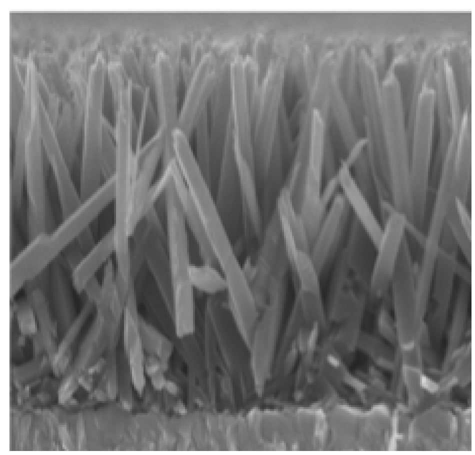
Energy & Environment Products

The appendix lists publications resulting from this project, including a special edition of the Journal of Law, Medicine, and Ethics.

Food and agricultural applications of nanotechnology were not well studied as recently as 5 years ago. Kuzma developed the first database on food and agricultural nanotechnology R&D in partnership with the Woodrow Wilson Center for International Scholars' Project on Emerging Nanotechnologies in Washington DC.[36] This database and the report from it received considerable national and international attention in scholarly communities and the media. It has also been used in Kuzma's subsequent research to look upstream at agrifood nano development and assess the risks, benefits, and potential societal issues (Upstream Oversight Assessment). It was also used by the United Nation's Food and Agricultural Organization in the preparation of its recent report on food and nanotechnology risk analysis (Kuzma was also an expert on the working group producing this report).

Two other federally funded grant collaborations are ongoing in nanotechnology and ELSI research. One is hosted by the Consortium and focusing on research ethics, like informed consent, for nanomedicinal products*: (Nanotherapeutics: Building Research Ethics and Oversight , NIH 1RC1HG005338-01, 2009-2011, Wolf, McCullough, Hall, and Kahn co-PIs)*. The other is examining public and stakeholder perception of nanotechnology in the context of risk communication: *(Intuitive Toxicology and Public Engagement, NSF NIRT SES-0709056 David Berube, North Carolina State University (PI), Dietram Scheufele, U of WI, Kevin Elliott, Univ. of South Carolina, Patrick Gehrke University of South Carolina , and Jennifer Kuzma (coPIs)).*

***Local Engagement*:** As part of the outreach mission of both the University of Minnesota and MNSCU faculty working on nanotechnology and ELSI are heavily involved in collaborations with stakeholders and engaging the public in conversations about nanotechnology. Faculty have presented at local private colleges, high schools, middle schools, community and professional organizations, companies, and for state governments. A sample is listed in the appendix. Talks on nanotechnology policy were given at St. Francis Xavier Middle School in Buffalo, MN; College of St. Catherine's; the College of St. Thomas; the Science Museum of MN; the 3M company; MN Pollution Control Agency; Bell Museum Café Scientifique; and Hennepin County Bar Association to name a few. MNSCU faculty and students have discussed nanotechnology and associated careers (which include ELSI related occupations) at multiple twin cities area high schools, Rochester area High School STEM



Eray Aydil (CEMS) has developed nanowires and nanoparticles to improve the performance of solar cells and lithium-ion batteries.

Energy & Environment Research

event, statewide MHTA Science Outreach events and many invited visits to elementary and middle schools.

Two collaborations are particularly worth noting. Faculty have been working closely with the Science Museum of Minnesota (SMM). Dave Chittenden, former VP for education, served on the working group for the NSF nanotechnology oversight grant, Gurumurthy Ramachandran, Jennifer Kuzma, Jordan Paradise, and David Pui served on the Science Museum's Nanoforum Advisory Board. The SMM has been developing ways to engage the public in nanotechnology and hosted exhibits and forum as part of the National Nanotechnology Informal Science Education Network (NISE-net). This advisory board helped to review materials and provide advice to SMM. Kuzma also participated as a speaker in three NISE-net public forums. A UMN graduate student of mechanical engineering, Gwideon Arefe, has been a speaker at these events too and is also featured on the SMM's public dialogue website "Science Buzz" for nanotechnology.

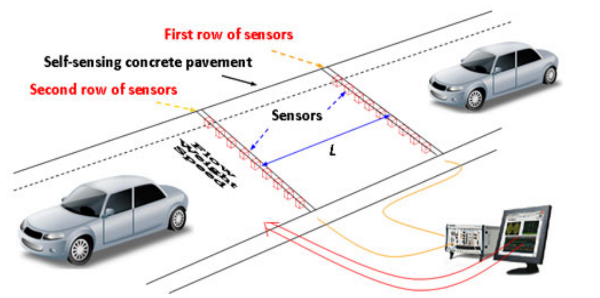
UMN scientists and scholars have been very active in engaging K-12 teachers in nanotechnology education. Leslie Flynn and Lee Penn received a MN Department of Education grant to host summer camps for teachers about nanotechnology. (Leslie Flynn (PI), Lee Penn, Frank Joseph, John Nelson, Baskar Dahal, Brandy Toner, Jeffrey Long, Chun Wang, Wei Zhang, Sashank Varma, Keisha Varma, Andreas Stein, Christy Haynes, Jennifer Kuzma co PIs) ELSI presentations have been part of these camps.

Since 2003, Dakota County Technical College has offered nanoscience training for high school teachers. Workshops on nanotechnology have also been presented at MN Science Teacher Conferences. Material presented includes nanotechnology concepts, safety considerations for lab experiments, societal aspects of nanotechnology (ELSI) and possible careers for students involving the study of nanoparticles on human health and the environment.

National and International Engagement: In service to the broader communities, faculty want their scholarly work to be relevant to national and international policy makers. As such, presentations at national and international meetings and service on advisory groups are essential. Presentations at national and international scholarly workshops are too numerous to list completely, but examples are provided below:

Kuzma has served on the United Nations FAO/WHO Expert Committee on Food and Nanotechnology, the Executive Committee of the International Society for the Study of Nanoscience and Emerging Technologies, and the European Commission Expert Group for the Science in Society Work Programme. She has presented at expert and stakeholder meetings with the United States Department of Agriculture, National Academy of Sciences' National Research Council, National Nanotechnology Coordination Office of the White House, Alberta Agricultural Research Institute, International Risk Governance Council (Zurich, Switzerland), Grocery Manufacturers of America, MidWestern States Risk Assessors, North American Hazardous Materials Management Association, World Conference of Animal Producers (CApetown, South Africa), Brazilian Agricultural Research Institute (EMBRAPA) (San Carlos, Brazil), and

American Association for the Advancement of Science (AAAS), among others. She has briefed U.S. Senate staff and has been interviewed for the NY Times, MPR, Earth and Sky radio, and other national, regional, and local media. Her interview for Earth and Sky is part of a long-term exhibit (“Take a Nanooze Break”) at the Walt Disney World Resort at Epcot Center. All these presentations and interviews focused on the ELSI dimensions of nanotechnology.



Professor Xun Yu (ME, Duluth), has developed a self-sensing carbon nanotube / cement composite for traffic monitoring. The resistance of the material changes with the weight of the car on the roadway.

Information Systems Research

Newberry has been involved with the IEEE Research and Development Policy Committee and the Medical Technology Policy Committee. Both of these committees are involved with nanotechnology – including research, education, safety and government regulation of technology. She has also participated in multiple National Science Foundation Workshops dealing with the societal aspects of nanotechnology. Through a working group specifically focused on K-12 education and supported by the National Science Foundation, Newberry is working with other educators, industry and policy makers to initiate nanoscience safety standards and training at multiple levels as well as raising awareness about the safety aspects of nanoscience.

3.5 Recommended ethical standards and guidelines for UMN/MNSCU

In summary, the UMN has been a leader in integrating ELSI with research and development in nanotechnology. The UMN is one of the few universities strong in both ELSI and nanotechnology R&D, and it showed early leadership in local, national, and international dialogues about nanotechnology and ELSI. MNSCU institutions and faculty interact with UMN work as well as being involved in separate outreach and educational activities.

It is important to continue ELSI work at UMN and MNSCU institutions and enhance public engagement, stakeholder dialogue, scholarly contributions to policy making, and the integration of ELSI work with nano-scale science, engineering, and technology. ELSI work is important from normative (ethical), legitimacy (trust) and substantial (responsible technology development and decision making) perspectives. It should occur alongside of research and development in nanotechnology. Below are some specific suggestions for improving ELSI work and its integration at the UMN:

- Raise awareness among all researchers about ELSI dimensions of nano by increasing SEI training and dialogue.
- Encourage students working in nanoscience and engineering to take classes related to ELSI issues of nanotechnology

- Continue stakeholder dialogue through roundtables, workshops, and consensus conferences
- Promote future collaborations between the SMM and ELSI researchers at the UMN.
- Integrate Anticipatory Governance, Upstream Oversight & Technology Assessment into research at UMN.
- Create a forum and space where ELSI, natural science, and engineering scholars at the UMN can collaborate and communicate.
- Foster stronger collaboration between UMN and MNSCU institutions with a focus on ELSI education at all levels and community outreach
- Actively participate in a national consortium focusing on training in nanoscience safety.
- Educate people working with nanomaterials about the EHS issues associated with nanotechnology broadly, and the available data and information on the materials with which they are working.
- Include stakeholders (especially graduate and other student workers) on institutional decisions about standard setting and safety measures.

4.0 Nanotechnology Education

4.1 Introduction

Study of our world at the nanoscale has been a part of the educational landscape for hundreds of years. Each time physicists, chemists and biologists study or work with molecules and atoms – they are working at the nanoscale. However, because of thee recent development of new tools that allow us to observe the nanoscale in much more detail – the "age of nanotechnology" has arrived. Many voices believe that nanotechnology offers an opportunity for change in the educational landscape within the U.S. by:

- Nanotechnology has the ability to energize and fuel student interest in science math and engineering – schools are one of the best places to provide that energy.
- There is a huge need for a nanotechnology aware workforce – will drive all market segments and economic growth.
- Government dollars will be spent on nanotechnology – the public needs to be aware of nanotechnology in order to assess and guide legislative decisions.

Many people have hoped that nanotechnology would energize student and public interest in science, math and engineering in the same way that President John Kennedy's challenge of putting a man on the moon did in the 1960s. That challenge issued by the President fueled a generation of scientists and engineers that met the challenge. The excitement and vision of space exploration also energized new markets and economic growth in the United States. The challenge of exploring the world of molecules and atoms (nanoscience) has the potential to create the same energy and interest in science and engineering in a new generation of students.

Also, to remain economically sound the United States must provide industry with a skilled and knowledgeable workforce. As previously discussed, nanotechnology will impact every market segment, therefore there is a significant need for a skilled workforce which is the impetus behind most education. Finally, the public needs to be aware at some level of the opportunity and challenges of any new science or technology. From an historical viewpoint the subject of nanotechnology is a new addition to the library of educational content.

In the 1980s nanotechnology knowledge and practice was focused in researchers in industry an educational institutions, It was also much more of a theoretical study rather than engineering or application driven. The focus was on trying to understand the interactions of specific molecules and atoms. It was during this decade that development of scanning probe microscopes and the discovery of buckyballs occurred. Both of these discoveries would win Nobel Prize awards a decade later. During the 80s there were no formal nanoscience or nanotechnology classes or programs. Nothing from an educational or training standpoint has been formalized at this time.

As two Nobel Prizes were awarded for discoveries in the nanotechnology area it slowly grew as an area of interest and knowledge for a small group of people to being involved in more and more disciplines and at more institutions.

During this time the National Science Foundation began to fund nanoscience research at high educational levels. Finally in the late 1990s an electronic device company in Pennsylvania approached the electrical engineering group at Penn State and asked them to develop a program to train nanoscience technologists. This training was necessary because the electronic device industry was approaching the nanoscale which required new equipment and new training for the operators of that equipment. From this request Penn State became the first NSF funded nanotechnologist training/educational program in the United States.

In the most recent decade multiple educational institutions hve received funding from several agencies to bring nanotechnology education into th more traditional educational pathways. DCTC was the second 2 year institution in the United States to create a nanoscience technologist program. During this decade approximately 20 institutions (2 year and 4 year) have begun nanoscience courses or programs. Nanotechnology has also obtained a more prominent place in traditional science and engineering courses.

Also, of significance is the aspect that nanotechnology "education" has moved from the exclusive arena of post secondary education and into middle and high school venues as well as informal education. Informal education includes not only the outreach activities that have been discussed in the previous sections but also talks given to various civic organizations and media coverage of nanotechnology.

Nanotechnology concepts and subjects are also being taught to high school educators for insertion into traditional programs and also to students as a part of day long outreach activities, summer camps, field trips and career fairs.

4.2 Nano at the K-12 level

Educational researchers are in the process of investigating appropriate age levels to introduce the concepts of nanotechnology. Even without defined guidelines or research results, nanoscience concepts and the wonders of the world at the molecular level are being introduced to children at a younger and younger age.

However, because nanotechnology and nanoscale phenomena are so directly tied to and a part of traditional science courses, nanotechnology is finding it's ay into more and more high school science classes. In some cases, English and civics instructors are using nanotechnology and societal impacts as a subject for class discussion or perhaps a written assignment. Currently, nanoscience is not considered as a separate course within high school – the concepts are imbedded into traditional courses. This may change in Minnesota in the fall of 2011. Four high schools have approached DCTC with the request to create and provide a year-long nanoscience course for high school junior and senior grade students. This will be the first year long nano focused course for high school students in the United States.

In 2010 Project Lead The Way has integrated a nanoscience module into their pre engineering curriculum. This is focused on high school age students.

DCTC faculty and students have visited several elementary and middle schools and have given nanoscience demonstrations and presentations. Nanoscience education at grades below 10 or 11 is very informal.

4.3 Nano at the AAS level and Community Outreach

In 2004 DCTC received a grant from the National Science Foundation to create a two year nanoscience technologist program. This program was unique in several ways. First, because of the industry strength within the Twin Cities area, the program would be multi-disciplinary – with emphasis on nanoelectronics, nanobiotech and nanomaterials. This was also the second 2 year AAS degree program in the United States. Finally, the program relied on a strong partnership with the University of Minnesota. DCTC program students have the 4th semester of the program at the University of MN, being taught by UMN professors and with lab experience in the extensive University labs discussed in a previous section. This collaboration is somewhat unique and has served as a model for other U.S. educational institutions and partnerships.

Note that the content of this program and courses that are taught at both institutions include societal and ethical aspects as well as safety training. The program at DCTC has fostered and served as an example for the creation of other 2 year nanoscience programs throughout the country. These additional programs also serve as partners in the effort to promote ELSI knowledge and content throughout various educational institutions.

In 2008 DCTC was awarded a regional center grant. Nano-Link, a regional center for nanotechnology education is an upper midwest center with partners in 5 states and continues the strong partnership with the University of MN. Nano-Link will serve as a vehicle to further research and education regarding nanotechnology, technical knowledge, societal impacts and ethical issues associated with the evolution of nanoscience. Nano-Link is also focused on the creation of modularized nanotechnology educational content. Aspects of ELSI comprise the topical content for several of the planned modules.

Medtronic (Minneapolis) uses a variety of nano coatings on implantable devices

Nanomedicine Product

In addition to the category of informal education or outreach that occurs at museums, career fairs and in the media, community outreach also includes presentations that are given to civic groups such as Chambers of Commerce, workforce development organizations, rotary clubs, lions clubs and so on. DCTC personnel have been involved in presentations at all of these organizations in many regions of the state. In each of these presentations, not only is the possibility of nanoscience discussed but the responsibilities of all involved parties to be aware of any ELSI subjects associated with the continuing development of nanotechnology.

4.4 Nano at the Bachelors and Graduate Level

Many universities have grappled with the question of how to organize nano content in their Bachelors and post graduate education. While many have established centers or institutes to facilitate research collaborations (often involving dedicated nano buildings), very few have decided to establish nano departments or nano-specific degrees. Rather the content is delivered in courses housed in traditional science and engineering departments. The University of Minnesota has established the Center for Nanostructure Applications to perform these functions. Information on CNA can be found at www.nano.umn.edu. The Center sponsors seminars and workshops which bring world-renowned experts to Minnesota. In addition, CNA organizes hands-on training and short courses that are attended by both University and local industry participants who want to gain exposure to this technology area. The Center also publishes a newsletter. Interested parties can subscribe to either print or soft copy versions of the newsletter from the website. Finally, CNA seeds cross disciplinary projects that pairs experts in nano materials with technical area experts to apply these materials to problems of interest.

Like the vast majority of its peers, the University of Minnesota incorporates nano concepts into many of its science and engineering courses more or less automatically since more than one hundred of the faculty of the University are also active researchers in this area. In addition to the classroom content, University students often receive hands-on training in for-credit labs and by participating in research, either at the undergraduate level through UROP (www.research.umn.edu/undergraduate/) or REU (www.nsf.gov/home/crssprgm/reu/) opportunities, or at the graduate level as part of the student's thesis or project research.

The University has a particular strength in nanoparticle-related research. As a result, the Institute of Technology (now the College of Science and Engineering), developed a special graduate minor program in Nanoparticle Science and Engineering (NPSE). This program has created a series of specialized courses in the topic and allows students to complete a minor in NPSE to complement a traditional graduate degree in a field of science or engineering.

5.0 Role of the Proposed Physics and Nanotechnology Building

The University is currently working on the design of a new Experimental Physics and Nanotechnology Building. The 140,000 square foot building is intended to:

- House an expansion of the Nanofabrication Center (NFC). NFC enables a great deal of nano-related research and education for faculty and enables industrial R&D by providing access to costly fabrication equipment on a fee-for-service basis. This is particularly useful for small companies that do not have the capital resources to create their own facility.
- Provide space and resources for multidisciplinary nano research including new areas such as energy and nanomedicine. These labs are outside of the conventional departmental control. This enables multidisciplinary teams to coalesce around research ideas and pursue those ideas in a common lab close to NFC and other resources.
- House the Physics Department Office and many of its faculty and research staff, including a wide variety of nano-related researchers in solid state and bio physics.

The age and inadequacies of the current facilities have negatively impacted retention and recruiting of top-tier graduate students and faculty. This is a very competitive area and researchers are being recruited to schools such as Cornell, Georgia Tech, Michigan, Ohio State, Illinois, Wisconsin, Berkeley, Utah, and Santa Barbara, all of which have recently built much more modern facilities.

The need for this new building arises from multiple factors. First, the number of nano researchers continues to grow, while their interest areas continue to diversify. This requires an expanded toolset to serve the user community. Clean room space is needed to house these tools, not only for University of Minnesota researchers; the private sector and MNSCU also make extensive use of these labs. Second, the emerging nano fields are highly multidisciplinary. Lab space is being reserved for "hotel" style assignments, allowing multidisciplinary teams to have a single lab that would support students from multiple departments. Once that project has been completed, the space will be reassigned to a new group. Finally, the facilities requirements for modern research and development in nanotechnology have become more stringent. The current facilities, which include the 80 year old Tate Hall, are no longer adequate to the task. The safety concerns raised in this report underscore the need for facilities with adequate filtration, ventilation, monitoring, and other experimental infrastructure to allow new developments in nanotechnology to be done safely and responsibly.

The proposed Experimental Physics and Nanotechnology Building will house new clean room and other facilities to support research and development in this emerging field.

6.0 Summary

Nanotechnology, which involves the control of matter at very small length scales, is a rapidly growing area, based on the development of novel materials structured at the nanoscale. In many cases, the properties of these materials depend of the size of this structure, allowing one to tune the properties for the desired application. Applications of nanoscale materials include consumer products, electronics, sensors, aerospace, and increasingly, medicine, energy, and environmental remediation. The market place for nano-enabled products is growing rapidly. This is bringing with it a need for workers trained in this discipline. MNSCU and the University are among the leading institutions in developing the curriculum to train these workers. This report highlights some of the leading nano-related research and product development that is underway in nanotechnology.

Nanotechnology, however, carries with it several concerns. Primary among them is the safety of people who are involved in the manufacture of nanoscale materials. The University has been working with NIOSH and other government agencies to develop these guidelines. In the mean time, the University has set up a set of best practices to mitigate risk to researchers who have exposure potential. Details of these best practices are presented in this report and in the appendices.

Nano also poses significant societal and ethical concerns such as regulatory policy, privacy protection, equity and access, informed consent and product use, funding structures and decisions, intellectual property and transparency, laboratory oversight, and human enhancement. The University is at the forefront of work in this area and has active groups that bring together engineers, biomedical researchers, ethicists, public policy experts, lawyers, and other stakeholders to develop recommendations for regulatory oversight models that will enable the responsible development of the technology.

The University and MNSCU have also been a leader in the development of educational activities around nano. A joint center for technical education in nano is one of only two in the country. This center is training the technical workforce, providing them the hands-on skill that they need to contribute to the growing nano economy.

Finally, this report briefly reviews the need for nano infrastructure at the University. A new Physics and Nanotechnology building is currently under design. This facility would enable the safe and responsible development of the next generation of nano, especially in emerging areas such as energy and medicine.

Appendices

A. EHS #1

1. Ramachandran, G., Watts, W.F., Kittelson, D. "Mass, surface area, and number metric in diesel occupational exposure assessment". *Journal of Environmental Monitoring*. 2005, 7(7), 728 – 735. (Deals with the importance of the exposure metric)

2. Kandlikar, M., Ramachandran, G., Maynard, A.D., Murdock, B., Toscano, W.A., Health risk assessment for nanoparticles: A case for using expert judgment. *Journal of Nanoparticle Research*. 9:137-156, 2007. (Framework for health risk assessment).

3. Choi, J.Y, Ramachandran, G. Review of the OSHA Framework for Oversight of Occupational Environments. *Journal of Law, Environment, and Ethics*, 37(4):633-650, 2009.

4. Park, J.Y., Ramachandran. G., Raynor, P.C., Olson, G.M. Determination of particle concentration rankings by spatial mapping of particle surface area, number, and mass concentrations in a restaurant and a die casting plant. *Journal of Occupational and Environmental Hygiene,* 7(8): 466-476, 2010.

5. Park, J.Y., Ramachandran. G., Raynor, P.C., Eberly, L.E., Olson, G.M. Comparing exposure zones by different exposure metrics for nanoparticles using statistical parameters: contrast and precision. *Annals of Occupational Hygiene,* 54(7):799-812 2010.

6. Park, J.Y., Ramachandran. G., Raynor, P.C., Kim, S.W. Estimation of surface area concentration of workplace incidental nanoparticles based on number and mass concentrations. Submitted for publication in *Journal of Nanoparticle Research.*

B. EHS #2

1. Dynamic Measurement of Altered Chemical Messenger Secretion after Cellular Uptake of Nanoparticles using Carbon-Fiber Microelectrode Amperometry, Marquis, B. M., McFarland, A. D., Braun, K. L., and Haynes, C. L., *Anal. Chem.*, 80, 3431-3437 (2008).
2. Toxicity of Therapeutic Nanoparticles, Maurer-Jones, M. A., Love, S. A., Bantz, K. C., Marquis, B. J., and Haynes, C. L., *Nanomedicine*, 4 (2), 219-241 (2009).
3. Amperometric Assessment of Functional Changes in Nanoparticle-Exposed Immune Cells: Varying Au Nanoparticle Exposure Time and Concentration, Marquis, B.J., Maurer-Jones, M.J., Braun, K.L., and Haynes, C.L., *Analyst*, 134, 2293-2300 (2009).
4. Analytical methods to assess nanoparticle toxicity, Marquis, B. J., Love, S. A., Braun, K. L., and Haynes, C. L., *Analyst*, 134 (3), 425-439 (2009).
5. Functional Assessment of Metal Oxide Nanoparticle Toxicity in Immune Cells, Maurer-Jones, M. A., Lin, Y.-S. and Haynes, C. L., *ACS Nano*, 4 (6) 3363-3373 (2010).
6. Assessment of Functional Changes in Nanoparticle-Exposed Neuroendocrine Cells with Amperometry: Exploring the Generalizability of Nanoparticle-Vesicle Matrix Interactions, Love, S. A. and Haynes, C. L., *Anal. Bioanal. Chem.*, in press (2010).
7. Impacts of Mesoporous Silica Nanoparticle Size, Pore Ordering, and Pore Integrity on Hemolytic Activity, Lin, Y.-S. and Haynes, C. L., *J. Am. Chem. Soc.*, 132 (13) 4834-4842 (2010).
8. The Bench Scientist's Perspective on the Unique Considerations in Nanoparticle Regulation, Marquis, B. J., Maurer-Jones, M. A., Ersin, Ö. H., Lin, Y.-S., and Haynes, C. L., submitted for publication in *J. Nanoparticle Research.*

C. Selected ELSI Papers

1. Kuzma, J. Editor. The Nanotechnology-Biology Interface: Exploring Models for Oversight. September 15, 2005. Workshop Report, Center for Science, Technology, and Public Policy, University of Minnesota.
2. Kuzma, J._ "Moving Forward Responsibly: Oversight for the Nanotechnology-Biology Interface," *Journal of Nanoparticle Research*, 9:165-182 (2007).
3. S.M. Wolf, G. Ramachandran, J. Kuzma, and J. Paradise (eds.) Developing Oversight Approaches to Nanobiotechnology: The Lessons of History." Special Symposium of Journal of Law, Medicine and Ethics. 37 (4) (2009).
4. Kuzma, J., Paradise, J., Kim, J., Kokotovich, A., G. Ramachandran, and Wolf, S.. "Integrated Oversight Assessment: A Historical Case Study and Multicriteria Approach" Risk Analysis 28(5): 1179-1195 (2008).
5. Paradise, J., Alison W. Tisdale, Ralph F. Hall, Efrosini Kokkoli Evaluating Oversight of Human Drugs and Medical Devices: A Case Study of the FDA and Implications for Nanobiotechnology. J. of Law, Med. & Ethics 37(4): 598-624 (2009).
6. Kuzma, J. and J.C. Besley. "Ethics of Risk Analysis and Regulatory Review: From Bio- to Nanotechnology," Nanoethics 2(2): 149-162 (2008).
7. Paradise, J.. Wolf, S., Kuzma, J., Kuzhabekova, A., Wedekind, A., Kokkoli, E., and G. Ramachandran. "Developing Oversight Strategies for Nanobiotechnology: Learning from Past Oversight Experiences." Journal of Law, Medicine, and Ethics 37 (4): 688-705 (2009).
8. Kuzma, J. and Kuzhabekova, A, Wilder, K. "Improving Oversight of Genetically Engineered Organisms" Policy & Society 28: 279-299 (2009).
9. Kuzma, J. and S. Priest. "Nanotechnology, Risk and Oversight: Learning Lessons from Related Emerging Technologies," *Risk Analysis* DOI: 10.1111/j.1539-6924.2010.01471.x (2010).
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13. Kuzma J. and Z. Meghani . "A possible change in the U.S. risk -based decision making for emerging technological products: Compromised or enhanced objectivity?" *EMBO Reports* 10: 1-6 (2009).
14. Kuzma, J. and Kuzhabekova, A, Wilder, K. "Improving Oversight of Genetically Engineered Organisms" *Policy & Society* 28: 279-299 (2009).
15. Kuzma, J. Larson, J. and P. Najmaie. "Evaluating Oversight Systems for Emerging Technologies: A Case Study of Genetically Engineered Organisms," *Journal of Law Medicine and Ethics* 37 (4): 546-586 (2009).

16. Wolf, S. M., Gupta, R. and Kohlhepp, P. (2009), Gene Therapy Oversight: Lessons for Nanobiotechnology. *The Journal of Law, Medicine & Ethics*, 37: 659–684.

17. Paradise, Jordan K., Diliberto, Gail, Tisdale, Alison and Kokkoli, Efrosini, Exploring Emerging Nanobiotechnology Drugs and Medical Devices. Food & Drug Law Journal, Vol. 63, No. 2, pp. 407-420, 2008

D. Selected ELSI Talks

1. Kuzma, J. “Nano and health: an Ethical Perspective,” Exploratorium, San Franciso, Nanoforum keynote presentation. June 6, 2007. (invited speaker)
2. Kuzma, J. “Nano and health: an Ethical Perspective,” Science Museum of Minnesota, Nanoforum keynote presentation. April, 26, 2007. (invited speaker)
3. Kuzma, J. MN Attorney General’s CLE workshop, “Emerging Technologies, Policy, and Law: Getting It Right.” June 2006. (invited speaker)
4. Invited keynote speaker for Science Museum of Minnesota’s Nanoforum. “The Brave New World of Nano Policy” August 2006.
5. Invited reviewer for Science Museum of Minnesota’s Nanoscale Informal Science Education Network’s Exhibits and Programs Workshop. July 2006.
6. Kuzma, J. Café Scientifique, Bell Museum of Natural History, “GEOs: An Intersection Between Science and Society.” November 2006. (invited speaker)
7. Kuzma, J. “Nanotechnology and Society: no Small Matter” MN Society of Professional Engineers, Feb 19, 2008. (invited speaker)
8. Kuzma, J. “Nanotechnology: What’s new, what isn’t and why it matters?” Mindstretch keynote speaker. October 31, 2007. (invited speaker)
9. Kuzma, J. “Nanotechnology, Oversight Policy”. Hennepin Country Bar Association, April 2008. (invited speaker)
10. Kuzma, J. MN Pollution Control Agency, “Grand Challenges for Nanotechnology Policy and the Environment,” February 2007. (invited speaker)
11. Kuzma, J. 3M company’s Technology Forum. “Nano-policy: No small matter” November 2006. (invited speaker)
12. Kuzma, J.” Nanotechnology: The Science of the Small” St. Francis Xavier Middle School, Buffalo, MN, April 20, 2009.
13. Kuzma, J. “Where Science Meets Policy: Oversight for Genetic Engineering” College of St. Catherine’s, St. Paul, MN. April 7, 2009. (invited speaker)
14. Kuzma, J.” Emerging Technologies, S&T Policy, and the (Your) Future.” University of St. Thomas. October 3, 2008 (invited speaker)
15. Kuzma, J. “No Small Matter: Nanotechnology and Social Issues”, Microscopy Camp! For grades 7-12 Metro High School Science Teachers. July 28, 2009.

Appendix E

To receive appropriate safety manuals or for further information call 612-626-6002, or visit the web at http://www.dehs.umn.edu/

RAR must be notified within 2 weeks of the administration of any hazardous agent to laboratory animals.

1. **Laboratory Safety Plan:** DEHS will verify that the PI and laboratory are covered by a current Laboratory Safety Plan (information and templates are available from DEHS or on the web at http://www.dehs.umn.edu/safety/lsp). Does your laboratory have a copy of your department's current (updated within the last calendar year) Laboratory Safety Plan?

☐**Yes.**
☐**No**.

Name of your department's Research Safety Officer (RSO):

2. **Annual Safety Training:** DEHS will verify that personnel involved in this protocol have current training records. Have all laboratory workers (including PI) listed in this protocol completed their annual update laboratory specific safety training?

☐**Yes. Date of safety training:**
☐**No**.

3. Chemicals: DEHS will verify that there are written Standard Operating Procedures (SOP) for the use of high hazard chemicals and materials. An SOP must also be written when the use of a nanomaterial is planned. SOP must include provisions to notify RAR when the first date of administration is scheduled and when administration will cease.

NOTE: Researchers may be required to care for animals if administration is expected to result in excretion of potentially hazardous materials.

Material safety data is available from the manufacturer. Information is also available at http://www.dehs.umn.edu/hazwaste_msds.htm If a novel compound is synthesized, conservatively estimate hazards based on similar compounds. The hazards of chemicals are reduced from those listed in the MSDS when diluted or mixed with less hazardous chemicals.

Contact the Chemical Hygiene Officer at 612-626-2330 with any questions regarding chemical usage. We have listed below examples of types of chemicals that should be listed on Appendix G; including hazardous chemicals which may cause irritation or acute health effects, carcinogens, and reproductive hazards. All chemicals that may cause adverse human health effects due to exposure during research, including those that could cause treated animals or their excrement to be hazardous, must be listed on Appendix G.

High Hazard Chemicals and Materials

Nanomaterials:
Nanoparticles are defined as being in the range of 1 to 100 nanometers. Traditional measures of exposure and toxicity assessment do not necessarily describe hazards

associated with exposure to some nanoparticles. Both exposure mechanisms and risks are poorly understood.

Highly toxic chemicals definition: Dept. of Transportation
Note: The DOT considers the terms “toxic” and “poisonous” synonymous
Poisonous Material (Division 6.1) or
Toxic Gas (Division 2.3)
Definition: A chemical is presumed to be toxic to humans if it falls within any one of the following categories when tested on laboratory animals
Dermal Toxicity. A material with an LD_{50} for acute dermal toxicity of not more than 1000 mg/kg.
Inhalation Toxicity. A dust or mist with an LC_{50} of not more than 4 mg/L; or a LC_{50} for acute toxicity on inhalation of vapors of not more than 5000 mL/m^3; or is an irritating material, with properties similar to tear gas, which causes extreme irritation.
Oral Toxicity. A liquid or solid with an LD_{50} for acute oral toxicity of not more than 300 mg/kg.

Material safety data is found on material safety data sheets and hazard classification information is found on shipping labels http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=082ca0261e385142205b65c51d1e3dae&rgn=div6&view=text&node=49:2.1.1.3.7.5&idno=49

Carcinogens of concern
International Agency for Research on Cancer (IARC)
Group 1 – Carcinogenic to Humans
Group 2A – Probably Carcinogenic to Humans
http://monographs.iarc.fr/ENG/Classification/index.php
NIOSH Alert: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings

Reproductive toxins of concern
U.S. National Library of Medicine Reproductive Toxin, National Institute of Health
http://hazmap.nlm.nih.gov/hazmapadv.html
http://www.nlm.nih.gov/

Examples of high hazard chemicals (NOTE- this is a non-exhaustive list, only a list of examples):

Toxic

	CAS #
Acrolein, inhibited	107028A
Acrylamide	79061A
Ammonia, anhydrous	7664417A
Cyanogen 41 gelling agent(acrylamide)	79061B
Methyl phenyl tetrahydropyridine (MPTP)	28289-54-5
Streptozotocin	18883-66-4
Warfarin, & salts (>0.3 %)	81812A

Carcinogen Group1

	CAS#
Benzo[a]pyrene	50-32-8
Ciclosporin	79217-60-0
Cyclophosphamide	50-18-0 & 6055-19-2
Estrogens, nonsteroidal	
Formaldehyde	50-00-0
N'-Nitrosonornicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK)	16543-55-8 & 64091-91-4
Tamoxifen	10540-29-1

Carcinogen Group 2A

	CAS#
Acrylamide	79-06-1
Adriamycin	23214-92-8
Chloramphenicol	56-75-7
Dimethyl sulfate	77-78-1
Ethyl carbamate (urethane)	51-79-6
Nitrogen mustard	51-75-2
Tris(2,3-dibromopropyl) phosphate	126-72-7

Reproductive Toxins

	CAS#
Bromodeoxyuridine (BRDU)	59-14-3
Halothane	151-67-7
Hormones	---
Nitrous oxide	10024-97-2
1-Methyl 4-phenyl 1,2,3,6-tetrahydropyridine (MPTP)	28289-54-5

Chemicals involved in this protocol	**Where will the chemical be used (Bldg, Room #)?**	**Has an SOP for this chemical been submitted to DEHS?**	**Dose Regimen (dose, frequency of dosing, total number of doses)**	**Is a fume hood available?**	**Is the carcass hazardous?**

4. Anesthetic Gases DEHS will verify the training records and Standard Operating Procedures for the use of anesthetic gases in the laboratory. All anesthetic gas use must be in accordance with University Policy: http://www.dehs.umn.edu/PDFs/AnestheticGases.pdf

Anesthetic gas (es)	Room where used (Bldg, Room number)	Delivery Method (s)	Scavenging Method (s)
		☐ intubation ☐ induction chamber ☐ nose cone ☐ bell jar or other container ☐ other (describe)	☐ fume hood ☐ downdraft table ☐ absorption canister ☐ other (describe)

5. Radiation: Contact Radiation Protection (612-626-6764) for radiation protection forms or assistance, or visit the web at http://www.dehs.umn.edu/rpd/

Where will the radiation be used (building and room no.)?	
Name of approved radioisotope permit holder *or* source owner:	
Duration of permit:	

Radioisotope or radiation source	Route of Administration	Dosage (activity)	Route of excretion (Is bedding radioactive?)	Is the carcass radioactive?

NOTICE: ALL OF THE FOLLOWING REQUIRE A PROTOCOL TO BE SUBMITTED TO THE INSTITUTIONAL BIOSAFETY COMMITTEE (IBC):

6. Human blood, body fluids, normal or neoplastic tissue (including human cell lines): Will human tissue, human cells, blood or body fluid be used in your research?

☐**Yes. Type:**
☐**No**.

Will Universal Precautions be followed when handling human blood, body fluids, or tissues?

☐**Yes. Type:**
☐**No**.

If no, please explain.

Please attach documentation indicating that all laboratory personnel have completed annual blood borne pathogen training.

P*lease note*: Principal Investigators are responsible for:

- Ensuring that employees working with human blood, body fluids or tissues have been offered vaccination for Hepatitis B vaccine. Contact Boynton Health Service for information (612-625-8400 or http://www.bhs.umn.edu/).
- Ensuring that employees working with human blood, body fluids or tissues obtain annual bloodborne pathogen training. Training records should be accessible. For information on training see: www.dehs.umn.edu/training.

7. **Infectious Agents (including bacteria, viruses, parasites, prions)**. Use of infectious agents requires review and approval by the Institutional Biosafety Committee (IBC). Visit the web at http://www.ibc.umn.edu to obtain forms for the IBC. SOP must include provisions to notify RAR when the first date of administration is scheduled and when administration will cease.

Name of agent	Biosafety Level	Animal Species	Route of Administration	Is the agent infectious to humans or animals? (indicate)) If so, is the agent shed in urine, feces or bodily secretions?	Dose Regimen (dose, frequency of dosing, total # of doses)	SOP Attached?

8. **Are biologically-derived toxins (derived from plants, bacteria, fungi, etc.) used in this protocol?**

☐**Yes.**
☐**No**.

If yes, please list toxin used.

9. Recombinant DNA (including transgenic animals): Use of recombinant DNA requires review and approval by the Institutional Biosafety Committee (IBC). Visit the web at http://www.ibc.umn.edu to obtain forms for the IBC.

What is the gene that will be modified? Is this a gain or loss of function?	Route of Administration	Dose Regimen (dose, frequency of dosing, total # of doses)	Is the agent infectious to humans or animals? (indicate) If so, is the agent shed in urine, feces or bodily secretions?	Is the carcass infectious?

Describe the host/vector system:

Appendix F

Standard Departmental Laboratory Safety Plan
Chapter 2 - Standard Operating Procedures

RSOs note and delete: Subsections 1, 2, and 3 present the topic headings for the detailed Standard Operating Procedures already included in Appendices D, E, and F. Ask PIs to review these subsections and appendices and train staff on all the SOPs which pertain to the chemicals and procedures used in the laboratory. Work with particularly hazardous or unique chemicals and/or procedures may not be covered by the SOPs listed below. In this case, the PI must ensure the researchers follow written SOPs that describe the work to be conducted, and the safety measures to mitigate any hazards. Procedures and written safety precautions included in laboratory notebooks may serve as laboratory-specific SOPs. Ensure the PIs keep these individual SOPs in the laboratory and train employees on their contents.

As noted in Chapter 1, Principal Investigators are responsible for ensuring there are written standard operating procedures (SOPs) for the research protocols conducted in their area. The SOPs must identify the hazards of the protocol, as well as measures to be taken to mitigate those hazards. The references listed below may provide enough detail to serve as the SOPs for some research protocols. Other protocols may require more tailoring, as described in Section 5 of this chapter.

1. Chemical Procedures
A. Prudent Practices in the Laboratory (Appendix D)

Laboratory standard operating procedures found in Prudent Practices in the Laboratory: Handling and Disposal of Chemicals (National Research Council, 1995) are adopted for general use at the University of Minnesota. Departmental Research Safety Officers have hard copies of this text, and the entire contents are accessible on the web. Note especially the following topics which are covered in Chapters 5 and 6 of Prudent Practices:

Chapter 5 Working with Chemicals

- Introduction
- Prudent Planning
- General Procedures for Working with Hazardous Chemicals
- Working with Substances of High Toxicity
- Working with Biohazardous and Radioactive Materials
- Working with Flammable Chemicals
- Working with Highly Reactive or Explosive Chemicals
- Working with Compressed Gases

Chapter 6 Working with Laboratory Equipment

- Introduction
- Working with Water-Cooled Equipment
- Working with Electrically Powered Laboratory Equipment
- Working with Compressed Gases
- Working with High/Low Pressures and Temperatures
- Using Personal Protective, Safety, and Emergency Equipment
- Emergency Procedures

B. Controlled Substances and Alcohol

In conducting research with controlled substances, University authorized employees must comply with federal and state laws and regulations regarding their uses, including registration with the Drug Enforcement Administration (DEA), storage requirements, inventory maintenance and substance disposal. A condensed guide to federal regulations as well as policies and forms pertaining to controlled substances are available on the Controlled Substances webpage.

Alcohol used for education, scientific research, or medicinal purposes can be purchased tax-free through University Stores (www.ustores.umn.edu), which holds the University of Minnesota site license for alcohol purchases with the Federal Bureau of Alcohol, Tobacco, and Firearms (BATF). Further information and links to the ordering form are available by clicking on Tax Free Alcohol Ordering Procedures.

C. The American Chemical Society's "Safety in Academic Chemistry Laboratories"

ACS's "Safety in Academic Chemistry Laboratories" is another useful text. This manual presents information similar to that found in Prudent Practices, but in a considerably condensed format.

D. Hazardous Waste Management

Extensive and detailed policies regarding hazardous waste management are specified in the University's guidebook "Hazardous Chemical Waste Management, 5th edition". Please refer to this text for approved waste handling procedures.

E. Emergency Procedures for Chemical Spills

The procedures listed below are intended as a resource for your department in preparing for emergencies before they happen. If you are currently experiencing an emergency such as a chemical or blood spill, please contact the Department of Environmental Health and Safety at 612-626-6002.

Complete spill response procedures are described in the Hazardous Chemical Waste Management Guidebook. However, the quick reference guide is included for convenience in this Laboratory Safety Plan.

Quick Reference Guide

Evacuate

- Leave the spill area; alert others in the area and direct/assist them in leaving.
- Without endangering yourself: remove victims to fresh air, remove contaminated clothing and flush contaminated skin and eyes with water for 15 minutes. If anyone has been injured or exposed to toxic chemicals or chemical vapors, call 911 and seek medical attention immediately.

Confine

- Close doors and isolate the area. Prevent people from entering spill area.

Report

- From a safe place, call the Department of Environmental Health and Safety (EHS) (612) 626-6002 during working hours, 911 after hours (Twin Cities Campus 911 operators will contact on-call EHS personnel).
- Report that this is an emergency and give your name, phone and location; location of the spill; the name and amount of material spilled; extent of injuries; safest route to the spill.
- Stay by that phone, EHS will advise you as soon as possible.
- EHS or the Fire Department will clean up or stabilize spills, which are considered high hazard (fire, health or reactivity hazard). In the case of a small spill and low hazard situation, EHS will advise you on what precautions and protective equipment to use.

Secure

- Until emergency response personnel arrive: block off the areas leading to the spill, lock doors, post signs and warning tape, and alert others of the spill.
- Post staff by commonly used entrances to the area to direct people to use other routes.

- After an accident, supervisor(s) must complete and fax in reporting forms within 24 hours. Workers' Compensation policy and reporting forms are available on the web (Appendix J).

2. Biohazardous Procedures

All researchers working with human blood or body fluids, or other pathogens must follow the university's **Exposure Control Plan**, and complete **Boodborne Pathogens Training**, available on the web. All researchers working with infectious material including attenuated lab & vaccine strains (bacteria, viruses, parasites, fungi, prions), biologically-derived toxins, rDNA, and artificial gene transfer must follow requirements of the University's Biosafety Program detailed in the **Biosafety Manual** and on the **Institutional Biosafety Committee's website**.

A. Biosafety Manual

The University's Biosafety Manual is made up of three components; researchers must implement all three components in their lab safety manual.

- Biosafety Principles and Practices;
- CDC/NIH's text Biosafety in Microbiological and Biomedical Laboratories (BMBL).
- Individual lab-specific Standard Operating Procedures (SOPs) that:
- – specify the biohazards being used
- – identify the material handling steps that may pose a risk of exposure (sharps, injecting animals, centrifugation, aerosol production, transport, etc.)
- – describe equipment and techniques used to reduce the above risk of exposure
- – give instructions for what to do in case of an accidental exposure/spill
- – list wastes that will be generated and how to properly dispose of wastes

B. Institutional Biosafety Committee (IBC)

The IBC is charged under Federal Regulations (NIH) and University of Minnesota Regents' Policy with the oversight of all teaching and research activities involving:

- Recombinant DNA

- Artificial gene transfer
- Infectious agents including attenuated lab & vaccine strains
- Biologically derived toxins

See the IBC web site for procedures to apply for approval for the above work.

C. Select Agents

Labs in possession of organisms or toxins that are federally designated as select agents are required to be registered with the Centers For Disease Control if quantities exceed the exemption amounts. See the Biosafety Section of the DEHS web site for a list of select agents, exemption quantities, and procedures for their use.

D. Additional Biosafety References

World Health Organization (WHO) *Laboratory Safety Manual*, available on the web at, http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/

National Research Council's text *Biosafety in the Laboratory: Prudent Practices for Handling and Disposal of Infectious Materials* (1989), available on the web at: http://books.nap.edu/books/0309039754/html/R1.html#pagetop.

Biological Material Safety Data Sheets (MSDS) available at http://www.phac-aspc.gc.ca/msds-ftss/index.html.

3. Radioactive Procedures

All researchers using radioactive materials at the University of Minnesota must:

- obtain a permit for the possession and use of radioactive materials (contact the Radiation Protection Division);
- complete required training modules; and
- comply with the radiation policies and procedures of the university (contained in the Radiation Protection manual).

The Radiation Protection manual contains information on a number of topics including license committees, the permitting process, purchasing procedures, transfer procedures, general safety, personnel dosimetry, waste management, emergency management (spill control), record keeping, and regulatory guides on occupational exposure and prenatal exposure.

Training is required for all personnel who require access to areas where radioactive materials are used or stored. This training can be completed on line (http://www.dehs.umn.edu/rad_radmat_training.htm).

4. Nanoparticles

Departments must establish a process to review research involving particularly hazardous materials such as nanoparticles. Certain laboratory operations, procedures or activities may warrant prior approval from a designated supervisor. Work with nanoparticles involving animal use will be approved by the Institutional Animal Care and Use Committee after review by DEHS staff. The PIs in the department must consider the toxicity of the chemicals used, the hazards of each procedure, and the knowledge and experience of the laboratory workers to decide which will require pre-approval.

- The RSO must work with the PIs to develop a prior approval procedure. This procedure should be described in the LSP.
- Research may require formal review and approval by a researcher's departmental safety committee, perhaps with involvement of DEHS personnel.
- RSOs should consult with Principal Investigators to identify research programs which may fall into this 'high hazard' category.
- PIs whose research is identified as 'high hazard' should provide copies of their SOPs to the RSO and their department's safety committee for review and approval.
- Establish a lab inspection procedure. RSOs should inspect PI labs at least once per year
- DEHS will review inspection findings and periodically conduct independent inspection.
- DEHS can conduct work place exposure monitoring when there is a potential for worker exposure.

5. General Safety Procedures

Other lab and general safety information is available on the University of Minnesota website as indicated below.

A. Lab Safety

- Emergency Eyewash and Safety Shower Installation (http://www.cppm.umn.edu/standards/AppendixS.pdf)
- Personal Protective Equipment for Animal Care and Use (http://www.ohs.umn.edu/ppe/home.html)
- Respiratory Protection for Lab Animal Allergens (http://www.ohs.umn.edu/laa/home.html)
- Controlled Substances (http://www.research.umn.edu/riop/controlsubst.htm)
- Lock Out/Tag Out (http://www.dehs.umn.edu/train_factsheet_lkouttagout.htm)
- Respiratory Protection Program (http://www.dehs.umn.edu/Docs/Respiratory%20Protection%20Program%20Instruction.doc)
- Hearing Conservation Program (http://www.ohs.umn.edu/hcp/home.html)
- Laboratory Close-out Procedure (http://www.dehs.umn.edu/Docs/LaboratoryCloseout.doc)

- **B. General Safety**
- Emergency Procedures (http://www1.umn.edu/prepared/)
- Temperature Standard (http://www.dehs.umn.edu/iaq_tempstandards.htm)
- University of Minnesota Twin Cities Campus Smoke-Free Indoor Air Policy (http://www.policy.umn.edu/Policies/Operations/Safety/SMOKING.html)
- Supervisors Injury/Illness Investigation Form (http://www.policy.umn.edu/prod/groups/president/@pub/@forms/@hr/documents/form/supincidentinv.doc)

6.. Laboratory-Specific Standard Operating Procedures

Each PI must have written Standard Operating Procedures (SOPs) for the research protocols conducted in his or her laboratory. Like the Lab Safety Plan, the SOPs must be accessible to researchers. Keeping hard copies in the lab or having them on a computer in the laboratory fulfills the accessibility requirement. SOPs developed through DEHS will be posted periodically in Appendix H.

Laboratory-specific SOPs are valuable research tools that supplement the departmental Laboratory Safety Plan. The process of writing SOPs requires an individual to think through all steps of a procedure and perform a risk assessment before beginning work. The SOP provides a written means to inform and advise researchers about hazards in their work place, allows for standardization of materials and methods, and improves the quality of the research. A well-written SOP can be used to comply with the federal Laboratory Safety Standard, which states that the Laboratory Safety Plan must include:

- "Standard operating procedures relevant to safety and health considerations to be followed when laboratory work involves the use of hazardous chemicals."
- SOPs should include exposure controls and safety precautions that address both routine and accidental chemical, physical or biological hazards associated with the procedure. A laboratory safety information sheet is available in Appendix F. This checklist, which prompts researchers to identify hazards and safety measures for the protocol, can be attached to existing procedures which may lack safety information. A template for writing new SOPs is available in Appendix I and guidance for writing biologically-related SOPs is available on the Biosafety section of the DEHS website.

7. General Emergency Procedures

The procedures listed below are intended as a resource for your department in preparing for emergencies before they happen. If you are currently experiencing an emergency such as a chemical or blood spill, please contact the Department of Environmental Health and Safety at 612-626-6002.

For University employees who have been exposed to bloodborne or other infectious pathogens, please follow the procedures below under "Needle Stick." For all other emergencies call 911.

Campus Safety Information Guidebook
(http://www.dem.umn.edu/Emergency%20Response%20Guide/index.htm)

- bomb threats
- medical emergencies
- fire
- severe weather
- utility outages
- warning systems/sirens

Chemical Spills (http://www.dehs.umn.edu/hazwaste_chemwaste_umn_cwmgbk_sec3.htm)

First Aid for Laboratory and Research Staff (http://www.dehs.umn.edu/Docs/Lab_First_Aid.doc)

Needle Sticks (http://www.dehs.umn.edu/bio_pracprin_blood_needle.htm)

Radioactive Material Incidents (http://www.dehs.umn.edu/rad_radmat_incidents.htm)

Workplace Violence (contact Human Resources (ohr@umn.edu) for a hard-copy)

8. Planning for Shutdowns

Researchers should develop written procedures to deal with events such as loss of electrical power (affecting fume hoods, coolers etc.) or other utilities (water), or temporary loss of personnel due to illnesses such as pandemic flu. Guidance on factors to consider when developing shut-down plans is included in the Lab Hibernation Checklist in Appendix Q.

Standard Departmental Laboratory Safety Plan
Chapter 3 - Criteria for Implementation of Chemical Control Measures

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RSO's – note and delete: This section does not require extensive tailoring. However, research safety officers for some departments have provided descriptions and floor plans that identify the location of equipment such as fume hoods, biological safety cabinets, glove boxes, showers, eyewashes, fire extinguishers, etc.

Engineering controls, personal protective equipment, hygiene practices, and administrative controls each play a role in a comprehensive laboratory safety program. Implementation of specific measures must be carried out on a case-by-case basis, using the following criteria for guidance in making decisions. Assistance is available from the Department of Environmental Health and Safety.

1. Engineering controls
a) Fume Hoods
The laboratory fume hood is the major protective device available to laboratory workers. It is designed to capture chemicals that escape from their containers or apparatus and to remove them from the laboratory environment before they can be inhaled. Characteristics to be considered in requiring fume hood use are physical state, volatility, toxicity, flammability, eye and skin irritation, odor, and the potential for producing aerosols. A fume hood should be used if a proposed chemical procedure exhibits any one of these characteristics to a degree that (1) airborne concentrations might approach the action level (or permissible exposure limit), (2) flammable vapors might approach one tenth of the lower explosion limit, (3) materials of unknown toxicity are used or generated, or (4) the odor produced is annoying to laboratory occupants or adjacent units.

Procedures that can generally be carried out safely outside the fume hood include those involving (1) water-based solutions of salts, dilute acids, bases, or other reagents, (2) very low volatility liquids or solids, (3) closed systems that do not allow significant escape to the laboratory environment, and (4) extremely small quantities of otherwise problematic chemicals. The procedure itself must be evaluated for its potential to increase volatility or produce aerosols.

In specialized cases, fume hoods will contain exhaust treatment devices, such as water wash-down for perchloric acid use, or charcoal or HEPA filters for removal of particularly toxic or radioactive materials.

b) Safety Shields
Safety shields, such as the sliding sash of a fume hood, are appropriate when working with highly concentrated acids, bases, oxidizers or reducing agents, all of which have the potential for causing sudden spattering or even explosive release of material. Reactions carried out at non-ambient pressures (vacuum or high pressure) also require safety shields, as do reactions that are carried out for the first time or are significantly scaled up from normal operating conditions.

c) Biological Safety Cabinets
Biological Safety Cabinets (BSC), also known as tissue culture hoods or laminar flow hoods, are the primary means of containment for working safely with infectious microorganisms. Cabinets

are available that either exhaust to the outside or recirculate HEPA filtered air to the laboratory. They are not to be used for working with volatile or hazardous chemicals unless they are specifically designed for that purpose and are properly vented. Generally, the only chemical work that should be done in a BSC is that which could be done safely on a bench top involving chemicals that will not damage the BSC or the HEPA filter. For proper cabinet selection and use see, the CDC publication Primary Containment for Biohazards.

Biological Safety Cabinets for Nanotechnology

A Biological Safety Cabinet connected to building exhaust may be necessary for work with nanoparticles with high biological activity. A Class ll or Class lll cabinet may be required.

A Class ll cabinet provides personnel, product and environmental protection. They have a narrow opening below a vertical sash, a HEPA filtered work area and a HEPA filtered exhaust to protect exhaust duct work and the outside environment. There are several types which vary in the percentage of air exhausted:
Type A2 cabinets maintain a minimum of 100 FPM inflow velocity. They exhaust approximately 30% back into the laboratory and recirculate the remainder. They may be vented by a thimble or gas tight connection.
Type B1 cabinets must maintain a minimum of 100 FPM inflow velocity. They exhaust more than 50% of inlet air and recirculate the remainder.
Type B2 cabinets maintain a minimum of 100 FPM inflow velocity and exhaust 100% of the inlet air to a external ventilation system. There is no recirculation of air within the cabinet.

Class lll cabinets provide personnel protection, environmental protection and may provide product protection. It is a totally enclosed, gas-tight, negative pressure, HEPA filtered, ventilated workspace which is accessed through attached rubber gloves and has purged interchange chambers. Exhaust air is treated by HEPA filtration and can be treated by thermal oxidation or a chemical scrub.

d) Other Containment Devices
Other containment devices, such as glove boxes or vented gas cabinets, may be required when it is necessary to provide an inert atmosphere for the chemical procedure taking place, when capture of any chemical emission is desirable, or when the standard laboratory fume hood does not provide adequate assurance that overexposure to a hazardous chemical will not occur. The presence of biological or radioactive materials may also mandate certain special containment devices. High strength barriers coupled with remote handling devices may be necessary for safe use of extremely shock sensitive or reactive chemicals.

e) Highly Localized Exhaust ventilation
Highly localized exhaust ventilation, such as is usually installed over atomic absorption units, may be required for instrumentation that exhausts toxic or irritating materials to the laboratory environment.
Ventilated chemical storage cabinets or rooms should be used when the chemicals in storage may generate toxic, flammable or irritating levels of airborne contamination.

2. Personal Protective Equipment
a) Skin Protection
As skin must be protected from hazardous liquids, gases, vapors and nanoparticles, Proper basic attire is essential in the laboratory. Long hair should be pulled back and secured and loose clothing (sleeves, bulky pants or skirts) avoided to prevent accidental contact with

chemicals or open flames. Bare feet, sandals and open-toed or perforated shoes are not permitted in any laboratory. Short pants and short skirts are not permitted unless covered by a lab coat. Long pants should be worn to cover skin that could be exposed during a spill.

Lab coats are strongly encouraged as routine equipment for all laboratory workers. Remember that lab coats should be worn to protect employees against both chemical and biological hazards. Working in a biosafety level 1 laboratory does not excuse an employee from wearing a lab coat. It is the responsibility of the employer to purchase and wash lab coats for employees who request them or are required to wear them. Lab coats must not be taken home for laundering. Lab coats are required when working with radioactive materials, biologically-derived toxins and nanoparticles, Biosafety Level II organisms, carcinogens, reproductive toxins, substances which have a high degree of acute toxicity, and any substance on the OSHA PEL list carrying a "skin" notation. See Appendix B for chemical listings. Lab coats cannot be assumed to provide complete protection against all agents, but will provide an extra layer that can be removed if accidentally contaminated, buying time for the researcher to get to the emergency shower and minimize direct skin contact. For strong acids and bases, a lab apron impervious to liquids would be a more appropriate choice.

Gloves made of appropriate material are required to protect the hands and arms from thermal burns, cuts, or chemical exposure that may result in absorption through the skin or reaction on the surface of the skin. Gloves are also required when working with particularly hazardous substances where possible transfer from hand to mouth must be avoided. Thus gloves are required for work involving pure or concentrated solutions of select carcinogens, reproductive toxins, substances which have a high degree of acute toxicity, strong acids and bases, and any substance on the OSHA PEL list carrying a "skin" notation.

Since no single glove material is impermeable to all chemicals, gloves should be carefully selected using guides from the manufacturers. General selection criteria are outlined in Prudent Practices, p. 132, and glove selection guides are available on the web. However, glove-resistance to various chemicals materials will vary with the manufacturer, model and thickness. Therefore, review a glove-resistance chart from the manufacturer you intend to buy from before purchasing gloves. When guidance on glove selection for a particular chemical is lacking, double glove using two different materials, or purchase a multilayered laminated glove such as a Silvershield or a 4H.

b) Eye Protection

Eye protection is required for all personnel and any visitors whose eyes may be exposed to chemical or physical hazards. Side shields on safety spectacles provide some protection against flying particles, but goggles or face shields are necessary when there is a greater than average danger of eye contact with liquids. A higher than average risk exists when working with highly reactive chemicals, concentrated corrosives, or with vacuum or pressurized glassware systems. Contact lenses may be worn under safety glasses, goggles or other eye and face protection. Experts currently believe the benefits of consistent use of eye protection outweigh potential risks of contact lenses interfering with eye flushing in case of emergency.

c) Respiratory Protection

Respiratory protection is generally not necessary in the laboratory setting and must not be used as a substitute for adequate engineering controls. Availability of respiratory protection for emergency situations may be required when working with chemicals that are highly toxic and highly volatile or gaseous. If an experimental protocol requires exposure above the action level (or PEL) that cannot be reduced, respiratory protection will be required. Rarely, an experimental situation may potentially involve IDLH (immediately dangerous to life or health) concentrations of chemicals, which will require use of respiratory protection. All use of respiratory protective equipment is covered under the University of Minnesota Respiratory Protection Program.

3. Hygiene Practices

Eating, drinking and chewing gum are all strictly prohibited in any laboratory with chemical, biological or radioactive materials. Researchers must also be careful to restrict other actions (such as applying lip balm, rubbing eyes or using ipods or cell phones) which could inadvertently cause exposure to research materials. Consuming alcohol or taking illegal drugs in a research laboratory are strictly prohibited, as such actions potentially endanger the health and safety of not only the user, but everyone in the building. Infractions will be met with serious disciplinary action.

Before leaving the laboratory, remove personal protective equipment/clothing (lab coat and gloves) and wash hands thoroughly. Do NOT wear laboratory gloves, lab coats or scrubs in public spaces such as hallways, elevators or cafeterias.

4. Administrative Controls

Supervisors shall consider the hazards involved in their research, and in written research protocols, detail areas, activities, and tasks that require specific types of personal protective equipment as described above. Researchers are strongly encouraged to prioritize research so that work with hazardous chemical, biological or physical agents occurs only during working hours (8 am – 5 pm, Monday through Friday). After-hours work (on nights and weekends) should be restricted to nonhazardous activities such as data analysis and report writing. If hazardous materials must be used at nights or on weekends, ensure that at least one other person is within sight and ear-shot to provide help in an emergency. Undergraduate workers are prohibited from working alone in the laboratory unless there is a review and formal approval by the department's RSO and/or safety committee.

Research Safety Officers must coordinate and/or conduct inspections of laboratories in their area of responsibility and ensure laboratory supervisors address any noted deficiencies. An audit checklist is available in Appendix G. RSOs can report cases of continued non-compliance to the unit head and to the Department of Environmental Health and Safety (DEHS). The RSO, in conjunction with DEHS and the unit head, has the authority to halt research activities that present an imminent hazard.

In the event that a research lab is moving or leaving the university altogether, the principle investigator is responsible for cleaning up the lab space. If the principle investigator does not take proper care to clean-up the laboratory, then the department for which they worked under becomes responsible. We strongly encourage departments to develop administrative controls to prevent this from happening. A good tool to use is the laboratory closeout checklist available on the DEHS website. Otherwise, DEHS does offer laboratory clean-up services for an hourly fee.

Standard Departmental Laboratory Safety Plan

Chapter 9 - Additional Employee Protection for Work with Particularly Hazardous Substances

RSO's – note and delete: Like Section 6, this Section also requires action. Again, the PIs in the department must consider the toxicity of the chemicals used and the hazards of each procedure, and decide whether the procedure requires the use of additional protective measures. Chemicals listed in Tables 1-5 and work with nanoparticles should be considered for additional protective measures. The additional protective measures must be incorporated in a Standard Operating Procedure. Each PI should forward a list of these SOPs to the departmental Research Safety Officer for reference in this section of the LSP. If none of the SOPs require additional protective measures, the PI should note this fact and forward a brief explanation to the RSO. DEHS staff is available to help PIs evaluate the need for additional protective measures.

Additional employee protection will be considered for work with particularly hazardous substances. These include nanoparticles, select carcinogens, reproductive toxins and substances that have a high degree of acute toxicity (see Appendix B). Pp. 90-93 of the 1995 edition of Prudent Practices provides detailed recommendations for work with particularly hazardous substances. These pages may be accessed from DEHS's web site at www.dehs.umn.edu. Laboratory supervisors and principal investigators are responsible for assuring that laboratory procedures involving particularly hazardous chemicals have been evaluated for the level of employee protection required. Specific consideration will be given to the need for inclusion of the following provisions:

1. Planning;
2. Establishment of a designated area;
3. Access control
4. Special precautions such as:
    a. use of containment devices such as fume hoods or glove boxes;
    b. use of personal protective equipment;
    c. isolation of contaminated equipment;
    d. practicing good laboratory hygiene; and
    e. prudent transportation of very toxic chemicals.
5. Planning for accidents and spills; and
6. Special storage and waste disposal practices.

Appendix G

Working with Nanomaterials: Decision Matrix for Selecting Engineering Controls and Personal Protective Equipment

Q_{Ex} = Ventilation effect on exposure concentration

Risk Rank	Ventilation Rate	Example
4	n/a	Enclosed system
3	15	OR, clean room, LEV
2	6	Lab w fume hoods
1	2	Office, patient room

Note: new labs have VAV systems, 6 ac/h is IBC requirement, actual ac/h can be determined empirically

G ~ Aerosol generation

Risk Rank	Definition
1	No active generation
2	Low risk of accidental release
3	High risk of accidental release
4	Deliberate generation

Exposure factor C = G / Q_{Ex}

R = Risk ranking for nanomaterial

Risk Group	Description
1	Not associated with illness in healthy adults
2	Rarely causes serious illness
3	May cause serious illness

Hazard Classification for Selection of Personal Protective Equipment

Risk Rank “R”	3	B	B	C	C
	2	A	B	B	C
	1	A	A	B	C
Exposure Factor “C”		1	2	3	4

Minimum Personal Protective Equipment (PPE) required for hazard class

A: PPE - nitrile, PVC or neoprene gloves, lab coat, eye protection

B: Enhanced PPE - goggles, respirator APF 100

C: High level PPE – full face or hooded PAPR respirator, disposable non-woven coveralls, clothes change and shower facility

Other factors for PPE selection

- Comfort: skin irritation, heat stress, breathing resistance, psychological stress
- Infection control issues: maintenance, storage and use
- Compatibility with other PPE: clothing, shoes, eye protection
- Compatibility: corrective eye wear, microscopes and other optical equipment
- Other safety issues: slip, trip, fall, retrieval, emergency egress

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