COLORADO Nanotechnology ALLIANCE

1st Annual Rocky Mountain Nanotechnology Showcase

Continuing Legal Education (CLE) Seminar
September 18, 2007
University of Denver, Driscoll Hall

Nanotechnology "101" Primer

What is nanotechnology?

Nanotechnology is the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications. Encompassing nanoscale science, engineering and technology, nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale. A nanometer is one-billionth of a meter, or 10 to the -9 meters; a sheet of paper is about 100,000 nanometers thick.[1] Here are some scientists' graphic descriptions of nanoparticles: If you "spread a drop of water over a square meter, it would form a thin film of roughly one nanometer." "Think of the metal film layered onto tinted sunglasses: a nanometer is one-tenth that thickness." At the nanoscale, the physical, chemical, electrical, and biological properties of materials differ in fundamental and valuable ways from the properties of individual atoms and molecules or bulk matter.

Nanotechnology R&D is directed toward understanding and creating improved materials, devices, processes, and systems that exploit these new properties based on a tiny sized particle—in which the surface area far exceeds the volume. For example, one growing sector of nanotechnology R&D is medicine. Medical researchers work at the micro- and nano-scales to develop new drug delivery methods, therapies, pharmaceuticals, and "combination products" such as drug-devices. For a biochemical perspective, the diameter of DNA, our genetic material, is in the 2.5 nanometer range, while red blood cells are approximately 2 – 5 micrometers, or some scientists say between 2,000 and 8,000 nanometers wide.

---

[1] National Nanotechnology Initiative website.

The following widely adopted formal definition of nanotechnology[2] was coined by NSET (The Nanoscale Science, Engineering, and Technology, specifically its Subcommittee of the National Science and Technology Council's Committee on Technology) in February, 2000:

> Research and technology development at the atomic, molecular or macromolecular levels, in the length scale of approximately 1 - 100 nanometer range, to provide a fundamental understanding of phenomena and materials at the nanoscale and to create and use structures, devices and systems that have novel properties and functions because of their small and/or intermediate size. The novel and differentiating properties and functions are developed at a critical length scale of matter typically under 100 nm. Nanotechnology research and development includes manipulation under control of the nanoscale structures and their integration into larger material components, systems and architectures. Within these larger scale assemblies, the control and construction of their structures and components remains at the nanometer scale. In some particular cases, the critical length scale for novel properties and phenomena may be under 1 nm (e.g., manipulation of atoms at ~0.1 nm) or be larger than 100 nm (e.g., nanoparticle reinforced polymers have the unique feature at ~ 200-300 nm as a function of the local bridges or bonds between the nano particles and the polymer).

What are nanomaterials?

Nanomaterials are the building blocks of nanotechnology. To better understand nanotechnology, some background information on nanomaterials will help.

Nanometers: Nanomaterials are measure din nanometers. As noted above, one nanometer is one billionth, or 10^{-9}, of a meter. Nanoparticles such as nanotubes and nanocrystals are 1 to 100 nanometers thick, and form the building blocks of nanomaterials.

Surface Area: Nanoparticles have large surface areas relative to their small volume; this surface to volume ratio in conjunction with other factors means that nanoparticles have different properties— such as chemical, physical, and electrical, among other properties -- from larger molecules of the same substance.

Nanotubes: Nanotubes are sheets of carbon atoms called graphene, rolled into cylinders. The nanotube is essentially one large molecule and therefore does not have any weak spots. The atoms are arranged in a hexagon-shaped lattice, which results in a lightweight material with a density about one quarter that of steel. Additionally, the carbon atoms are chemically bonded in a fashion similar to diamonds. This makes carbon-based nanomaterials extremely strong. They are the world's toughest fibers. Another quality of nanotubes is that in its constituent graphene, "charge carrying particles act as if without mass." This makes the material an almost resistanceless conductor of electrons.

Nanotubes are also strong thermal conductors. "Heat energy in nanotubes is carried by sound waves" and "sound waves bearing thermal energy travel straight down individual carbon nanotubes at roughly 10,000 meters per second, behavior consistent with superior thermal

---

2 National Science Foundation website.

conductivity." While Nanotubes are expensive,[1] mixing them with other materials such as plastics creates nanocomposites--which show increased strength and conductivity, and thus greater efficiency.

Nanocrystals: The properties of crystalline materials change as their size approaches the nanoscale, and as the number of atoms clustered at the surface of the material increases, relative to the number in the bulk material. Due to this increased surface area, nanocrystalline materials are ultra-high activity chemical catalysts, which means that they are widely used in the formation of nanocomposite materials. Nanocomposites are materials made of distinctly dissimilar components and mixed at the nanometer scale. For example, nanomaterial-fillers are dispersed in the host polymer. Interactions between the host and filler particles result in materials which display new and improved properties when compared to their macrocomposite counterparts. Improvements include increased strength and enhanced electrical conductivity when nanotubes are used as filler.

Semiconductor nanocrystals, also known as quantum dots, have quantum optical properties that are absent in the bulk material. Quantum dots have a tunable band gap, which means that the wavelength at which they will absorb or emit radiation can be adjusted at will. The greater the band gap of a solar cell semiconductor, the more energetically the photons are absorbed, and the greater the output voltage. Recent research demonstrated that when quantum dots are irradiated with energy that is to 2 - 4 times their band gap energy, two or more electron-hole pairs are produced, thus increasing the solar power.[3]

What are the key applications for nanotechnology in renewable energy?

Wind: Because the addition of nanomaterials increases the strength of polymers such as plastics, nanocomposites are used to strengthen wind turbine blades, without adding to their weight.

Solar: The superior electrical conductivity of nanotubes increases the performance of solar cells. So too can quantum dots, which can produce twice as many electrons from a single photon, as conventional photovoltaic cells. Nanotech solar cells are simultaneously more efficient and less expensive.

Fuel Cells: A polymer-electrolyte membrane fuel cell generates current by stripping hydrogen atoms from a chemical source, breaking them apart on a catalyst (such as platinum), and harvesting the electrons. When nanocrystals are added to the catalyst, the high surface area of nanocrystals brings more fuel into contact with the catalyst, therefore increasing the efficiency of the fuel cell.

Geothermal: A circuit made from two dissimilar metals, with junctions at different temperatures, can produce electricity. The strong thermal conductivity of nanotubes is used to manufacture electrical generators, which produce electricity from heat, in a very efficient and cost-effective way.

---

[3] Kyaw Tin & Susan Brienza, Patton Boggs LLP memorandum, July 19, 2007.

Overall, some researchers and R&D companies believe that the overlap between nanotechnology and renewable energy technologies is so great that they are converging into one field.[4]

Commercial Applications

There are well over 600 existing commercial products using *engineered nanomaterials*, including self-cleaning windows (cars, homes), anti-graffiti paints, sunscreens, cosmetics, antimicrobial bandages, clothing, sports equipment, and car components, among many other products. Indeed, the exact number of nanotech products is difficult to estimate because nanotech labeling and claims are not currently required. The Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars maintains a Nanotechnology Consumer Products Inventory that contains information on products that the center believes use some form of *nanotechnology*: http://www.nanotechproject.org/index.php?id=44. The center also provides information regarding a myriad of existing and future applications for nanotechnology: http://www.nanotechproject.org/. The National Nanotechnology Initiative also provides information regarding applications available today: http://www.nano.gov/html/facts/appsprod.html.

Nanoparticles play a role in dozens of product types many Americans already use—scientists estimate between 350 and 700 consumer products (manufactured in at least 17 different countries) on the market employ nanotech. As of October 2006, the FDA estimated that over 60 cosmetics and 20 dietary supplements employ nanotech, but these numbers have already been well surpassed. Here's a sampling of what is currently marketed:

- Supplements more Bioavailable: Israeli researchers have uncovered ways to increase the bioavailability of CoQ10 in drugs and dietary supplements. At a trade show in 2006, Supply Side West, a new supplement for blood lipid health was announced, using "nanodispersion" of Policosanol and Omega-3, called Nanocosanol™ (from Valensa).
- Functional foods: A major application of the technology could be a time release mechanism in functional foods that would allow certain molecules to be activated when the body's levels of a nutrient are especially low. In this way, nanotech would enable a biofeedback process at the molecular level.
- Food packaging and safety detection. One group of researchers is developing packaging in which nanoparticles embedded in plastic film can detect whether the food product inside has decomposed. A potential application of this technology would be to prevent or detect acts of bioterrorism on the nation's food supply.
- Cosmetics: Nanotech sunscreen, in which nanoparticles of zinc oxide are used to eliminate sunscreen's white pasty appearance. Cosmetics use nanoparticles to increase stability, and to modify the release and penetration of ingredients. Some nanotech skin creams are claiming to remove wrinkles, *via* a nanotech process—which, of course, raises the issue of possible fraudulent advertising claims, if the nanotech nature of the product or ingredients does not actually have the effect claimed: as produced by nanotechnology.

Use of *engineered nanomaterials* will result in more effective medications, reduce the rate of infections in hospitals, diagnose diseases (such as cancer) at a much earlier stage and treat them

4 Kyaw Tin & Susan Brienza, Patton Boggs LLP memorandum, July 19, 2007.

more effectively and with substantially less side effects (e.g., as with some chemotherapeutic treatments), create longer lasting and more biocompatible artificial joints, make artificial tissues that replace diseased organs and repair nerve damage.

- The National Nanotechnology Initiative (NNI) publication, Nanobiotechnology, describes applications in nanomedicine: http://www.nano.gov/nni_nanobiotechnology_rpt.pdf.

- The NNI provides links to NNI Centers, Networks, and Facilities describing applications and research and development of nanotechnology in the medical field: http://www.nano.gov/html/centers/nnicenters.html.

- The National Cancer Institute (NCI) provides a site that explores nanotechnology in the fight against cancer and maintains a scientific bibliography on nanomedicine:
  http://nano.cancer.gov/resource_center/exploring.asp.
  http://ncl.cancer.gov/working_ncl-nano.asp.
  http://nano.cancer.gov/resource_center/scientific_bibliography.asp.

- The National Institute of Health provides a site that containing information on (1) currently active NIH and Bioengineering Consortium research and training opportunities and (2) listings of funded grants for NIH and Bioengineering Consortium program announcements related to nanotechnology and nanoscience: http://www.becon.nih.gov/nano.htm..

- A site maintained by Ion Channel Media provides information on recent high impact publications in nanomedicine and recent nanomedicine news: http://www.nano-biology.net/.

- The Alliance for NanoHealth has collaborative research projects to address a multitude of medical issues, ranging from better drugs and more powerful diagnostic techniques to portable monitoring devices and smaller, more reliable implants, such as miniature, nanoscale, pacemakers: http://www.nanohealthalliance.org/.

- Information on nanomedicine applications is available at the Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars: http://www.nanotechproject.org/114/nanofrontiers-visions-for-the-future-of-nanotechnology.

Engineered nanomaterials may be used to improve human health and the environment by more effectively filtering the pollutants in our air and water, by reacting with toxic chemicals (e.g., at polluted sites) and making them less toxic, as well as enabling the use of cleaner energy sources which could result in less environmental pollution.

- The Meridian Institute presents applications for nanotechnology in water treatment: http://www.merid.org/nano/.

● The U.S. Environmental Protection Agency Nanotechnology website and White Paper (February 2007) provide potential applications of nanomaterials:
http://es.epa.gov/ncer/nano/index.html.
http://www.epa.gov/osa/pdfs/nanotech/epa-nanotechnology-white-paper-final-february-2007.pdf.

● Information on green nanotechnology applications is available at the Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars:
http://www.nanotechproject.org/.
http://www.nanotechproject.org/tags?tag=green.

Engineered nanomaterials may make us less reliant on foreign oil and solve many of our energy problems, for instance, resulting in significantly more energy efficient vehicles, power transmission lines, and solar panels, as well as enabling the use of cleaner energy sources which could result in less environmental pollution. The NNI document, Nanoscience Research for Energy Needs describes potential applications: http://www.nano.gov/nni_energy_rpt.pdf.

Computers will become smaller, yet have significantly faster processing speeds and storage capacity. The Institute for Nanoelectronics and Computing provides relevant information in this area: http://www.inac.purdue.edu/.

Personal protective equipment (e.g., respirators, clothing, etc.) will become lighter and more effective against harmful objects and substances, and in some cases, be able to detect, destroy, or otherwise actively respond to harmful substances.

Instruments used to detect harmful chemical, biological, and radiological materials in the air, water, and soil will become smaller, lighter, have faster response times, and detect concentrations at lower levels with greater accuracy and specificity.

The U.S. government is investing heavily in applications research and development of *engineered nanomaterials*: http://www.nano.gov/NNI_07Budget.pdf. Again, many government agencies and departments participate in the National Nanotechnology Initiative: http://www.nano.gov/html/gov/home_gov.html.

A space elevator is another, very recent, application. A rocket would take two spools, each the size of a living room with 31,000 miles of carbon nanotube ribbon wrapped around it, to create an orbit of 22,000 miles. Both would be unrolled, one being allowed to waft back to earth, the other pulled up and away from earth by a spacecraft and then anchored with a weight at the end. Then they'd be joined in the middle. The bottom portion would be secured onto an oil rig-like platform located along the equator, 1,500 miles west of Mexico, a location chosen for its uneventful weather. The actual cab of the elevator -- the "climber" -- would attach to the ribbon via rollers. It would zip up at 120 miles an hour, requiring a week to reach the very top. The space elevator is mostly conceived as an all-cargo affair, especially for satellites. Remarkably, it could also be used for trips to the moon, Mars or beyond. The earth rotates once every 24 hours, meaning that something tethered to it 62,000 miles up travels at more than 20,000 miles an hour. If you're at the top of the elevator and time it right when you let go, you can be whipped, launched to just about anywhere you want to go, with a nudge or two from booster rockets.

What is known about risks that accompany emerging nanotechnologies?

Like any other commercial products, nanotechnology cannot be allowed to create undue risk to the environment, health, and safety. Because these new nanoscale materials behave so differently than their conventional-sized counterparts, there are not many studies testing and quantifying their risks. Moreover, the existing regulatory programs for environmental, health and safety were not necessarily designed to cover nanoscale materials, leaving uncertainty as to whether these materials are regulated and, if so, how they are to be regulated. Another challenge is that the instruments of measurement typically used in the environmental, health and safety industry are not able to detect nanoscale materials. Very sophisticated equipment is needed, but is not readily available.

Research on health risks can take many years. While we await the results, the nanotechnology economy marches on, leaving businesses to provide traditional services for novel materials. How does one protect the environment, employees, workers, and consumers when the health risks are not known and you cannot readily detect the materials? How are nanomaterials to be measured when the traditional instruments cannot see them? How do you know what is there? Will nanomaterials create liability risk? These are but a few of the challenges with nanotechnology and nanotech products.

ENVIRONMENTAL, HEALTH, AND SAFETY (EHS) RESEARCH FINDINGS AND RESEARCH NEEDS

The Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars has developed an inventory that catalogs global government-funded research into the human health, safety and environmental risk implications of *nanotechnology*: http://www.nanotechproject.com/index.php?id=18.

The International Council on Nanotechnology (ICON) provides an on-line database and journal regarding the scientific findings to-date related to the EHS benefits and risks of *nanomaterials*: http://icon.rice.edu/virtualjournal.cfm. The NIOSH Nanoparticle Library is linked to the ICON database: http://www.cdc.gov/niosh/topics/nanotech/NIL.html.

The National Institute for Occupational Health and Safety (NIOSH) is responsible for conducting research and making recommendations to prevent work-related injury, illness, and death. The NIOSH Nanotechnology Research website contains information-specific activities that NIOSH is conducting in the field of nanotechnology, including identifying and controlling health and safety hazards of nanomaterials in the workplace: http://www.cdc.gov/niosh/topics/nanotech/research.html. The NIOSH document "Progress Toward Safe Nanotechnology in the Workplace" (2007) is a report of the progress of the NIOSH Nanotechnology Research Center since its inception in 2004 through 2006: this report describes NIOSH research efforts from hazard identification to risk management: http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf.

There are many unanswered questions with regard to the environmental, health, and safety implications of *engineered nanomaterials*, but which only further research will adequately answer. To meet this need, the U.S. government published a document in 2006 that identified EHS research needs related to the understanding and management of potential risks of engineered *nanoscale* materials that may be used, for example, in commercial or consumer products, medical treatments, environmental applications, and research: http://www.nano.gov/NNI_EHS_research_needs.pdf.

The U.S. Environmental Protection Agency (EPA) Nanotechnology White Paper (February 2007) includes the research needs they see for environmental applications and implications: http://www.epa.gov/osa/pdfs/nanotech/epa-nanotechnology-white-paper-final-february-2007.pdf.

CHARACTERIZATION: ENVIRONMENT, SAFETY, AND HEALTH

Physical-Chemical Parameters that may be Toxicologically Important

Current research indicates that particle size, surface area, and surface chemistry (or activity) may be more important metrics than mass and bulk chemistry. A number of sources have isolated the precise physical and chemical characteristics that may have important health implications. The toxicity and health risk of nanotech products may be a function of the following properties, all or some of which may be significant, in increasing the overall toxicity.

(a) size and size distribution
(b) shape and shape distribution: e.g., fiber diameter, length, and aspect ratios for individual nanotubes and bundles/ropes
(c) state of agglomeration, aggregation, and dispersion
(d) biopersistence/durability/solubility
(e) surface area: biologically available surface area, specific surface area, external (geometric surface area), and internal (if material is porous). Microporous or mesoporous powders exhibit much higher surface areas than nonporous powders.
(f) porosity
(g) surface chemistry: surface composition, surface energy/wettability, surface charge, surface reactivity, adsorbed species, and surface contamination.
(h) trace impurities/contaminants (e.g., metal catalysts, polycyclic aromatic hydrocarbons, etc.)
(i) chemical composition, including spatially averaged (bulk) and spatially resolved heterogeneous composition
(j) physical properties: e.g., density, hardness, conductivity, etc.
(k) crystal structure/crystallinity: e.g., amorphous or crystalline, crystalline form/phase/polymorph (e.g., rutile or anatase titanium dioxide, etc.)
(l) surface roughness

Characterization of Physical-Chemical Parameters

The following references pertain to the task of characterizing physical and chemical parameters of nanomaterials:

ASTM, WK8705 New Measurement of particle size distribution of nanomaterials in suspension by Photon Correlation Spectroscopy (PCS). Under development: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851.

ASTM, WK9952 New Standard Practice for Measuring Length and Thickness of Carbon Nanotubes Using Atomic Force Microscopy Methods. Under development: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851.

ASTM, WK9953 New Standard Practice for Measuring Diameter and Wall Thickness of Multi-wall Carbon Nanotubes (MWNT) Using Transmission Electron Microscopy Methods. Under development**:** http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851.

ASTM, WK13577 New Standard Practice for Calculation of Mean Sizes/Diameters and Standard Deviations of Particle Size Distributions. Under development: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851.

ASTM, WK10417 New Standard Practice for the Preparation of Nanomaterial Samples for Characterization. Under development: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851.

Borm, P. eT al., Research Strategies for Safety Evaluation of Nanomaterials, Part V: Role of Dissolution in Biological Fate and Effects of Nanoscale Particles, Toxicological Sciences 90(1), 23-32, 2006.

Donaldson K. et. al., "Carbon Nanotubes: A Review of Their Properties in Relation to Pulmonary Toxicology and Workplace Safety," Toxicological Sciences 92(1), 5-22, 2006.

Environmental Protection Agency Nanotechnology White Paper (February 2007), http://www.epa.gov/osa/pdfs/nanotech/epa-nanotechnology-white-paper-final-february-2007.pdf.

Klaus, U. et. al., Cellular responses to nanoparticles: Target structures and mechanisms, Nanotoxicology, 1:1, 52 – 71, March 2007. Available at: http://www.informaworld.com/smpp/title~content=t716100760.

ISO, Use of transmission electron microscopy (TEM) in single walled carbon nanotubes (SWCNTs), ISO/AWI TS 10797. Under development: http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME.

ISO, Scanning electron microscopy (SEM) and energy dispersive X-ray analysis (EDXA) in the characterization of single walled carbon nanotubes (SWCNTs), ISO/AWI TS 10798. Under development: http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME.

ISO, Workplace Atmospheres – Ultrafine, nanoparticle and nano-structured aerosols – Exposure characterization and assessment. Geneva: Switzerland: International Standards Organization. Document no. ISO/TR 27628, 2007. Available for purchase from ANSI, http://www.ansi.org/.

National Institutes of Health, National Cancer Institute, Nanotechnology Characterization Laboratory, Assay Cascade: http://ncl.cancer.gov/assay_cascade.asp, http://ncl.cancer.gov/newsletter_vol_001.asp , http://ncl.cancer.gov/newsletter_vol_002.asp.

National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, "Approaches to Safe Nanotechnology -- An Information Exchange with NIOSH," July 2006. Online Available: http://www.cdc.gov/niosh/topics/nanotech/safenano/.

Nel et. al., Toxic Potential of Materials at the Nanolevel, Science, Vol. 311, pp. 622-627, 3 February 2006.

NIST, Center for Nanoscale Science and Nanotechnology, http://physics.nist.gov/Divisions/Div841/Gp3/cnst_home.html.

Oberdorster, et al., Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy, Particle and Fibre Toxicology, 2:8, 2005, Online, Available: http://rsi.ilsi.org/Nanomaterial+Toxicity.htm.

Powers, et. al., Research Strategies for Safety Evaluation of Nanomaterials. Part VI. Characterization of Nanoscale Particles for Toxicological Evaluation, Toxicological Sciences 90(2), 296-303, 2006.

Powers, et. al., Characterization of the size, shape, and state of dispersion of nanoparticles for toxicological studies Nanotoxicology, 1:1, 42 – 51, March 2007. Available at: http://www.informaworld.com/smpp/title~content=t716100760.

Note: The web links to the ASTM E56.02 Committee on Characterization and ISO TC 229 Nanotechnologies should be regularly consulted for the latest developments related to documents relating to characterizing physical-chemical parameters that may be of toxicological importance. http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851.

http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME.

Note: The International Conference on Nanotechnology: Occupational and Environmental Health & Safety, 4-7 December 2006, Cincinnati, OH, slide presentations are available online, and include characterization presentations: http://www.uc.edu/noehs/conference_program.asp.

Assessment of Cancer Treatment Particles

Working in concert with the National Institute of Standards and Technology (NIST) and the U.S. Food and Drug Administration (FDA), the National Cancer Institute (NCI) established the Nanotechnology Characterization Laboratory (NCL) to perform and standardize preclinical efficacy and toxicity testing of nanoparticles intended for cancer therapeutics and diagnostics. The NCL is a national resource and knowledge base for cancer researchers from academia, government and industry, facilitating the development and translation of nanoscale particles and devices for clinical applications.

Organizations can have their *engineered nanomaterials* characterized by the NCL if the applications meet the required criteria. The NCL generally does not accept proposals for characterization of *nanomaterials* intended for application in areas other than cancer, but it does consider other applications with regard to *nanomaterials* intended for medical applications within the human body. Cancer-related nanostrategies proposed to the NCL for characterization are ranked according to their projected impact on clinical cancer applications and/or furthering nanotechnology's compatibility with biological systems.

Characterization includes physical and chemical characterization and in toxicity characterization (*in vitro* and in *vivo*). The NCL is working with ASTM and ISO to develop standardized protocols. At the request of NIH NCL, NIST is preparing gold colloid reference materials (not standard reference materials, which take much longer) of 10 nm, 30 nm, and 80 nm sizes, which correspond to three biological barriers : 10 nm (kidney filtration), 30 nm (endothelial pores), and 80 nm (liver bile duct filtration). Filtration barrier sizes are not absolute: for example, with regard to liver filtration, pore sizes are 150-200 nm and bile duct (where clearance takes place) is about 80-100 nm.

Toxicological assessment

There exists a battery of validated toxicity and ecotoxicity tests for chemicals. However, much work is required to optimize these tests for *nanomaterials* that are often poorly understood in terms of their behavior in living organisms and in soil and water (Oberdorster et. al., p. 20, 2007). Special consideration will need to be given to the way in which particles are prepared in order to generate a relevant protocol (Oberdorster et. al., p. 20, 2007; Powers, et. al., 2007). Until standardized, well characterized, and relevant and validated protocols are in place, it will be difficult to interpret toxicity studies and compare results between laboratories (Oberdorster et. al., p. 20, 2007). Also essential is the use of standard reference materials to compare behavior, e.g., titanium dioxide, carbon black, quartz, etc. (Nel, 2006).

The ASTM and ISO links should be regularly consulted for developments related to toxicological assessment. The following references pertain to the toxicological assessment of nanomaterials:

ASTM, WK8997 New Standard Practice for Analysis of Hemolytic Properties of Nanoparticles. Under development: **http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851**.

ASTM, WK9326 New Standard Practice for Evaluation of the Effect of Nanoparticulate Materials on the Formation of Mouse Granulocyte-Macrophage Colonies. Under development: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851.

ASTM, WK9327 New Standard Practice for Evaluation of Cytotoxicity of Nanoparticulate Materials on Porcine Kidney Cells. Under development: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5602.htm?L+mystore+cprk8709+1177002851.

ISO, Nanotechnologies -- Generation of silver nanoparticles for inhalation toxicity testing, ISO/AWI 10801. Under development: http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME.

ISO, Nanotechnologies -- Monitoring silver nanoparticles in inhalation exposure chambers for inhalation toxicity testing. Under development: http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME.

ISO, Nanotechnologies -- Endotoxin test on nanomaterial samples for in vitro systems. Under development: http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME.

Note: The International Conference on Nanotechnology: Occupational and Environmental Health & Safety, 4-7 December 2006, Cincinnati, OH, slide presentations are available online, and includes toxicology presentations: http://www.uc.edu/noehs/conference_program.asp.

Occupational Health and Safety

The NIOSH, ASTM, ISO, and OSHA links below should be regularly consulted for the latest developments related to occupational health and safety:

ASTM, WK8985 New Standard Guide for Handling Unbound Engineered Nanoparticles in Occupational Settings. Under development: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5603.htm?L+mystore+cprk8709+1177117315.

ICON, Online EHS journal and database: http://icon.rice.edu/virtualjournal.cfm.

International Conference on Nanotechnology: Occupational and Environmental Health & Safety, 4-7 December 2006, Cincinnati, OH. Slide presentations online, available: http://www.uc.edu/noehs/conference_program.asp.

ISO, Workplace Atmospheres – Ultrafine, nanoparticle and nano-structured aerosols – Exposure characterization and assessment. Geneva: Switzerland: International Standards Organization. Document no. ISO/TR 27628, 2007. Available for purchase from ANSI, http://www.ansi.org/.

Maynard, A.D. and Aitken, R.J., Assessing exposure to airborne nanomaterials: Current abilities and future requirements, Nanotoxicology, Volume 1:1, 26-41, March 2007. Available at: http://www.informaworld.com/smpp/title~content=t716100760.

NIOSH, Approaches to Safe Nanotechnology -- An Information Exchange with NIOSH. Available at: http://www.cdc.gov/niosh/topics/nanotech/safenano/.

NIOSH, Progress Toward Safe Nanotechnology in the Workplace, February 2007. Available at: http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf.

NIOSH, Nanoparticle Information Library: http://www.cdc.gov/niosh/topics/nanotech/NIL.html.

NIOSH, Evaluation of Health Hazard and Recommendations for Occupational Exposure to Titanium Dioxide, DRAFT Current Intelligence Bulletin" Online, available: http://www.cdc.gov/niosh/review/public/TIo2/ .

Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars, Health and Environmental Implications: an inventory of current research: http://www.nanotechproject.com/index.php?id=18.

Occupational Medical Surveillance

NIOSH will be developing medical surveillance guidelines in collaboration with other federal agencies, industry, and other interested parties. Consult the NIOSH Nanotechnology homepage regularly for developments: http://www.cdc.gov/niosh/topics/nanotech/default.html.

NIOSH, Trout, D., NIOSH Medical Officer, Medical Evaluations and Worker Health, International Conference on Nanotechnology: Occupational and Environmental Health & Safety, 4-7 December 2006, Cincinnati, OH. Slide presentation online, available: http://www.uc.edu/noehs/conference_program.asp.

NIOSH, NTRC Epidemiology and Surveillance Projects (IN: Progress Toward Safe Nanotechnology in the Workplace, February 2007, pp. 24-25). Available at: http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf.

NIOSH, NTRC Epidemiology and Surveillance Projects (IN: Progress Toward Safe Nanotechnology in the Workplace (2007) is a report of the progress of the NIOSH Nanotechnology Research Center since its inception in 2004 through 2006: research describes NIOSH research efforts from hazard identification to risk management: http://www.cdc.gov/niosh/docs/2007-123/pdfs/2007-123.pdf.

Occupational Exposure Registries (IN: EHS research needs for Engineered nanoscale materials, p. 37, http://www.nano.gov/NNI_EHS_research_needs.pdf).

Environmental Protection

The following EPA links provide information about environmental risks:

EPA, Nanotechnology White Paper, February 2007: http://www.epa.gov/osa/pdfs/nanotech/epa-nanotechnology-white-paper-final-february-2007.pdf.

EPA Nanotechnology Website: http://es.epa.gov/ncer/nano/.

Lifecycle EHS Risk Management

Environmental Defense-DuPont, Nano Risk Framework (DRAFT): http://www.nanoriskframework.com/page.cfm?tagID=1095.

Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars, Nanotechnology and Life Cycle Assessment – A Systems Approach to Nanotechnology and the Environment: http://www.nanotechproject.org/111/32007-life-cycle-assessment-essential-to-nanotech-commercial-development.

Areas of legal focus for nanotechnology

One of the key issues is whether the existing legal EHS frameworks—FDA, EPA, and OSHA laws and regulations-- adequately provide for oversight, monitoring, governing, and enforcement with respect to nanomaterials and nanotechnology. With many laws and regulations, this is a complicated issue.

The FDA's jurisdictional predicament is that while products such as drugs and biologics require pre-market approval as to safety and efficacy, other categories such as foods, dietary supplements, and cosmetics require no such pre-market approval. Thus, manufacturers of such products are permitted to market and sell nanoparticle versions of such products with no FDA oversight—until post-market safety problems arise. This problem and many other scientific and regulatory concerns are addressed in the Report of the FDA's Task Force on Nanotechnology, just recently issued on July 25, 2007.

Recommendations of the Task Force to address regulatory challenges of nanotech products, "taking into account the evolving state of the science in this area."

1. Requesting data and other information about effects of nanoscale materials on safety and, as appropriate, effectiveness of products.

2. Suggestions that FDA provide guidance to manufacturers about when the use of nanoscale ingredients may require submission of additional data, change the product's regulatory

status or pathway, or merit taking additional or special steps to address potential safety or product quality issues.

3. Seeking public input on the adequacy of FDA's policies and procedures for products that combine drugs, biological products, and/or devices containing nanoscale materials to serve multiple uses, such as both a diagnostic and a therapeutic intended use.

4. Encouraging manufacturers to communicate with the agency early in the development process for products using nanoscale materials, particularly with regard to such highly integrated combination products. Thus, industry is encouraged to have in-person meetings with the appropriate branch or office of the FDA to discuss its product development.

The American Bar Association (ABA) Section of Environment, Energy, and Resources (SEER) reviewed the core federal environmental statutes to assess the suitability of each to address issues pertinent to human health and the environment arising from applications of nanotechnology. The assessment is found in several briefing papers submitted to the U.S. Environmental Protection Agency (EPA). SEER prepared briefing documents on each of the six core environmental statutes, and also a briefing document on innovative governance mechanisms, that identify key legal and regulatory issues that EPA can be expected to encounter as it considers how best to address issues likely to arise in connection with nanotechnology. The documents may be found at http://www.abanet.org/environ/nanotech/.

In general, the SEER papers concluded that the core environmental statutes were found to provide EPA with sufficient legal authority to address adequately the challenges EPA is expected to encounter as it assesses the enormous benefits of and potential risks associated with nanotechnology. The papers assess the Clean Water Act; the Clean Air Act; the Resource Conservation and Recovery Act; the Comprehensive Environmental Response Compensation and Liability Act (CERCLA), the Toxic Substances Control Act (TSCA), and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

This general conclusion of the sufficiency of the current EPA regulatory schema is not shared by everyone. For example, the organization Environmental Defense believes that nanomaterials should be considered new materials that require new regulatory approaches. EPA generally is taking the position that it has legal authority to regulate nanomaterials, primarily via TSCA. In EPA's White paper of February 2007, the Agency focused on the need for more information, especially regarding methodologies for testing for and measuring nanoparticles and their multiple and long-term effects on the environment. As research provides more answers about risks, the law will likely evolve to address the risks.

Ethics and Legal Professional Responsibilities in the Field of Nanotechnology
Which rules apply, and when?

Nanotechnology's Ethical Issues

Although funding and expenditures on, and applications of nanotechnology ("NT" in this section) have risen dramatically in the last decade, ethical questions and policies have lagged behind.[5] Unless the global community makes a serious and substantive commitment to studying the ethical, environmental, economic, legal and social implications of NT, the NT industry is at risk of being undermined by activist groups which are seeking to exaggerate and exploit the risks and myths associated with NT.[6]

The lack of emphasis put on ethical issues compared to the R & D funding can be seen in the disparity between the number of scientific publications addressing NT versus the number of academic publications addressing the ethical and social implications of NT.[7] A cursory listing of ethical concerns within NT includes: environmental contamination, military applications, personal privacy, risks of nanoparticle medicines and cosmetics, and workplace safety.[8]

Why is the lack of a consensus on ethical/philosophical/societal issues regarding NT a concern? This lack of consensus is a concern because private industry often suffers when the public's enthusiasm for innovative technology shifts to fear of the unknown, as happened with bio-engineering and genetically modified organisms (GMO), for example, in foods.[9] This fear can manifest itself through knee-jerk legislation and regulation or through the application of inconsistent health and safety standards across jurisdictions and communities.

For example, in 2002 at Johannesburg, the *World Summit on Sustainable Development* advocated a moratorium on the deployment of nanomaterials.[10] In December 2006, the German Society for Institutional Analysis issued a report, "The Legal Appraisal of Nano Technologies," which suggests that nanomaterials should be regulated as a new substance rather than under existing

---

[5] Anisa Mnyusiwalla, Abdallah Daar and Peter Singer, 'Mind the gap': science and ethics in nanotechnology, Institute of Physics Publishing, Nanotechnology 14 (2003) R9-R13 *available at* www.iop.org/EJ/abstract/0957-4484/14/3/201/.

[6] *Id.*

[7] *Id.*

[8] *Id.; see also* Vicki Colvin, Responsible Nanotechnology: Looking Beyond the Good News, EurekAlert! In Context, November 2002, *available at* www.eurekalert.org.

[9] Colvin, *supra* note 4.

[10] Mnyusiwalla, *supra* note 1.

European Union chemical regulations.[11] In 2004, the well-respected UK Royal Society and the Royal Academy of Engineering concluded that the unique hazards of nanoparticles warranted a moratorium on their release into the environment.

In May 2006, the International Center for Technology Assessment (CTA) spearheaded a coalition of consumer, health, and environmental groups in filing the first legal action as to the risks of nanotechnology. Specifically, they formally petitioned the FDA to review and address the human health and environmental risks of nanomaterials, which they characterized as "untested and unlabeled." The 80-page petition of the ICTA demanded comprehensive regulations specific to nanotech products, including "nano-specific toxicity testing and mandatory labeling of nano-ingredients."

In the U.S., the American National Standards Institute established a Nanotechnology Standards Panel, which was tasked with developing recommendations for toxicity effects, environmental impact and risk assessment. Similarly, the Woodrow Wilson International Center for Scholars stated that "new laws may be needed to manage the risks associated with nanotechnology, including a requirement that companies submit plans demonstrating that their products are safe."[12] Within the NT industry in the U.S., it is recognized that consumer confidence in the safety of nano-products is a significant issue for the growth of this industry.

How are Nanotechnology Ethics Related to Professional Responsibility?

Assuming that manufacturers will be required to demonstrate that NT products are non-toxic and safe, as advocated by the Woodrow Wilson Center above, manufacturers will be required to satisfy warranty and labeling standards before placing their products in the marketplace.[13] Furthermore, since manufacturers typically know more about the effects of their products than outsiders, these manufacturers would have a compelling incentive to delay admitting or to deny a claim that a product is unsafe.[14] It is at this juncture that a lawyer for a NT manufacturer would be faced with an ethical problem. At a broad and general level, the following questions are likely to arise:

---

[11] Mnyusiwalla, *supra* note 1; Legal appraisal of nano technologies, Existing legal framework, the need for regulation and regulative options at a European and a national level, Sofia, December 12, 2006, *available at* http://www.sofia-research.com.

[12] Jonathan Mansfield, Nanotech firms need legal strategies, Portland Business Journal, May 12, 2006, *available at* www.portland.bizjournals.com/portland/stories/2006/05/15/focus5.html; Patrick Thibodeau, Group calls for closer look at nanotech ethics, safety risks, Computer World, January 23, 2006, *available at* http://www.computerworld.com/action/article.do?command=viewArticleBasic&articleId=107990;

[13] Mansfield, *supra* note 8.

[14] Mary Lyndon, Secrecy and Access in an Innovation Intensive Economy: Reordering Information Privileges in Environmental Health and Safety Law, 78 U. Colo. L. Rev. 465, 482, (Spring 2007).

1. What are a lawyer's options if a client is unwilling to disclose that its nanotech product might be unsafe?

2. May a Colorado lawyer violate confidentiality to protect public safety?

3. To what extent may the lawyer violate her client's confidentiality?

4. To whom may/must the lawyer disclose this information if the lawyer represents an organization, as opposed to an individual?

5. May/should a lawyer give a client advice that goes beyond legal considerations and takes into account moral, economic, social or political factors?

6. If the laws and regulations of NT are in an embryonic state, what do the Colorado Rules of Professional Conduct require a lawyer to discuss with a client?

2008 Colorado Rules of Professional Conduct

The questions above are not overly difficult, but they merely scratch the surface of Professional Responsibility issues as related to NT. Moreover, the answers and rationales to these questions may be slightly different than in previous years when applying the 2008 edition of the Colorado Rules of Professional Conduct. The existing rules were adopted by the Colorado Supreme Court in 1993, and were based on the American Bar Association's (ABA) model rules in effect at the time. [15]

In 2002, based upon the recommendations of the ABA Ethics 2000 Commission, the ABA House of Delegates adopted the most current version of the Model Rules of Professional Conduct. Shortly thereafter, the Colorado Supreme Court established the Standing Committee on the Colorado Rules of Professional Conduct to determine whether Colorado should adopt the ABA's 2002 Model Rules.[16]

One of the Committee's preliminary determinations was that uniformity among jurisdictions that adopted the Model Rules was highly desired. This determination was due, in part, to the increase in multi-jurisdictional practices across the country, and also to make meaningful use of the precedent value of other jurisdictions' courts and ethics committees. To achieve uniformity across jurisdictions, one of the committee's presumptions was that each Model Rule would be recommended for adoption unless that rule contradicted Colorado law or Colorado public policy.[17] Accordingly, the 2008 Colorado Rules of Professional Conduct are very similar to the ABA Model Rules. Moreover, to answer the ethical questions set forth above, the following

---

[15] Report and Recommendations Concerning the American Bar Association Ethics 2000 Model Rules of Professional Conduct, Colorado Supreme Court Standing Committee on the Colorado Rules of Professional Conduct, December 30, 2005, *available at* http://www.courts.state.co.us/supct/committees/profconductdocs/sc-standingcommreport.pdf.

[16] *Id.*

[17] *Id.*

Rules and Comments offered for your consideration are nearly identical to the ABA provisions. Note that the use of underline and **bold** text is added for emphasis and is not contained in the actual Rules or Comments.

Confidentiality – CRPC 1.6, Revised 2008

Confidentiality is a fundamental principle of the lawyer-client relationship, and therefore it is the logical place to begin to examine the potentially divergent interests between a NT manufacturer and the public interest. Guidance for questions one, two and three can be found in Rule 1.6. Paragraph 1.6(a) states that "a lawyer shall not reveal information relating to representation of a client unless the client gives informed consent, the disclosure is impliedly authorized in order to carry out the representation, or the disclosure is permitted by paragraph (b). Paragraph (b) contains seven instances under which a lawyer may (discretionary) reveal information relating to representation of a client, to the extent the lawyer reasonably believes necessary. These exceptions are the same exceptions found in the ABA Model Rules.

Rule 1.6(b)(1) and (b)(2) – Death, Bodily Harm, and Intent to Commit a Crime

The first two exceptions give a lawyer the discretion to breach confidentiality in order to prevent "reasonably certain death or substantial bodily harm," or to "reveal the client's intention to commit a crime and the information necessary to prevent the crime." Obviously, disclosure of a client's involvement or contemplations involving death, bodily harm and criminal intent are going to be adverse to the client's interests. However, Comments (6) and (6A) acknowledge that the value of life and physical integrity trump the public interest in preserving client confidentiality. It must be noted that Comments (6) and (6A) do not give the lawyer *carte blanc* to disclose every piece of information about a client. Rather, to disclose client confidences, the harm must be reasonably certain to occur – which means the harm is either imminent, or if the harm will occur at a future date, the harm must be substantial. Also, if the client confidences relate to criminal conduct, the criminal act must be pending (not a completed crime).

Comment (6) even provides an example of "substantial harm" whereby a lawyer learns that a client has discharged toxic waste into the town's water supply. If the lawyer reasonably believes that a person who drinks the water will suffer a life threatening or debilitating disease and the lawyer's disclosure will eliminate or mitigate the harm, the lawyer may reveal the information. Applying Rule 1.6 to the NT industry, a lawyer who learns that a client has introduced an unsafe NT product to the market place, contaminated the environment with a dangerous NT product, or is contemplating whether or not to violate governmental regulations of the NT industry, the lawyer may (but is not required) to disclose this information. This rule could be applicable if the lawyer knows that there is a high likelihood that an FDA-regulated nanotech product will cause serious harm, and there is no Warning or Caution on the label.

Rule 1.6(b)(3) and (b)(4) – Substantial injury to financial interests or property through criminal or fraudulent activity, compared to Rule 1.2(d) – Scope of Representation

The third and fourth exceptions to Rule 1.6 pertain to preventing a client from committing fraud, or preventing/mitigating/rectifying the effects of a client's fraudulent or criminal actions. Both exceptions allow disclosure if the result of the fraud or crime will involve "substantial injury to the financial interests or property of another" **and** the lawyer's services were used in furtherance of the fraud or crime. Notably, these exceptions address the situation where a lawyer has unwittingly assisted the client's commission of a crime or fraud. Comment (7) states that such a serious abuse of the client-lawyer relationship by the client forfeits the protection of Rule 1.6.

Once again looking into the crystal ball of future NT laws and regulations, a lawyer who discovers that his services have been used to facilitate fraudulent labels or warranties, inadequate warnings and disclaimers, or fake or misleading product safety declarations, has the discretion (but is not required) to disclose client confidences in order to prevent or mitigate financial harm or property losses of third parties.

The situations described above, where the lawyer's services were exploited without the lawyer's knowledge, are distinguishable from situations where the lawyer is aware of the fraudulent or criminal activity. Rule 1.2(d) prohibits a lawyer from counseling a client or assisting a client in conduct the lawyer knows is criminal or fraudulent.

While Rule 1.2(d) prohibits the lawyer from assisting a client in the commission of a crime or fraud, the lawyer is permitted to discuss the legal consequences of any proposed conduct, and may also assist a client in making a good faith effort to determine the validity, scope, meaning or application of the law. The emergent nature of NT regulation will trigger the language of Rule 1.2(d) frequently as clients and lawyers work to abide by future laws and administrative regulations.

Rule 1.6(b)(5) and (b)(6) – Obtaining legal advice regarding compliance with the Rules and Conflicts between a lawyer and a Client

A lawyer may seek out confidential advice regarding compliance with the Rules of Professional Conduct without breaching a client's confidentiality. In fact, Comment (9) states that generally such external advice is impliedly authorized in order for the lawyer to represent the client.

In the event that a dispute arises between the lawyer and a client regarding the payment of fees, or allegations of misconduct by the lawyer, the lawyer is allowed to disclose client confidences to the extent necessary to establish a claim or a defense.

Rule 1.6(b)(7) Disclosures in Compliance with other Law or a Court Order

Rule 1.6(b)(7) and Comment (12) expressly recognize that other laws (e.g., Sarbanes-Oxley, the IRS code, a subpoena) may require a lawyer to disclose client confidences; but before the lawyer complies with the order, the lawyer must discuss the matter with the client per Rule 1.4.

Limiting the extent of the disclosure – Rule 1.6 Comments (14) and (15)

Although the provisions of Rule 1.6(b) contain several situations which permit a lawyer to breach a client's confidences, the final three comments to Rule 1.6 apply additional constraints to the manner in which a lawyer can breach confidentiality. First, when practicable, the lawyer should attempt to persuade the client to take suitable actions to alleviate the need for the disclosure. Second, the lawyer can disclose only to the extent the lawyer reasonably believes is necessary to accomplish the specified purpose. If the disclosure is to be made in connection with judicial proceedings, the disclosure should be limited to those persons who have a need to know.

Third, Rule 1.6(b) permits but does not require disclosure of information relating to the representation of a client. A lawyer who chooses not to disclose information that falls within Rule 1.6(b)(1) through (b)(7) does not violate the Rule.

Organization as a client – CRPC 1.13, Revised 2008

Rule 1.13(a) states, "A lawyer employed or retained by an organization represents the organization acting through its duly authorized constituents." Comment (1) states that since an organization is a legal entity that cannot act except through its officers, directors or shareholders, the decisions made by the constituents on behalf of the organization must be accepted by the lawyer. Similar to the business judgment rule, Comment (3) continues this line of thought, stating that the business decisions regarding the operation and policies of the organization (even high risk decisions) are not in the lawyer's province.

Under Rule 1.13(b), if the lawyer knows that a constituent's conduct is a violation of a legal obligation to the organization, or is a violation of law which could be imputed to the organization and will likely result in substantial injury to the organization, then the lawyer shall proceed as is reasonably necessary and in the best interest of the organization. Generally, this means that the lawyer shall refer the matter to higher authority in the organization (e.g., Corporate Officers, or the Board of Directors).

Paragraph (c) of Rule 1.13 indicates that if the highest authority within the organization fails (or refuses) to remedy the situation, and the situation is a clear violation of the law, **AND** the lawyer reasonably believes the violation is reasonably certain to result in substantial injury to the organization, the lawyer may reveal the information, whether or not Rule 1.6 permits the disclosure. However, this disclosure can only be made if, and to the extent necessary, to prevent substantial injury to the organization.

Comment (6) to this Rule summarizes the relationship between Rules 1.2, 1.6, and 1.13. First, the comment reiterates that public disclosure of an organization's confidences can only be made if the organization's highest level of authority insists upon conduct, or fails to address conduct, that is clearly a violation of the law. Second, unlike Rule 1.6(b)(3) and (b)(4), it is not required that the lawyer's services have been utilized in furtherance of the violation. All that is required is that the matter be related to the lawyer's representation of the organization.

Third, if the lawyer's services were being used by the organization to further a crime or fraud (by the organization or a constituent), then Rule 1.6(b)(2) through (b)(4) may permit disclosure by the lawyer. Fourth, Rule 1.2(d)'s prohibition on assisting a client in the commission of a crime or fraud would require the lawyer to withdraw from representing the organization in accordance with Rule 1.16(a)(1). The mandatory withdrawal has often been referred to as a "noisy withdrawal" because the lawyer's departure draws additional attention to the client's affairs.

Organizations within the NT community will consist of corporations, government agencies, non-profit entities, universities, etc. With each of these organizations, the lawyer must consider the severity of the violation and its consequences, the motivations of the constituents, and the policies of the organization concerning such matters. Once the lawyer has decided that a violation has occurred, she must raise the issue up the corporate ladder until it is rectified. As for public disclosures, until administrative adjudications and judicial precedent in the NT arena have moved beyond the infancy stage, it could be very difficult for a lawyer to satisfy the "clear violation of the law" provision of Rule 1.13(c)(1).

Lawyer's role as an Advisor – CRPC 2.1, Revised 2008

Rule 2.1 involves a far less stressful situation for a lawyer than what has been discussed with Rules 1.6 and 1.13: instead of acting against the client's interests, the lawyer is acting as an advisor to the client. During representation, a lawyer is required to exercise independent professional judgment and render candid advice. The lawyer may offer advice not only on legal issues, but also on moral, economic, social and political factors for the client's consideration—as well as business factors.

Comment (2) recognizes that advice that is given in narrow legal terms might not be of significant value to a client, especially where costs or effects on other people are predominant. It is proper for a lawyer to refer to relevant moral and ethical considerations when giving advice.

In an emerging field such as NT, Rule 2.1 and Comment (2) may provide a lawyer with the greatest latitude to encourage a client to consider ethical issues. Discussions with a client regarding tobacco settlements, asbestos litigation, and superfund cleanup sites could all be relevant and analogous to NT manufacturers who are preparing to develop, launch, and sell new products. In addition, Comment (5) cautions that when lawyer knows the client is undertaking action with substantial adverse consequences, <u>the lawyer's duty</u> under Rule 1.4 <u>may require</u> that the lawyer offer advice to the client, if the client's course of action relates to the representation.

Communication – CRPC 1.4 and Competence – CRPC 1.1, Revised 2008

Nanotechnology is a rapidly evolving field with a heavy emphasis on mathematics, engineering and science. While some lawyers are extremely conversant in these subject areas, most lawyers are not. Similarly, members of the NT industry may not have the same level of familiarity with nanotechnology laws and regulations marshaled (e.g., safety in the workplace) by industry members in other more stable industries. Thus, lawyers for NT clients may need to be more interdependent than in other lawyer-client relationships. Interdependent here means that the lawyer must learn more about science and the client must learn more about the law than in the usual attorney-client relationship. If so, two fundamental requirements for this interdependence will be communication and competence.

A lawyer is required to keep a client reasonably informed about the status of a matter, and a lawyer shall explain a matter to the extent reasonably necessary to permit the client to make informed decisions regarding the representation. These requirements are expressly stated in Rules 1.4(a)(3) and (b). To meet these requirements, a lawyer for an NT client must be able to understand the nature of the client's business, and determine whether pending laws and regulations will apply to the client. This understanding is often generally described as competence, which is addressed in Rule 1.1.

Competent representation, as defined in Rule 1.1, requires legal knowledge, skill, thoroughness and preparation reasonably necessary for the representation. The Comments to Rule 1.1 state that a lawyer can provide adequate representation in a completely novel field through necessary study, or by associating oneself with another lawyer with competence in that field. In addition, a lawyer is expected to stay abreast of changes in the law and its practice through continuing study and education. This will be a special challenge for the lawyer of an NT client, given that federal rule-making will no doubt increase in the next 3 years.

It is quite possible that the continuing study and education – in technical subjects – will pose the greater challenge to lawyers working in the NT field. Finally, although the judicial system strives for consistency and precedent, the very nature of nanotechnology may prevent the associated legal and ethical issues that will inevitably arise from being categorized into practice areas that exist today.

Ethics Beyond Legal Ethics

One very readable book, entitled Nanotechnology: A Gentle Introduction to the Next Big Idea (Ratner & Ratner 2003) discusses ethical issues in the broadest sense of "ethics," including public policy and social responsibility. But ethical decisions, for society as well as for attorneys, requires knowledge of at least the basics on the scientific issues. We hope that this Nano 101 Primer provides a start. The book's section called "Nano Ethics: Looking Beyond the Promise of Nanotechnology" (at pp. 158- 162) concludes as follows:

> Even more futurist concerns [than genetic engineering] also are from nanotechnology. Arguably, forms of nanocomputation that we've discussed (such as quantum computing, DNA computing, and nanoelectronic computing) may help unlock true artificial intelligence. If this occurs, how should artificial intelligence be treated? What rights and privileges should it have? What if it should become self-replicating? Also, if interfaces between humans and computers improve to the point where they are hard to differentiate, what will that mean for human civilization? How will we treat these cyborgs? Would this truly be the next stage in the evolution of the human race? Might it allow for the arbitrary extension of life through artificial organs or bodies? Even if nanocomputation fails to produce machines that think, one of its stated goals is to break codes. If this reaches fruition, all common forms of digital cryptography--from the sort that protects e-commerce to the kind that protects nuclear secrets--could be compromised. The implications for national security and for personal privacy cannot be overstressed.
>
> These are all heady questions, and it is time to begin to tackle them somewhere other than on TV and in the pages of science fiction books. The whole ethical debate over nanotechnology is one of the most important reasons for the public to know what nano is and what it could mean. Nanotechnology is already, by its very nature, a multi disciplinary science. Perhaps we don't need the involvement only of scientists and engineers, but of thinkers, ethicists, lawyers, theologians, and politicians as well.

Nanotechnology Glossary:

Buckyball or Fullerene or C60
One of three known pure forms of carbon (graphite and diamond being the other two) that takes a spherical shape with a hollow interior. Buckyballs, named because they resemble the geodesic domes built by architect Buckminster Fuller, were discovered in 1985 among the byproducts of laser vaporization of graphite in which the carbon atoms are arranged in sheets. Though C60, referring to the number of carbon atoms that make up one sphere, is the most common fullerene, researchers have found stable, spherical carbon structures containing 70 atoms (C70), 120 (C120), 180 (C180), and others.
Robert F. Curl Jr. and Richard E. Smalley, both of Rice University in Houston, Texas and Harold W. Kroto of the University of Sussex in England, won the 1996 Nobel Prize for Chemistry for their discovery of buckminsterfullerene, the scientific name for buckyballs.

Carbon Nanotubes
A form of carbon related to fullerenes, except that the carbon atoms form extended hollow tubes instead of closed, hollow spheres. Carbon nanotubes can also form as a series of nested, concentric tubes. Carbon nanotubes can be used as nanometer-scale syringe needles for injecting molecules into cells and as nanoscale probes for making fine-scale measurements. Carbon nanotubes can be filled and capped, forming nanoscale test tubes or potential drug delivery devices. Carbon nanotubes can also be “doped,” or modified with small amounts of other elements, giving them electrical properties that include fully insulating, semiconducting, and fully conducting.

Dendrimer
A dendrimer is a tree-like highly branched polymer molecule (Greek *dendra* = *tree*). Dendrimers are synthesized from monomers with new branches added in discrete steps ("generation") to form a tree-like architecture. A high level of synthetic control is achieved through step-wise reactions and purifications at each step to control the size, architecture, functionality and monodispersity. Several different kinds of dendrimers have been synthesized utilizing different monomers and some are commercially available. This picture shows a "3rd generation" polyamidoamine (PAMAM) dendrimer.

Dendrimers are of particular interest for cancer applications because of their defined and reproducible size, but more importantly, because it is easy to attach a variety of other molecules to the surface of a dendrimer. Such molecules could include tumor-targeting agents (including but not restricted to monoclonal antibodies), imaging contrast agents to pinpoint tumors, drug molecules for delivery to a tumor, and reporter molecules that might detect if an anticancer drug is working.

Imaging Contrast Agent
A molecule or molecular complex that increases the intensity of the signal detected by an imaging technique, including MRI and ultrasound. An MRI contrast agent, for example, might contain gadolinium attached to a targeting antibody. The antibody would bind to a specific target – a metastatic melanoma cell, for example – while the gadolinium would increase the magnetic signal detected by the MRI scanner.

Liposome
A type of nanoparticle made of lipids, or fat molecules, surrounding a water core. Liposomes, several of which are widely used to treat infectious diseases and cancer, were the first type of nanoparticle to be used to create therapeutic agents with novel characteristics.

Microfluidics
A multidisciplinary field comprising physics, chemistry, engineering and biotechnology that studies the behavior of fluids at volumes thousands of times smaller than a common droplet. Microfluidic components form the basis of so-called "lab-on-a-chip" devices that can process microliter and nanoliter volumes and conduct highly sensitive analytical measurements. The fabrications techniques used to construct microfluidic devices are relatively inexpensive and are amenable both to highly elaborate, multiplexed devices and also to mass production. In a manner similar to that for microelectronics, microfluidic technologies enable the fabrication of highly integrated devices for performing several different functions on the same substrate chip. Microfluidics is a critical component in gene chip and protein chip development efforts.

Nanocantilever
The simplest micro-electro-mechanical system (MEMS) that can be easily machined and mass-produced via the same techniques used to make computer chips. The ability to detect extremely small displacements make nanocantilever beams an ideal device for detecting extremely small forces, stresses and masses. Nanocantilevers coated with antibodies, for example, will bend from the mass added when substrate binds to its antibody, providing a detector capable of sensing the presence of single molecules of clinical importance.
http://nano.cancer.gov/resource_center/nanotech_glossary.asp - top.

Nanometer
A unit of spatial measurement that equals one-billionth (10 -9) of a meter. The head of a pin is about 1 million nanometers across. A human hair is about 60,000 nanometers in diameter, while a DNA molecule is between 2-12 nanometers wide.
http://nano.cancer.gov/resource_center/nanotech_glossary.asp - top.

Nanoparticle
A nanoscale spherical or capsule-shaped structure. Most, though not all, nanoparticles are hollow, which provides a central reservoir that can be filled with anticancer drugs, detection agents, or chemicals, known as reporters, that can signal if a drug is having a therapeutic effect. The surface of a nanoparticle can also be adorned with various targeting agents, such as antibodies, drugs, imaging agents, and reporters. Most nanoparticles are constructed to be small enough to pass through blood capillaries and enter cells.
http://nano.cancer.gov/resource_center/nanotech_glossary.asp - top.

Nanoshell
A nanoparticle composed of a metallic shell surrounding a semiconductor. When nanoshells reach a target cancer cell, they can be irradiated with near-infrared light or excited with a magnetic field, either of which will cause the nanoshell to become hot, killing the cancer cell.
http://nano.cancer.gov/resource_center/nanotech_glossary.asp - top

Nanotechnology
The interactions of cellular and molecular components and engineered materials—typically clusters of atoms, molecules, and molecular fragments—at the most elemental level of biology. Such nanoscale objects—typically, though not exclusively, with dimensions smaller than 100 nanometers—can be useful by themselves or as part of larger devices containing multiple nanoscale objects.
http://nano.cancer.gov/resource_center/nanotech_glossary.asp - top.

Nanowire
A nanometer-scale wire made of metal atoms, silicon, or other materials that conduct electricity. Nanowires are built atom by atom on a solid surface, often as part of a microfluidic device. They can be coated with molecules such as antibodies that will bind to proteins and other substances of interest to researchers and clinicians. By the very nature of their nanoscale size, nanowires are incredibly sensitive to such binding events and respond by altering the electrical current flowing through them, and thus can form the basis of ultra sensitive molecular detectors.
http://nano.cancer.gov/resource_center/nanotech_glossary.asp - top.

Quantum dot (Qdots)
Nanometer sized semiconductor particles, made of cadmium selenide (CdSe), cadmium sulfide (CdS) or cadmium telluride (CdTe) with an inert polymer coating. The semiconductor material used for the core is chosen based upon the emission wavelength range being targeted: CdS for UV-blue, CdSe for the bulk of the visible spectrum, CdTe for the far red and near-infrared, with the particle's size determining the exact color of a given quantum dot. The polymer coating safeguards cells from cadmium toxicity but also affords the opportunity to attach any variety targeting molecules, including monoclonal antibodies directed to tumor-specific biomarkers.

Because of their small size, quantum dots can function as cell- and even molecule-specific markers that will not interfere with the normal workings of a cell. In addition, the availability of quantum dots of different colors provides a powerful tool for following the actions of multiple cells and molecules simultaneously. In August 2004, researchers announced the successful preparation of water-soluble gold quantum dots that can also be constructed to emit light at a variety of wavelengths. These polymer-coated quantum dots may prove to be more suitable for use in human clinical applications.

(Source for Glossary: NIH, National Cancer Institute, Alliance for Nanotechnology in Cancer.)

References:

ASTM, Terminology for Nanotechnology, E-2456-06, December 2006. Available for free download at: http://www.astm.org/cgi-bin/SoftCart.exe/DATABASE.CART/REDLINE_PAGES/E2456.htm?E+mystore.

ASTM, Standard Terminology for Nanotechnology, WK8051. Under development: http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/SUBCOMMIT/E5601.htm?L+mystore+cprk8709+1177002851.

Baron, P.A. and Willeke, K., Aerosol Measurement, Principals, Techniques, and Applications, 2nd edition, John Wiley and Sons, Inc., 2001.

BSi, Vocabulary – Nanoparticles, PAS 71:2005. Available for free download at: http://www.bsi-global.com/en/Standards-and-Publications/Industry-Sectors/Nanotechnologies/PAS-71/.

Hinds, W.C., Aerosol Technology – Properties, Behavior, and Measurement of Airborne Particles, 2nd Edition, John Wiley and Sons, Inc., 1999.

ISO, Nanoparticles – Terminology and definitions, ISO/AWI TS 27687. Under development: http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME .

ISO, Workplace Atmospheres – Ultrafine, nanoparticle and nano-structured aerosols – Exposure characterization and assessment. Geneva: Switzerland: International Standards Organization. Document no. ISO/TR 27628, 2007. Available for purchase from ANSI, http://www.ansi.org/.

NCI, Nanotechnology Glossary, http://nano.cancer.gov/resource_center/nanotech_glossary.asp.

WEBSITES

American Industrial Hygiene Association (AIHA): http://www.aiha.org/Content/Topics/nano/

ASTM E56 Nanotechnologies:
http://www.astm.org/cgi-bin/SoftCart.exe/COMMIT/COMMITTEE/E56.htm?L+mystore+cprk8709+1179181259

Environmental Protection Agency (EPA): http://es.epa.gov/ncer/nano/

Food and Drug Administration (FDA): http://www.fda.gov/nanotechnology/

International Conference on Nanotechnology: Occupational and Environmental Health & Safety, 4-7 December 2006, Cincinnati, OH. Slide presentations online, available: http://www.uc.edu/noehs/conference_program.asp.

International Council on Nanotechnology (ICON):
http://cohesion.rice.edu/centersandinst/cben/industry.cfm?doc_id=5023

International Organization for Standardization (ISO) TC 229 Nanotechnologies:
http://www.iso.org/iso/en/CatalogueListPage.CatalogueList?COMMID=5932&scopelist=PROGRAMME

National Cancer Institute (NCI): http://nano.cancer.gov/

National Institute for Occupational Safety and Health (NIOSH):
http://www.cdc.gov/niosh/topics/nanotech/

National Nanotechnology Initiative (NNI): http://www.nano.gov/

Occupational Safety and Health Administration (OSHA): http://www.osha.gov/

Organisation for Economic Co-operation and Development (OECD):
http://www.oecd.org/department/0,2688,en_2649_37015404_1_1_1_1_1,00.html

Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies:
http://www.nanotechproject.org/

ABBREVIATIONS AND ACRONYMS

AIHA: American Industrial Hygiene Association

DOE: Department of Energy

EHS: Environment, health, and safety

EPA: Environmental Protection Agency

FDA: Food and Drug Administration

g/cc: grams per cubic centimeter

ICON: International Council on Nanotechnology

ISO: International Organization for Standardization

mg/m^3: milligrams per cubic meter

mm: millimeter

MURI: Multi-disciplinary University Research Initiative

NASA: National and Aeronautics Space Administration

NCI: National Cancer Institute

NCL: Nanotechnology Characterization Laboratory

NIOSH: National Institute for Occupational Safety and Health

NIST: National Institute of Standards and Technology

nm: nanometers

NNI: National Nanotechnology Initiative

OECD: Organisation for Economic Co-operation and Development

OSHA: Occupational Safety and Health Administration

PM: particulate matter

µm: micrometers

Note: This Nanotechnology 101 Primer was authored by Griff Kundahl, Esq. with the assistance of Susan Brienza, Esq. and Maki Iatridis, Esq. The Ethics section was authored by Susan Brienza, Esq. and Erik Dullea (soon to be Esq.)