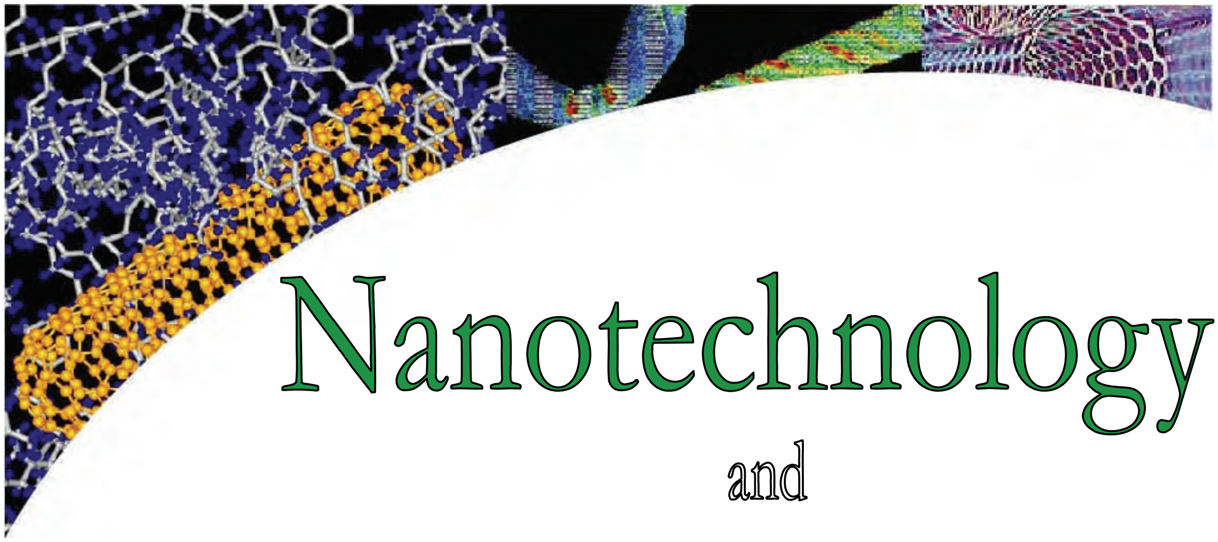

Nanotechnology

and

OSWER

New opportunities and challenges

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

July 12-13, 2006

Ronald Reagan Building and International Trade Center

Washington DC

DISCLAIMER

ACKNOWLEDGMENTS

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Table of Contents

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

JUN 9 2006

OFFICE OF
SOLID WASTE AND
EMERGENCY RESPONSE

MEMORANDUM

FROM: Susan Parker Bodine
Assistant Administrator

TO: OSWER Office and Staff Directors
Superfund Directors, Regions 1-10
RCRA Directors, Regions 1-10

SUBJECT: Nanotechnology and OSWER: New Opportunities and Challenges Symposium

The Environmental Protection Agency's (EPA) Office of Solid Waste and Emergency Response (OSWER) is hosting a symposium: *Nanotechnology and OSWER: New Opportunities and Challenges* at the Ronald Reagan International Trade Center (Polaris Rooms A, B, and C), 1300 Pennsylvania Ave. NW, Washington, DC on July 12 and 13, 2006. The purpose of this symposium is to provide information about nanotechnology and its possible influence on waste management practices.

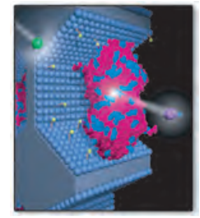
Nanotechnology is the art and science of manipulating matter at the nanoscale to create new and unique materials and products. The use of nanotechnology has enormous potential to change the way we do things. An estimated global research and development investment of nearly $9 billion per year is anticipated to lead to new medical treatments and tools; more efficient energy production, storage and transmission; better access to clean water; more effective pollution reduction and prevention; and stronger, lighter materials. Also, nanotechnology brings a series of challenges to solid waste practices, such as, the ability of current analytical techniques to detect nanoparticles in the environment, the fate and transport of nanomaterials in the environment, and the potential toxicity of nanomaterials.

A series of renowned international, legal, academic and industrial experts in the field of nanotechnology will present and discuss technical issues and implications of nanomaterials related to solid waste practices. This symposium is intended for EPA employees, other federal agency representatives and invited guests. Please join us to learn about nanotechnology and its opportunities and challenges in our solid waste programs.

For more information, agenda and online registration visit the website at http://esc.syrres.com/nanotech/.

Nanotechnology and OSWER

new opportunities and challenges



Symposium July 12-13, 2006

Ronald Reagan Building and International Trade Center
1300 Pennsylvania Ave., NW • Washington, DC
Polaris Rooms A,B,C

Experts, researchers, and industry leaders will present and discuss technical issues relevant to nanotechnology and waste management practices, with a primary focus on the life cycle of nanomaterials and policy issues.

- Nanotechnology and the Environment
- Lifecycle of Nanomaterials
- Detection and Characterization
- Potential Toxicity
- Fate and Transport
- Waste Management
- Regulations, Positions, Policies, and Actions
- Panel Discussion on Policy

Agenda Day 1 - Wednesday, July 12

TIME	TOPIC	SPEAKER
8:00 - 9:00 AM	**Registration**	
9:00 - 9:30 AM	**Welcome and Opening Remarks** (*2 speakers*)	***Ms. Renee Wynn*** U.S. EPA - Washington, DC ***Ms. Susan Parker Bodine*** AA OSWER/U.S. EPA - Washington, DC
9:30 - 10:30 AM	**Introduction**: Overview of Nanotechnology and the Environment • Applications of Nanotechnology • Benefits and Potential Threats to the Environment	***Dr. Vicki Colvin*** Rice University - Houston, TX
10:30 - 11:30 AM	**Session 1**: Life Cycle of Nanomaterials	***Dr. Stig Irving Olsen*** Technical University of Denmark - Lyngby, Denmark
11:30 -1:00 PM	**Lunch** (on your own)	
1:00 - 2:00 PM	**Session 2**: Potential Exposure Scenarios and Potential Toxicity of Nanomaterials	***Dr. David Warheit*** E.I. DuPont de Nemours & Co., Inc. - Newark, DE
2:00 - 3:00 PM	**Session 3**: Detection and Characterization of Nanomaterials in the Environment (*2 speakers*)	***Mr. John Scalera*** U.S. EPA - Washington, DC ***Dr. Anil K. Patri*** National Cancer Institute - Frederick, MD
3:00 - 3:30 PM	**Break**	
3:30 - 4:30 PM	**Session 4**: Fate and Transport of Nanomaterials	***Dr. Gregory V. Lowry*** Carnegie Mellon University - Pittsburgh, PA
4:30 PM	**Wrap-up and Adjourn**	

Agenda Day 2 - Thursday, July 13

TIME	TOPIC	SPEAKER
8:30 - 9:00 AM	**Registration**	
9:00 - 10:00 AM	**Session 5**: Waste Management of Nanomaterials • New Nanoproducts • Impacts on Current Waste Management Practices • Pollution Prevention	***Dr. Lou Theodore*** Manhattan College - New York, NY
10:00 - 10:15 AM	**Break**	
10:15 - 12:00 PM	**Session 6**: Review of Regulations, Positions, Policies, Guidance, and Actions for Nanomaterials (*2 speakers*) • General Environmental Law Framework • RCRA/CERCLA • Policies on Redevelopment, Institution Controls, Land Reuse	***Mr. Mark Greenwood*** Ropes & Gray - Washington, DC ***Mr. Tracy D. Hester*** Bracewell & Giuliani LLP - Houston, TX
12:00 - 1:00 PM	**Lunch** (on your own)	
1:00 - 3:00 PM	**Session 7**: Panel Discussion • OSWER Policy and Regulatory Questions • Data Evaluation and Gaps • Next Steps	***All Speakers and Special Guests***
3:00 PM	**Adjourn**	

to register visit
http://esc.syrres.com/nanotech/

DEFINITIONS OF ACRONYMS

AFM	Atomic force microscopy
ASTM	American Society for Testing and Materials
ATOFMS	Aerosol tome-of-flight mass spectrometry
CBEN	Center for Biological and Environmental Nanotechnology
CBI	Confidential Business Information
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CNC	Condensation nuclei counter
CPC	Condensation particle counter
CVD	Chemical vapor deposition
DMA	Differential mobility analyzer
DNAPL	Dense non-aqueous phase liquid
EC	European Commission
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECB	European Chemicals Bureau
EDX	Energy dispersive X-ray analysis
EELS	Electron energy lost spectroscopy
EPCRA	Emergency Planning & Community Right to Know Act
FDA	Food and Drug Administration
HEPA	High efficiency particulate arrestance
IARC	International Agency for Research on Cancer
ILSI-HESI	International Life Sciences Institute Health and Environmental Sciences Institute
ILSI-RSI	International Life Sciences Institute Risk Science Institute
ISO	International Organization for Standardization
LCA	Life cycle assessment
MECO	Materials, energy, chemicals, and others
MNIMBS	Michigan Nanotechnology Institute for Medicine and Biological Sciences
MSDS	Material Safety Data Sheet
MTBE	Methyl tertiary butyl ether
MTX	Methotrexate
NCI	National Cancer Institute
NCL	Nanotechnology Characterization Laboratory
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Health
NIH-SBIR	National Institutes of Health Small Business Innovation Research
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology
NLLAP	National Lead Laboratory Accreditation Program
NNI	National Nanotechnology Initiative
NPEG	Nanotechnology Public Engagement Group
NSET	Nanoscale Science, Engineering and Technology

DEFINITIONS OF ACRONYMS

NT	Nanotechnology
OAR	Office of Air and Radiation
OECD	Organisation for Economic Co-operation and Development
OIAA	Office of Analysis and Access
OPPT	Office of Pollution Prevention and Toxics
ORD	Office of Research and Development
OSHA	Occupational Safety and Health Administration
OSRTI	Office of Superfund Remediation and Technology Innovation
OSW	Office of Solid Waste
OSWER	Office of Solid Waste and Emergency Response
PCBs	Polychlorinated biphenyls
PPE	Personal protective equipment
RCRA	Resource Conservation and Recovery Act
ROS	Reactive oxygen species
SAR	Structure-activity relationship
SEM	Scanning electron microscopy
SETAC	Society of Environmental Toxicology and Chemistry
SRM	Standard reference material
STAR	Science to Achieve Results
TCE	Trichloroethylene
TCLP	Toxicity characteristic leaching procedure
TEM	Transmission electron microscopy
TiO_2	Titanium dioxide
TSCA	Toxic Substances Control Act
US EPA	United States Environmental Protection Agency
ZnO	Zinc oxide

Nanotechnology and OSWER – Symposium Summary

The symposium, which included presentations from leading experts in the field of nanotechnology as well as question-and-answer sessions and a panel discussion, was an opportunity to exchange ideas and learn about nanotechnology in order to inform future OSWER decision-making. Important considerations include how nanotechnology is being used today, and how it will be used in the future; how people are being exposed to nanotechnology products; and the fate and transport of nanomaterials.

Nine leading experts in the field of nanotechnology gave presentations:

Overview of Nanotechnology and the Environment
Dr. Vicki Colvin, Rice University
Dr. Colvin discussed some of the unique properties of nanoparticles (e.g., large surface area, which can lead to increased reactivity). She discussed examples of applications of nanomaterials (e.g., the use of magnetite for water treatment). Balancing risks and benefits is key to the future of nanotechnology. We must be proactive in understanding risks, and ask difficult questions about risks/benefits for any new technology. It is also important for the Agency to be open about what we know and do not know.

Life Cycle of Nanomaterials
Dr. Stig Irving Olsen, Technical University of Denmark
Dr. Olsen provided an overview of life cycle assessment (LCA) and its use and application to nanotechnology, with a focus on the cost of nanotechnology resources with respect to rebound effects and scarce resources. Nanotechnological products are emerging on the market, but studies on the life cycle environmental impacts are still very limited. Nonetheless, several potential environmental aspects can be identified which can question the sustainability of nanotechnologies. Energy intensive manufacturing efforts (e.g., maintaining a clean nanotechnology production environment to ensure pure products – this requires lots of high-energy input) and potential impacts due to release of nanomaterials are potential environmentally problematic properties of nanotechnologies.

Nanotechnologies should not be considered environmentally beneficial just because products are small. A life cycle perspective should be applied during design and technological development in order to reduce potential environmental impacts in the life cycle of the "nano-products."

Potential Exposure Scenarios and Potential Toxicity of Nanomaterials
Dr. David Warheit, E.I. DuPont de Nemours & Co., Inc.
Dr. Warheit's research involves health effects resulting from respiratory exposures to nanomaterials. Some common perceptions of pulmonary toxicity include the idea that nanoparticles are more inflammogenic and/or tumorigenic than fine-sized particles of identical chemical composition. However, not all nano-sized particles are more toxic. Some factors that may influence toxicity are surface coatings, species differences, particle aggregation potential, and whether the particle was fumed vs. precipitated in its manufacture.

Results of pulmonary bioassay hazard/safety studies have demonstrated that fine-sized quartz particles (1.6 µm) may produce greater pulmonary toxicity in rats compared to nanoscale quartz particles (50 nm), but not compared to smaller nanoquartz sizes (e.g., < 30 nm).

It cannot be assumed that nanomaterials are the same as their bulk counterparts; the biology changes with chemistry and physics. Each particle type should be tested on a case-by-case basis.

Detection and Characterization of Nanomaterials in the Environment

Mr. John Scalera, US EPA
Mr. Scalera presented an overview of some available analytical techniques used for the detection and characterization of nanoparticles in environmental including particle size analysis, particle fraction concentration counts, surface area analysis, morphology and particle chemical composition analysis. He discussed measurement limitations and how measurement for nanomaterials in soil and sediments is a challenge.

Mr. Scalera also discussed methods for nanoparticle collection and size determination (e.g., differential mobility analyzer, condensation particle counters). The challenge of detecting nanomaterials in the environment is compounded by the extremely small size of the particles and their potential sequestration and agglomeration, and also by their unique physical and chemical characteristics.

Dr. Anil K. Patri, National Cancer Institute
Dr. Patri discussed the collaboration between NCL at NCI Frederick, the National Institute of Standards and Technology (NIST) and the U.S. Food and Drug Administration (FDA) to perform pre-clinical characterization and assessment of nanomaterial intended for cancer therapeutics and diagnostics. He discussed some tools and techniques used to evaluate nanomaterial properties (e.g., detection and quantitation of nanomaterials in blood by capillary electrophoresis).

Fate and Transport of Nanomaterials
Dr. Gregory V. Lowry, Carnegie Mellon University
Dr. Lowry discussed topics including pathways of exposure, fate, and transport; sources of nanomaterials; how they travel; what factors affect their mobility; whether nanomaterials can be transformed; and whether they're toxic. Processes that will control the fate and transport of nanomaterials in the environment include redox processes, aggregation, and deposition. Environmental geochemical conditions (e.g. pH, ionic strength, and ionic composition) can greatly affect the rate and extent of each of the processes controlling the fate and transport of nanomaterials. He indicated that the fate and transport as well as toxicity of nanomaterials are open questions.

Waste Management of Nanomaterials
Dr. Lou Theodore, Manhattan College
Dr. Theodore discussed the importance of nanotechnology, health and hazard risk assessment, and regulations. Nanoscale particles have unique properties, which lead to infinite possible uses. Quality control is an issue in the development of nanoparticles because of the unique chemical and physical properties of particles (of the same chemical composition) of different size. There are two necessary elements of hazard assessment: (1) what is the probability; and (2) what are the consequences. From this information, one can estimate risk. If either the probability or the consequences is low, then hazard is low. Regarding regulation of engineered nanoparticles, OSHA is likely to regulate nanoparticles before EPA, but that risks to civilians will fall under the domain of EPA. A cost-benefit analysis is needed for any new regulation.

Review of Regulations, Positions, Policies, Guidance, and Actions for Nanomaterials

Mr. Mark Greenwood, Ropes & Gray, Washington DC
Mr. Greenwood addressed the issue of responding to public concerns about nanotechnology and identified key environmental protection policy issues related to nanotechnology from the perspective of managers of air, water, and waste programs. He said that the general public has a positive reaction to medical improvement and improved consumer products, but has concerns with adequate testing and movement to other routes of exposure. It will be important for OSWER to define its role in nanotechnology and look more deeply at the issue. There is a need to develop capabilities in

responding to spills, managing workplace exposure, and determining risks. There is also a need to prepare information for the public (for general dissemination and in response to questions).

Mr. Tracy D. Hester, Bracewell & Giuliani, LLP
Mr. Hester discussed the application of RCRA and CERCLA requirements to nanoscale materials and wastes. Because nanomaterials may display unusual or unique qualities, they may pose challenges to existing RCRA and CERCLA regulations designed to control releases of regularly-sized versions of the same materials. Issues include: how to handle spills; how to dispose of nanomaterials; and how to measure/demonstrate the amount of nanoparticles in waste media to show that it is not hazardous. This is a difficult challenge due to the difference in activity and toxicity of nanoparticles with only small changes to the molecule.

A Panel composed of the conference speakers and additional EPA personnel held a discussion during which they addressed two charge questions from OSWER: Based on what is currently known in the nanotechnology area, what can be inferred about the properties and characteristics of nanotechnology waste? How can nanotechnology impact current waste management practices for wastes?

Panel Members:

Dr. Elizabeth Lee Hofmann, US EPA OSWER, Moderator
Mr. Jim Willis, US EPA OPPT
Dr. Barbara Karn, US EPA ORD, Woodrow Wilson International Center for Scholars/Emerging Nanotechnologies Project
Dr. Nora Savage, US EPA ORD, National Center for Environmental Research/Environmental Engineering Research Division
Ms. Marti Otto, US EPA OSRTI
Mr. Tracy D. Hester, Bracewell & Giuliani LLP, Houston TX
Mr. Mark Greenwood, Ropes & Gray, Washington DC
Dr. Stig Irving Olsen, Technical University of Denmark, Lyngby Denmark
Dr. Lou Theodore, Manhattan College, Department of Chemical Engineering
Mr. John Scalera, US EPA, Washington DC
Dr. Anil K. Patri, National Cancer Institute, Frederick MD
Dr. Gregory V. Lowry, Carnegie Mellon University, Pittsburgh PA
Dr. David Warheit, E.I. DuPont de Nemours & Co., Inc Newark DE

Question: Based on what is currently known in the nanotechnology area, what can be inferred about the properties and characteristics of nanotechnology waste?

Points made by various Panel members in response to this question are summarized below.

- Most technology waste streams will end up containing nanomaterials or nanotechnology products.

- The issue of how to identify nanoparticles in waste is a very difficult problem. Even when one controls for all of the variables in the lab, different results can be obtained depending on what is looked for and what methods are used, even when working with the same material. Also, aggregation and agglomeration are issues when dealing with waste streams. Additionally, nanoparticles can be coated.

- One of the biggest issues is the depletion of scarce resources. A means to improve recovery of valuable materials from waste is needed.

- There is a need to develop a life cycle assessment framework for product stewardship. Experimental simulations should be carried out using one or two standardized materials, to determine which methods and which parameters to use (size, shape, charge, and surface characteristics).

- OSWER should understand stability and degradation of nanomaterials and their waste products.

- OSWER should consider whether it is possible to categorize nanomaterials or identify subsets of materials that are of less interest than free nanoparticles (e.g., nanomaterials bound in a matrix, or one-dimensional nanomaterial coatings).

- OSWER should review the nanotechnology white paper, the ORD research strategy, and more importantly the NNI research strategy to make sure that its needs get reflected in the research areas being considered.

- OSWER should be very open to the public with respect to how waste streams are managed.

Question: How can nanotechnology impact current waste management practices for wastes?

Points made by various Panel members in response to this question are summarized below.

- Nanoparticles have unique, novel properties that can be utilized for waste remediation (waste water, air pollutants, etc.). There is the possibility of creating nanomaterials that have reactive and physical properties that allow us to remediate hard-to-reach wastes.

- This can be approached from a pollution prevention point of view; current chemicals can be replaced with new nanomaterials that don't have toxicological issues.

- Chemistry required for understanding nanowaste is typically not a part of traditional waste management. There is a need to know a lot more about what's in the waste stream, how it behaves in the environment, etc. Reevaluation and revalidation of our methods for waste treatment will be needed, to see if they work with nanomaterials.

- Some Agency management changes may be needed. Nanotechnology is a good opportunity to look at the link between waste management and the time when a chemical comes into commerce. Management programs typically consider product development and waste separately. Can we be proactive in asking these questions simultaneously? There is a need to align waste management and product programs and ask the right questions in the beginning.

The standardization and characterization of nanosized particles is a must. It is important to be able to compare particles from different laboratories. NIST is developing standard reference materials (SRMs) that will be thoroughly characterized.

Dr. Vicki Colvin

Rice University
Professor of Chemistry and Professor of Chemical Engineering

Dr. Vicki Colvin has been on the faculty at Rice since the fall of 1996. As a physical chemist interested in complex materials problems, her group includes a diverse range of synthetic chemists, physical chemists and applied physicists. Specific research areas include template chemistry, meso- and macroporous solids, nanocrystalline oxides, photonic band gap materials and confined glasses.

Prior to her start at Rice, she was a member of the technical staff at Bell Labs where she developed new materials for holographic data storage. She received her PhD in 1994 at U.C. Berkeley under the direction of Dr. Paul Alivisatos. Her undergraduate degree, a B.S. in chemistry and physics, was completed in 1988 at Stanford University. In 1996, Colvin was recruited by Rice University to expand its nanotechnology program. Today, she serves as Professor of Chemistry at Rice University as well as Director of its Center for Biological and Environmental Nanotechnology (CBEN). CBEN was one of the nation's first Nanoscience and Engineering Centers funded by the National Science Foundation. One of CBEN's primary areas of interest is the application of nanotechnology to the environment.

Colvin has received numerous accolades for her teaching abilities, including Phi Beta Kappa's Teaching Prize for 1998-1999 and the Camille Dreyfus Teacher Scholar Award in 2002. In 2002, she was also named one of Discover Magazine's "Top 20 Scientists to Watch" and received an Alfred P. Sloan Fellowship.

Selected Publications

Bunge, S. D., Krueger, K. M., Boyle, T. J., Rodriguez, M. A., Headley, T. J. and Colvin, V. L. "Growth and morphology of cadmium chalcogenides: the syntheses of nanorods, tetrapods, and spheres from CdO and Cd $(O_2CCH_3)_2$." *J. Mater. Chem.*, 13 (2003): 1705-1709.

Bertone, J. F., Cizeron, J., Wahi, R. K., Bosworth, J. K., and Colvin, V. L. "Hydrothermal Synthesis of Quartz Nanocrystals." *Nano Lett.*, 3 (2003): 655-659.

Buhro, W. E., and Colvin, V. L. "Semiconductor Nanocrystals - Shape Matters." *Nature Materials*, 13 (2003): 1705-1709.

Mittleman, D., Prasad, T., Colvin, V. "Superprism phenomenon in three-dimensional macroporous polymer photonic crystals." *Phys. Rev. B*, 67 (2003): 165103-1 - 165103-7.

Colvin, V. L. "The potential environmental impact of engineered nanomaterials." *Nat. Biotechnol.*, 21 (2003): 1166-1170.

Y. Gao, R. Wahi, A. T. Kan, J. C. Falkner, V. L.Colvin, and M. B.Tomson "Adsorption of cadmium on anatase nanoparticles: Effect of crystal size and pH." *Langmuir*, 20 (2004): 8585-8593.

W. Yu, J. C. Falkner, B. Shih, and V. L. Colvin "Preparation and characterization of monodisperse PbSe nanocrystals in a non-coordinating solvent." *Chem. Mater.*, 16 (2004): 3318-3322.

A. M. Al-Somali, K. M. Krueger, J. C. Falkner, and V. L. Colvin "Recycling size exclusion chromatography for the analysis and separation of nanocrystalline gold." *Anal. Chem.*, 76 (2004): 5903-5910.

W. W.Yu, J. C. Falkner, C. T. Yavuz, V. L. Colvin "Synthesis of monodisperse iron oxide nanocrystals by thermal decomposition of iron carboxylate salts." *Chem. Commun.*, 20 (2004): 2306-2307.

C. M. Sayes, J. D. Fortner, W. Guo. D. Lyon, A. M. Byd, K. D. Ausman, Y. J. Tao, B. Sitharaman, L. J. Wilson, J. B. Hughes, J. L. West, V. L. Colvin "The differential cytotoxicity of water-soluble fullerenes." *Nano Lett.*, 4 (2004): 1881-1887.

Presentations

Presenter. "From Opals to Optics: Colloidal Crystals and Photonic Structures." University of Bologna, Departments of Chemistry and Chemical Engineering, Bologna, Italy. (Jan. 30, 2002)

"From Opals to Optics: Colloidal Crystals and Photonic Structures." Materials Forum, Georgia Institute of Technology, Atlanta, GA. (January, 2003)

"From Opals to Optics: Colloidal Crystals and Photonic Structures." University of Michigan, Ann Arbor, MI. (January, 2003)

Presenter. "From Wow to Yuck: The Environmental Implications of Nanotechnology." NSF International Workshop on Societal Implications of Nanotechnology, Lecce Italy. (Feb. 1, 2002)

Presenter. "From Opals to Optics: Colloidal Crystals and Photonic Structures." AMRI Conference/University of New Orleans, New Orleans, LA. (Feb. 8, 2002)

Awards

Research Fellow, Alfred P. Sloan. (2000).

Young Investigator, Beckman. (2000).

Award: “Top 20 Young Scientists to Watch,” Discover Magazine. (2000).

Introduction: Overview of Nanotechnology and the Environment

July 12, 9:30-10:30 AM

Dr. Vicki Colvin, Professor of Chemistry and Professor of Chemical Engineering, Rice University

Abstract

Traditionally, nanotechnology has been motivated by the growing importance of very small (d < 50 nm) computational and optical elements in diverse technologies. However, this length scale is also an important and powerful one for living systems. At Rice, we believe that the interface between the 'dry' side of inorganic nanostructures and the 'wet' side of biology offers enormous opportunities for medicine, environmental technologies, as well as entirely new types of nanomaterials. As part of our work on the potential biological applications, we also consider the unintended environmental implications of water soluble nanomaterials. Given the breadth of nanomaterial systems, we use a carefully selected group of model nanoparticles in our studies and focus on natural processes that occur in aqueous systems. We characterize the size and surface-dependent transport, fate and facilitated contaminant transport of these engineered nanomaterials. Models from larger colloidal particles can be extended into the nanometer size regime in some cases, while in others entirely new phenomena present themselves. We also consider biological interactions of nanoparticles and specifically address the interactions of a classic nanomaterial, C_{60}, with cellular systems. While the water-suspendable nano-C60 nanocrystal is apparently cytotoxic to various cell lines, the closely related fully hydroxylated, $C_{60}(OH)_{24}$, is non-toxic, thus producing no cellular response. Similarly, we have also found that functionalized single-walled carbon nanotubes are non-toxic to cells in culture. More specifically, as the functionalization density of the SWNT increases, the nanotube becomes more inert to cultures.

Introduction: Overview of Nanotechnology and the Environment

July 12, 9:30-10:30 AM

Dr. Vicki Colvin, Professor of Chemistry and Professor of Chemical Engineering, Rice University

Highlights

Nanoparticles are defined as being less than 100 nm in size. Such small particles have huge surface areas, which can lead to increased reactivity. A vast array of nanomaterials is possible, each with its own exposure scenarios and applications. Manufacturing processes can allow for very specific control over size and chemical composition. Some examples of nanomaterials in commerce include sunscreens formulated with nano-sized TiO_2 and ZnO to be transparent, tennis balls lined with ceramic nanoparticles to enhance gas impermeability, and fabrics embedded with nanowhiskers to be stain/wrinkle resistant.

Balancing risks and benefits is key to the future of nanotechnology. We must be proactive in understanding risks, and ask difficult questions about risks/benefits for any new technology. We must be informed about implications as well as applications.

There are important applications for nanotechnology in drinking and waste water treatment – for example, magnetic filtration to treat arsenic in drinking water. The magnetic properties of iron oxide (magnetite) are such that arsenic strongly sorbs onto iron oxide. Smaller size improves magnetization because all dipoles point in the same direction. This can be applied to filtration by using magnets to control flow and distribution of the nano-sorbent. Advantages to magnetic filtration include the fact that there are no pressure gradients and no fouling of filters. Obstacles to the commercialization of this treatment system include the need for a testing site, a market, public confidence in the safety of the system, and funds for development.

Nanoparticles can interact with proteins, can be bioactive, and can be difficult to remove from environmental matrices or living organisms. There can be ecological, occupational, and residential risks for applications. Additionally, smaller materials are not necessarily more mobile; surface interactions can impact soil mobility. Strong interactions with clays, soils, etc. are possible. One example is C_{60} fullerenes. Fullerenes typically cluster in water, although the clustering is affected by water impurities (dirt, humic acid, etc.) and preparation conditions. Additionally, developmental toxicity investigations of C_{60} fullerenes in zebra fish indicate that oxidative stress can occur.

It is important to know the mechanisms by which nanomaterials behave in order to engineer safe nanoparticles. EPA has a crucial role to play in nanotechnology. Agency collaborations with researchers can help determine research directions and identify problems.

Question-and-Answer Session

A questioner asked how one sorts out conflicting information on mechanisms of toxicity of nanomaterials (e.g., sometimes reactive oxygen species (ROS) are the issue; sometimes surface area is the issue). Dr. Colvin replied that we aren't yet sure how to evaluate these things. Complete and careful characterization is essential; peer-reviewed journals should encourage publication of characterization papers. Researchers should participate in setting standards for characterization so that data from different studies can be compared. We can't compare papers, because nanoparticles are made and characterized differently each time. Quality control is an issue of emergent technology. A questioner asked about developing a strategy for gleaning data from incomplete datasets. Dr. Colvin indicated that there is no way to conduct conventional risk assessments for nanomaterials and obtain full data sets. Testing of nanomaterials needs to be performed, especially by companies that already have products on the market. In order to know about the toxicity of nanoparticles as a regulator, you need structure/function relationships and predictive tools. A commenter suggested parallel research tracks: 1) generic research to determine mechanistic attributes; and 2) product development on a specific product, investigating toxicity endpoints as part of the development process.

A questioner asked, what past lessons can be used to inform the present situation? Dr. Colvin noted that risk communication is very important; we should always focus on giving the public the highest level of information possible as quickly as possible, and without spin. The key is to educate consumers on risks and benefits. Engaging the public early in the process is important to public acceptance.

A questioner asked what kind of testing has been done on materials that are in the marketplace now. Dr. Colvin indicated that it depends on whether the materials considered new. If they are not new, then no new testing is required. A questioner wondered about the difference between nanotechnology and colloid chemistry. Dr. Colvin indicated that the understanding of nanoparticles in liquids is based on colloid chemistry, but colloid chemistry does not explain structure/function of nanoparticles. Nanomaterials can be highly structured, often with additional optical and/or magnetic properties. One can't rely on colloids to predict all nanoparticle behavior.

A questioner asked how we develop principles for being honest about what we know/don't know about nanotechnology. Dr. Colvin responded that people want to hear either "these are the risks," or "we don't know what the risks are." In development of other new technologies, investigators have engaged social scientists and ethicists early on (e.g., genome project). You can't say "this is new and cool, so give me money to develop it" and at the same time say that it is no different from existing materials and does not need additional scrutiny. An industry representative commented that his industry is developing a product stewardship and framework for new products for health and environmental effects. A commenter also noted that the Federal government is doing work in this area (e.g., a report outlining needed information on environmental health and safety of nanoparticles, NSETC committee).

Nanotechnology and the Environment

OSWER Conference
July 12-13, Washington DC

CBEN
Center for Biological and Environmental Nanotechnology

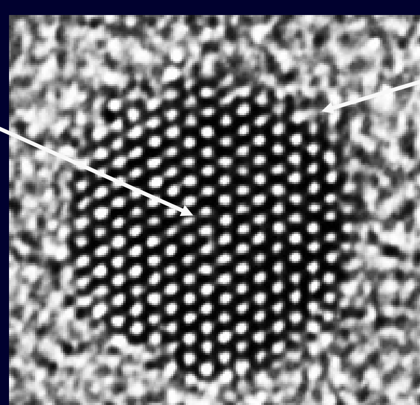
Dr. Vicki Colvin
Director, CBEN
Professor of Chemistry
Rice University

Small is Beautiful

Highly crystalline

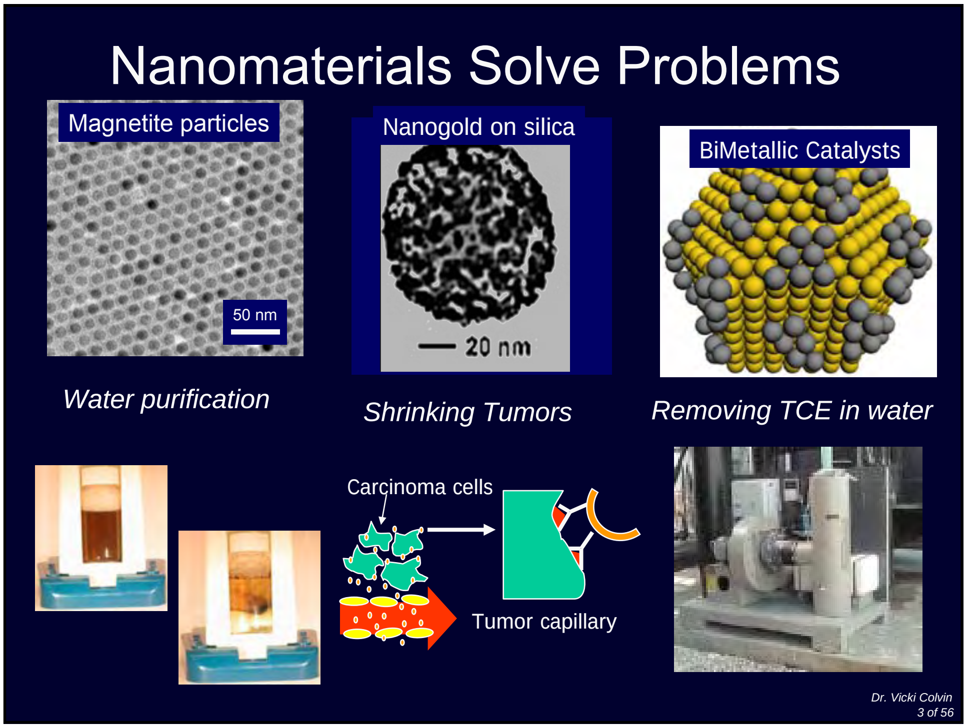
Huge surface areas

C-sixty
1nm



Cadmium Selenide nanocrystal
6 nm

Lysozyme
3 nm


Nanomaterials Solve Problems
Magnetite particles
50 nm
Nanogold on silica
20 nm
BiMetallic Catalysts
Water purification
Shrinking Tumors
Removing TCE in water
Carcinoma cells
Tumor capillary
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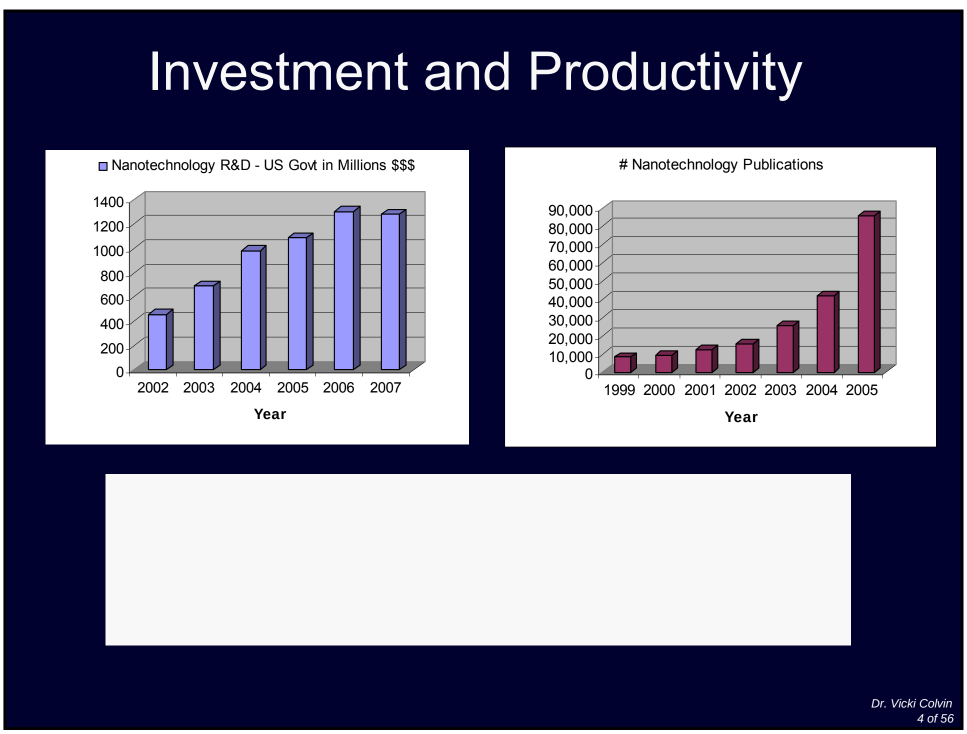
3 of 56


Investment and Productivity
Nanotechnology R&D - US Govt in Millions $$$
1400
1200
1000
800
600
400
200
0
2002 2003 2004 2005 2006 2007
Year
Nanotechnology Publications
90,000
80,000
70,000
60,000
50,000
40,000
30,000
20,000
10,000
0
1999 2000 2001 2002 2003 2004 2005
Year
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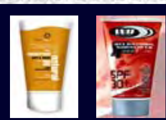
4 of 56

Nanotechnology: It's Here

Product	"Nano Inside"	Value Added
	Active Ingredient: Nanoscopic TiO_2/ZnO	Transparency
	Lined with Ceramic Nanoparticles	Gas Impermeability
	Embedded with "Nano Whiskers"	Stain- and Wrinkle-Resistance

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5 of 56

From "Wow" to "Yuck"?

DDT cured malaria → Endangered birds

Pesticides improved crop yields → Toxic to animals

Refrigerants made houses cool → Lead to ozone hole

Asbestos improved insulation → Liability expenses

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6 of 56

Today's Talk

Benefits

Risks

1. Applications of nanomaterials in water treatment
   Example: Nanosized magnetite for arsenic removal

2. Is size dangerous? Implications of nanotechnology

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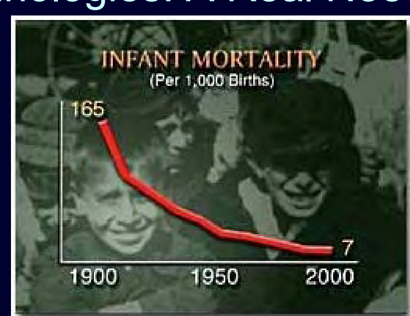
7 of 56

Water Treatment Technologies: A Real Need



- Waterborne illnesses major cause of death
- Increasing contamination in water
- Population growth increasing demand

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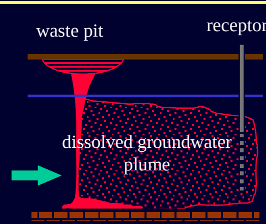
8 of 56

Nanomaterials in Water Treatment

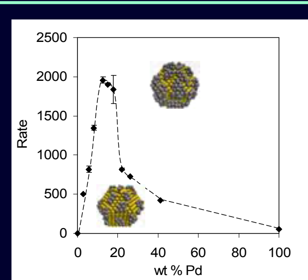


J. Zhang, LeHigh University

Small size provides high surface area

↓

In-situ remediation of contaminated wells



M. Wong, Rice University

Small size provides reactive surface

↓

100-fold improvement in TCE removal

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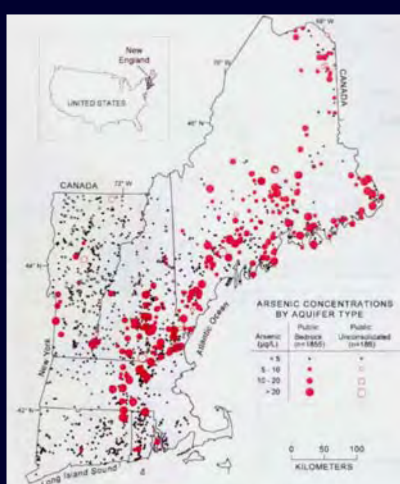
9 of 56

Arsenic in Drinking Water



Ayotte et al, Envi. Sci. Tech. 2003 37, p.2075

- Arsenic in water linked to cancer
- EPA standards: 50 ug/L to 10 ug/L
- Natural and anthropogenic sources
- Enormous interest in removal
  - Plants (phytofiltration)
  - Muds and sediments
  - Zero valent iron – in-situ
  - Mine tailings (e.g. iron oxides)

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10 of 56

Existing Sorbents for Arsenic Removal

" Our two year study showed that none of the (18) Arsenic Removal Plants could maintain arsenic in … water … below the WHO guidelines ...."
- Hossain *et al* in ES&T 2005, p. 4300

Material	Sorbent (kg) / month	1 gram treats _____ L water	Waste to dispose of kg (1 yr)	Backwash frequency (day)
Alumina + Metal Oxide	0.24	3.8	2.88	14
Red Mud [As(III)]	360.7	0.002	4328.1	Periodic
Ion Exchange	No Removal of Toxic As(III)			~ 3

For a family of four, using 900 L water/month, at 500 ppb As levels (7.9 pH)

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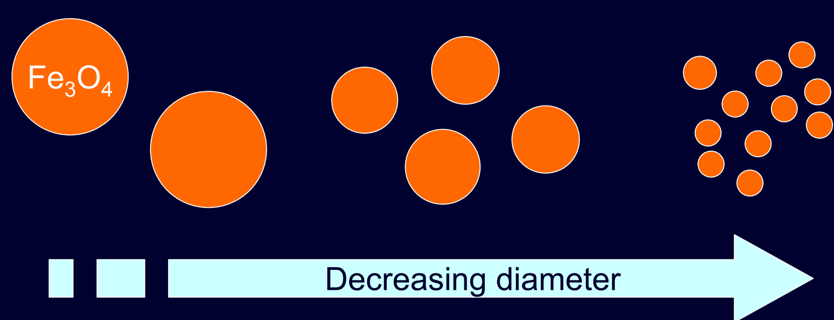
11 of 56

Nanomagnets: Two Advantages



1. Increased surface area for arsenic sorption

2. Enhanced magnetic susceptibilities improve separations

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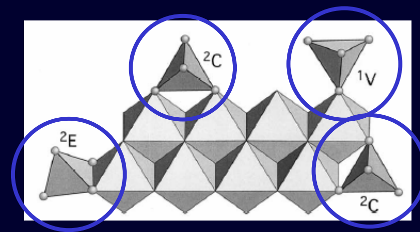
12 of 56

Arsenic sorption onto iron oxides

- *Strong and specific sorption*
- *Chemical transformation*
- *Subjected to interferences*
  - *Silicate and phosphates*
  - *Humic acids*



Models for surface interactions*

Are Nanoscale iron oxides are good candidates for sorbents?

MASON TOMSON, AMY KAN, SUJIN YEAN

* D. M. Sherman, S. R. Randall Geochimica et Cosmochimica v. 67 no. 22 p. 4223

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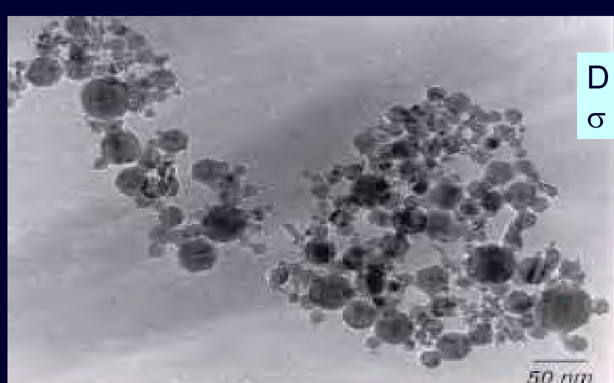
13 of 56

Commercial nanoscale iron oxides



D = 25 nm
σ ~ 35%

http://www.kemcointernational.com/IronOxide.htm

As particle size gets smaller sorptive area increases with R^2

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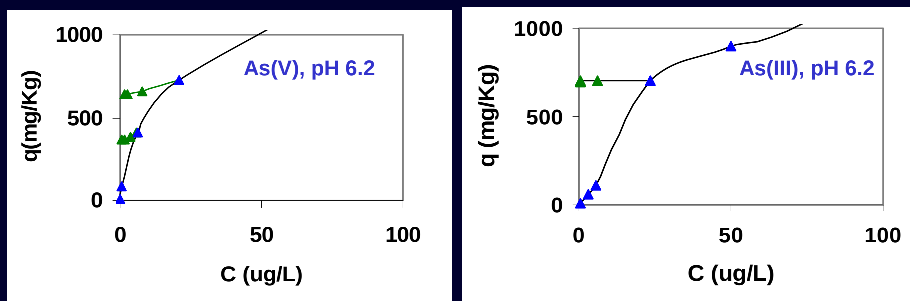
14 of 56

Sorption of Arsenic Onto Magnetite



- 20 nm Magnetite can sorb both As(V) and As(III)
- Sorption capacities (▲) of .1 % (w/w)
- Arsenic is irreversibly sorbed (▲) stable in storage

MASON TOMSON, AMY KAN – Rice University

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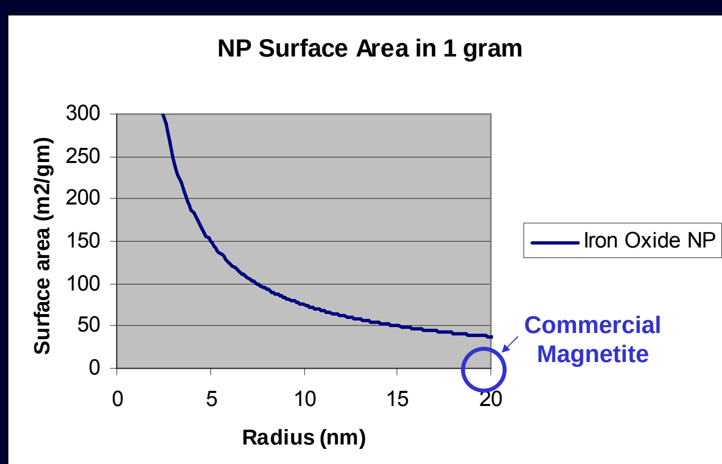
15 of 56

Size dependence: Surface Area



Surface area in 1 gram ~ $4 \pi r^2 / (4/3 \pi r^3 \cdot \text{density})$

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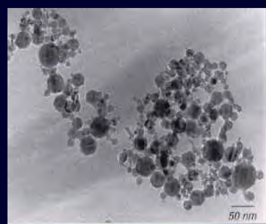
16 of 56

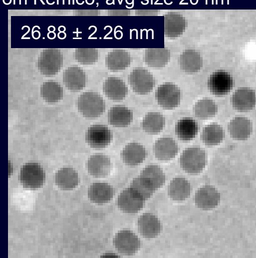
Synthesis of monodisperse nano-Fe_3O_4

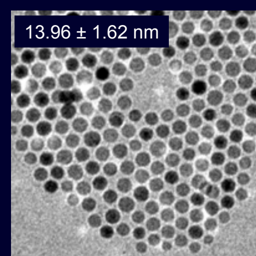


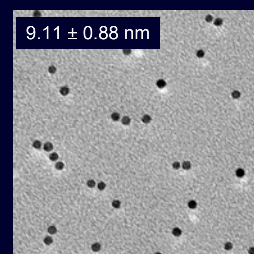
From Kemico, avg size 20 nm

Commercial nano-oxides have problems

- Agglomerated → poor magnetic separation
- Larger nanoparticles → lower sorption
- Bad size distribution → no optimization







W. Yu, V. L. Colvin, Chem. Comm. (2004)

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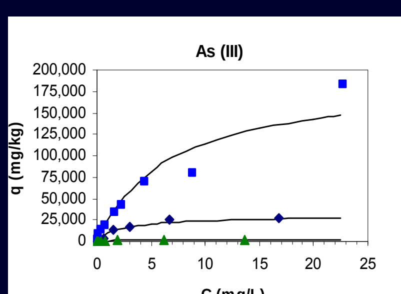
17 of 56

Nanomagnets: Large Sorption Capacity

Volume of water treatable by 1 Kg magnetite



Particle Size (nm)		Volume of Water (L)
12	As(III)	2,283
20	As(III)	594
300	As(III)	21
12	As(V)	1,435
20	As(V)	1,145
300	As(V)	150

Remaining Challenge: Nanoparticles are difficult to remove

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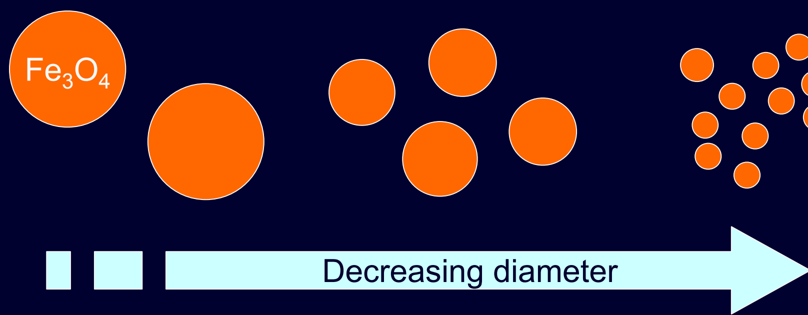
18 of 56

Nanomagnets: Two Advantages



1. Increased surface area for arsenic sorption
2. Enhanced magnetic susceptibilities improve separations

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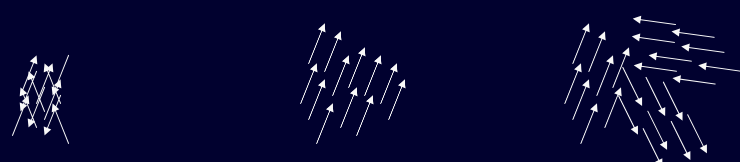
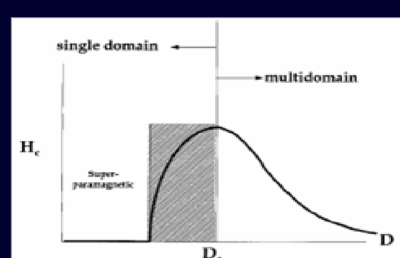
19 of 56

"Nano" Improves Magnetic Behavior



Small cluster: Supraparamagnetic	Larger cluster: Single Domain	Bulk solid: Permanent magnet
Easy to magnetize	Magnetization can shift	Small magnetization

Nanocrystals are better magnets than larger bulk materials



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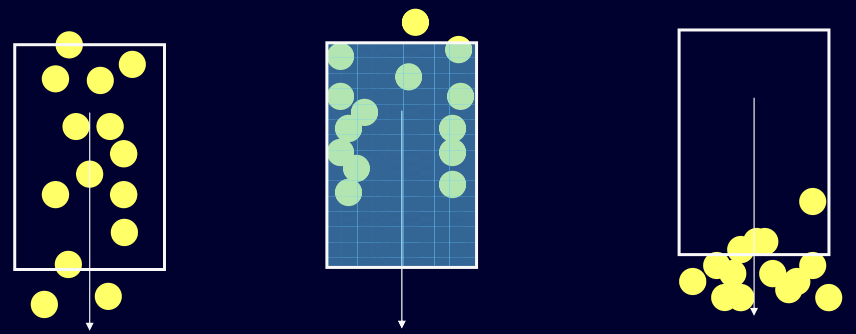
20 of 56

Magnetic Filtration for Nanosorbents



- Requires no pressure gradients
- No fouling of separation system

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21 of 56

Magnetic Separations in Water Treatment

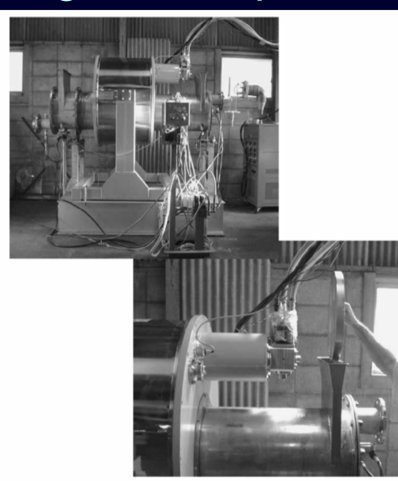

Fig. 4. Superconductive magnet used in the 500 tons/day plant.

- Gravitational settling
- Filtration
- Induced coagulation
- Magnetic Separations

External fields >> 1- 2 Tesla
Particle sizes >> 50 nm

Kakihara, Y., T. Fukunishi, et al. (2004). "Superconducting high gradient magnetic separation for purification of wastewater from paper factory." Ieee Transactions on Applied Superconductivity **14**(2): 1565-1567.

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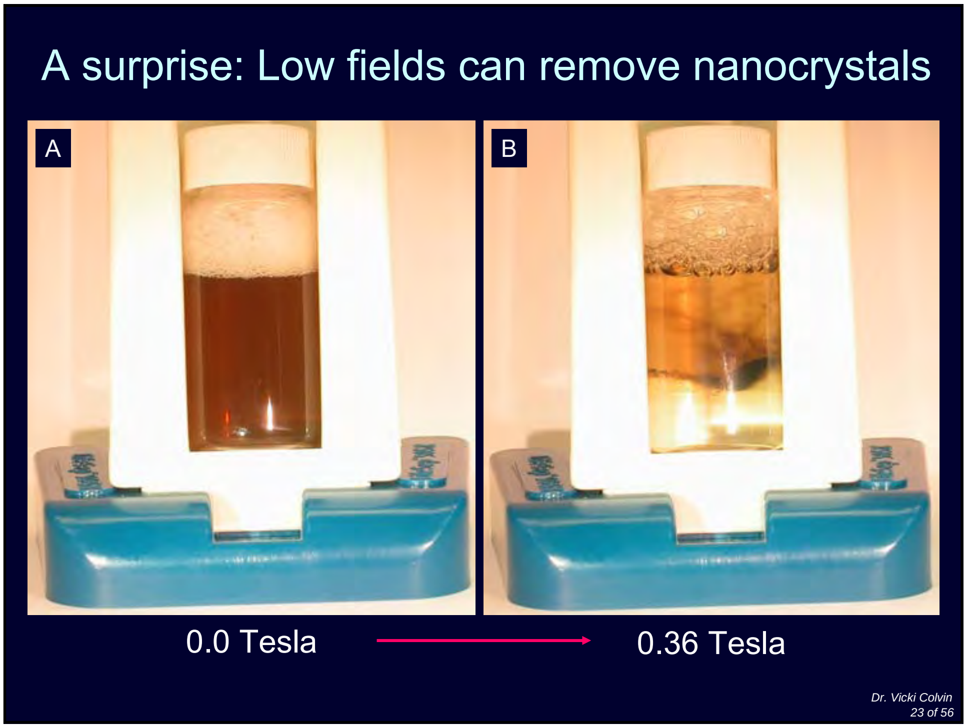
22 of 56


A surprise: Low fields can remove nanocrystals
A
B
0.0 Tesla
0.36 Tesla
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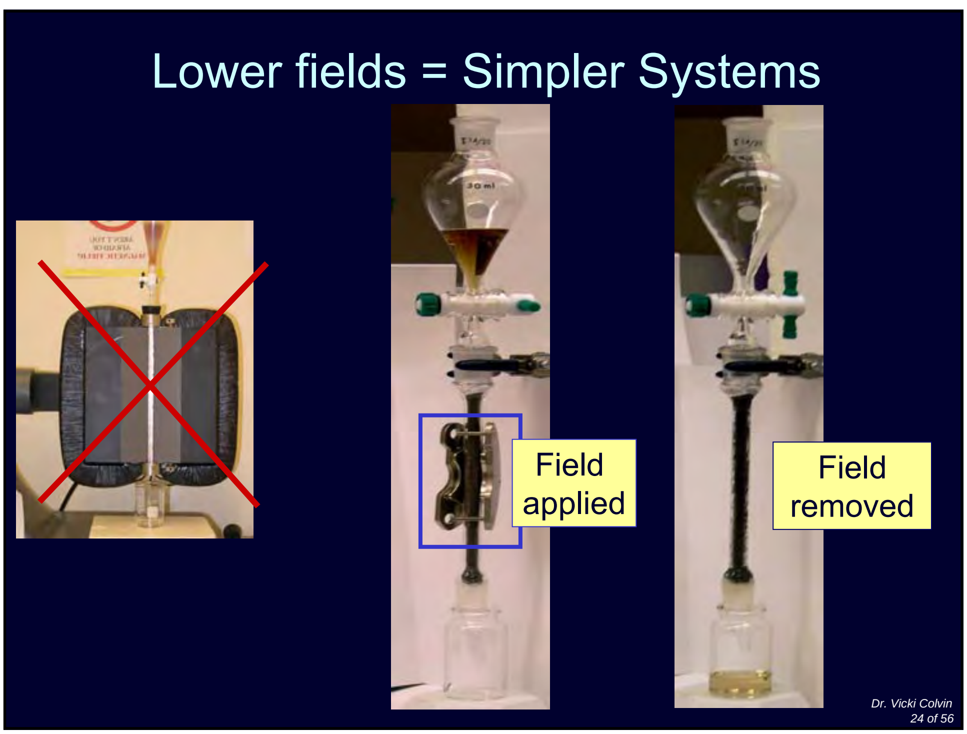
23 of 56


Lower fields = Simpler Systems
Field applied
Field removed
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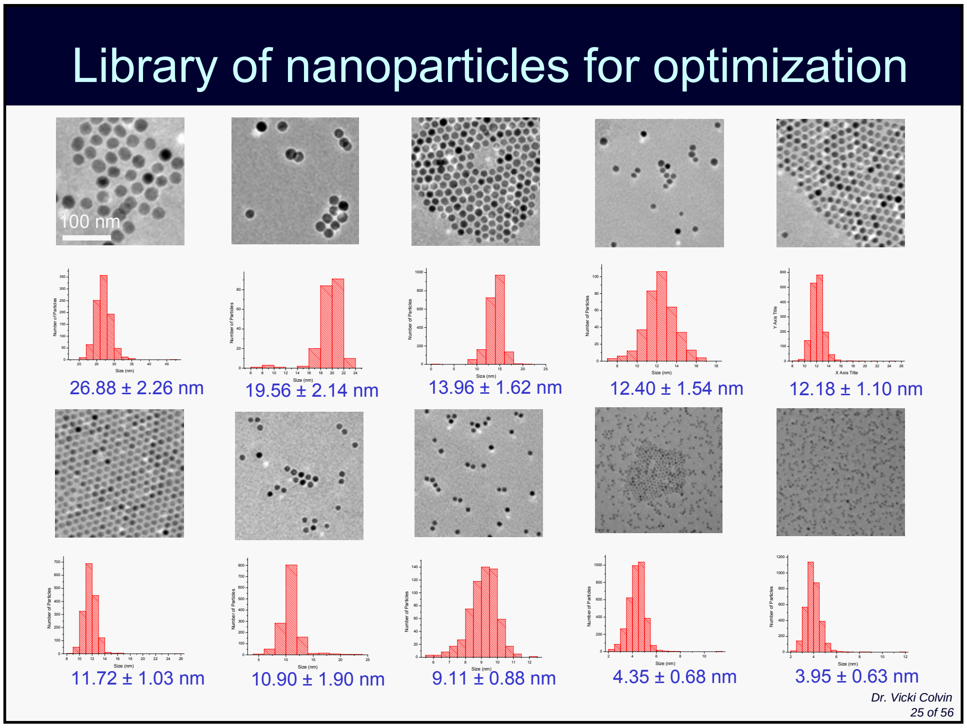
24 of 56


Library of nanoparticles for optimization
100 nm
26.88 ± 2.26 nm
19.56 ± 2.14 nm
13.96 ± 1.62 nm
12.40 ± 1.54 nm
12.18 ± 1.10 nm
11.72 ± 1.03 nm
10.90 ± 1.90 nm
9.11 ± 0.88 nm
4.35 ± 0.68 nm
3.95 ± 0.63 nm
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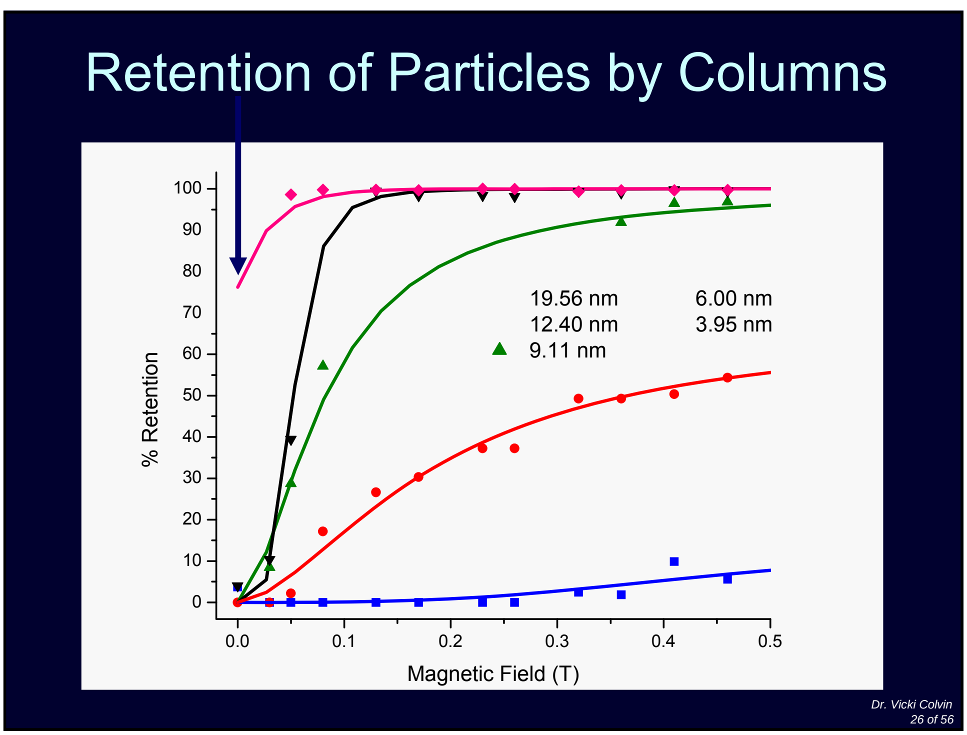
25 of 56


Retention of Particles by Columns
% Retention
100
90
80
70
60
50
40
30
20
10
0
0.0
0.1
0.2
0.3
0.4
0.5
Magnetic Field (T)
19.56 nm
12.40 nm
9.11 nm
6.00 nm
3.95 nm
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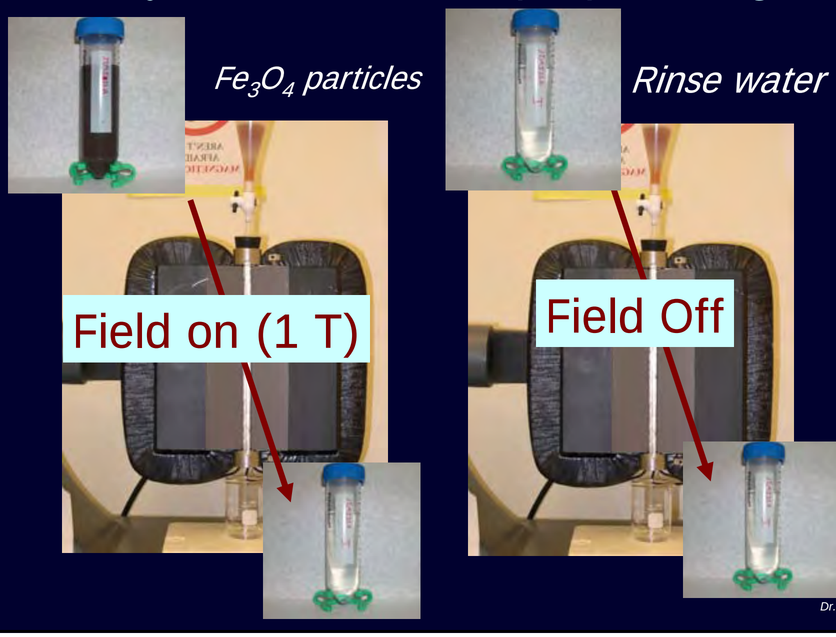
26 of 56

Nanocrystals must be supraparamagnetic



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27 of 56

Existing Sorbents for Arsenic Removal

Material	Sorbent (kg)/ month	1 gram treats ____ L water	Annual waste to dispose kg [3]	Backwash Frequency (day)	Efficiency[1]
Alumina + Metal Oxide	0.24	3.8	2.88[3]	14	0.003
Red Mud [As(III)]	360.7	0.002	4328.1[3]	Periodic	~0.003
Ion Exchange	No Removal of Toxic As(III)			~ 3	0.014
Nanoscale Iron Oxides	**0.09**	**10**	**1.1**	**0**	**~7.5 to 75 [2]**

1. "Efficiency" as defined by NAE in the "Granger Challenge, June, 2005" The object is to maximize the efficiency.
2. 12 nm magnetite cost estimated as a synthesized chemical at $2.00/lb and a multiplication factor of cost by 3x to 30x for estimated conditioning chemicals and packaging.
3. The amount (kg) + the backwash frequency

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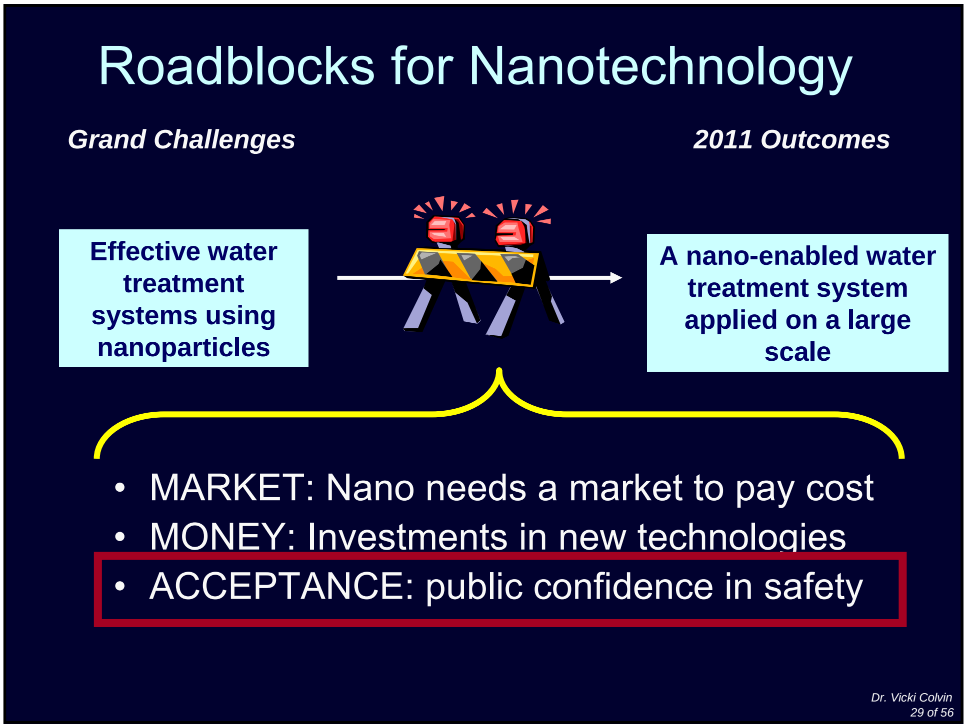
28 of 56


Roadblocks for Nanotechnology
Grand Challenges
2011 Outcomes
Effective water treatment systems using nanoparticles
A nano-enabled water treatment system applied on a large scale
• MARKET: Nano needs a market to pay cost
• MONEY: Investments in new technologies
• ACCEPTANCE: public confidence in safety
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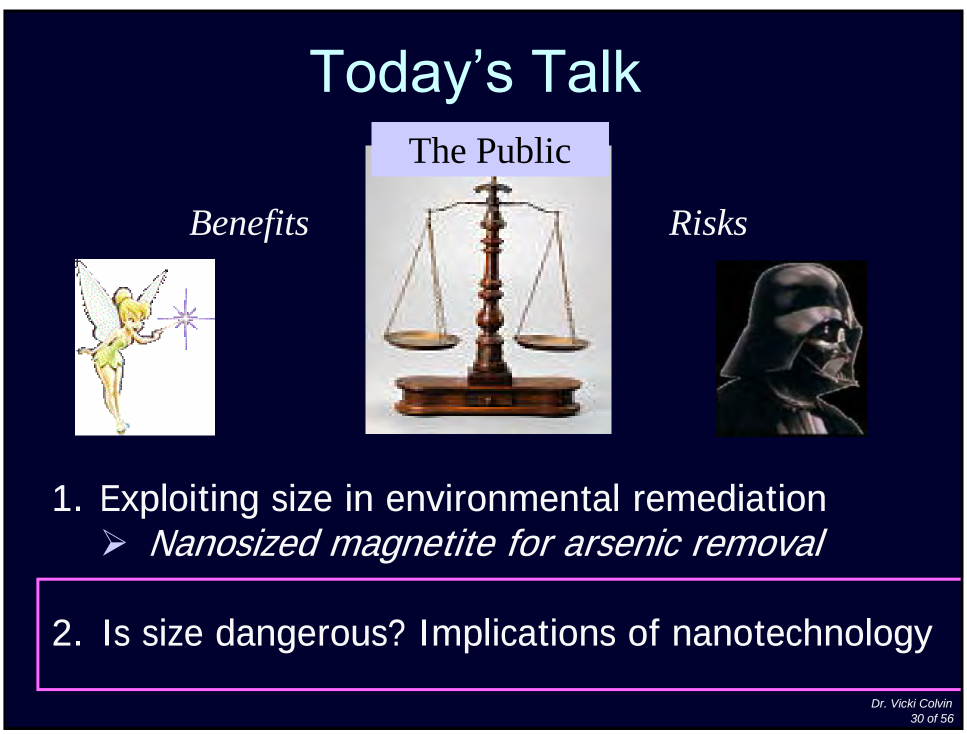
29 of 56


Today's Talk
The Public
Benefits
Risks
1. Exploiting size in environmental remediation
➢ Nanosized magnetite for arsenic removal
2. Is size dangerous? Implications of nanotechnology
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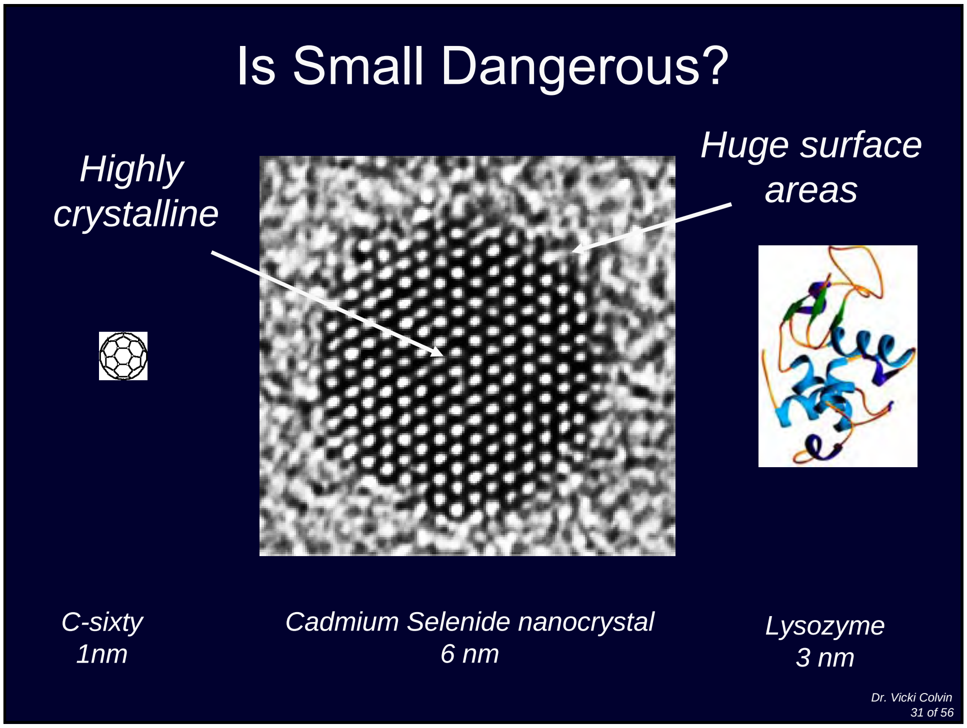
30 of 56


Is Small Dangerous?
Highly crystalline
Huge surface areas
C-sixty
1nm
Cadmium Selenide nanocrystal
6 nm
Lysozyme
3 nm
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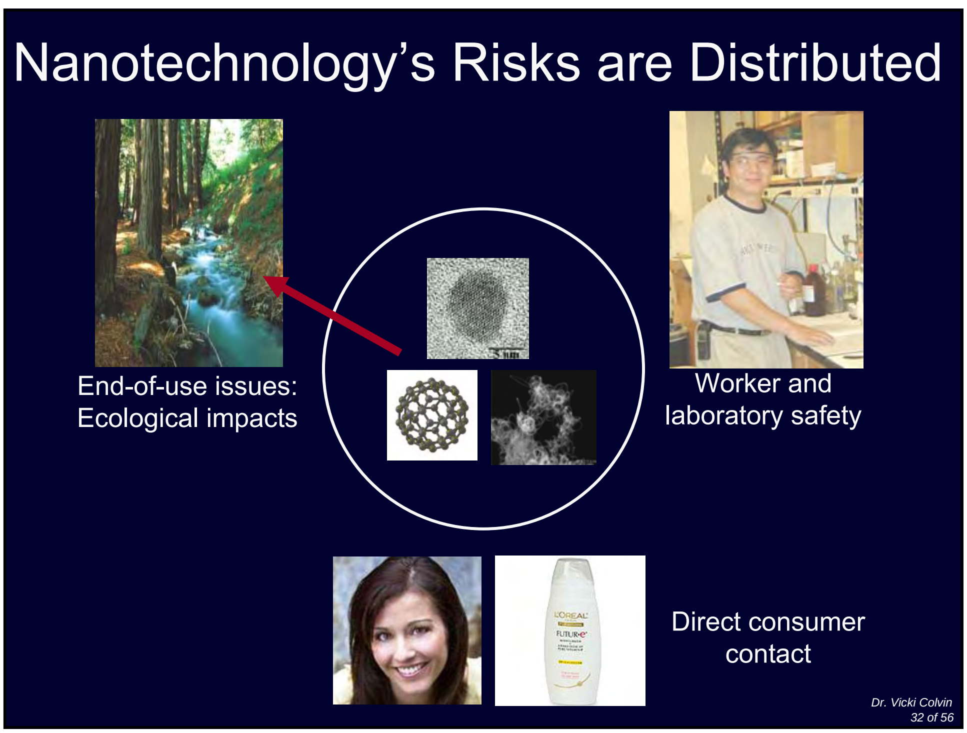
31 of 56


Nanotechnology's Risks are Distributed
End-of-use issues:
Ecological impacts
Worker and
laboratory safety
Direct consumer
contact
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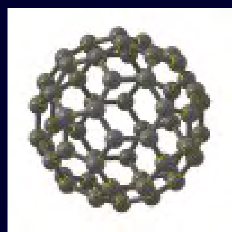
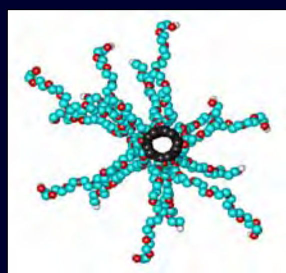
32 of 56

Carbon nanostructures: Model Systems



C-sixty or C_{60}
- Factory production (Frontier Carbon)
- Highly controlled "molecular" species
- Fuel cells, face creams, medical treatments
- Extremely hydrophobic in pristine state



Single-walled Carbon Nanotubes (SWNT)
- Factory production (CNI, NEC, Samsung)
- Complex mixtures, distributions of types
- Flat panel displays, composites
- Extremely hydrophobic in pristine state

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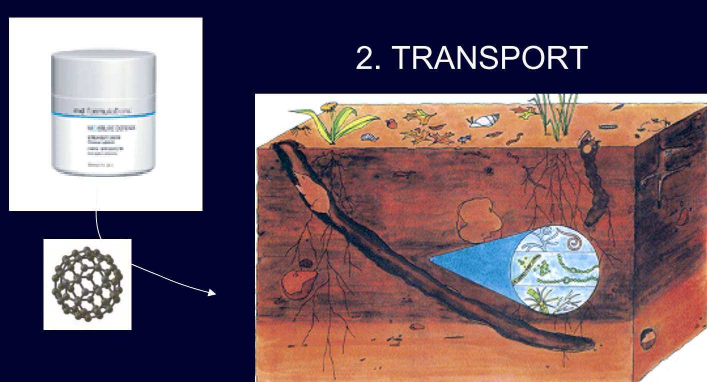
33 of 56

Risk : From Source to Receptor



Risk = Exposure • Effect

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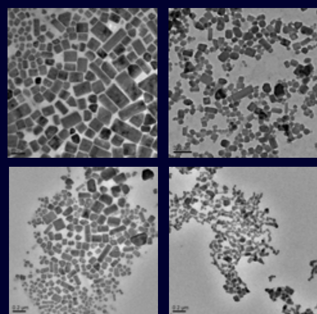
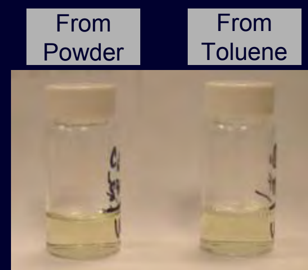
34 of 56

Environmental Chemistry of Fullerenes





Yellow suspensions

Hydrophobic fullerenes CLUSTER when they sit in water

Preparation conditions affect CLUSTERING and BEHAVIOR

Dirt and other residues stick to CLUSTERS in groundwater

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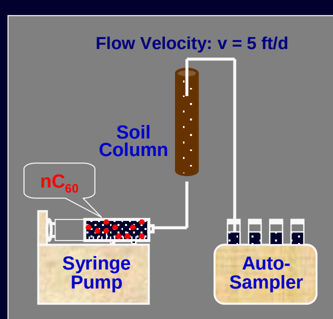
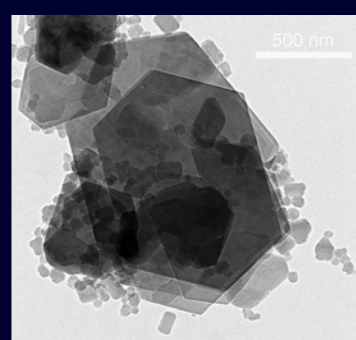
Movement of Nanoparticles in Soils





- SMALL ≠ MOBILE (nanoparticles are sticky)
- MODELS too predict distribution in soil/water

Wiesner (Duke); Hughes (GaTech)

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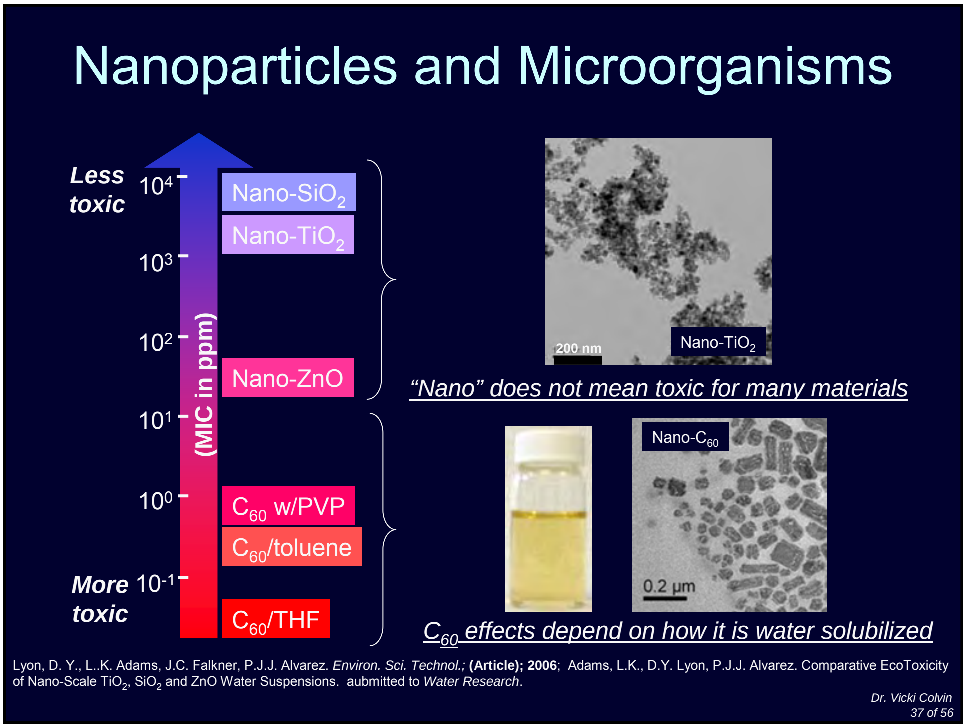
36 of 56


Nanoparticles and Microorganisms
Less toxic
More toxic
(MIC in ppm)
10^4
10^3
10^2
10^1
10^0
10^-1
Nano-SiO2
Nano-TiO2
Nano-ZnO
C60 w/PVP
C60/toluene
C60/THF
200 nm
Nano-TiO2
"Nano" does not mean toxic for many materials
Nano-C60
0.2 μm
C60 effects depend on how it is water solubilized
Lyon, D. Y., L..K. Adams, J.C. Falkner, P.J.J. Alvarez. Environ. Sci. Technol.; (Article); 2006; Adams, L.K., D.Y. Lyon, P.J.J. Alvarez. Comparative EcoToxicity of Nano-Scale TiO2, SiO2 and ZnO Water Suspensions. submitted to Water Research.
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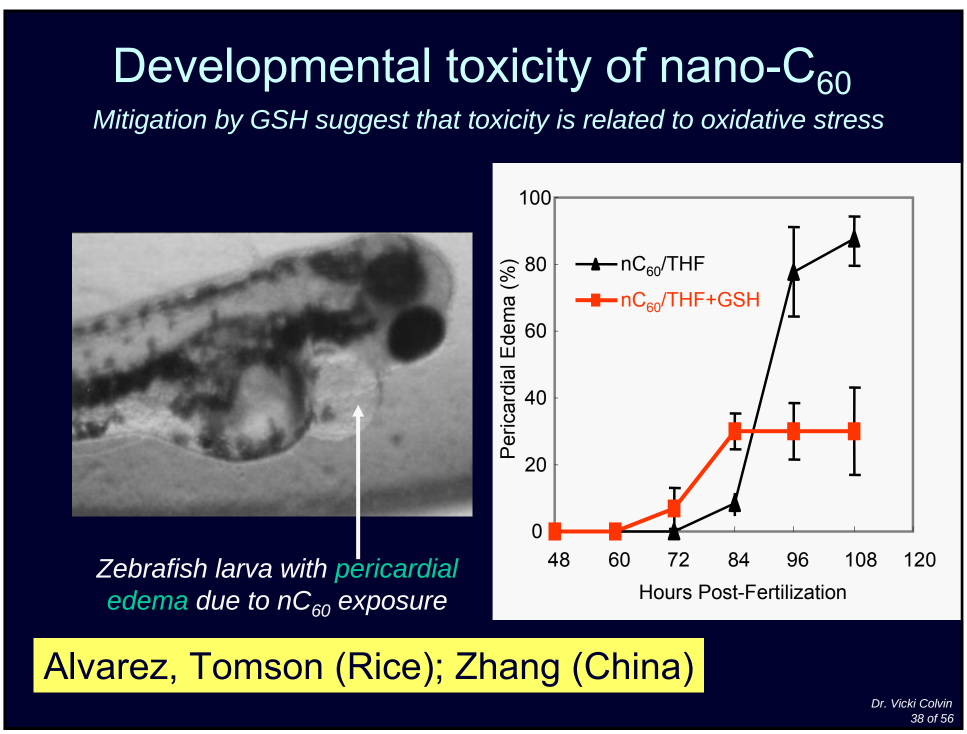
37 of 56


Developmental toxicity of nano-C60
Mitigation by GSH suggest that toxicity is related to oxidative stress
Zebrafish larva with pericardial edema due to nC60 exposure
Pericardial Edema (%)
100
80
60
40
20
0
nC60/THF
nC60/THF+GSH
48
60
72
84
96
108
120
Hours Post-Fertilization
Alvarez, Tomson (Rice); Zhang (China)
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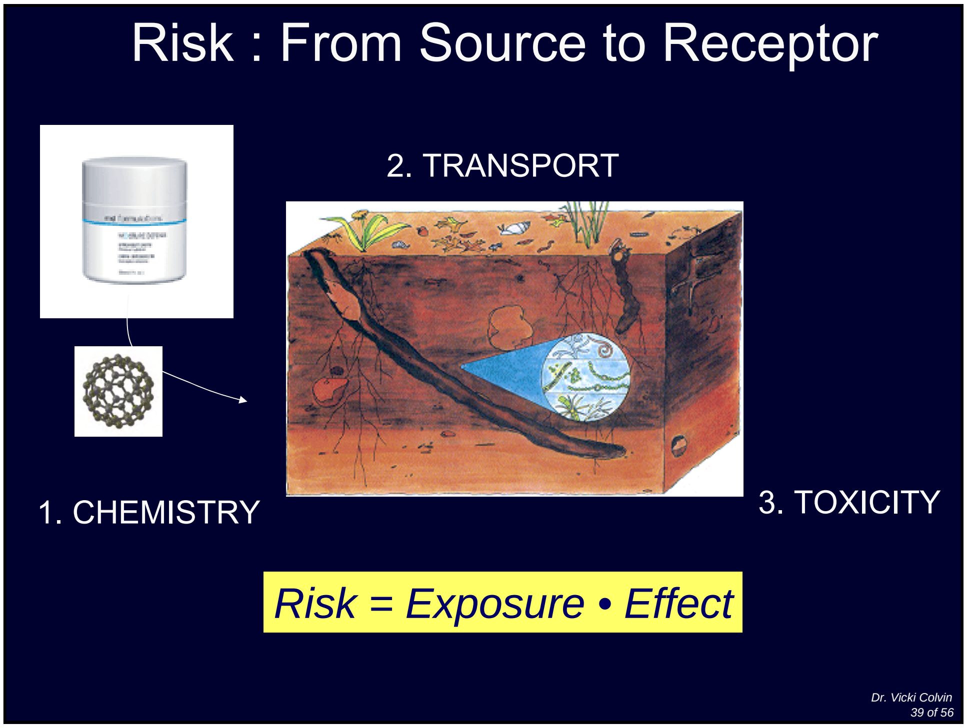
38 of 56


Risk : From Source to Receptor
2. TRANSPORT
1. CHEMISTRY
3. TOXICITY
Risk = Exposure • Effect
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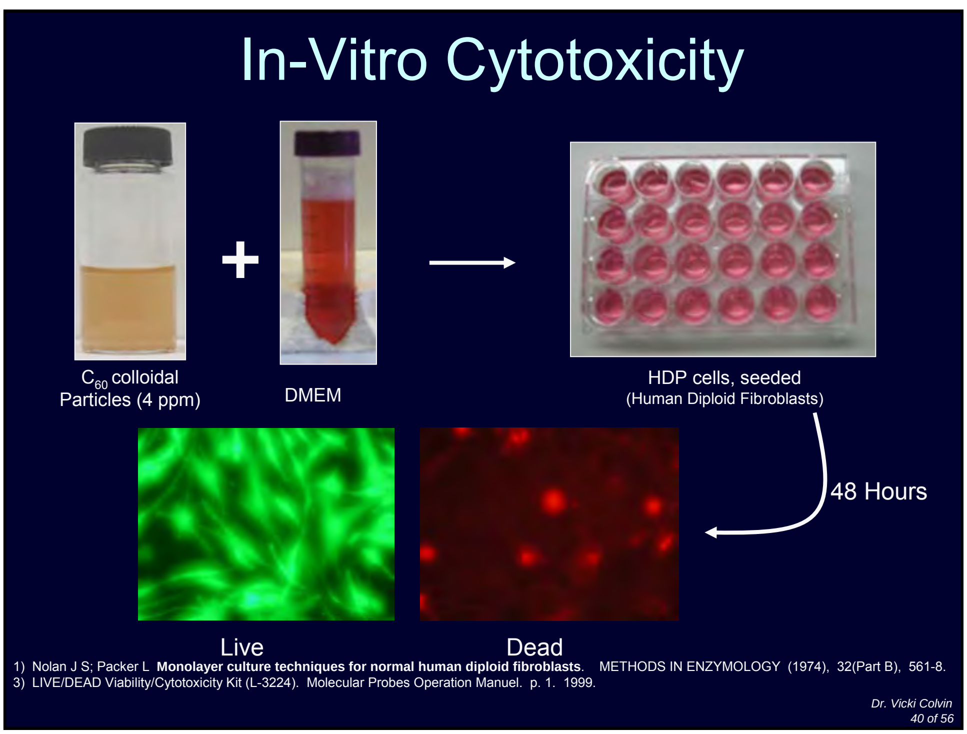
39 of 56


In-Vitro Cytotoxicity
C60 colloidal Particles (4 ppm)
DMEM
HDP cells, seeded
(Human Diploid Fibroblasts)
48 Hours
Live
Dead
1) Nolan J S; Packer L Monolayer culture techniques for normal human diploid fibroblasts. METHODS IN ENZYMOLOGY (1974), 32(Part B), 561-8.
3) LIVE/DEAD Viability/Cytotoxicity Kit (L-3224). Molecular Probes Operation Manuel. p. 1. 1999.
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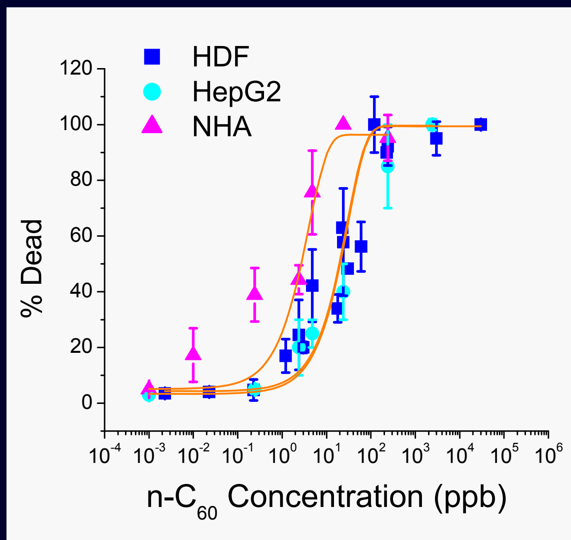
40 of 56

Dose Response Curve for n-C_{60}



Human Cell Line	LC_{50} (ppm)
HepG2	0.05
HDF	0.02
NHA	0.002

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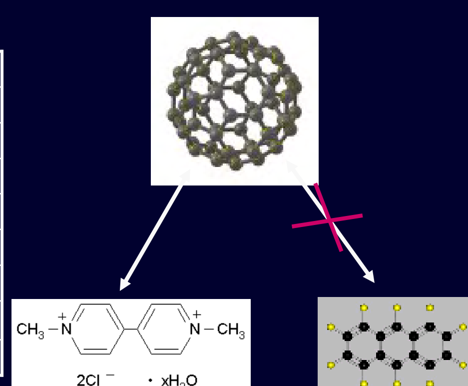
41 of 56

n-C_{60} Relative Cytotoxicity

Toxin	LC50, mg/kg
C_{60}-$(OH)_x$	> 100,000
Ethyl Alcohol*	17,000
THF	11,000
Toluene	1,600
Paraquat	100
Benzo[a]pyrene*	10
n-C_{60}	**0.02**
Dioxin*	0.001



* National Institute of Health, Registry of Cytotoxicity Data (ZEBET)

Aggregated C-sixty is a very toxic substance in cell culture

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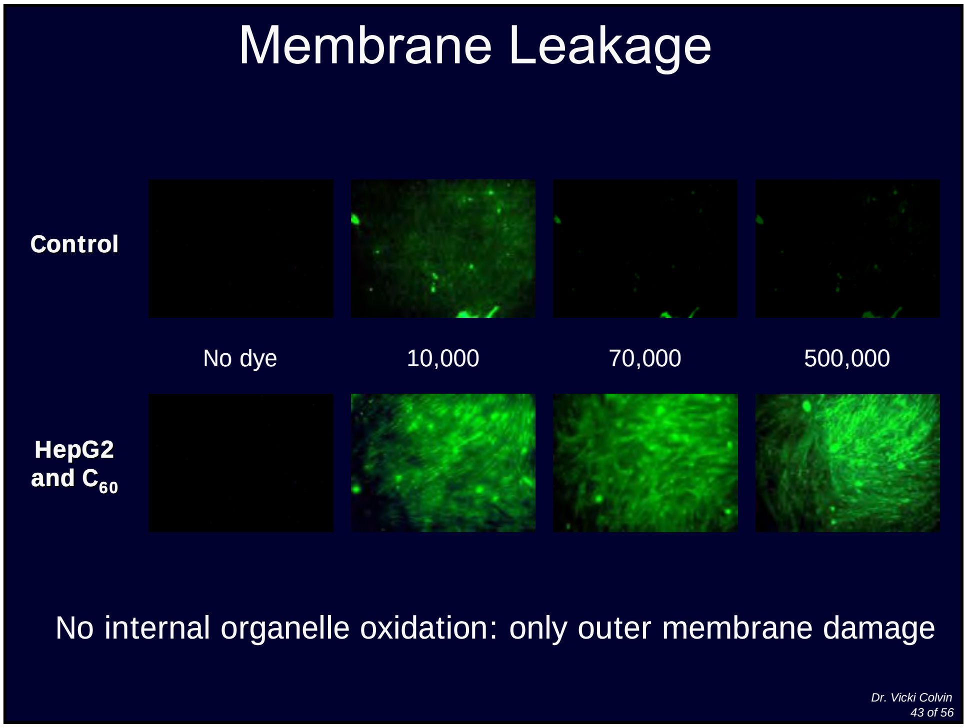
42 of 56


Membrane Leakage
Control
No dye
10,000
70,000
500,000
HepG2 and C60
No internal organelle oxidation: only outer membrane damage
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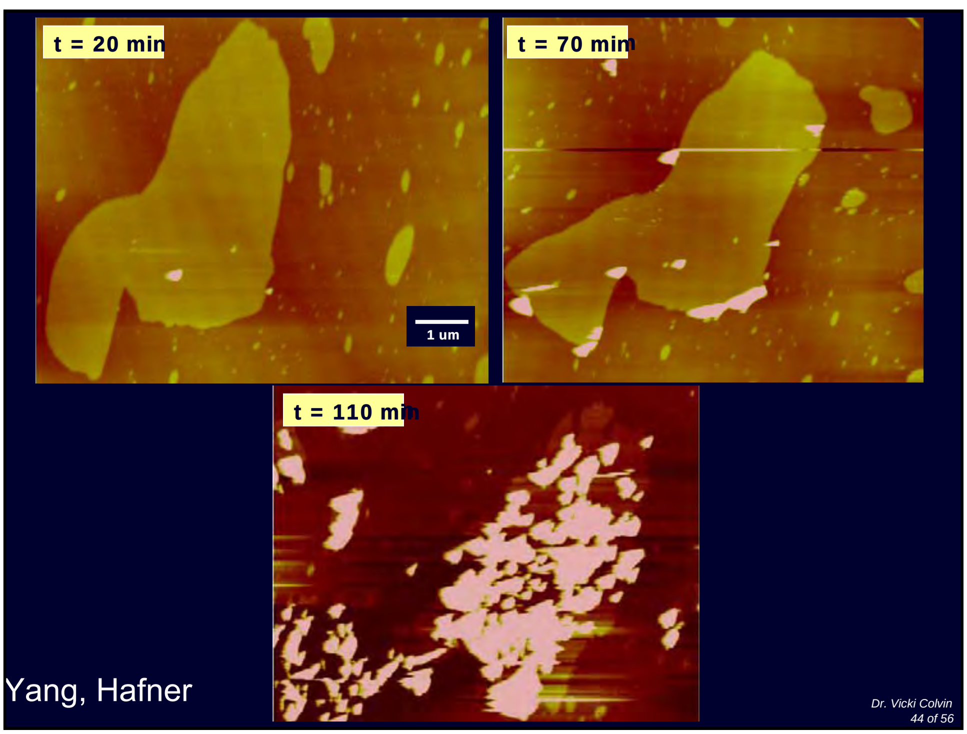
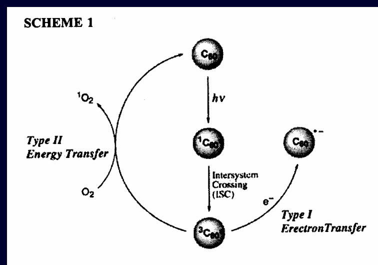
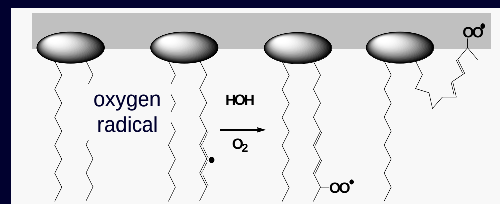
43 of 56


t = 20 min
t = 70 min
1 um
t = 110 min
Yang, Hafner
Dr. Vicki Colvin
44 of 56

Origins of fullerenes bioactivity





C_{60} can form superoxide anion, and singlet oxygen

C_{60} is also a highly lipophilic substance

Cytotoxic substance which destroys lipid membranes

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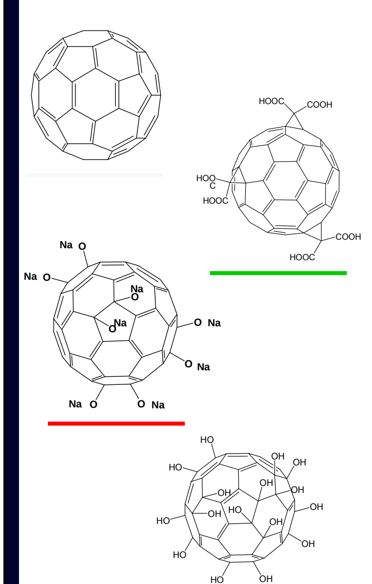
45 of 56

Systematic Variation of Surface Chemistry



Increasing derivatization lowers photoinduced singlet oxygen generation

More polar functionality creates higher water solubility in materials

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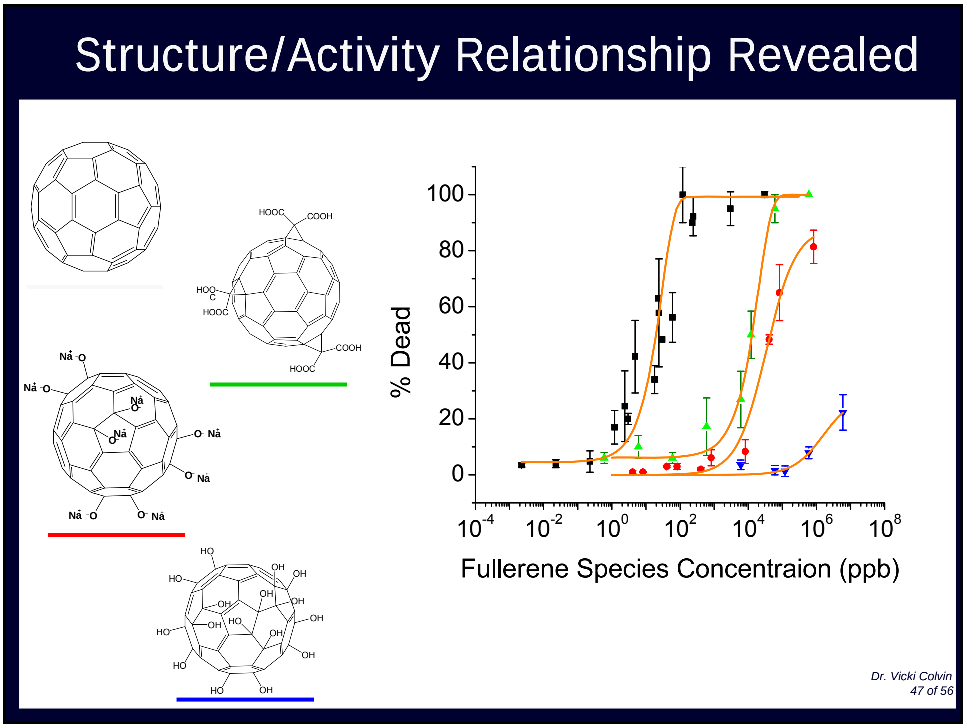
46 of 56


Structure/Activity Relationship Revealed
HOOC
COOH
HOOC
COOH
HOOC
Na O
Na O
Na
O Na
O Na
Na O
O Na
HO
OH
% Dead
100
80
60
40
20
0
10^{-4}
10^{-2}
10^{0}
10^{2}
10^{4}
10^{6}
10^{8}
Fullerene Species Concentraion (ppb)
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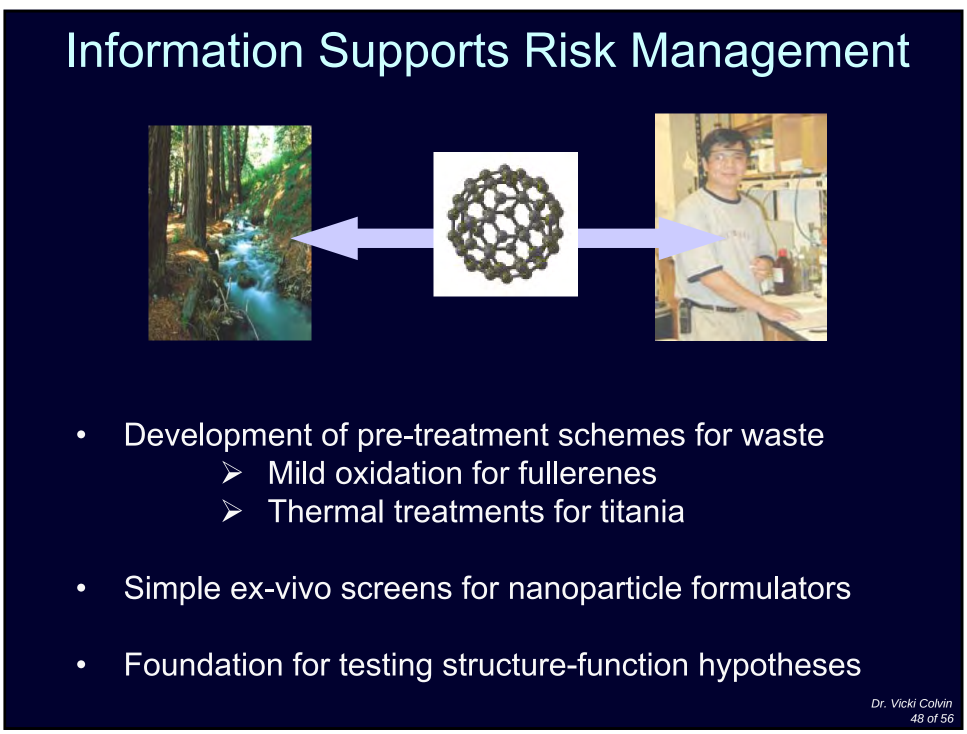
47 of 56


Information Supports Risk Management
• Development of pre-treatment schemes for waste
➢ Mild oxidation for fullerenes
➢ Thermal treatments for titania
• Simple ex-vivo screens for nanoparticle formulators
• Foundation for testing structure-function hypotheses
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48 of 56

Framing a new question

Are engineered nanoparticles dangerous?

↓

How can we engineer safe nanoparticles?

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49 of 56

Today's Talk

Benefits

Risks

1. Nanocrystalline magnetite irreversibly sorbs Arsenic
2. "Nano" makes magnetic separations practical
   1. *Higher removal at lower fields*
   2. *Very high surface areas increase capacity*
3. Ongoing implications work improves technology

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50 of 56

Acknowledgements

- **Dr. Christie Sayes**
- **John Fortner**
- Dr. Joe Hughes
- Dr. Jennifer West
- Joe Mendez
- Delina Lyon
- Adina Boyd
- Andre Gobin
- Yi Yang
- Raj Wahi
- Dr. David Warheit (DuPont)
- Dr. Wenh Guo
- Dr. Yitzhi Jane Tao
- Dr. Mason Tomson
- Dr. Kevin Ausman
- Dr. Jane Grande-Allen
- Dr. Lon Wilson
- Dr. Jason Hafner

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Center for Biological and Environmental Nanotechnology

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51 of 56

Want to learn more? Do more?

- Copies of presentation: colvin@rice.edu
- Center web page: http://cben.rice.edu//
- Check-out
  – ICON: http://icon.rice.edu/. Multi-stakeholder group devoted to minimizing risks of nanotechnology
  – Standards activities: http://www.astm.org. (E56) Help write standards on nanotechnology and risk assessment, management.

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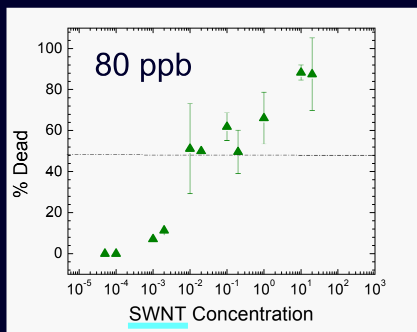
NanoX: Not Toxicology As Usual

Are single-walled carbon nanotubes toxic?



- 20 major types of SWNT
- 4 manufacturing types (trace impurities)
- Lengths ranging from 5 – 300 nm
- 5 methods of purification
- 10 possible surface coatings

> 50,000 SWNT samples

Basic structure-function relationships for nanomaterials and biological impacts are necessary

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53 of 56

Acknowledgements

- **Professor Mason Tomson**
- **Dr. Amy Kan**
- **Sunjun Yean**
- **Cafer Yavuz**
- **J. T. Mayo**
- **Arjun Prakash**
- **Dr. William Yu**
- **Yi Hua**
- **Josh Falkner**

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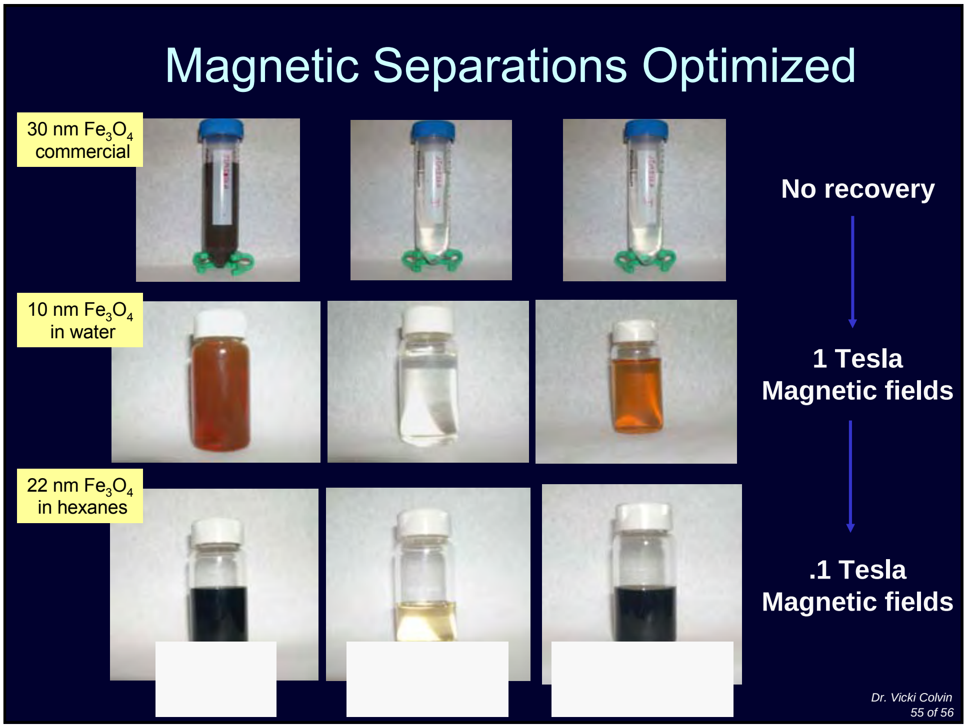

Arsenic Removal, with Magnetic Field

Particle Size (nm)	As(V) or As(III)	Initial As Concentration (mg/L)	Residual As Concentration (mg/L)	% Removal
12	As (III)	500	3.9	99.2
20	As (III)	500	45.3	90.9
300	As (III)	500	375.7	24.9
12	As (V)	500	7.8	98.4
20	As (V)	500	17.3	96.5
300	As (V)	500	354.1	29.2

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Dr. Stig Irving Olsen

Technical University of Denmark
Department of Manufacturing Engineering Management
Lyngby, Denmark

Dr. Stig Irving Olsen is a biologist with 17 years of experience in environmental science. The key areas of his work have been eco-toxicological and toxicological assessments of chemical substances and life cycle assessment.

Dr. Olsen has, among other assignments, worked on eco-toxicological and toxicological evaluation of pesticides, elaboration of EU-classification proposals for substances, toxicological evaluation of plastic materials, and methodological development of toxicological and ecotoxicological assessments in LCA where comparative evaluation are important. In this connection he was a co-chairman of the SETAC-Europe working group on assessment of toxicological impacts in LCA.

Dr. Olsen spent one year at European Chemicals Bureau (ECB) acquiring further, extensive knowledge about the EU risk assessment scheme a.o. through working on the revision of the technical guidance document for risk assessment of chemicals. Particular emphasis was put on the comparative aspects of LCA and RA in, e.g., substitution and the feasibility of using LCA in the risk management of chemicals.

Since January 2005 the focus of his work has been on environmental assessment of micro/nano production in a life cycle perspective. Dr. Olsen is an expert member of the Danish Technological Council work group on nanotechnology and toxicology.

Session 1: Life Cycle of Nanomaterials

July 12, 10:30-11:30 AM

Dr. Stig Irving Olsen, Technical University of Denmark, Department of Manufacturing Engineering Management, Lyngby, Denmark

Abstract

The concept of life cycle assessment (LCA) is built upon the functional unit, i.e., all impacts, etc., are related to a specific service or function in the society. In an LCA context, the assessment of emerging technologies like Nanotechnology is challenging due to a number of knowledge gaps. It may not be known exactly what the function is (or functional unit) or what the technology may substitute, and production may still be at an experimental level, raising questions about technology or choice of materials.

Nanotechnology apparently has great potentials in reducing energy requirement of products use stage, increasing energy production efficiency, reducing materials in the use stage, etc. Nanotechnological products are emerging on the market, but studies on the life cycle environmental impacts are still very limited. Nonetheless, several potential environmental aspects can be identified which can question the sustainability of nanotechnologies. For example, energy intensive manufacturing efforts, high requirement to materials, potential impacts due to release of nanomaterials in the use stage or end of life, and problems with recycling of materials are all potential environmentally problematic properties of nanotechnologies.

Due to the state of development of nanotechnologies prospective, LCA studies methodologies like “consequential LCA” may be useful because future changes are taken into account. However, it still does not suffice for emerging technologies. In a recent “Green Technology Foresight” project a methodology was developed based on five elements:

- Life-cycle thinking,
- systems approach,
- a broad dialogue based understanding of the environment,
- precaution as a principle and,
- prevention as preferred strategy.

When assessing emerging technologies, three levels should be considered.

- First order effects are connected directly to production, use, and disposal.
- Second order are effects from interaction with other parts of the economy from more intelligent design and management of processes, products, services, product chains, etc., and the effect on the stocks of products. An example could be dematerialisation.
- Third order effects may be considered rebound effects, e.g., when efficiency gains stimulate new demands, which balances or overcompensates the savings.

Nanotechnologies should not be considered environmentally beneficial just because products are small. A life cycle perspective should be applied during design and technological development in order to reduce potential environmental impacts in the life cycle of the “nano-products.”

Session 1: Life Cycle of Nanomaterials

July 12, 10:30-11:30 AM

Dr. Stig Irving Olsen, NANO DTU, Technical University of Denmark, Department of Manufacturing Engineering Management, Lyngby, Denmark

Highlights

Nanotechnologies imply a vast array of benefits to society many of which may also be environmentally beneficial, e.g. reductions in energy use and improved functionality of material. But apart from the potential toxicological risks of nanoparticles nanotechnology may also imply an increased use of scarce resources, a high energy demand and waste in production, problems in recycling etc. To ensure a sustainable development of nanotechnologies it is important to adequately meet human demand and to assess the entire system.

Life cycle assessment (LCA) is a useful tool for this but a simplified approach may be needed. LCA is an environmental assessment tool that focuses on the services provided to society, very often the functionalities provided by a product. LCA has a holistic perspective since the entire life cycle of a product from the extraction of raw materials to the final disposal is included and because all relevant environmental impacts and consumption of resources are assessed. It can be used for the identification of problematic impacts in the life cycle and for comparisons between products and/or life cycle stages. ISO standards are developed for LCA.

In nanotechnology manufacturing, the use of scarce metals and materials may increase; since only small amounts are needed, cost is not so prohibitive. This creates increased impact upstream. For example, it is 2000 times more energy-intensive to extract gold from ore than steel. Also, the use of Sc (scandium)-doped fullerenes in automobile fuel cells could quickly deplete Sc, a rare material. Experiences from electronics show that disassembly and recycling of scarce materials is very difficult.

Maintaining a clean nanotechnology production environment to ensure pure products requires lots of high-energy input both in the process and upstream.

Using three real cases of fullerenes application some environmental aspects of the life cycle were illustrated, e.g. the need to purify nanoparticles in organic solvent prior to use in composite and low yield as well as the potential release during incineration of nanotubes in composites.

Both the induced impact of nanotechnology function as well as the impact of whatever the new technology is replacing needs to be assessed. Forecasting methods are needed in environmental assessment. It is important to interpret risks during the life cycle. And finally the need to make environmental concerns inherent to nanoresearch was emphasized.

Question-and-Answer Session

When asked whether benefits of nanotechnology outweigh risks, Dr. Olsen indicated that there are many applications for which it will be difficult to weigh benefits versus risks. For example, environmental impact assessments are typically not performed for medical applications. When asked about the importance of recycling of nanomaterials, Dr. Olsen indicated that recycling will be critical to realizing energy savings, especially for products/processes that use scarce resources. A commenter noted that the Woodrow Wilson Center and the EC will hold a workshop on LCA and nanotechnology. The Woodrow Wilson Center website has two databases available (visit www.nanotechproject.org).

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Life Cycle Assessment of Micro/Nano products

Nanotechnology and OSWER: New Opportunities and Challenges

Stig Irving Olsen, M.Sc., Ph.D.
Department of Manufacturing Engineering and Management
NANO•DTU, Technical University of Denmark

With contributions from
Michael Søgaard Jørgensen and Michael Hauschild, IPL, NANO•DTU
Antonio Franco and Steffen Foss Hansen, E&R, NANO•DTU

Nano•DTU
Center for Nanoteknologi på DTU

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Outline

- Why environmental assessments in life cycle perspective are important
- LCA overview
- Exemplification of environmental issues in micro and nano production
- Product cases on fullerenes
- Other studies
- Conclusion and the way forward

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Potential benefits of nano technology

Material science: strength, hardness, flexibility, heat conductivity/resistance, electrical conductivity/resistance.

Medicine and biology: nano-engineered biomolecules and structures can let medicine for the first time intervene in a sophisticated and controlled way at the cellular and molecular level. disease diagnosis or molecular imaging

Information and electronics: minimization of scale of devices, optoelectronics, chips and storage

Environment: Improve efficiency of a number of environmental applications such as enhanced and self-cleaning filtration devices for the purification of water, or remediation technologies. Nanoscale solid state sensors and biosensor for detection of pollutants

Energy: Improved efficiency of energy usage, devices for enhanced exploitation of solar energy, hydrogen storage, fuel cells or nano-fabricated catalysts

Military technology: nanocomputers and nanosensors may allow a more capable surveillance of potential aggressors. Nanotechnological enhancements could make smaller, cheaper and more precise conventional weapons. A better target discrimination could minimize unintended damages in a war scenario

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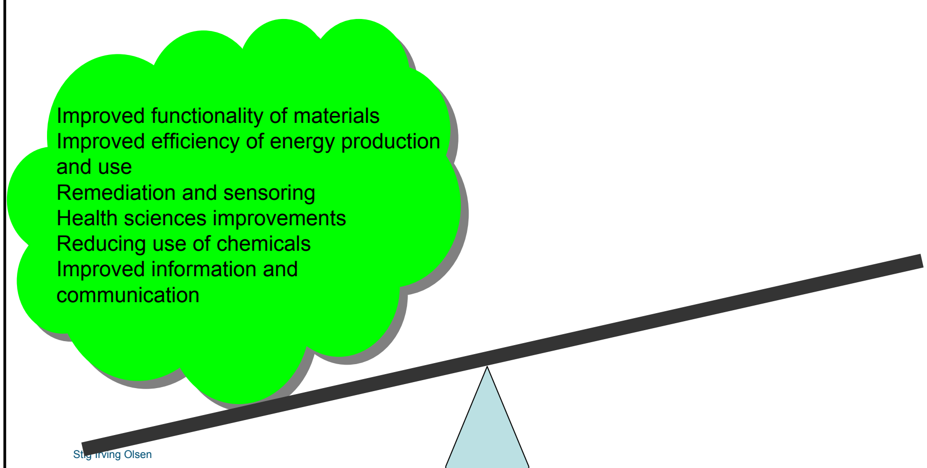

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Potential environmental impacts

Toxicological risks to humans and the environment
Increased exploitation and loss of scarce resources
Higher requirement to materials and chemicals
Increased energy demand in production lines
Increased waste production in top down production
Rebound effects (horizontal technology)
Increased use of one way systems
Disassembly and recycling problems

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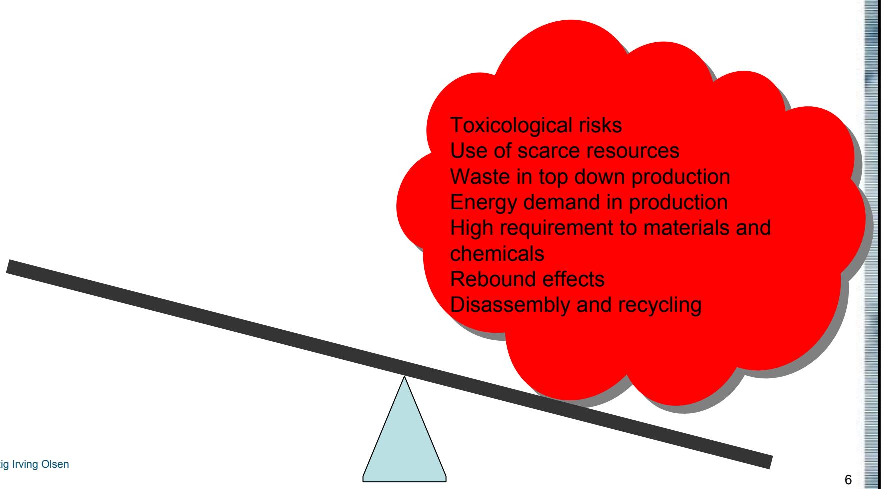

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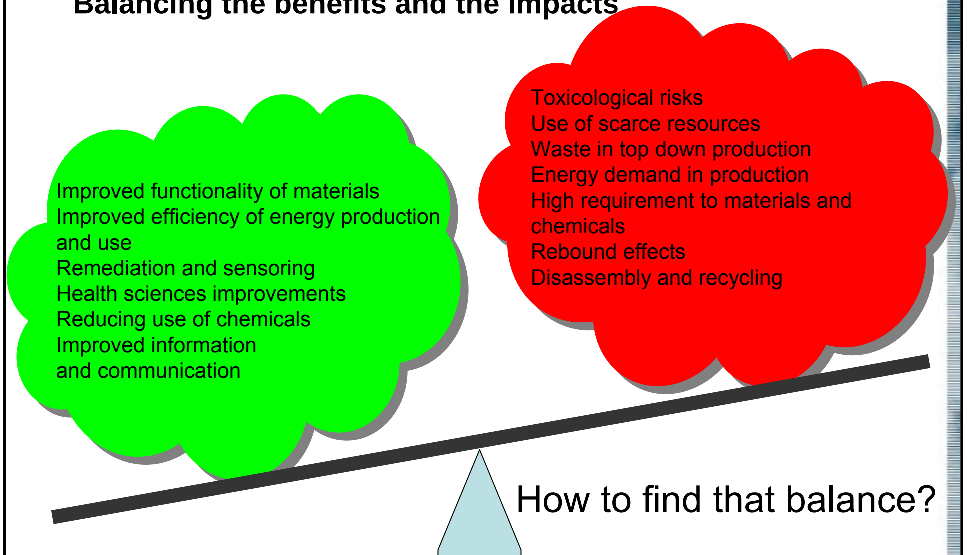
Balancing the benefits and the impacts



Environmental Assessment Concept – an outline

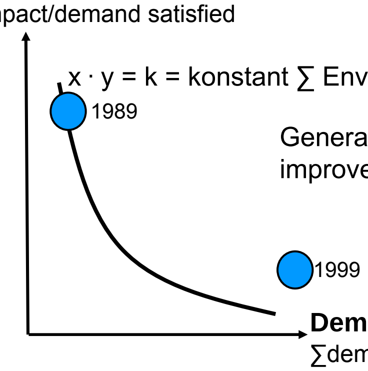
Supply side (substitution)

Eco-efficiency:
impact/demand satisfied

The Master Equation:

∑ Env. impact = P · E · T

=∑demand · impact/demand satisfied



Generalised criterion for environmental improvement: x · y < k

Demand side (expansion)
∑demand

(After Henrik Wenzel, 2005)

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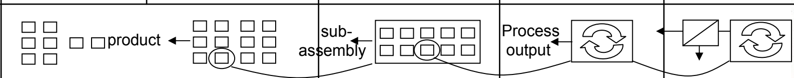
The levels of intervention for Eco-efficiency improvement in the demand-supply chain – a closer look

	Level 0	Level 1	Level 2	Level 3	Level 4
The demand & supply chain	The human need/demand ⇄	The product ⇄	The production ⇄	The process ⇄	The input/output from/to nature
The demand side	The consumer demands a product or service	The product is the demand of a chain of production facilities	The production is the demand of a series of processes/unit operations	The process demands the resulting input and output	
The supply side		The product supplies the service and satisfies the customer demand	The production facility supplies the material or sub-assembly of the product	The process/unit operation supplies the requested properties	Nature supplies the resources and receives the emissions
The system level of intervention	Not targeted by Eco-efficiency measures	The product system The product life cycle The product chain The supply chain	The company/ individual production facility in the supply chain	The individual unit operation in the production facility	The resource consumption & emission from the individual process
Pictograms of the four intervention levels	 product **The product chain**		sub-assembly **The production facility**	Process output **The unit operation**	**The emission**
Concepts for Eco-efficiency improvement	Life Cycle Engineering Eco-design Design for Environment		Process Integration Cleaner Production Waste Minimisation	Process Intensification Cleaner Production	Treatment

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(Reproduced from Wenzel and Alting, 2004) 9

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Life Cycle Thinking

- What is environmental assessment of products?
- How is the environmental impacts of a product assessed?
- Why is the environmental impacts from products interesting?

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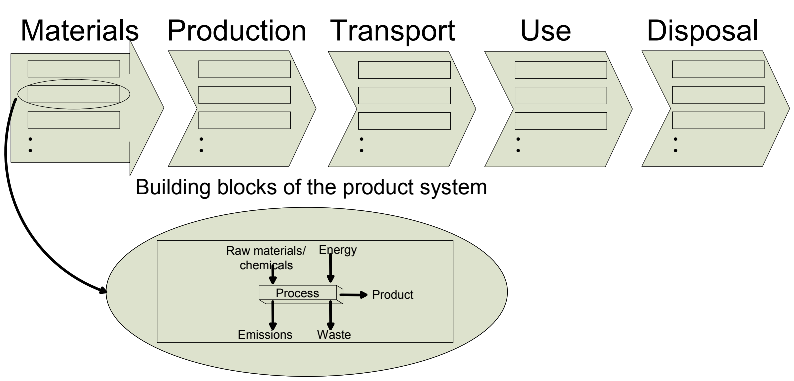
Inventory

<u>Product system</u>



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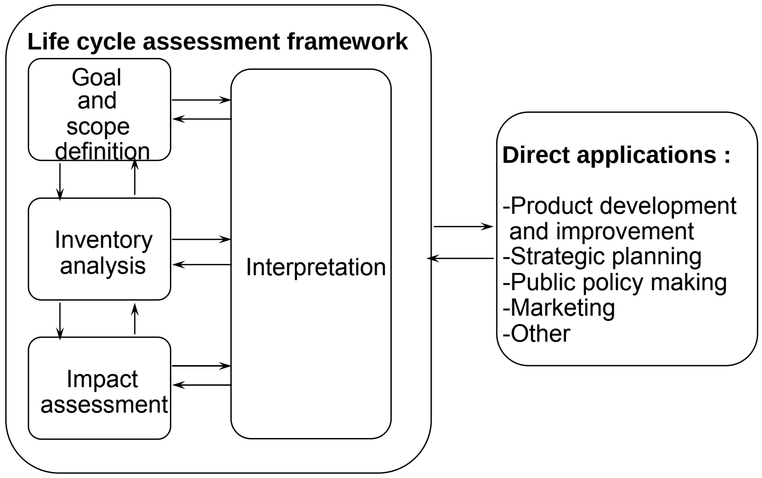
Elements of LCA



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Environmental impacts

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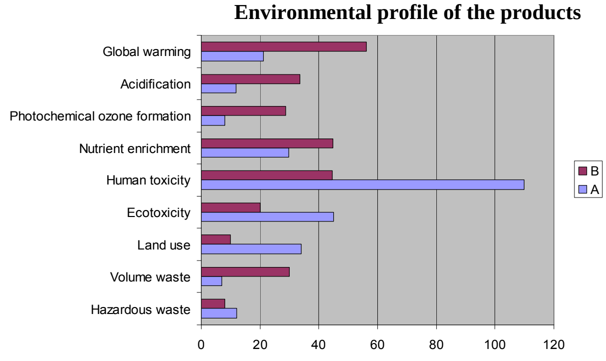
Inventory of emissions

Substance	CAS.no.	Emission to air g	Emission to water g
2-hydroxy-ethanacrylate	816-61-0	0,0348	
4,4-methylenebis cyclohexylamine	1761-71-2	5,9E-02	
Ammonia	7664-81-7	3,7E-05	4,2E-05
Arsenic (As)	7440-38-2	2,0E-06	
Benzene	71-43-2 (cur	5,0E-02	
Lead (Pb)	7439-92-1	8,5E-06	
Butoxyethanol	111-76-2	6,6E-01	
Carbondioxide	124-38-9	2,6E+02	
Carbonmonoxide (CO)	630-08-0	1,9E-01	
Cadmium (Cd)	7440-46-9	2,2E-07	
Chlorine (Cl2)	7782-50-5	4,6E-04	
Chromium (Cr VI)	7440-47-3	5,3E-06	
Dicyclohexane methane	86-73-6	5,1E-02	
Nitrous oxide(N2O)	10024-97-2	1,7E-02	
2,4-Dinitrotoluene	121-14-2	9,5E-02	
HMDI	5124-30-1	7,5E-02	
Hydro carbons (electricity, stationary combustic	-	1,7E+00	
Hydrogen ions (H+)	-		1,0E-03
i-butanol	78-83-1	3,5E-02	
i-propanol	67-63-0	9,2E-01	
copper (Cu)	7740-50-8	1,8E-05	
Mercury(Hg)	7439-97-6	2,7E-06	
Methane	74-82-8	5,0E-03	
Methyl i-butyl ketone	108-10-1	5,7E-02	
Monoethyl amine	75-04-7		7,9E-06
Nickel (Ni)	7440-02-0	1,1E-05	
Nitrogen oxide (NOx)	10102-44-0	1,1E+00	
NMVOC, diesel engine (exhaust)	-	3,9E-02	
NMVOC, power plants (stationary combustion)	-	3,9E-03	
Ozone (O3)	10028-15-6	1,8E-03	
PAH	ikke specifik	2,4E-08	
Phenol	108-95-2		1,3E-05
Phosgene	75-44-5	1,4E-01	
Polyeter polyol	ikke specifik	1,6E-01	
1,2-propylenoxide	75-56-9	8,2E-02	
Nitric acid	7782-77-6 (c	8,5E-02	
Hydrochloric acid	7647-01-0 (c	1,9E-02	
Selenium (Se)	7782-49-2	2,6E-05	
Sulphur dioxide(SO2)	7446-09-5	1,3E+00	
Toluene	108-88-3	4,8E-02	
Toluene-2,4-diamine	95-80-7	7,9E-02	
Toluene diisocyanat (TDI)	26471-62-5	1,6E-01	
Total-N	-		2,6E-05
Triethylamine	121-44-8	1,6E-01	
Unspecified aldehydes	-	7,5E-04	
Uspecified organic compounds	-	1,5E-03	
Vanadium	7440-62-2	1,8E-04	
VOC, diesel engine (exhaust)	-	6,4E-05	
VOC, stationary combustion (coal fired)	-	4,0E-05	
VOC, stationary combustion (natural gas fired)	-	2,2E-03	
VOC, stationary combustion (oil fired)	-	1,4E-04	
Xylene	1330-20-7	1,4E-01	
Zinc (Zn)	7440-66-6	8,9E-05	

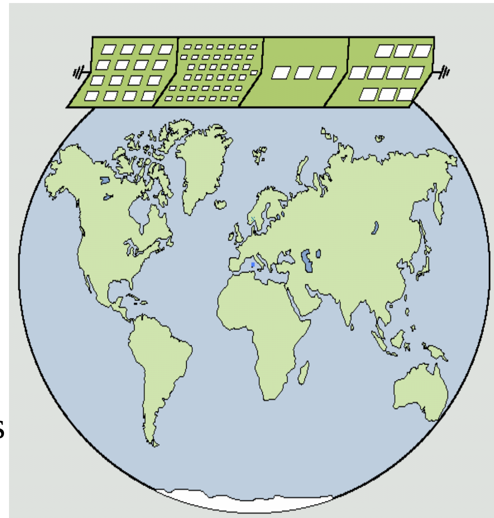
Global warming	174.000	kg CO_2- equ.
Ozone depletion	0	kg CFC11- equ.
Acidification	868	kg SO_2- equ.
Photochemical ozone formation	200	kg C_2H_4- equ.
Eutrophication	3.576	kg NO_3^- equ.
Toxicity to humans	$3{,}40 \cdot 10^{11}$	m^3 air
Ecotoxicity	$2{,}16 \cdot 10^{7}$	m^3 water
Land use	170	ha·yr
Bulk waste	9.450	kg
Hazardous waste	248	kg

Environmental profile of the products



Environmental impact assessment in LCA

- The Life Cycle is *global*
- The product system extends over time
- Focus is on a single product
- The assessment predicts impacts not actual effects



Characteristic features of LCA

Focus on services (the functional unit) ➠ products

Holistic perspective
- life cycle from cradle to grave
- all relevant environmental impacts, resource consumption (biotic and abiotic) and sometimes working environment
- Identification of problematic impacts

Comparative (relative statements)

Aggregation over time and space
- The life cycle is global
- The life cycle may last for decades or centuries

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How is an LCA performed?

Three levels with increasing extent of detail, effort of work and strenght of decision

Stops when question is answered with adequate certainty

1. Life Cycle Check
2. Life Cycle Screening
3. Detailed Life Cycle Assessment

To perform an LCA imply an iterative approach – *also within each of the three levels*

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Elements in a Life Cycle Check

- Choice of product
- Identification of the service - the functional unit
- Establishing boundaries for the product system
- Collection of data
- Preliminary environmental assessment – the MECO principle
- Interpretation

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Life Cycle Check – the preliminary environmental assessment

The MECO principle

	Life Cycle Phase			
Reasons for Environmental Impact	Extraction of raw materials	Production	Use	Disposal
Materials				
Energy				
Chemicals				
Other				

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Life Cycle Check

	ife Cycle Phase			
Reasons for Environmental Impact	Extraction of raw materials	Production	e	sposal
aterials				
nergy				
hemicals				
ther				

Strenghts of the MECO analysis:

- It covers the whole Life Cycle
- All environmental impacts are included through the choices and actions that causes them
- Simpel and quick
- Sometimes provides adequate answers
- Identifies needs for more detailed analyses

It is used quantitative or qualitative

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20

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Environmental input output analysis

- The economic input-output life cycle assessment (EIO-LCA) relates economic activity across sectors to energy requirements and environmental discharges
- input-output matrix of economic activities is used to calculate economic activity generated across all sectors by purchases in a particular sector. It also uses public datasets, such as EPA's Toxic Release Inventory (TRI), to calculate unit environmental output per unit economic output for each sector.
- The model provides aggregate results and therefore does not distinguish between different grades or types of materials produced in the same sector.

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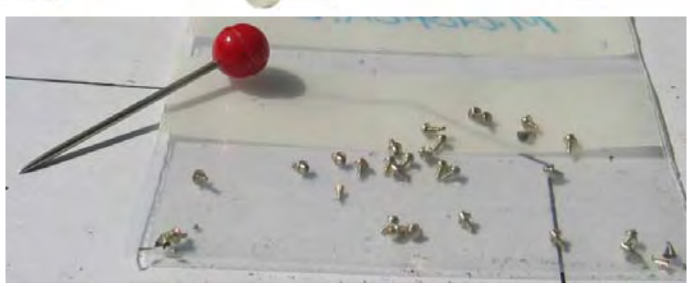
Some materials issues in micro manufacturing

Micro screw for hearing aid



Ordinary turning produces more than 50% metal waste
Cold forging puts requirements to materials

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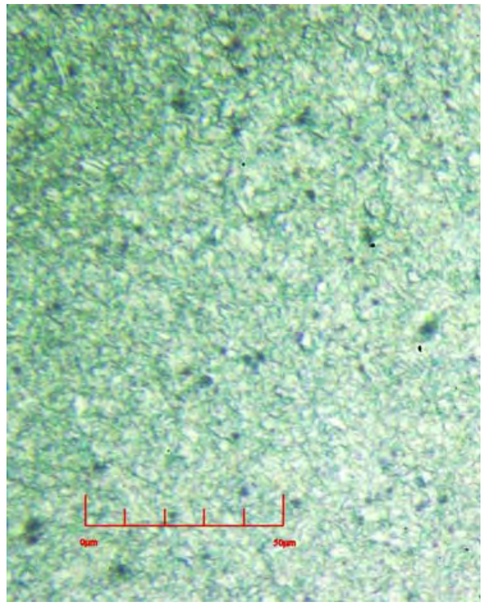
Material analysis



Micro structure
- Homogenious material
- Small grains

Better specifications must be met

Withen og Marstrand

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Use of scarce resources

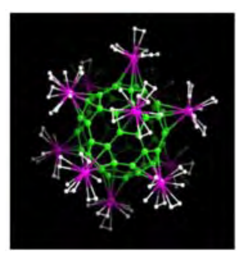
More frequent use of rare metals due to reduced importance of price in the single product and/or specific properties

Rare metals imply higher energy use in extraction (e.g. Gold is 2000 times more energy intensive than steel)

For example the use of gallium arsenide in electronics

Or the use of other types of metals in Endo- or ectohedral fullerenes

For example Carbon trimetaspheres in which lathanide series metals incorporated inside (e.g. galolinium)



Three-dimensional Scandium (pink) C60 (green) complex with 8.7 wt.% total H2 (white) capacity and 7.0 wt% reversible hydrogen storage.
Dillon et al., 2006.
Mater. Res. Soc. Symp. Proc. Vol. 895

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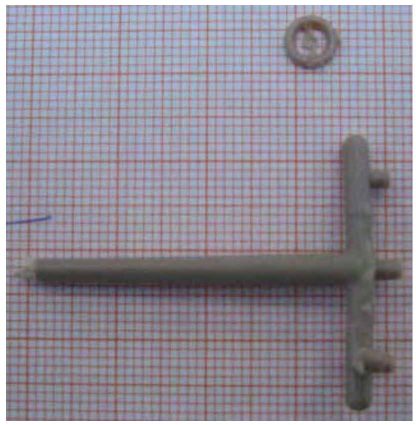
Some materials issues in Micro manufacturing

Micro injection moulding – big runners are necessary for handling and assembly – up to 99% of the total weight is waste



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Problems with recycling:

Material quality reduction

Disassembly

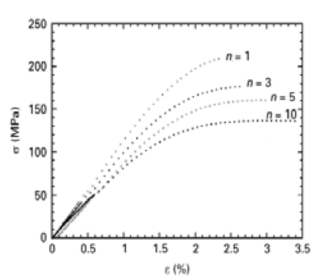

Figure 6 Stress–strain curves of recycled CPEEK30.

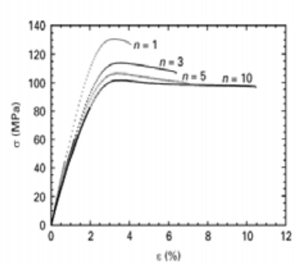

Figure 5 Stress–strain curves of recycled CPEEK10.

Sarasua & Pouyet, 1997

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26

Top down production

Inputs	*Outputs*
460 kWh energy	0.007 kg silicon wafer
1.7 m^3 water	1.7 m3 waste water
1.0 kg inorganic acid	3.3 kg inorganic waste/emission
2.3 kg inorganic chemical	0.7 kg organic waste/emission
5 kg nitrogen	
0.1 kg other technical gases	
0.7 kg organic chemicals	

From K. Schischke, O. Deubzer, H. Griese, I. Stobbe, 2002

Waste management issues

Waste hierarchy
- prevention
- recycling/reuse
- Energy recovery
- disposal

How does NT fit into this?

Over the life cycle probably not prevention due to waste produced in raw materials extraction and production stages

Recycling is seen to be difficult with current technologies for small amount (problems related to e.g. disassembly) as seen for electronics today

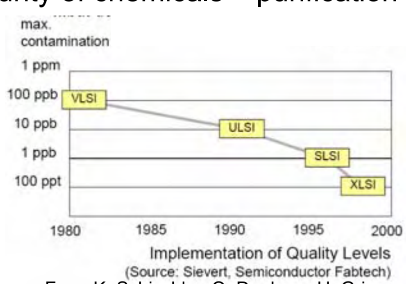
Some energy issues in Micro manufacturing

Clean room requirements increasing:

HVAC (heating, ventilation and air conditioning)

class 10,000	2280 kWh/m^2
class 100	8440 kWh/m^2

High purity of chemicals – purification energy requiring



(7% of total energy use by US chemical industry)

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From K. Schischke, O. Deubzer, H. Griese, I. Stobbe, 2002

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Production of a digital telephone

Main group	Mass (g)	TPI (*1000)	GWP (g CO_2 equivalents)	ADP (g/year)	EPS (ELU)	Eco99 (millipoints)
Mechanics	941	130	9049	589	3087	623
Frequency determined components	0.5	3	25.2	0.3	1.3	1.3
Discrete semiconductors	77	21	1044	4	9	47
Electromechanics	53	19	440	55	311	46
Passives	8	33	599	4	262	26
Magnetic	14	42	403	26	142	23
Integrated circuits	6	9	1637	102	566	998

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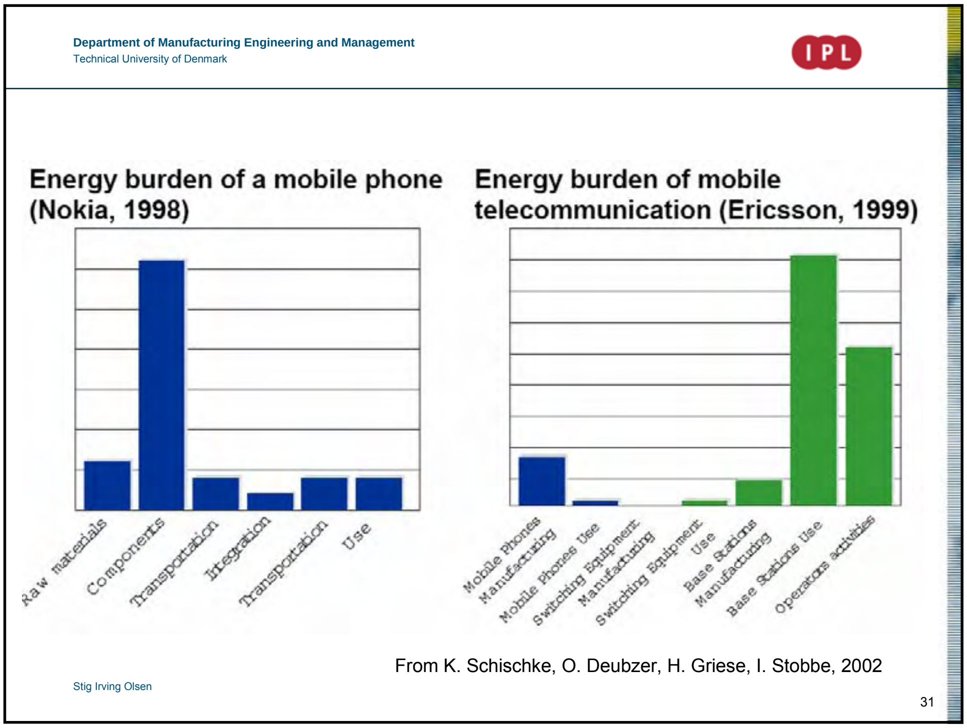
Andræ, 2002. PhD Thesis
Chalmer University of technology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Energy burden of a mobile phone (Nokia, 1998)
Energy burden of mobile telecommunication (Ericsson, 1999)
Raw materials
Components
Transportation
Integration
Transportation
Use
Mobile Phones Manufacturing
Mobile Phones Use
Switching Equipment Manufacturing
Switching Equipment Use
Base Stations Manufacturing
Base Stations Use
Operators activities
From K. Schischke, O. Deubzer, H. Griese, I. Stobbe, 2002
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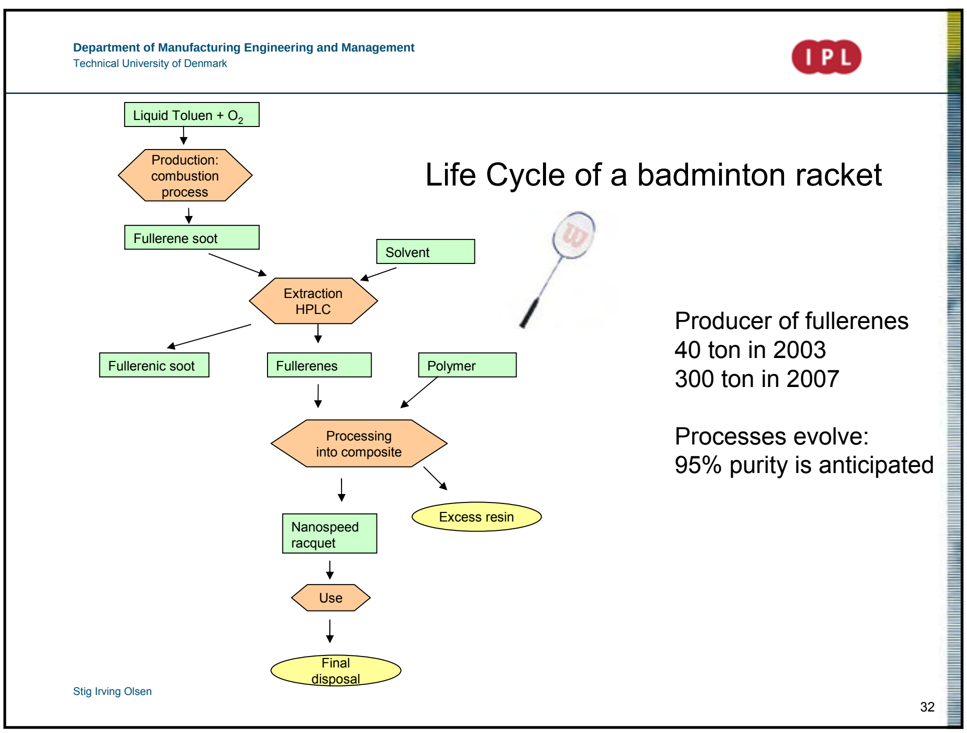
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Life Cycle of a badminton racket
Liquid Toluen + O_2
Production: combustion process
Fullerene soot
Solvent
Extraction HPLC
Fullerenic soot
Fullerenes
Polymer
Processing into composite
Excess resin
Nanospeed racquet
Use
Final disposal
Producer of fullerenes
40 ton in 2003
300 ton in 2007
Processes evolve:
95% purity is anticipated
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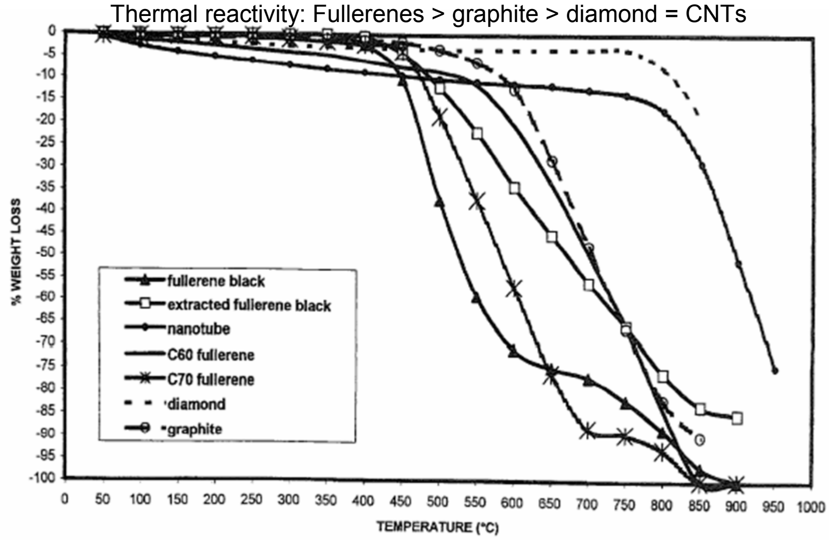
Thermal reactivity: Fullerenes > graphite > diamond = CNTs



Cataldo, F, 2002. Fullerenes, 20(4), p.293-311

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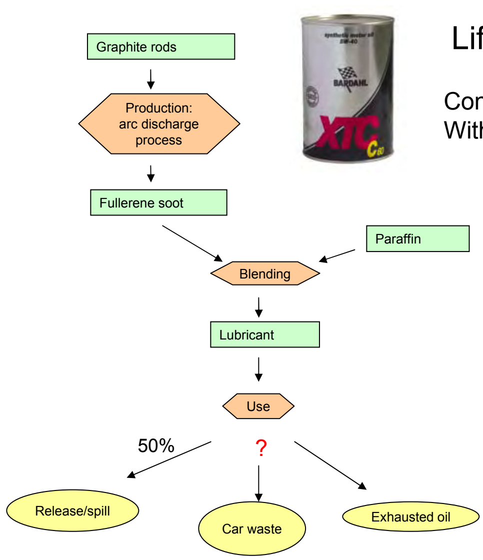
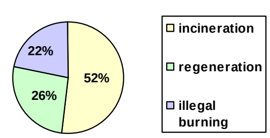
Life Cycle of a motor oil

Content 9% fullerenic soot
With a content of 7% fullerenes





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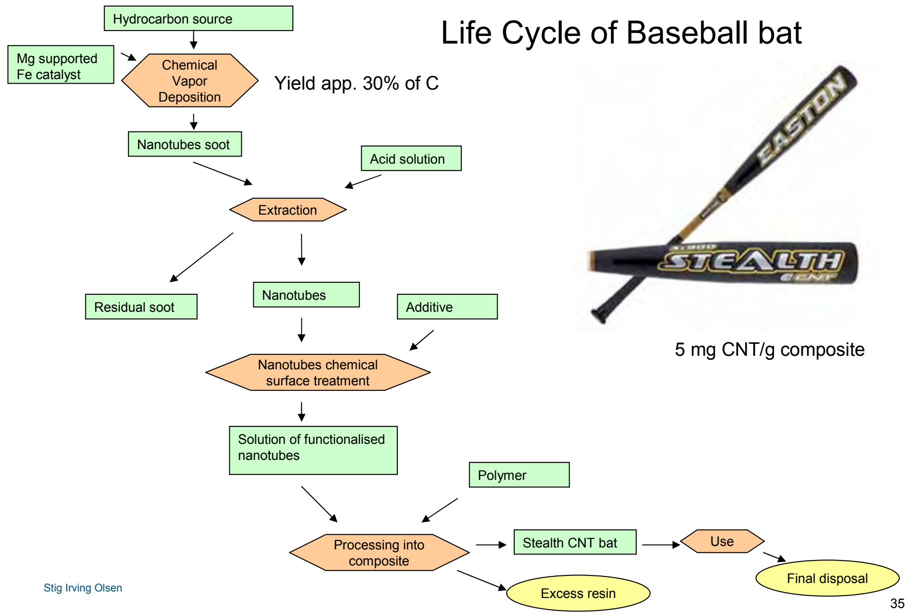
Life Cycle of Baseball bat



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From Haum et al, 2004 IÖW

Table 3: Overview production processes of nanotechnology

Nanotechnology based products	Nanostructure	Manufacturing process	potential hazards	industrial sector
Application Area: New Surface Functionalities and Finishing				
tribological layers: e.g. superhard surfaces	ultrathin layers; nano-crystallites; nano-particles in an amorphous matrix	vapour phase deposition, PECVD	PVD/CVD production process: risk of disposal of nano-particles is small (process is running in a vacuum environment) use stage: low scale disposal of nano-particles possible	engineering, automotive
thermal and chemical protection layers	ultrathin layers; organic-inorganic hy-brid-polymers; nanocomposites	vapour phase deposition; sol-gel		aerospace, automotive, ICT, food
self-cleaning and antibacterial surfaces	ultrathin (polymer) layers, nano-crystallites in an amourphous matrix	vapour phase deposition, sol-gel, soft lithography		textile, ICT, food, building, medicine...
scratch resistant and anti-adhesive surfaces	ultrathin layers; organic-inorganic hy-brid-polymers	sol-gel; SAM	use stage: low scale disposal of nano-particles possible	building, automotive, textile, consumer goods
products with "nanoparticle effects" : e.g. colour effects in lacquers	nano-particles, ultrathin layers	flame assisted deposition, flame hydrolysis, sol-gel	production: deposition possible; use stage: low scale disposal possible	building, automotive, consumer goods, textile
Application Area: Catalysis, Chemistry, Advanced Materials				
catalysts	nanoporous oxides, polymers or zeo-lithes; ultrathin layers	precipitation, sol-gel, SAM, molecu-lar imprinting	not known	chemistry, automotive, environmental, biotech
sieves and filtration	sintered nano-particles, nanoporous polymers	self assembly, colloid chemistry		chemistry, environmental
Application Area: Energy Conversion and Utilisation				
fuel cells	ceramics from sintered nano-particles	div.	not known	energy, automotive
super-capacitors	nanotubes, nanoporous carbon aerogels	div.	nanotubes possibly toxic when inhaled	energy
superconductors	ultrathin layers	e.g. vapour phase deposition	production: risk of disposal is small	energy, medicine
Application Area: Construction				
nanoscale additives: e.g. carbon black in car tires	nanocrystals and -particles	flame assisted deposition, flame spray pyrolysis	production process: disposal of nano-particles possible, danger of inhaling for workers; use stage: low scale disposal of nano-particles possible	building, automotive
nanoparticle-reinforced products: e.g. tem-perature resistant components	(amorphous) nano-particles	flame assisted deposition, flame hydrolysis		automotive, ICT, consumer goods, medi-cine, aerospace
Application Area: Information Processing and Transmission				
nanoelectronic components	ultrathin lateral nanostructured semicon-ductor	PVD, CVD, lithography	PVD/CVD production process: risk of disposal of nano-particles is small	ICT
Displays	utrathin layers	PVD, spin-coating		ICT, automotive
Application Area: Nanosensors and Nanoactuators				
sensors: e.g. GMR-sensors	metallic ultrathin layers; ultrafine tips	CVD/PVD/MBE; etching, SAM	PVD/CVD production process: risk of disposal of nano-particles is small	automotive, engineering, ICT, analytics
probes e.g. for scanning tunneling microscope	utrathin layers, ultrafine tips and mole-cules	PVD, etching, SAM		analytics
Application Area: Life Sciences				
active agent carrier: e.g. drug carriers	organic molecules, nanoporous oxides	self assembly, anodic treatment	flame hydrolysis production process: disposal of nano-particles possible; use stage: particles might be absorbed dermally; very small TiO_2-particles possi-bly toxic	Pharma, medicine
Cosmetics: e.g. pigments	utrathin layers from nano-particles, (amorphous) nano-particles	wet-chemical separation; colloid chemistry		cosmetics
sunscreen	nanocrystalline titanium dioxide (TiO_2)	flame hydrolysis		cosmetics

Source: IOW

LCA of Nano technologies

Mentioned specifically as a research area in official reports

Only few studies has as yet been identified:

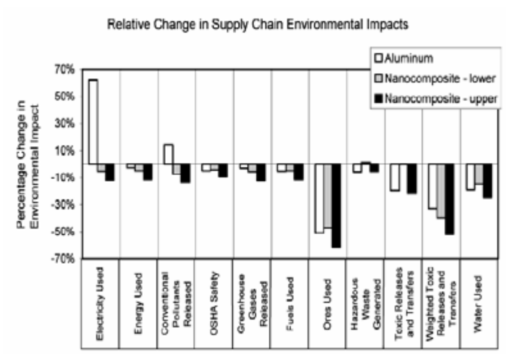
Carnegie-Mellon University
Two studies: Nanocomposite automotive body parts
Automotive catalysts

IÖW (Institute for ecological economy research)
Ecological efficiency of nanovarnish
Process innovation with styrene synthesis
Nano-innovation within the display sector
Nano-applications within the lights sector

Carnegie Mellon studies (1)

Combination of process based and EIO LCA
-Steel→ nanocomposite or aluminum – weight reduction
-Design requirements e.g. energy absorption, durability, costs etc.

	Mass reduction	CO_2 - savings
Nanocomposite	38-67%	4.6 – 8.5%
Aluminum	50%	5.5%



(Lloyd and Lave, 2003)

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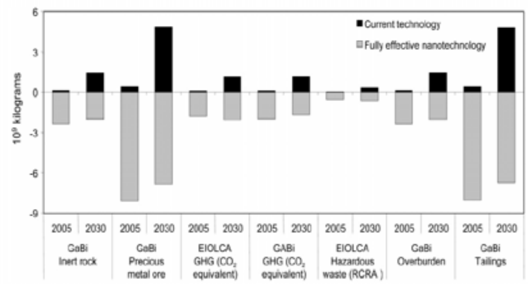
Carnegie Mellon studies (2)

Reduction of PGM (platinum group metals) in automotive catalysts

-Using Nanotechnology a 95% reduction is feasible by controlling shape, size and location of PGM particles



(Lloyd et al., 2005)

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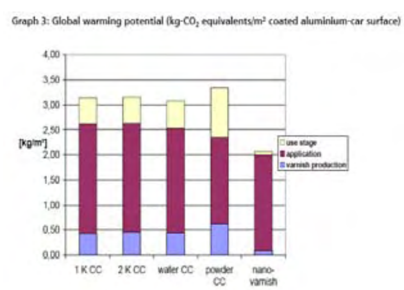
Studies from IÖW (1) *(Steinfeldt et al., 2004)*

Nano varnish



Styrene synthesis: Nanostructured catalytic converters

50% energy reduction

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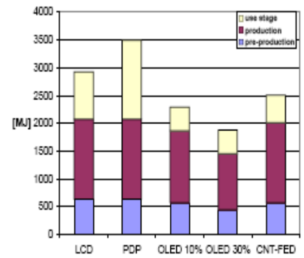
Studies from IÖW (2) *(Steinfeldt et al., 2004)*

Displays (many assumptions due to immature technology)
Reduction of energy use in LC of 20% feasible



Nanotechnology in lights sector:
White LEDs compared to traditional tungstenlamp and fluorescent lamps. LEDs more efficient than tungsten lamps but still significantly less so than fluorescent lamps.

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Environmental Assessment Concept

Foresight concept	Life Cycle Assessment concept	Scope of assessment
1. order assessment	Induced → Nanotechnologies → Application	Substitution - supply side only
2. order assessment	Avoided → Alternative technology → Application	Compare **eco-efficiency**: impact/satisfied demand
3. order assessment	Rebound effects - technology induced changes of the demand side	Expansion - demand side also Include impacts of changes in demand

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42

Challenges for future work

Nanotechnology is an enabling technology and probably introduces radically new technologies of production and functionalities of products

Implementation of techniques for technology forecasting in environmental assessment – scenarios, roadmapping, others?

Prospective LCAs

- Data for marginal technologies
- Inventory data for nanotechnologies

Making environmental concern inherent to nano research

Interpreting risks during the life cycle

Overall policy recommendations for research

Visions for the anticipated use => shaping the attention and priorities for environmental concern

Environmental screening of research proposals

Environmental concerns as part of research:
Internal/external competence. Independence. Dialogue

Dr. David B. Warheit

E.I. Dupont de Nemours and Co., Inc.
Haskell Laboratory for Toxicity and Industrial Medicine

David B. Warheit graduated from the University of Michigan in Ann Arbor with a BA in Psychology; received his Ph.D in Physiology from Wayne State University School of Medicine in Detroit. Subsequently, he was awarded an NIH Postdoctoral Fellowship, and 2 years later, a Parker Francis Pulmonary Fellowship, both of which he took to NIEHS to study mechanisms of asbestos-related lung disease with Arnold Brody. In 1984, he moved to DuPont Haskell Laboratory to develop a pulmonary toxicology research laboratory. His major research interests are pulmonary toxicological mechanisms and corresponding risk related to inhaled particulates, fibers, and nanomaterials.

Dr. Warheit is the author/co-author of >100 publications and has been the recipient of the ILSI Kenneth Morgareidge Award (1993 - Hannover, Germany) for contributions in Toxicology by a Young Investigator and the Robert A. Scala Award and Lectureship in Toxicology (2000).

Dr. Warheit has also attained Diplomat status of the Academy of Toxicological Sciences (2000) and the American Board of Toxicology (1988). He has served and currently serves on NIH review committees (NIH SBIR, NIH Bioengineering) and has participated on working groups at IARC, ECETOC, ILSI RSI and ILSI-HESI and the National Academy of Sciences, as well as several journal editorial boards (including current Associate Editor – *Inhalation Toxicology and Toxicological Sciences*).

Currently Dr. Warheit is the chairman of the ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) Task force on “Health and Environmental Safety of Nanomaterials,” and serves on the NIOSH Board of Scientific Counselors and National Toxicology Program - Nano Working Group.

Session 2: Potential Exposure Scenarios and Potential Toxicity of Nanomaterials

July 12, 1:00-2:00 PM

Dr. David B. Warheit, E.I. Dupont de Nemours and Co., Inc. Haskell Laboratory for Toxicity and Industrial Medicine

Abstract

Impact of Nanoparticulates on Respiratory Health Effects: Toxicity is not always dependent solely upon Particle Size and Surface Area.

“Environmental Impact of Nanotechnology: Big Things Come in Little Packages”

The results of several lung toxicology studies in rats have demonstrated that ultrafine or nanoparticles (generally defined as particles in the size range < 100 nm) administered to the lungs produce enhanced inflammatory responses when compared to fine-sized particles of similar chemical composition at equivalent doses. However, the common perception that nanoparticles are always more toxic than fine-sized particles is based upon a systematic comparison of only 2 particle-types, namely, titanium dioxide and carbon black particles. Apart from particle size and corresponding surface area considerations, several additional factors may play more important roles in influencing the pulmonary toxicity of nanoparticles. These include, but are not limited to: **1) surface treatments/coatings of particles; 2) the aggregation/disaggregation potential of aerosolized particles; 3) the method of nanoparticle synthesis – i.e., whether the particle was generated in the gas or liquid phase (i.e., fumed vs. colloidal/precipitated); 4) translocation potential of the particle; 5) particle shape; and 6) surface charge.**

Results of pulmonary bioassay hazard/safety studies will be presented demonstrating that fine-sized quartz particles (1.6 µm) may produce greater pulmonary toxicity (inflammation, cytotoxicity, cell proliferation and/or histopathology) in rats when compared to nanoscale quartz particles (50 nm), but not when compared to smaller nanoquartz sizes (e.g., < 30 nm). In addition, other studies have demonstrated no measurable difference in pulmonary toxicity indices among particle-types when comparing exposures in rats to 1) fine-sized TiO_2 particles (300 nm – 6 m^2/g (surface area); 2) TiO_2 nanodots (6-10 nm – 169 m^2/g); or 3) TiO_2 nanorods (25 m^2/g). Finally, studies will be presented which demonstrate that varying surface treatments on finesized TiO_2 particles influence lung responses. In summary, some important take-home messages are the following:

1) Risk is a product of Hazard and Exposure;

2) In general, one cannot assume that nanomaterials have the same chemistry or biology (i.e., toxicity) as their bulk counterparts; therefore, the hazards of each particle-type should be tested on a case-by-case basis.

Session 2: Potential Exposure Scenarios and Potential Toxicity of Nanomaterials

July 12, 1:00-2:00 pm

Dr. David B. Warheit, DuPont Haskell Laboratory for Health and Environmental Sciences.

Highlights

Dr. Warheit's research involves health effects resulting from respiratory exposures to nanomaterials. There are parallel research tracks: generic mechanistic research, and product-specific testing.

Nanoparticles are equivalent in size to ultrafine particles (<100 nm). Ultrafine nanoparticles are <100 nm in size, and fine particles are 100 nm to 3 µm in size. Certain particle sizes are respirable (e.g., <3 µm in rat, <5 µm in human).

Regarding lung structure as it relates to particle deposition: rats have 3 to 5 bronchoalveolar duct bifurcations; humans may have 15 to 20. Ciliated Clara cells are positioned at the junctions of bronchial tubes and alveolar duct bifurcations. At the first of these junctions is where inhaled particles deposit in the distal lung. Macrophages engulf foreign particles to clear them from the lung. They engulf the particles, then move to the mucociliary escalator on the airway surface, and move up the bronchial tubes to be coughed up or swallowed.

Some common perceptions of pulmonary toxicity include the idea that nanoparticles are more inflammogenic and/or tumorigenic than fine-sized particles of identical chemical composition. However, not all nano-sized particles are more toxic. Some factors that may influence toxicity are surface coatings, species differences, particle aggregation potential, and whether the particle was fumed vs. precipitated in its manufacture.

Pulmonary bioassays can be used as measures of lung toxicity. It is important to consider dose response characteristics and the time post-exposure. Data from 24 hours post-exposure are not as useful because there is always an inflammatory response from the intratracheal instillation exposure. Thus the sustainability or nonsustainability of the response is very important (often measured at 1 week, 1 month or 3 months postexposure).

There can be a heterogeneous cellular response in the lung to inhalation of crystalline silica – macrophages, neutrophils and lymphocytes can respond. This can be indicative of an ongoing inflammatory response. Alternatively, the cellular response can be homogeneous (macrophages only). This is indicative of no sustained inflammation.

Regarding lung toxicity, generally there has been good correlation between the findings of instillation and inhalation studies.

In an experiment with TiO_2, two concentrations of nano sized particles (nanoscale rods or nanoscale dots) were tested and compared with fine sized TiO_2 particles. The positive control was quartz particles (Min-U-Sil). Physical-chemical characterization of the particles was robust -- crystal form, crystal size, shape, surface area etc. were measured and recorded. The surface area of Nanorods was four times greater than the corresponding fine particles, and the surface area of Nanodots was thirty times greater than fine TiO_2 particles. Following intratracheal instillation of particles into the lungs of rats, there were no toxicity differences among the groups of TiO_2 –exposed rats for various biomarkers. The quartz positive control produced an active inflammatory response.

Nanoquartz is a form of alpha quartz crystalline silica. The hypothesis states that nanoquartz should be more toxic than fine-sized Min-U-Sil quartz particles, but results show that one nanoquartz sample was less toxic and another one was equivalent in toxicity to Min-U-Sil. Three quartz-particle types of different sizes were tested along with a negative control. Nanoquartz 2 (size: 12 nm) produced a greater or equivalent response compared to Min-U-Sil, and fine quartz was less toxic than Min-U-Sil. Nanoquartz 2 has eighteen times the surface area of Min-U-Sil. All quartz particle-types produced ongoing inflammatory responses to varying degrees. Min-U-Sil and Nanoquartz 2 produced greater accumulation of macrophages that did not get cleared.

A red blood cell hemolysis assay can be useful as a measure of surface reactivity for quartz samples. In our study, surface reactivity was more predictive for toxicity than surface area or size. Hemolytic potential does not correlate well for other particle types.

Inhalation of zinc oxide particles can cause metal fume fever. Tests were performed by Dr. Warheit to see if nano-sized zinc oxide was more potent than fine zinc oxide. As an aerosol, the particles were observed to aggregate in the inhalation chamber. The question then arises, following deposition in the lung - do particles then behave as an aggregate or do they disaggregate? Both nano-sized and fine zinc oxide produced aggregates of similar sizes and both had similar toxicity profiles based on pulmonary biomarkers.

To investigate impacts of particle surface coatings, six grades of TiO_2 with various coatings/surface treatments were examined. Although titanium dioxide is generally considered a low toxicity material, the TiO_2 with the highest level of surface coating caused an inflammatory response that was maintained longer than for the other TiO_2 samples, and also produced the greatest cytotoxicity (still minor compared to quartz particles).

To summarize, it cannot be assumed that nanomaterials are the same as their bulk counterparts. The chemistry and physics (physical properties) change as one moves down the nanoscale – but what about the biology or toxicology? Each particle type should be tested on a case-by-case basis.

Question-and-Answer Session

A questioner asked what causes the toxicity of nanoquartz. Dr. Warheit answered that quartz is listed as a class 1 human carcinogen; it is a variable entity. Epidemiologists believe that quartz has lead to lung cancer and fibrosis in some cases but not in others; experts don't know why. There may be a difference between synthetic and mined quartz; iron content may play a role. A questioner asked whether one can correlate inflammation and cytotoxicity with the amount of material removed via the mucociliary elevator. Dr. Warheit indicated that it depends on particle type. Those not cleared can cause inflammation. Even low toxicity materials have clearance half-times of 55 days in rats and much longer in humans. Overloading can produce longer clearance times, and inflammation. A commenter stated that the standard for "nano-sized" materials had been set at approximately 1-100 nanometers and that he found it curious that hemolysis was used instead of a cell apoptosis test. The commenter wondered if Min-U-Sil could be used as a positive control for hemolysis. Dr. Warheit responded that hemolysis studies were performed using fourteen particle types. The preliminary conclusion was that it was not instructive for particles other than quartz and that most available nanoparticle studies are *in vitro*. Comparisons have been done *in vitro* and *in vivo*. For diesel extracts, *in vitro* tests have given opposite results compared to the *in vivo* tests when assessing toxicity ranking of the same particulate materials. In a current ongoing study comparing *in vitro* results with *in vivo* effects for 5 different dusts, the *in vitro* data appear to be problematic in terms of validating the *in vivo* results.

Impact of Nanoparticulates On Respiratory Health Effects: Toxicity Is Not Always Dependent Solely Upon Particle Size and Surface Area

David B. Warheit, Ph.D.
DuPont Haskell Laboratory
Newark, DE

Nanotechnology and OSWER: New Opportunities and Challenges
July 12, 2006

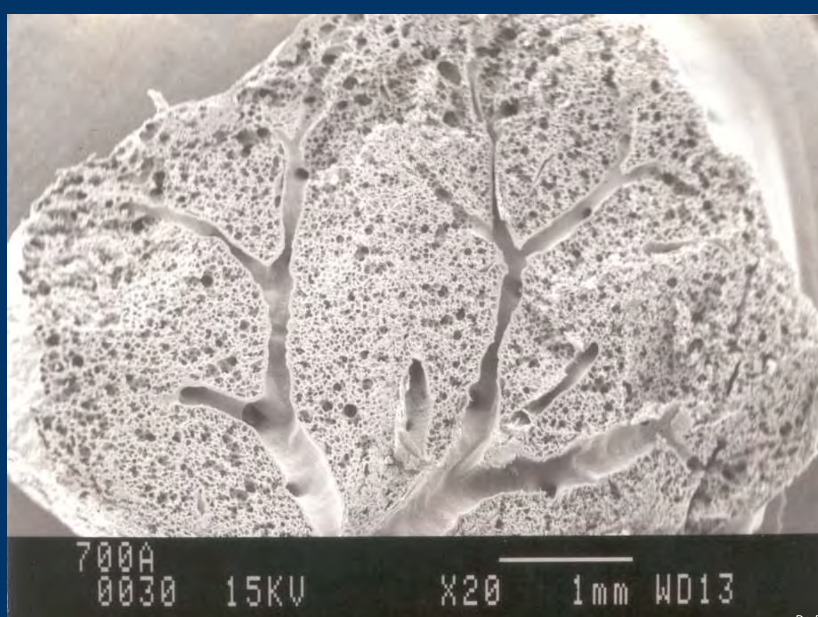
Outline

- Lung structure and particle deposition
- Pulmonary bioassay as a measure of lung toxicity- Hazard Assessment
- Pulmonary bioassay with Fine/Nanoscale TiO_2 dots and rods; Fine/Nanoscale Quartz particles, and Fine/Nanoscale ZnO particles
- Impacts of Particle Surface Coatings
- Summary

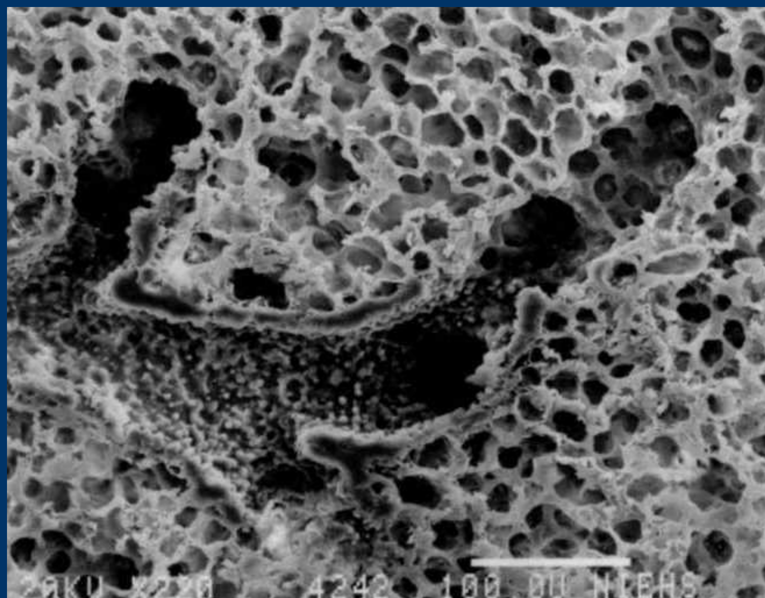
Definitions- Particle Size

- Nano = Ultrafine = < 100 nm
- Fine = 100 nm - 3 µm
- Respirable (rat) = < 3 µm (max = 5 µm)
- Respirable (human) = < 5 µm (max = 10 µm)
- Inhalable (human) = ~ 10 - 100 µm

Rat Lung Microdissection



Rat Lung Tissue Dissected to Demonstrate the Junction of the Terminal Airway and Proximal Alveolar Region



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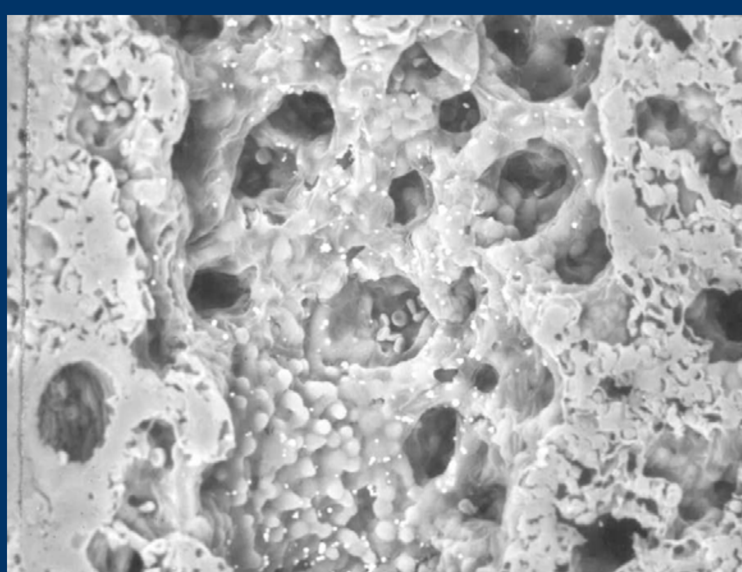
5 of 79

Iron Particle Deposition at Bronchoalveolar Junction



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6 of 79

Iron Particle Deposition at Bronchoalveolar Junction

(Backscatter Image)

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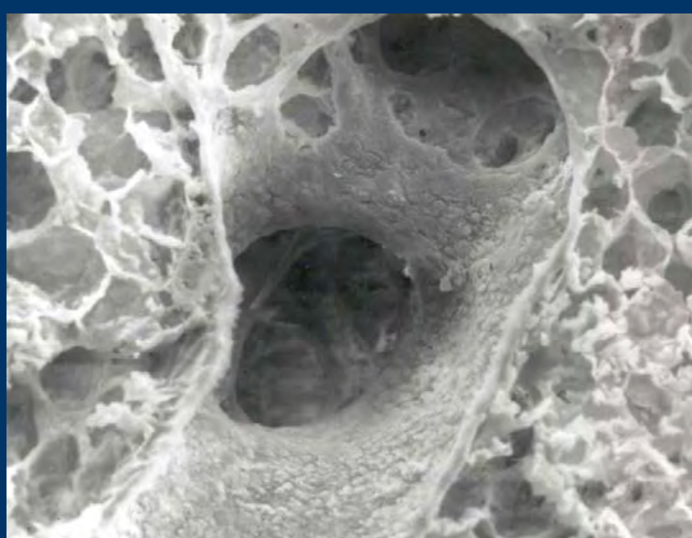
7 of 79

Alveolar Macrophage Clearance of Inhaled Iron Particles



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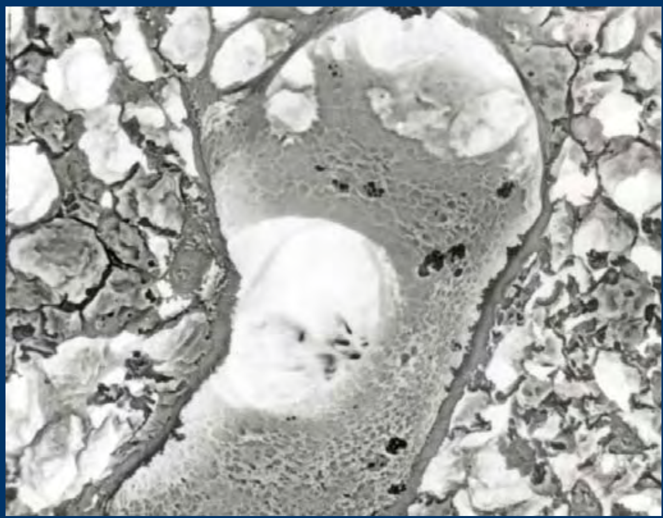
8 of 79

Alveolar Macrophage Clearance of Inhaled Iron Particles

(Backscatter Image)



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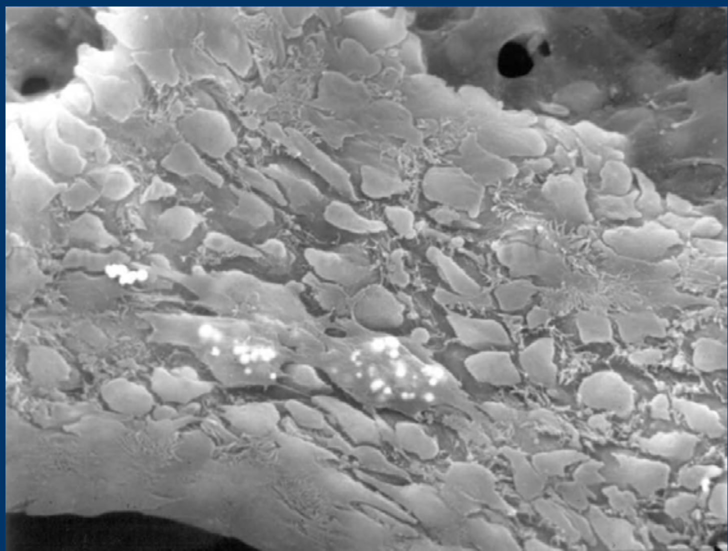
9 of 79

Alveolar Macrophage Migration to Iron Particle Deposition and Phagocytosis



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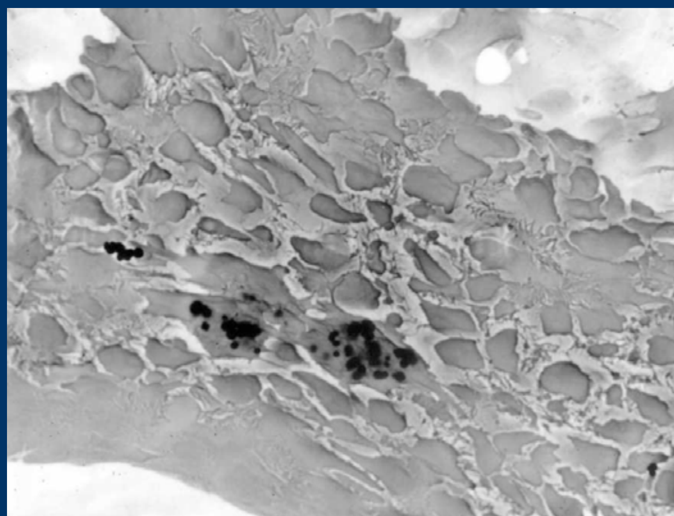
10 of 79

Alveolar Macrophage Migration to Iron Particle Deposition and Phagocytosis

(Backscatter Image)



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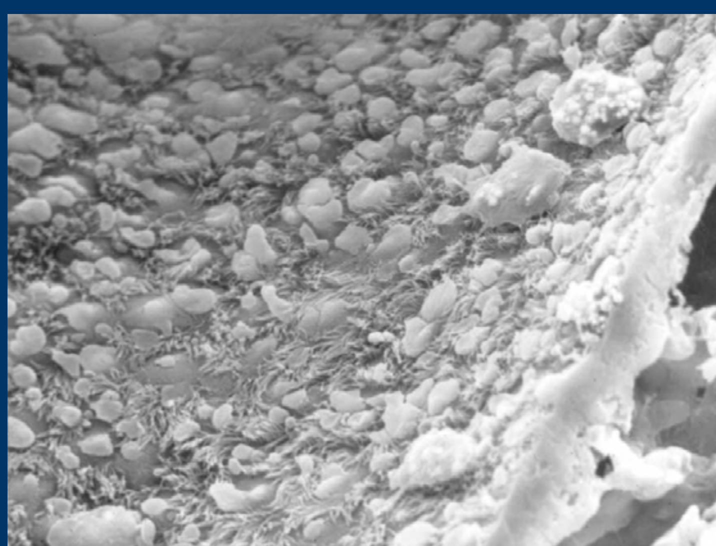
11 of 79

Clearance of Iron Particles on the Airway Mucociliary Escalator



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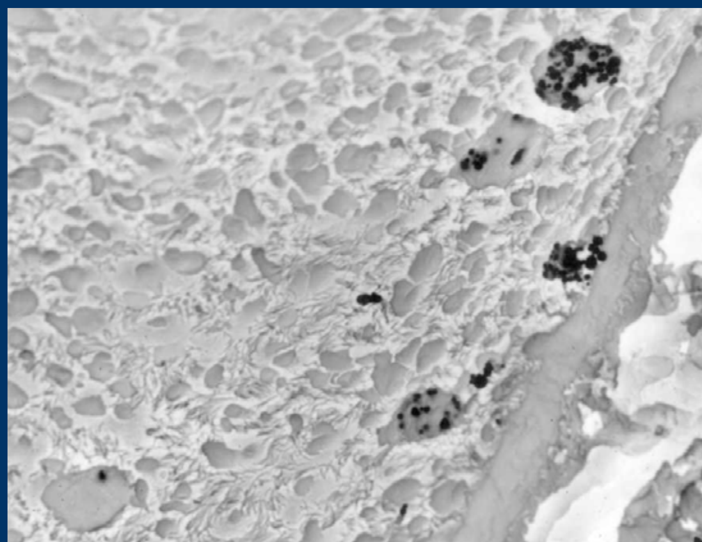
12 of 79

Clearance of Iron Particles on the Airway Mucociliary Escalator



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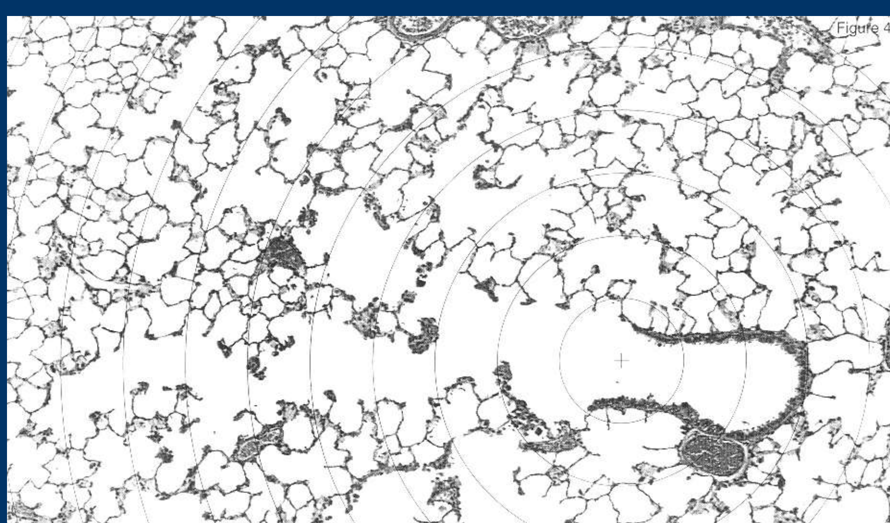
13 of 79

Morphometry at Bronchoalveolar Junctions



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14 of 79

Common Perceptions on Pulmonary Toxicity of Nanoparticles

- Nanoparticles are more toxic (inflammogenic, tumorigenic) than fine-sized particles of identical composition.
- Concept generally based on 3 particle-types:
  - Titanium Dioxide particles
  - Carbon Black particles
  - Diesel Particles

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15 of 79

Complications related to the Dogma of Nanoparticulate Toxicology

- Not all Nanoparticles are more toxic
- Surface coatings of particles
  - Coatings - passivated or dispersion
- Species Differences in Lung Responses
  - Rat is the most sensitive species
- Particle aggregation/disaggregation potential
- Fumed vs. precipitated Nanoparticles
- Surface charge of particles

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16 of 79

The Key Issue: Risk

Health Risk is a product of

- **Hazard and Exposure**

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17 of 79

Studies to Assess Pulmonary Hazards to Nanoparticulates

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18 of 79

Pulmonary Bioassay Studies

- Working hypothesis
- Four factors influence the development of pulmonary fibrosis
  1) inhaled materials which cause cell/lung injury
  2) inhaled materials which promote ongoing inflammation
  3) inhaled materials which reduce alveolar macrophage function
  4) inhaled materials which persist in the lung

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19 of 79

Pulmonary Bioassay Components

Bronchoalveolar Lavage Assessments

Lung Inflammation & Cytotoxicity

- Cell Differential Analysis
- BAL Fluid Lactate Dehydrogenase (cytotoxicity)
- BAL Fluid Alkaline Phosphatase (epithelial cell toxicity)
- BAL Fluid Protein (lung permeability)

Lung Tissue Analysis

- Lung Weights
- Lung Cell Proliferation (BrdU)
  - Parenchymal
  - Airway
- Lung Histopathology

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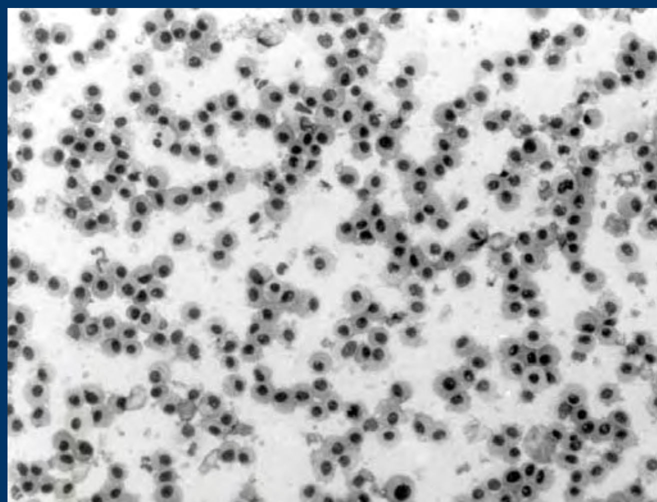
20 of 79

Cytocentrifuge Preparation of BAL – Recovered Cells From a Sham – Exposed Rat



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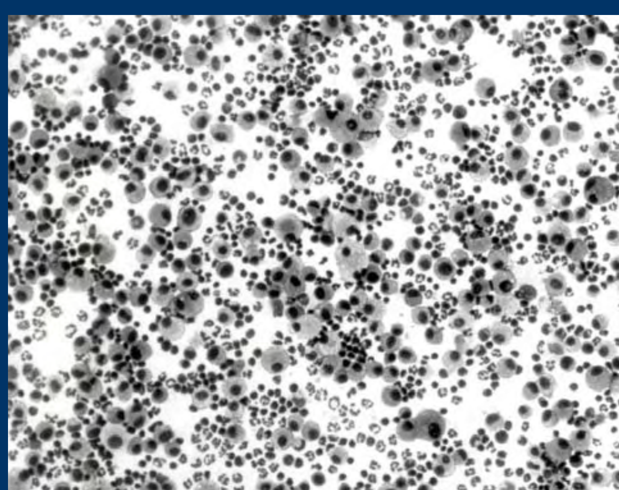
21 of 79

Cytocentrifuge Preparation of BAL – Recovered Cells From a Quartz (Crystalline Silica) – Exposed Rat



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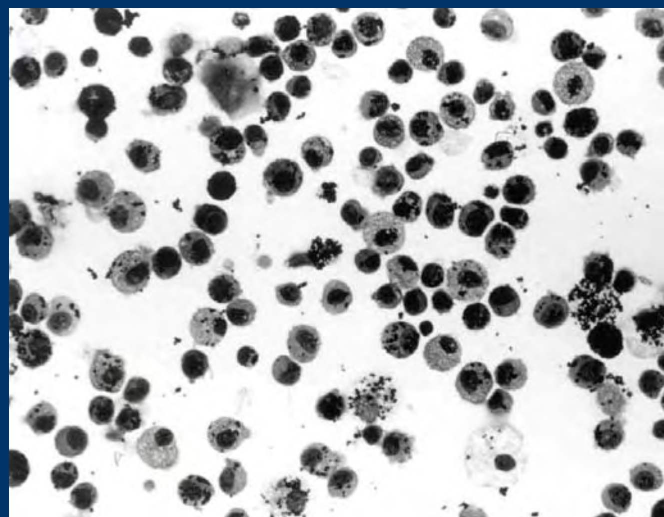
22 of 79

Cytocentrifuge Preparation of BAL – Recovered Cells From a Carbonyl Iron – Exposed Rat



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23 of 79

Use of Bronchoalveolar Lavage, Cell Proliferation, and Histopathology to Assess the Lung Toxicity of Particulate samples

(BALF = Bronchoalveolar Lavage Fluid Analysis)

Parameter	Indicator
BALF Cells and Differentials	Lung Inflammation
BALF Lactate Dehydrogenase	Non-specific cytotoxicity
BALF Alkaline Phosphatase	Type 2 cell epithelial toxicity
BALF Protein	Permeability ↑ of alveolar/ capillary barrier
Lung Weights	Pulmonary edema or fibrosis
Macrophage phagocytosis	Lung clearance functions
Cell Proliferation	Inflammation/lung fibrosis and tumor potential
Histopathology	Evaluation of lung tissue responses

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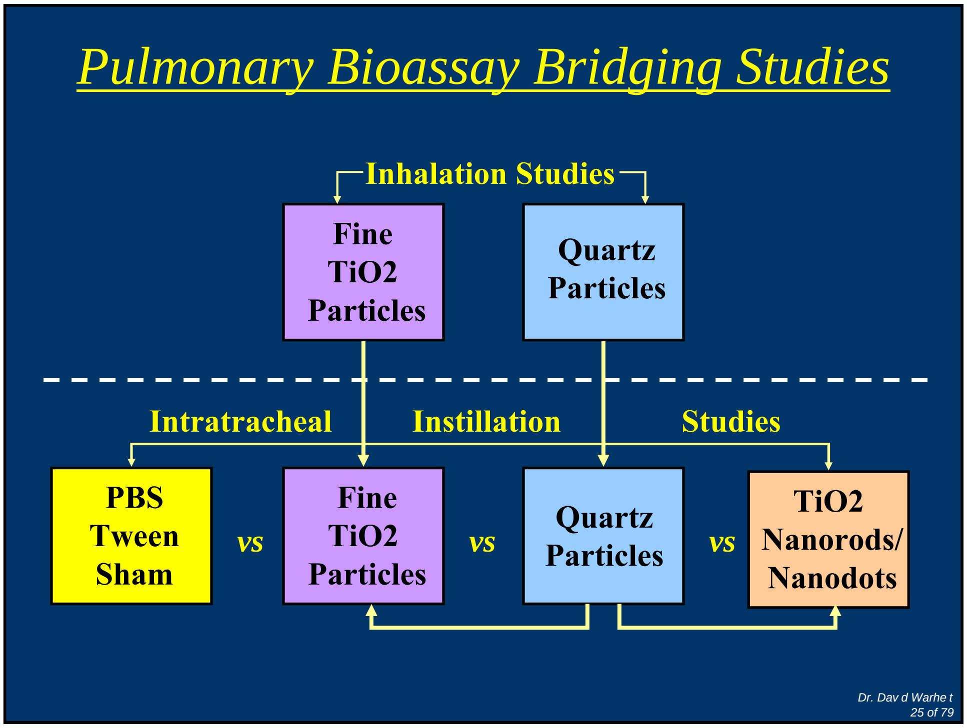
24 of 79


Pulmonary Bioassay Bridging Studies
Inhalation Studies
Fine TiO2 Particles
Quartz Particles
Intratracheal
Instillation
Studies
PBS Tween Sham
vs
Fine TiO2 Particles
vs
Quartz Particles
vs
TiO2 Nanorods/ Nanodots
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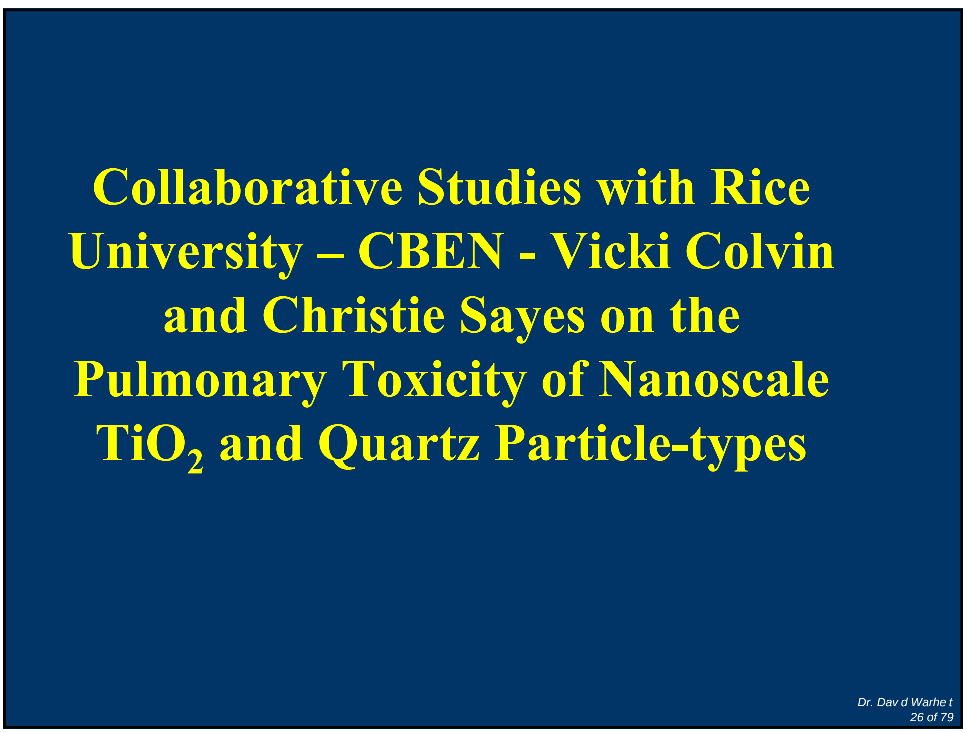
25 of 79


Collaborative Studies with Rice University – CBEN - Vicki Colvin and Christie Sayes on the Pulmonary Toxicity of Nanoscale TiO_2 and Quartz Particle-types
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26 of 79

TiO_2

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27 of 79

Pulmonary Instillation Studies with Nanoscale TiO_2 Rods and Dots in Rats: Toxicity is not Dependent upon Particle Size and Surface Area

DB Warheit, TR Webb CM Sayes, VL Colvin and KL Reed

- **Toxicological Sciences 91:227-236, 2006**

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28 of 79

Protocol for Nanoscale TiO2 Pulmonary Bioassay Study

Intratracheal Instillation Exposure Doses of 1 and 5 mg/kg

Exposure Groups
- PBS (control)
- Particulate Types (1 and 5 mg/kg)
  - Fine-sized TiO2 particles
  - Nanoscale TiO2 rods
  - Nanoscale TiO2 dots
  - Quartz Particles (positive control)

Instillation Exposure

Postexposure Evaluation via BAL and Lung Tissue

24 hr | **1 wk** | **1 mo** | **3 mo**

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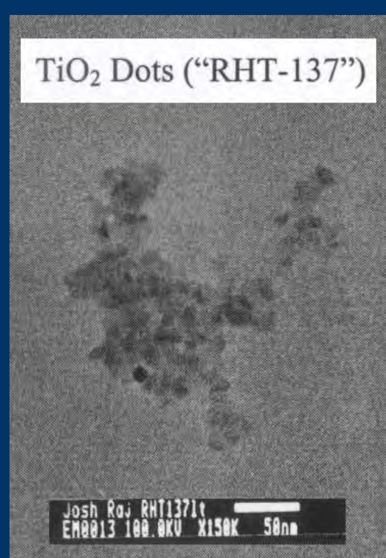
29 of 79

TiO2 Nanoscale Dots



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30 of 79

TiO2 Nanoscale Rods

Dr. Dav d Warhe t
31 of 79

TiPure® R-100

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32 of 79

Characterization of Nanoscale TiO_2 and Quartz Particles

	XRD	particle size	Surface Area
• **Fine TiO_2**	rutile	d_{50} = 300 nm	**6.0 m^2/g**
• **TiO_2 Nanorods**	anatase	length= 90 - 233 nm width = 20 – 35 nm	**26.5 m^2/g**
• **TiO_2 Nanodots**	anatase	d_{50} = 6 nm	**169.4 m^2/g**
• **Min-U-Sil**	αQ	d_{50} = 1.3 µm	**4.0 m^2/g**

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33 of 79

RESULTS

Biomarkers =
Pulmonary Inflammation
Pulmonary Cytotoxicity

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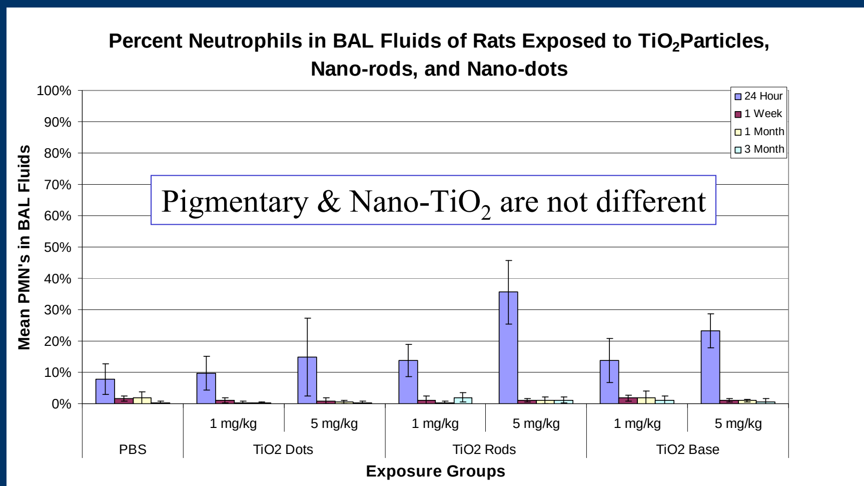
34 of 79

Collaborative Studies with Rice University: TiO_2



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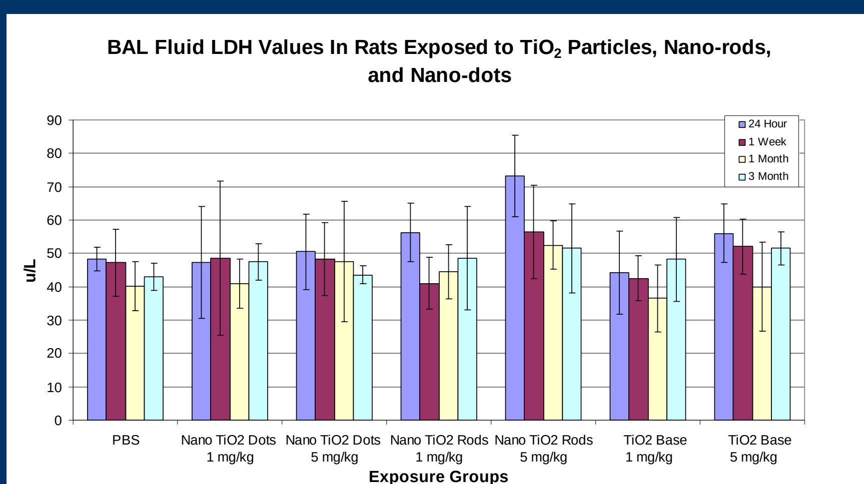
35 of 79



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36 of 79

Second Nanoscale TiO2 Study

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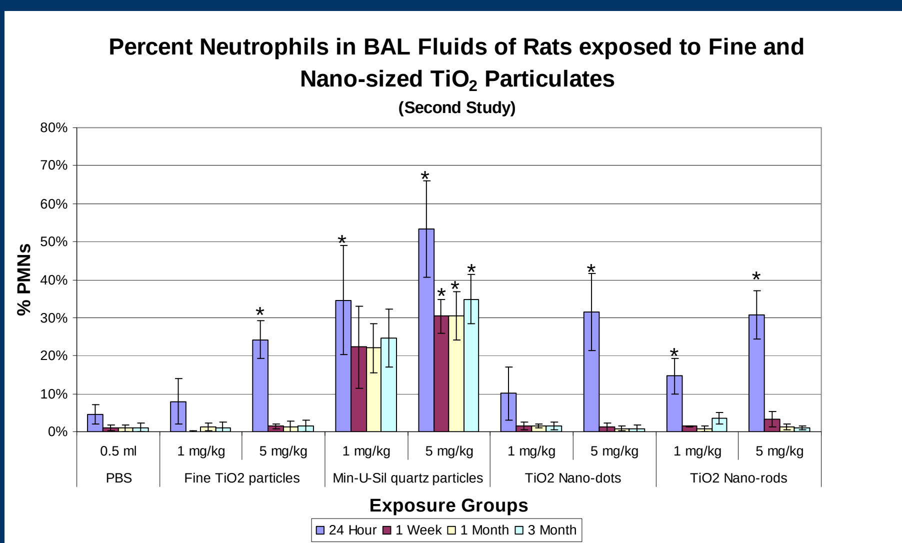
37 of 79

Pulmonary Inflammation



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38 of 79

Characterization of Nanoscale TiO_2 and Quartz Particles

	XRD	particle size	Surface Area
• **Fine TiO_2**	rutile	d_{50} = 300 nm	**6.0 m^2/g**
• **TiO_2 Nanorods**	anatase	length= 90 - 233 nm width = 20 – 35 nm	**26.5 m^2/g**
• **TiO_2 Nanodots**	anatase	d_{50} = 6 nm	**169.4 m^2/g**
• **Min-U-Sil**	αQ	d_{50} = 1.3 µm	**4.0 m^2/g**

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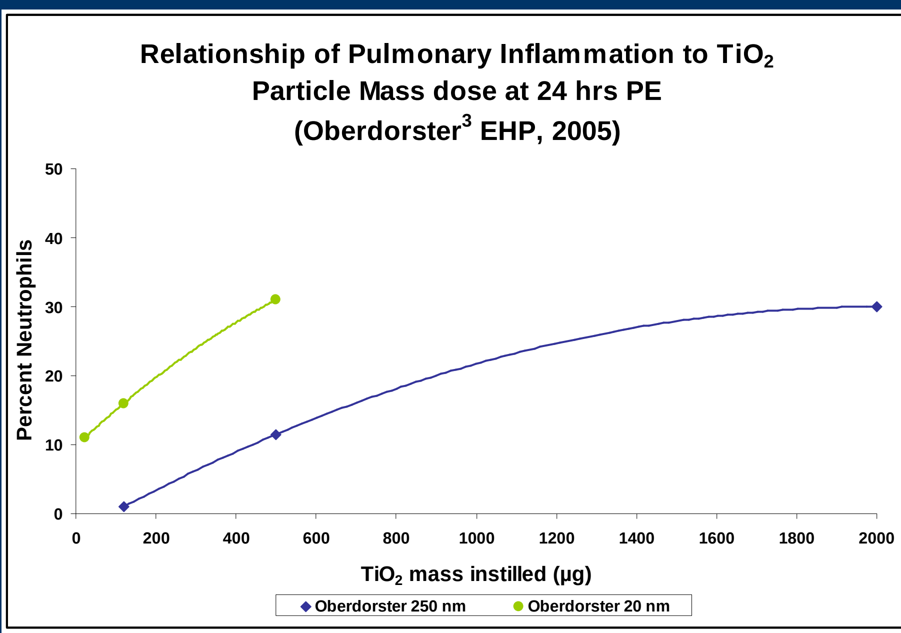
39 of 79



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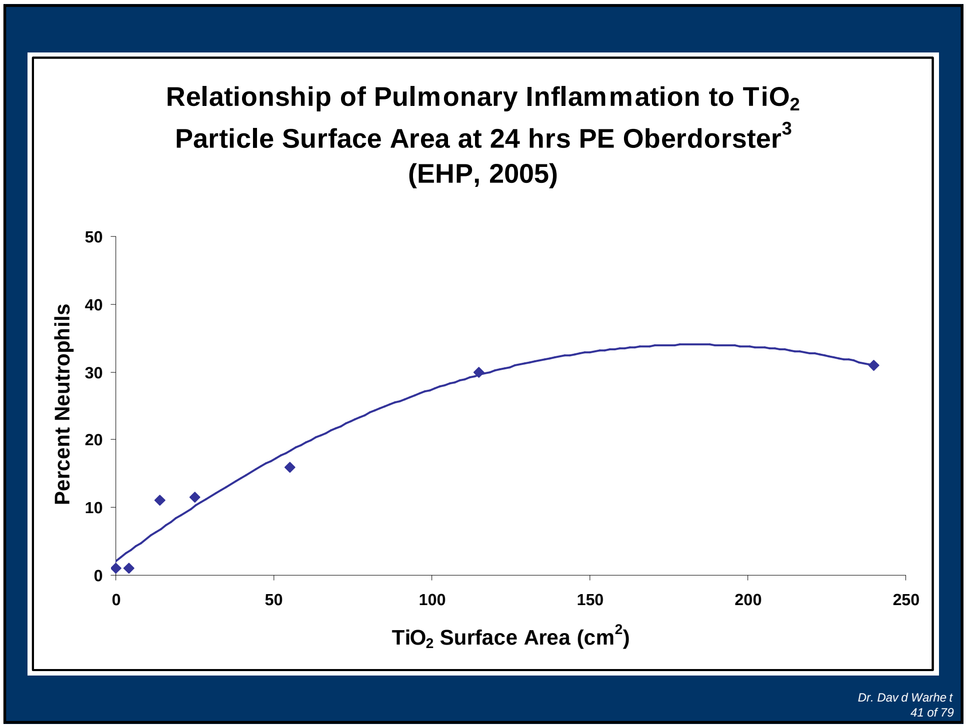
40 of 79


Relationship of Pulmonary Inflammation to TiO2
Particle Surface Area at 24 hrs PE Oberdorster3
(EHP, 2005)
Percent Neutrophils
0
10
20
30
40
50
0
50
100
150
200
250
TiO2 Surface Area (cm2)
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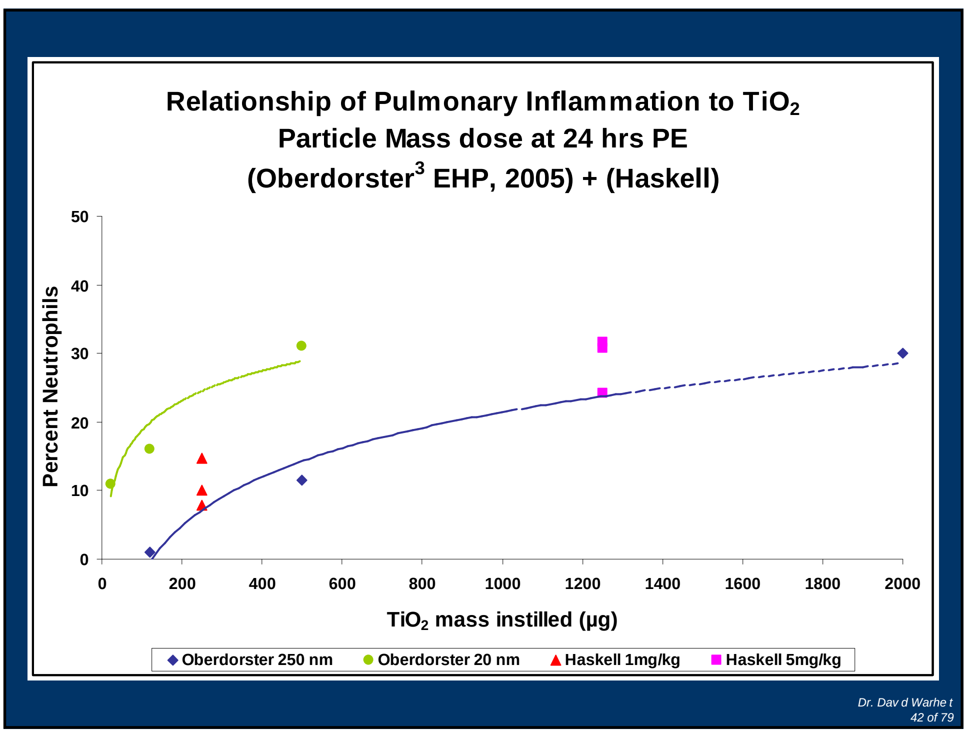
41 of 79


Relationship of Pulmonary Inflammation to TiO2
Particle Mass dose at 24 hrs PE
(Oberdorster3 EHP, 2005) + (Haskell)
Percent Neutrophils
0
10
20
30
40
50
0
200
400
600
800
1000
1200
1400
1600
1800
2000
TiO2 mass instilled (µg)
Oberdorster 250 nm
Oberdorster 20 nm
Haskell 1mg/kg
Haskell 5mg/kg
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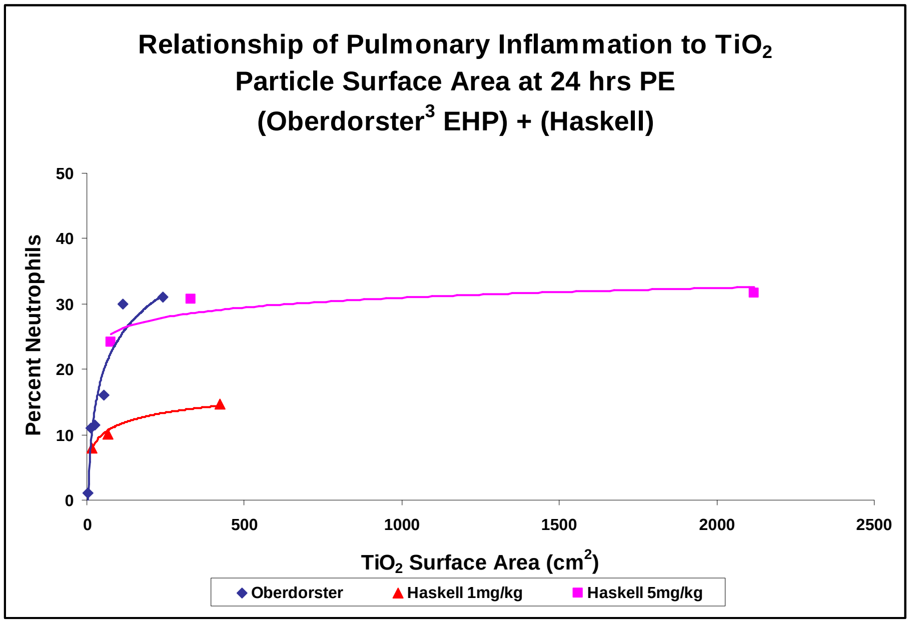
42 of 79



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43 of 79

Hypothesis and a Question

- Hypothesis: At similar doses - Ultrafine (Nano) particles have greater pulmonary toxicity than fine-sized particles of identical composition.
- Question – generally this dogma applies to low toxicity particulates. However, in considering a cytotoxic particle such as crystalline silica – would nanoquartz particles be even more toxic than fine-sized Min-U-Sil quartz particles?

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44 of 79

Nanoscale Quartz

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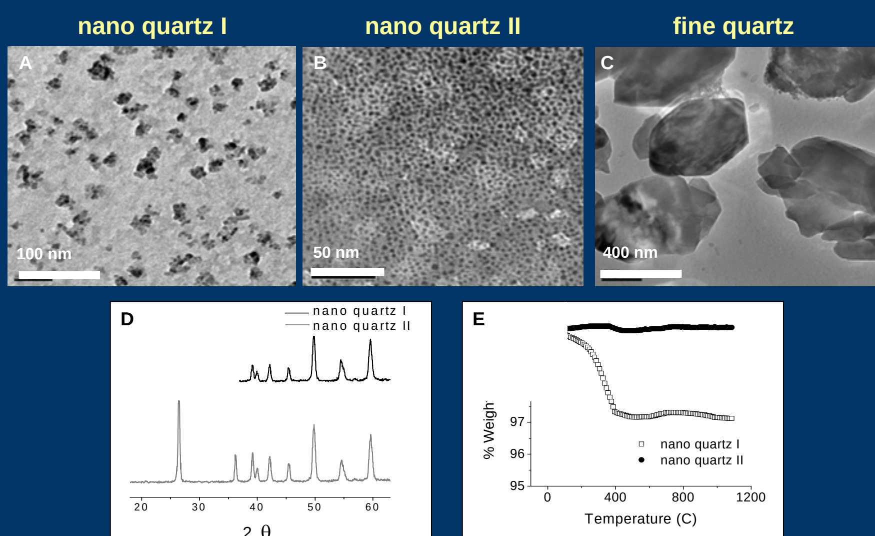
45 of 79

Physicochemical Characterization of Quartz Particulates



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46 of 79

Physicochemical Characterization of Quartz Particulates (cont.)

Sample	Average Size (nm)	Size Range (nm)	Surface Area (m^2/g)	Crystallinity	ICP-AES (% Fe content)
nano quartz I	50	30-65	31.4	α-quartz	0.080%
nano quartz II	12	10-20	90.5	α-quartz	0.034%
fine quartz	300	100-500	4.2	α-quartz	0.011%
Min-U Sil	534	300-700	5.1	α-quartz	0.042%

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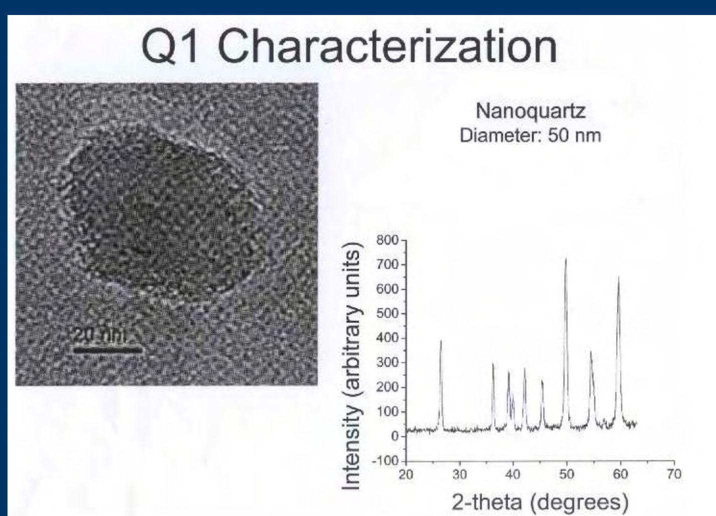
47 of 79

Nanoscale Quartz Particles



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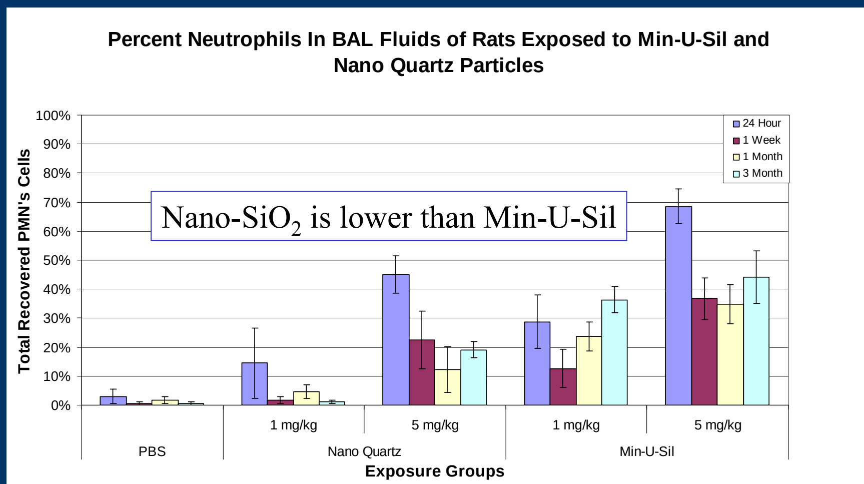
48 of 79

Preliminary Collaborative Studies with Rice University: SiO_2



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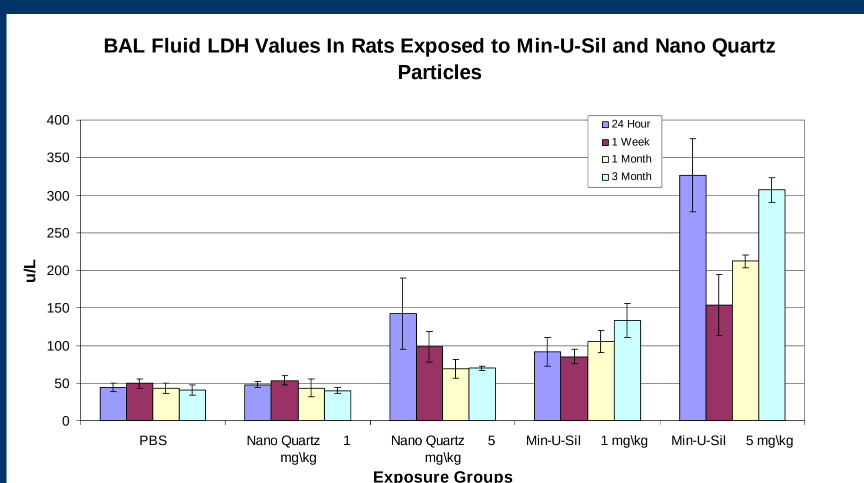
49 of 79



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50 of 79

Characterization of Quartz Particles

	XRD particle size	Surface Area
• **Nanoscale-Q I**	αQ d_{50} = 50 nm	**31.4 m^2/g**
• **Min-U-Sil**	αQ d_{50} = 534 µm	**5.1 m^2/g**

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51 of 79

Second Nanoscale Quartz Study

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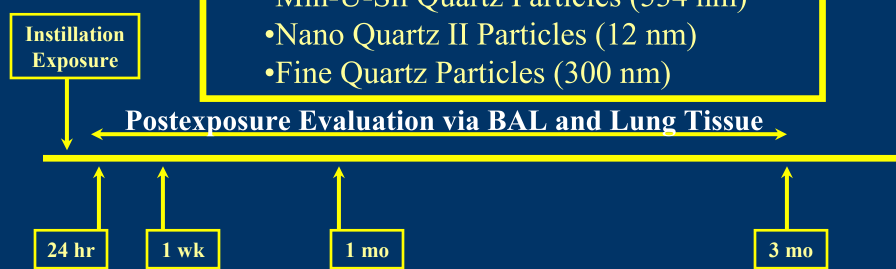
52 of 79

Protocol for Second Nano quartz Pulmonary Bioassay Study

Intratracheal Instillation Exposure Doses of 1 and 5 mg/kg

Exposure Groups
- PBS (vehicle control)
- Particulate Types (1 and 5 mg/kg)
  - •Carbonyl Iron Particles (negative control)
  - •Min-U-Sil Quartz Particles (534 nm)
  - •Nano Quartz II Particles (12 nm)
  - •Fine Quartz Particles (300 nm)



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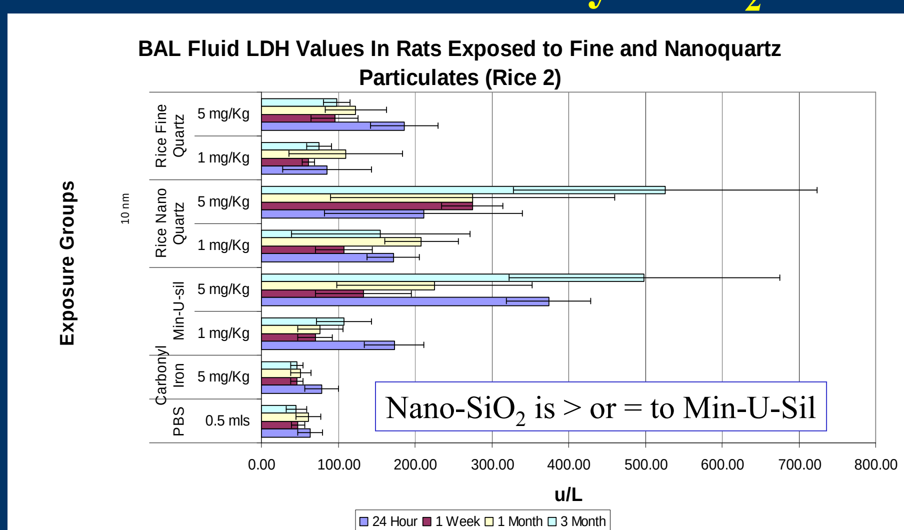
53 of 79

Follow-up Collaborative Studies with Rice University: SiO_2



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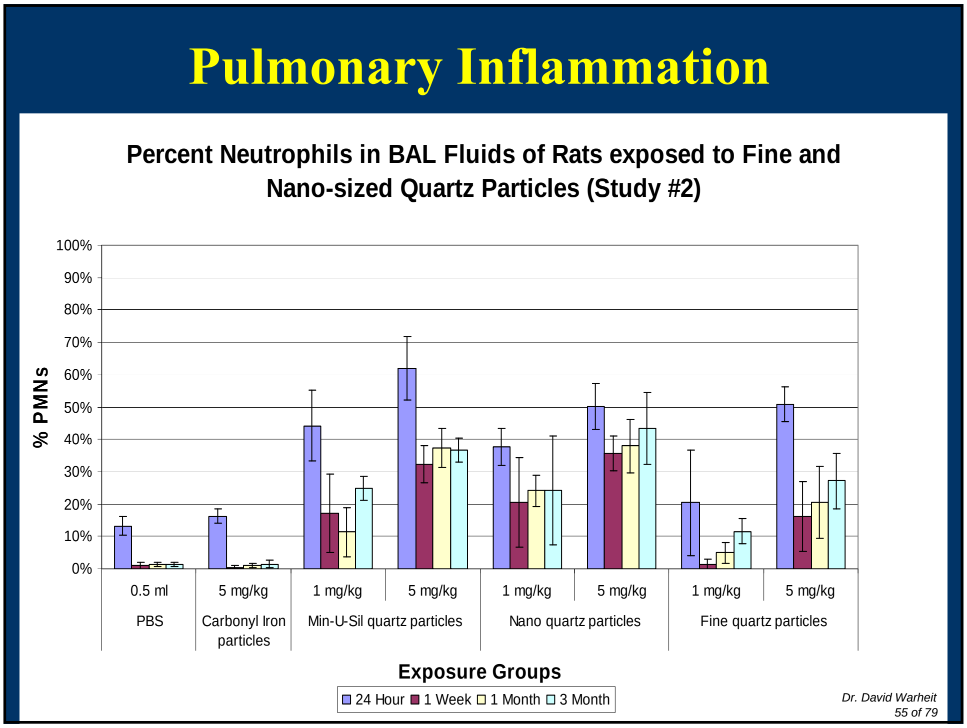
54 of 79


Pulmonary Inflammation
Percent Neutrophils in BAL Fluids of Rats exposed to Fine and Nano-sized Quartz Particles (Study #2)
% PMNs
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0.5 ml
PBS
5 mg/kg
Carbonyl Iron particles
1 mg/kg
5 mg/kg
Min-U-Sil quartz particles
1 mg/kg
5 mg/kg
Nano quartz particles
1 mg/kg
5 mg/kg
Fine quartz particles
Exposure Groups
24 Hour
1 Week
1 Month
3 Month
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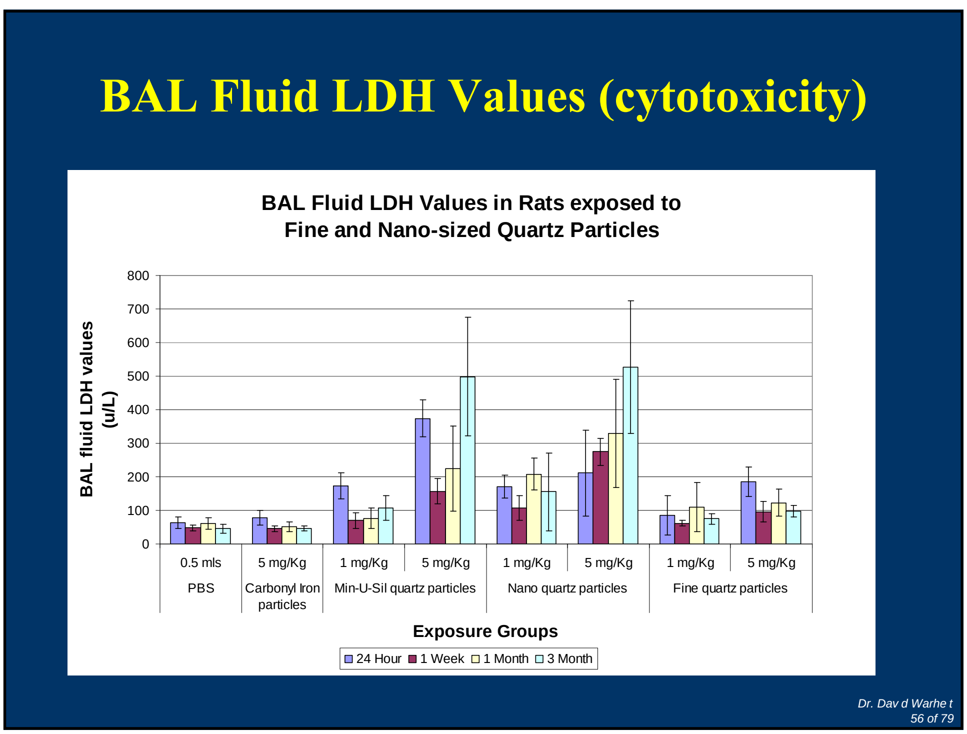
55 of 79


BAL Fluid LDH Values (cytotoxicity)
BAL Fluid LDH Values in Rats exposed to Fine and Nano-sized Quartz Particles
BAL fluid LDH values (u/L)
800
700
600
500
400
300
200
100
0
0.5 mls
PBS
5 mg/Kg
Carbonyl Iron particles
1 mg/Kg
5 mg/Kg
Min-U-Sil quartz particles
1 mg/Kg
5 mg/Kg
Nano quartz particles
1 mg/Kg
5 mg/Kg
Fine quartz particles
Exposure Groups
24 Hour
1 Week
1 Month
3 Month
56 of 79

Characterization of Quartz Particles

	XRD particle size	Surface Area
• **Fine Quartz**	αQ d_{50} = 300 nm	**4.2 m^2/g**
• **Nanoscale-Q II**	αQ d_{50} = 12 nm	**90.5 m^2/g**
• **Min-U-Sil**	αQ d_{50} = 534 nm	**5.1 m^2/g**

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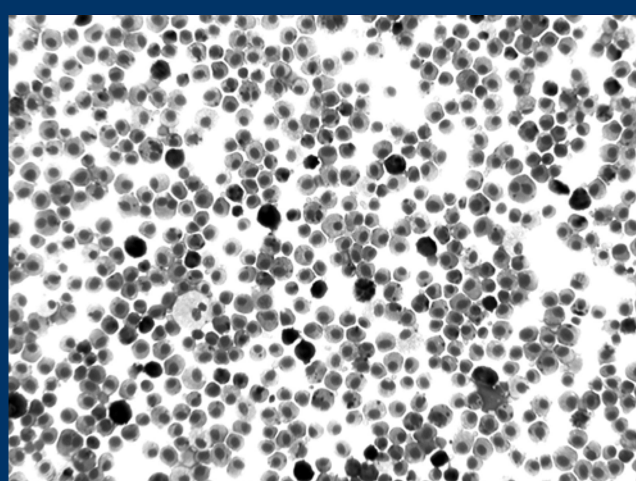
57 of 79

CI – 2B-3M – 2aab – 20x



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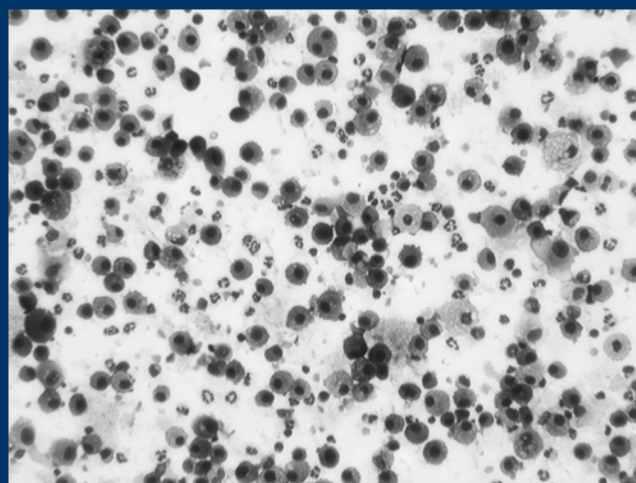
58 of 79

FineQ-5B-3M-2a-20x



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59 of 79

FineQ-5B-3M-5-10x

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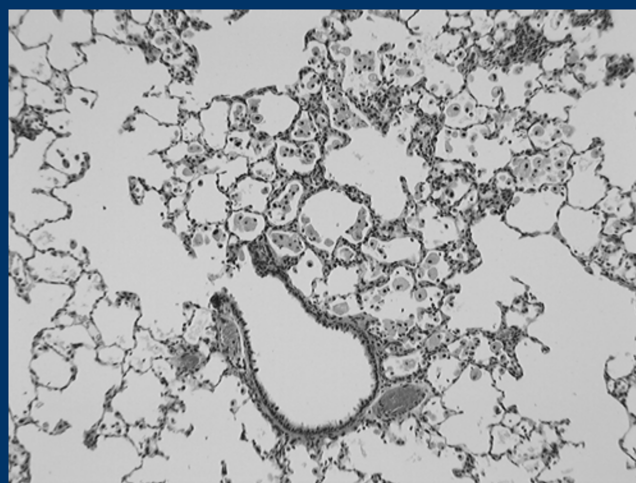
60 of 79

Min-U-Sil-3B-3M - 2-10x



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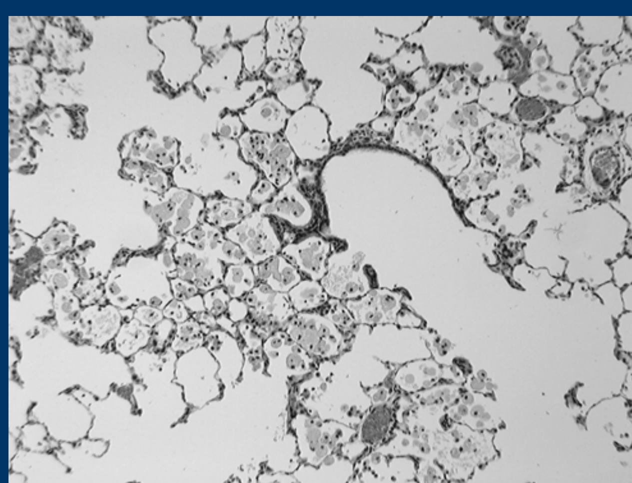
61 of 79

NanoQ-4B-3M-5



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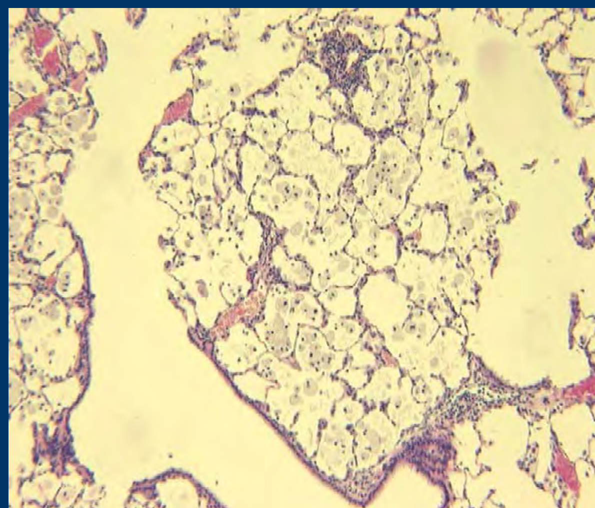
62 of 79

Lung Section of Rat exposed to Nanoquartz Particles (3M pe)



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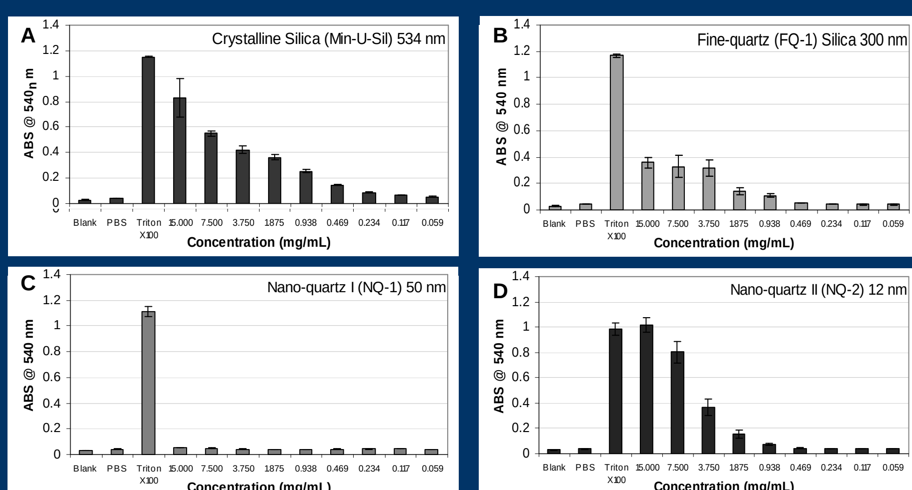
63 of 79

Hemolytic Potential of Quartz Samples (Surface Reactivity)



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64 of 79

Summary of α-Quartz Results

Endpoint	Nano quartz I	Nano quartz II	Fine quartz	Min-U-Sil
Particle size	++	+	+++	++++
Surface area	+++	++++	++	+
Fe content	+++	++	+	++
Crystallinity	++++	++++	++++	++++
Radical content	+	++	+	+++
Hemolytic potential	+	+++	++	+++
Lung inflammation	++	+++	++	+++
Cytotoxicity	++	+++	+	+++
Airway BrdU	NA	++	+	++
Lung paren. BrdU	NA	++	+	++
Histopathology	NA	++++	++	+++

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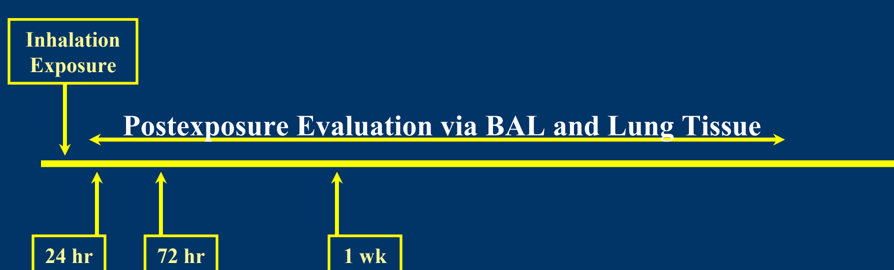
65 of 79

Protocol for Fine and Nanoscale ZnO Pulmonary Bioassay Studies

Inhalation Exposure at concs of 25, 35 or 50 mg/m^3 for 1 or 3 hours



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66 of 79

Aerosol Generation Equipment and Set-up

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67 of 79

Mean Particle Size Determinations in the ZnO and MgO Inhalation Studies

Study	MMAD (cascade impactor)
• ZnO 25 mg/m^3	3.3 µm
• ZnO 35 mg/m^3	2.7 – 3.2 µm
• ZnO 50 mg/m^3	3.2 µm
• MgO 50 mg/m^3	3.0 µm
• Nano ZnO 25 mg/m^3	2.8 µm

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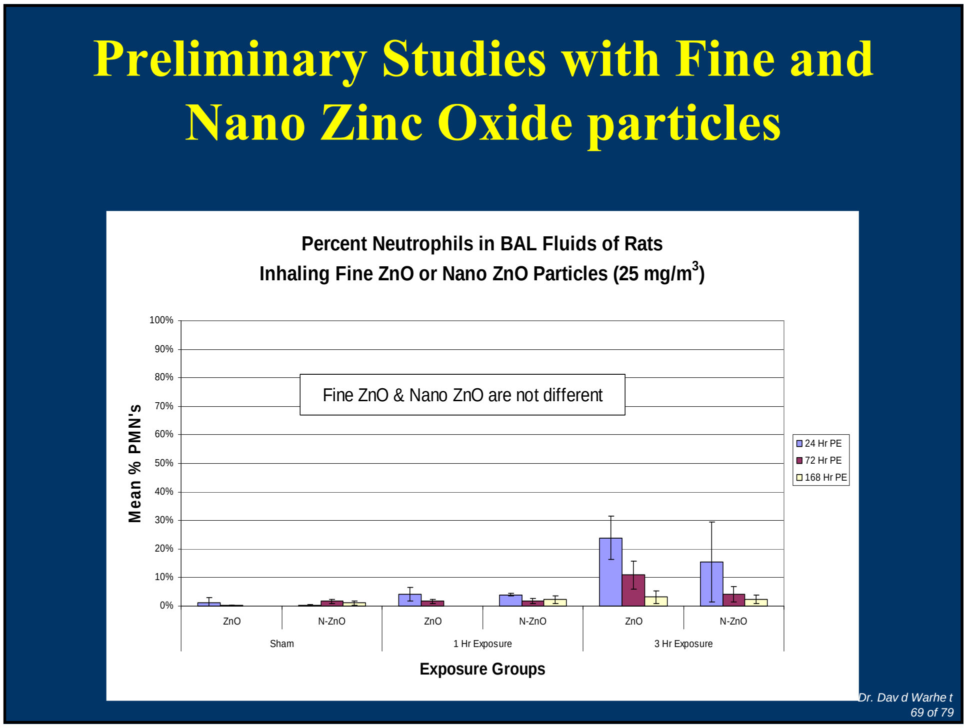
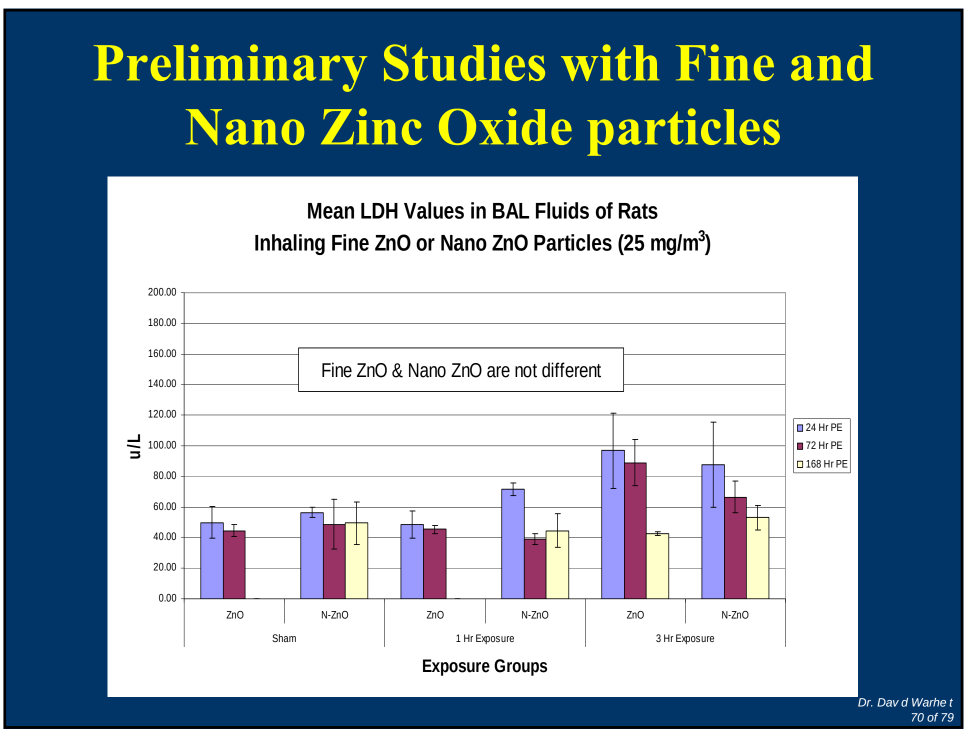
68 of 79



Preliminary Studies with Fine and Nano Zinc Oxide particles
Percent Neutrophils in BAL Fluids of Rats
Inhaling Fine ZnO or Nano ZnO Particles (25 mg/m3)
Mean % PMN's
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Fine ZnO & Nano ZnO are not different
24 Hr PE
72 Hr PE
168 Hr PE
ZnO
N-ZnO
ZnO
N-ZnO
ZnO
N-ZnO
Sham
1 Hr Exposure
3 Hr Exposure
Exposure Groups
69 of 79



Preliminary Studies with Fine and Nano Zinc Oxide particles
Mean LDH Values in BAL Fluids of Rats
Inhaling Fine ZnO or Nano ZnO Particles (25 mg/m3)
u/L
200.00
180.00
160.00
140.00
120.00
100.00
80.00
60.00
40.00
20.00
0.00
Fine ZnO & Nano ZnO are not different
24 Hr PE
72 Hr PE
168 Hr PE
ZnO
N-ZnO
ZnO
N-ZnO
ZnO
N-ZnO
Sham
1 Hr Exposure
3 Hr Exposure
Exposure Groups
70 of 79

Impact of Surface Treatments/Coatings on TiO_2 Particles

- **Inhalation Studies**
- **Pulmonary Bioassay Intratracheal Instillation Studies**

Dr. Dav d Warhe t
71 of 79

Comparative Pulmonary Toxicity Inhalation and Instillation Studies with Different TiO_2 Particle Formulations: Impact of Surface Treatments on Particle Toxicity

DB Warheit, WJ Brock, KP Lee, TR Webb, and KL Reed

- **Toxicological Sciences 88:514-524, 2005**

Dr. Dav d Warhe t
72 of 79

TiO_2 Coatings Formulations

TiO2 base - 99% TiO2 - 1% alumina

TiO2 I - 99% TiO2 - 1% alumina + organic grinding aid

TiO2 II - 96% TiO2 - 4% alumina

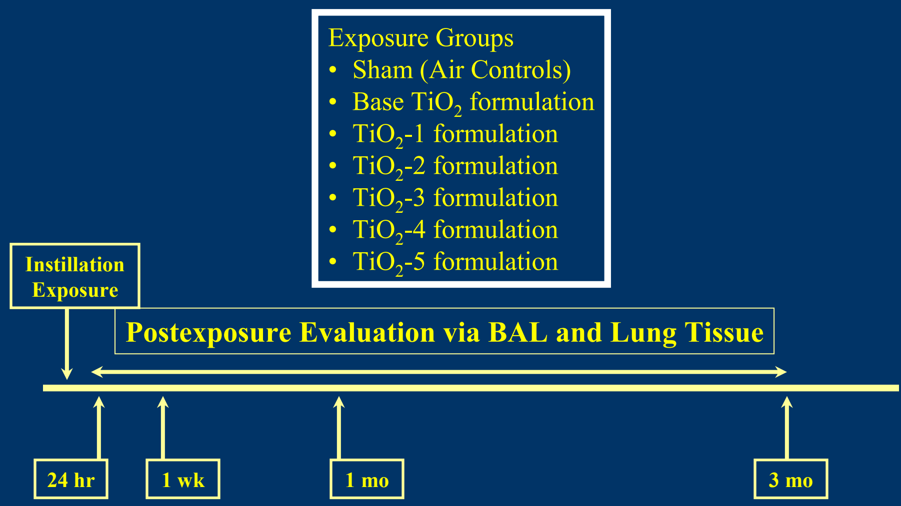
TiO2 III - 83% TiO2 - 6% alumina 11% amorphous silica

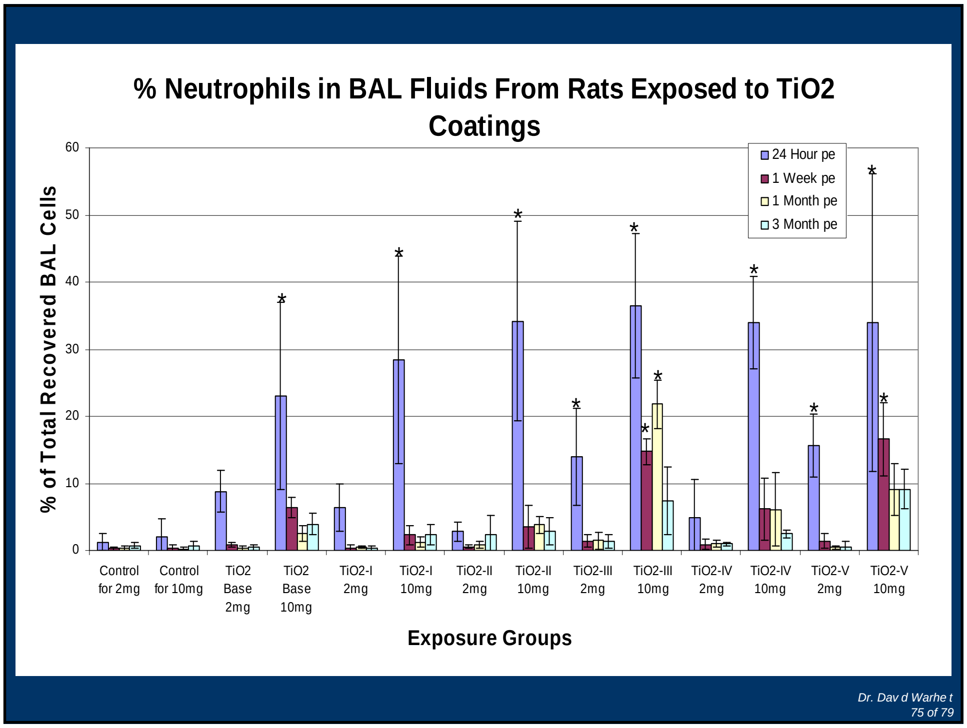
TiO2 IV - 91% TiO2 - 3% alumina - 6% amorphous silica

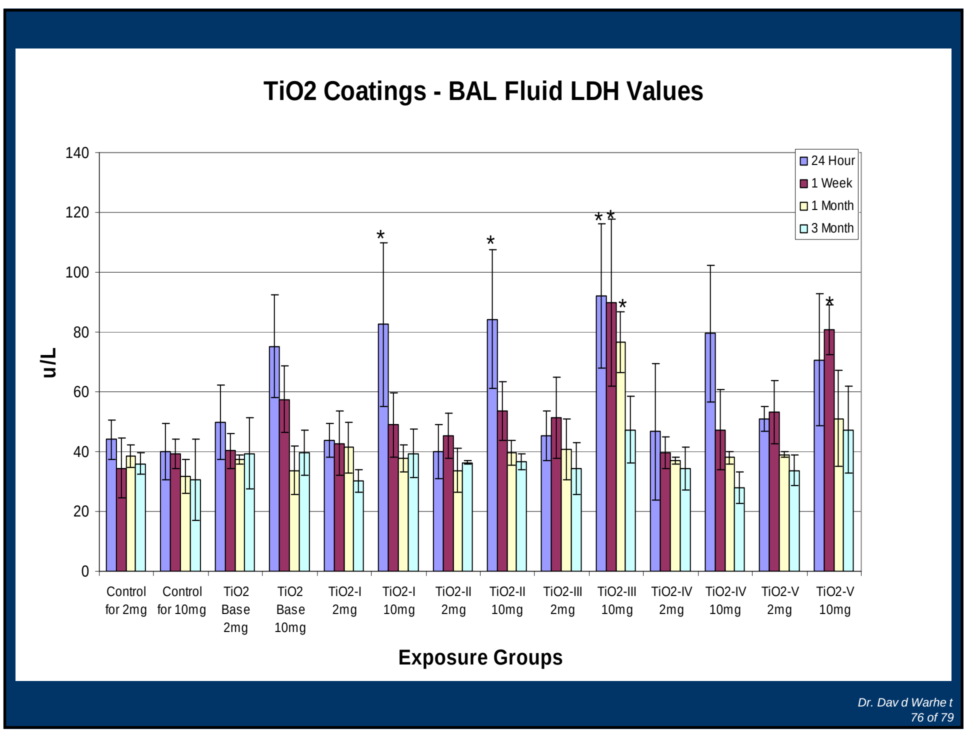
TiO2 V - 94% TiO2 - 3% alumina - 3% amorphous silica

Protocol for TiO_2 Coatings Bioassay Study

Instillation Study




% Neutrophils in BAL Fluids From Rats Exposed to TiO2 Coatings
% of Total Recovered BAL Cells
24 Hour pe
1 Week pe
1 Month pe
3 Month pe
Control for 2mg
Control for 10mg
TiO2 Base 2mg
TiO2 Base 10mg
TiO2-I 2mg
TiO2-I 10mg
TiO2-II 2mg
TiO2-II 10mg
TiO2-III 2mg
TiO2-III 10mg
TiO2-IV 2mg
TiO2-IV 10mg
TiO2-V 2mg
TiO2-V 10mg
Exposure Groups
Dr. Dav d Warhe t
75 of 79


TiO2 Coatings - BAL Fluid LDH Values
u/L
24 Hour
1 Week
1 Month
3 Month
Control for 2mg
Control for 10mg
TiO2 Base 2mg
TiO2 Base 10mg
TiO2-I 2mg
TiO2-I 10mg
TiO2-II 2mg
TiO2-II 10mg
TiO2-III 2mg
TiO2-III 10mg
TiO2-IV 2mg
TiO2-IV 10mg
TiO2-V 2mg
TiO2-V 10mg
Exposure Groups
Dr. Dav d Warhe t
76 of 79

Important Particle Characteristics

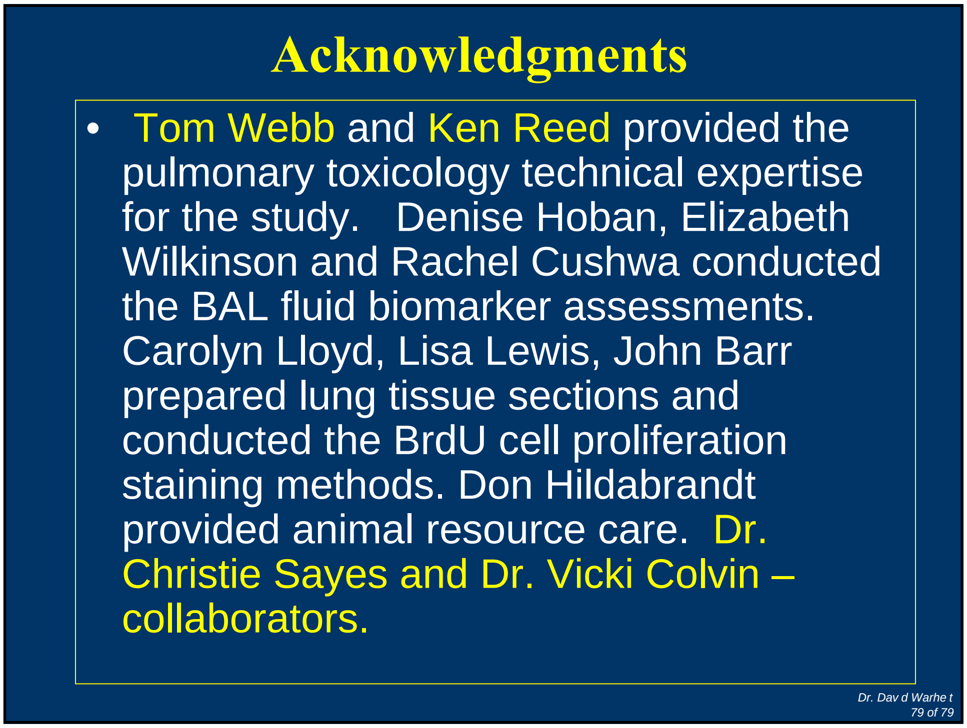
- Primary particle size
- Particle shape (SEM)
- Surface area
- Surface charge
- Composition- e.g crystalline vs.amorphous
- Surface Coatings
- Aggregation status
- Particle number
- Method of synthesis (gas vs. liquid phase)

Dr. Dav d Warhe t
77 of 79

Summary

- Risk is a product of Hazard and Exposure
- Cannot assume that nanomaterials are the same as their bulk counterpart
- Each particle-type should be tested on a case-by-case basis
- A variety of factors (in addition to particle size/surface area) influence toxicity of nanoparticulates

Dr. Dav d Warhe t
78 of 79


Acknowledgments
• Tom Webb and Ken Reed provided the pulmonary toxicology technical expertise for the study. Denise Hoban, Elizabeth Wilkinson and Rachel Cushwa conducted the BAL fluid biomarker assessments. Carolyn Lloyd, Lisa Lewis, John Barr prepared lung tissue sections and conducted the BrdU cell proliferation staining methods. Don Hildabrandt provided animal resource care. Dr. Christie Sayes and Dr. Vicki Colvin – collaborators.
Dr. Dav d Warhe t
79 of 79

Mr. John Scalera

US EPA Office of Environmental Information
Washington, DC

John Scalera, a native of Washington DC, graduated magna cum laude from American University in Washington DC with a B.S. in Chemistry in 1977. In 1979 he received a B.S. in Secondary Science Education from the University of Maryland, College Park. Over his 28 years of federal service as a chemist, he has had the opportunity to work in basic research and analytical chemistry in several federal laboratories including the National Institute for Standards and Technology, Walter Reed Army Institute of Research., U.S. Bureau of Mines, and the EPA Region III Laboratory in Annapolis Maryland. His experience as an analytical chemist exposed him to many techniques applicable to the analysis of nanomaterials including transmission electron microscopy, supercritical fluid chromatograph, X-ray diffraction, and differential thermal analysis.

In 1989 Mr. Scalera started his career at EPA Headquarters with the Office of Pollution Prevention and Toxics (OPPT). In 1994, in recognition of his efforts in designing and establishing the EPA National Lead Laboratory Accreditation Program (NLLAP), he received the Agency's Quality Assurance Manager of the Year award.

Currently he is working in the EPA Office of Environmental Information, Office of Information Analysis and Access (OIAA). In support of OIAA's Collaboration on Scientific Initiatives Program, he has supported the EPA Science Policy Council's Committee on Nanotechnology. His efforts for the committee include oversight on the drafting of the Detection and Analysis and Environmental Fate sections of the Science Policy Council's white paper "Nanotechnology."

Session 3: Detection and Characterization of Nanomaterials in the Environment

July 12, 2:00-3:00 PM

An Overview on Nanotechnology Detection and Analysis Methods

Mr. John Scalera, US EPA Office of Environmental Information, Washington DC

Abstract

The challenge in detecting nanomaterials in the environment is compounded not only by the extremely small size of the particles and their potential sequestration and agglomeration, but also by their unique physical and chemical characteristics. Unlike particles larger in size, nanoparticles can be subject to quantum effects that significantly impact their physical-chemical properties resulting in challenges when it comes to sample characterization. An overview will be presented of some of the available analytical techniques used for the detection and characterization of nanoparticles in environmental including particle size analysis, particle fraction concentration counts, surface area analysis, morphology and particle chemical composition analysis.

Session 3: Detection and Characterization of Nanomaterials in the Environment

July 12, 2:00-3:00 pm

An Overview on Nanotechnology Detection and Analysis Methods

Mr. John Scalera, US EPA Office of Environmental Information, Washington DC

Highlights

Physical-chemical characterization information provided by the manufacturers of nanotechnology materials can provide valuable information that can be used in analyzing for these materials in the environment. This information can include chemical composition, solubility, morphology, particle size distribution, and fluorescent and magnetic properties. Although there are many analytical techniques that can be applied to the analysis of nanoparticles in environmental samples, many challenges remain in obtaining accurate analytical results. These challenges include the environmental transformation of nanoparticles, agglomeration, analytical interferences from analytes of non-interest, particle size fractionation and concentration techniques and the lack of standard methods and reference materials. Some of the available methods/technologies for nanoparticles characterization in environmental samples are identified below.

Nanoparticle Characterization Methods/Technologies:

- Aerodynamic mobility collectors are used in the collection and isolation of nanoparticles fractions in aerosol samples based upon particle inertia. The two basic aerodynamic mobility based collectors employ either cyclones or impactor plate technologies to isolate nanoparticles fractions. The use of multiple impactor plates in series (cascade impactors) has reported particle size isolation down to a 6 nanometer limit.

- Differential mobility analyzers (DMAs) take advantage of an electrical force to isolate charged particles from an aerosol sample based upon the electrical mobility of the charges particles in reaction to the charge core lying within the DMA. Particle size fractions can be focused down to approximately 6 nanometers. Desired particle size fractions are focused to the exit of the DMA by varying the charge on the central core within the DMA. The desired particle fractions can be collected on filters for subsequent analysis by other technologies or sent to a particle counting device (CPCs or CNCs) set up in tandem with the DMA.

- Condensation particle counters (CPCs) or condensation nuclei counters (CNCs) are technologies designed to provide total counts of aerosol particle fractions. In general, these instruments increase the size of nanoparticles 100 to 1000 times by condensing a vapor about individual particles. This is accomplished in CPCs by sending particles into a supersaturated atmosphere (water, isopropyl or butyl alcohol). As the nanoparticles become larger do to the condensing of the liquid onto the surface, they become optically detectable.

- Aerosol time-of-flight mass spectrometry (ATOFMS) is a relatively expensive technology but capable of providing real-time particle size and chemical composition data on aerosol samples. Commercial instruments are available for field use with sensitivities down to approximately 30 nms.

- Field flow fractionation technology is a particle size fractionation technique applied to particle samples in a liquid media: Unlike HPLC, where a stationary phase is required, field flow fractionation uses the diffusion properties of particles in a liquid media to obtain separation of particles across a wide size range (1nm to several microns). There are several types of field fractionation techniques including those that employ magnetic or electrical or gravitational forces to enhance separation. The various sample fractions generated by this technology can be collected for subsequent analysis or analyzed on-line using technologies such as ICP- mass spectroscopy.

- Available electron microscopy techniques include scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The use of electron microscopy techniques combined with energy dispersive X-ray analysis (EDX) or electron energy loss spectroscopy (EELS) allows for the collection of particle size, morphology, and chemical composition data. These electron miscopy techniques are very labor intensive, expensive, require high vacuums environments and a high level of technician skill.

- Atomic Force Microscopy (AFM) is a relatively new technology. Unlike electron microscopy techniques, AFM do not require high vacuum environments and can be performed in air, liquid or gas atmospheres. The technology is based upon the van der Waals force generated between the interaction of a very fine tip (nominal 30 nms diameter) at the end of a cantilever with the surface of the particle being analyzed. Morphology and particle size information is generated with sensitivity down to the sub-nanometer range.

Question-and-Answer Session

A questioner asked about the best method for measuring an aerosol of asbestos in air. Mr. Scalera responded that it depends upon the size fraction, because degree of agglomeration differs with size. Mr. Scalera was then asked about development of a device for measuring nanoparticles in the workplace. Mr. Scalera responded that there is a need for methodologies that people are comfortable with, and that methods are standardized for personal protection. A questioner asked about the certainty of knowing what is captured when a cascade impactor is used. Mr. Scalera responded that capture (by impaction) in a cascade impactor takes advantage of diffusion properties of nanoparticles, and the use of a thirteen-stage cascade impactor have the ability to collect various fraction of nanoparticle down to 7 nm. Mr. Scalera further stated that more than one manufacturer have multi-stage impactors capable of this type of particle size collection resolution.

The Detection and Characterization of Nanoparticles in the Environment

An Overview on Nanotechnology Detection and Analysis Methods

John Scalera, U.S. EPA
Office of Environmental Information,
OIAA/ EAD
July 12, 2006

Mr. John Scalera
1 of37

Areas to be Presented

- What Are You Looking For?
- Analytical Hurdles
- Unique Properties, Analysis, and Source Identification
- Environmental Analysis Methods
- Development of Standards
- Additional Information Sources

DISCALIMER: The identification of manufacture supplied information or their products as a part of this presentation is for information purposes only and should not be perceived as an endorsement by the EPA.

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2 of37

What Are You Looking For ?

- **Manufacturer's Characterization Information:**
  - Organic versus inorganic structure/ chemical composition/molecular weight
  - Solubility
  - Type (fullerenes, single-walled nanotubes (SWNTs), [illegible] dots, dendrimers, complexed organics, contain a metal eleme[illegible]
  - Particle Size Distribution
  - Particle Surface Area
  - Zeta Potential
  - Use (pharmaceutical, gasoline additives, material properties enhancement, water purification)
  - Specific industries/locations involved in production

Mr. J

What Are You Looking For ? (cont.)

- **Environmental Transformation:**
  - Degradation (biotic and abiotic)
  - Oxidation to a more complex state
  - Morphological changes
  - Agglomeration/coagulation
  - Aggregation

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4 of37

Environmental Analysis Hurdles

- Trace levels of the nanoparticles of interest
- Other nanoparticles of non-interest (natural, incidentally formed)
- Particle size changes (agglomeration, aggregation, condensation)
- Chemical Impurities/Interferences
- Vaporization of Organics During Sample Preparation and Analysis

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5 of37

Environmental Analysis Hurdles

- Static charges
- Extraction Efficiencies (sequestration)
- Aquatic stability due to colloidal formations in the environment
- Lack of quality control reference materials/surrogates
- Lack of standard analytical methods
- Laboratory contamination/ background levels

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6 of37

Unique Properties, Analysis and Source Identification

- **Unique Physical Characteristics**
  - Particle Size
  - Diffusion Properties
  - Morphology

  Unique Chemical Characteristics
  - Radioactive Isotope Ratios
  - Marker chemicals
  - Elemental Ratio Characterization
- **Unique Spectroscopic Properties**
  - Gold particle reflection at nano level
  - Fluorescence freq.varies with particle size.
- **Unique Quantum Effects**
  - Magnetic properties

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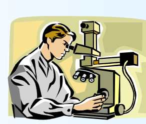
7 of37

Environmental Analysis Process

- Sample Collection 
- Extraction 
- Fractionation/Concentration/Cleanup 
- Analysis 

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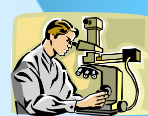
8 of37

Environmental Analysis Method Types

- Real-time analysis
  - single-particle analytical techniques
  - ensemble analytical techniques
- Subsequent analysis
  - single-particle analytical techniques
  - ensemble analytical techniques



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9 of37

Aerosol: Bulk Sample Collection

- Mechanical Collectors
  - HEPA filters , ultra-low particle air filters (down to 5 nms)
- Aerodynamic Mobility Based Collectors
  - Cyclones (down to about 60 nms)
  - Impactors (down to about 60 nms)

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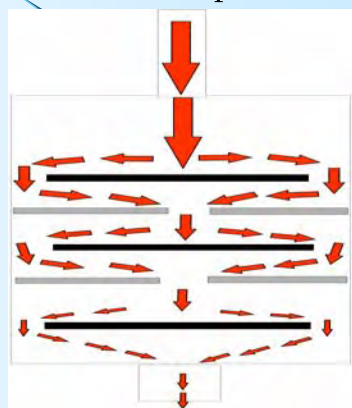
10 of37

Aerosols: Isolation of Nanoparticle Fractions- Aerodynamic Mobility

- **Inertia Impactors**
  - Particle size = “aerodynamic diameter”
  - Cascade impactor = multiple impactor plates in series
  - Nano- Micro-orifice uniform deposit impactor (MOUDI), 6 nm limit
- **Electrical Low Pressure Impacto (ELPI)**
  Real-time particle counts per size fraction
  - Incorporates multiple electrometers
  - Range 7 nms to 10 microns

Cascade Impactor



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11 of37

Aerosol: Bulk Sample Collection

- Electrostatic Collectors
  - Aerosol particles are charged in a chamber then electro-statically precipitated onto a collecting surface
  - Down to 5 nms
- Thermal Precipitators

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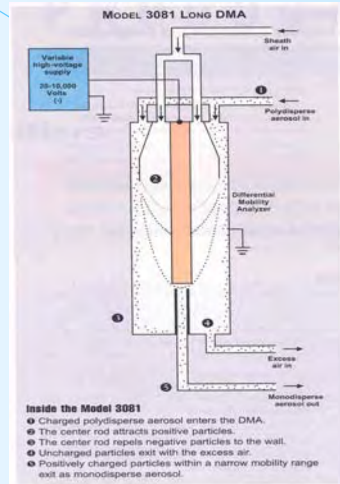
12 of37

Aerosols: Isolation of Nanoparticle Fractions-Electrical Mobility

- **Differential Mobility Analyzer (DMA)**
  - Particle size = “electrical mobility equivalent diameter”
  - 2 nm to 1micron
  - Alternate voltage to obtain various nanometer size fractions to outlet slit
- **Fast Mobility Particle Sizer (FMPS)**

  Real-time particle counts per size fraction
  - Incorporates multiple electrometers
  - Range 6 nm to 560 nm



TSI Model 3081 DMA

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13 of37

Aerosols: Particle Counting—CPC, CNC

- Condensation Particle Counters (CPC), or Condensation Nuclei Counters (CNC)
  - Detection of particles down to approximately 3 nm
  - Supersaturated vapor (water, isopropyl or butyl alcohol)
  - Particle grows 100 to 1000 times larger in size.
  - Optical detection

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14 of37

Aerosols: Nanoparticle Size Characterization—Diffusion Technology

- Diffusion Batteries
  - Particles demonstrating increasing diffusion character with smaller particle sizes.
    - Aerosol flows through a diffusion battery consisting of a series of fine capillaries or wi mesh screen grids. Smallest particles exit first where they are counted using CPC/CNC.
    - Sensitivity down to about 3 nanometers

Mass Analysis

- Mass of nanoparticle 10^{-18} gram
- Weighing of collection filters possible
  - concentration factor
  - significant collection time period
  - controlled env. (e.g, humidity control)
- Piezoelectric crystal balance
  - Quartz Crystal—alteration in resonance frequency as particles attach
  - Sensitivity limits is approximately 1 nanogram
- Beta Meter
  - Measures the change in detected beta radiation through a filter as particles deposit on the filter.
  - Particle mass is proportional to the degree of signal attenuation
  - sensitivity is approximately 25 ug per cm2

Mass Analysis(cont)

- Calculating an approximate mass of a particle fraction:
  - particle count for a size fraction
  - assume shape; get a particle volume
  - use a known or an approximate particle density

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17 of37

Aerosol Analysis: Single Particle Analyses, Size and Chemical Composition

- **Aerosol Time-of-Flight Mass Spectrometry (ATOFMS)**
  - **Real-time Analysis**
  - **Range = 30nm to 3 um.**

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18 of37

Non-Aerosol Bulk Samples

- Grab Samples: water/soils/sediments
  - **Agglomeration/Coagulation Issues**
    - **Sonication**
    - **Dispersing Agent**

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19 of37

Bulk Samples Analysis: Sample Preparation/Extraction

- Solid or Liquid Matrix: sieves—40 micron limit
- In a liquid matrix: filtration, centrifugation
- Liquid/Liquid Extraction: organic vs water soluble fractions; separatory flask
- Soxhlet Extraction: extraction of organic soluble fraction from sediments or soil.
- Solid Phase Extraction: extraction of analytes from liquid fraction
  - Ion Exchange Columns
- Supercritical Fluid Extraction (SFE)

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20 of37

Bulk Samples Analysis: Sample Preparation/Extraction/Fractionation

Filtration/Ultrafiltration Techniques (samples in liquid medium)

- Variable Cut-off size membranes
- Stirred filtration cells
- Continuous loops for maximized extraction and concentration /diafiltration techniques

Centrifugation/Ultracentrifugation

- Based upon particle density
- Centrifugal filters or membranes

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21 of37

Isolation of Nano Sample Fractions from Collected Samples (cont)

- **Field Flow Fractionation (FFF)**
  - Based upon particle diffusion; the diffusion coefficient is inversely proportional to particle size
  - Approximately 1nm to a few micrometers
    - **Asymmetric Flow Field Flow Fractionation (AF4)**
    - **Gravitational**
    - **Thermal**
    - **Magnetic**
    - **Electrical**

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22 of37

Isolation of Nano Sample Fractions from Collected Samples (cont.)

- **Asymmetric Flow Field Flow Fractionation (AF4)**

Channel height =100 to 500 um

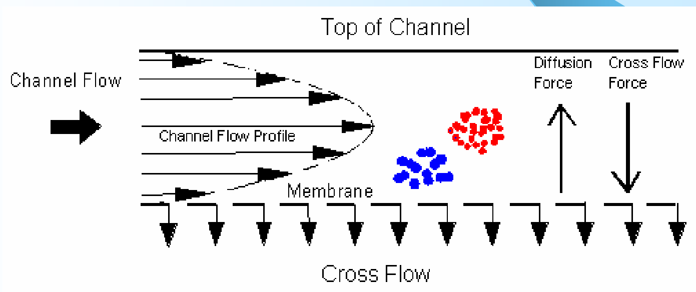

Diagram Courtesy of Postnova Analytics at www.postnova.com

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23 of37

Isolation of Nano Sample Fractions from Collected Samples (cont)

- **Field Flow Fractionation (FFF)**
  - **Greater the particle density, the lower the fractionation particle size limit**
  - **0.2000 mg mass in 20 to 100 uls injected**
  - **One hour analysis time at 1 to 2 mls of elutent per minute**

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24 of37

Sample Fractionation & Analysis: Chromatography

- Chromatographic Technologies
  - High Pressure Liquid Chromatography (HPLC)
    - Size exclusion chromatography-separation based on particle size, physical impedance
    - Ion Chromatography-separation based upon i properties of the particle
  - Supercritical Fluid Chromatography
    - Separation based on solvency in supercritical fluid

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Analytical Techniques: Particle Size Distribution

- Dynamic Light Scattering (DLS) or Photon Correlation Spectroscopy (PCS)
    - **Particle size analysis in liquids**
    - **Range less than 5 nm to over 1 micron**
    - **Can be used on-line in tandem with fractionation methods (e.g., HPLC-DLS)**

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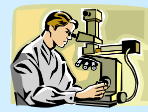
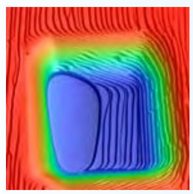
26 of37

Collected Fraction Off-Line Single Particle Analysis: Electron Microscopy



- Analysis on a particle by particle basis
  - Scanning Electron Microscopy (SEM)
  - Transmission Electron Microscopy(TEM)
    - – Energy dispersive X-ray analysis (EDX)
    - – Electron energy loss spectroscopy (EELS)
- Particle size, morphology, chemical composition



Silicon wafer structure
Image courtesy of the National Institute of Standards and Technology

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27 of37

Off-Line Single Particle Analysis: Electron Microscopy (cont.)

- Collection and preparation challenges:
  - Loss due to volatilization
  - Electrostatic forces
  - Resuspension and uniform deposit of onto analysis substrate.
- Cost
- Time
- Highly Skilled Analyst
- Statistical Accuracy requires large analyzed population of particles

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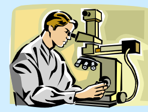
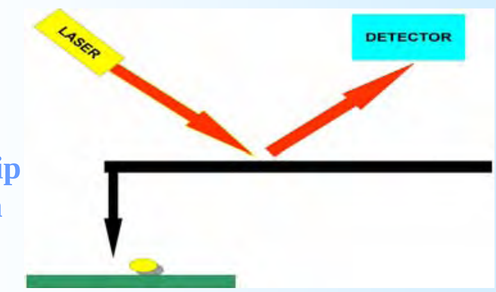
28 of37

Off-Line Single Particle Analysis: Atomic Force Microscopy (AFM)



- Applied in air or liquid mediums
- Uses the interaction of van der Waals forces between the microscopic tip of the AFM and the particle.
- Provides information down to the molecular level
  - **– particle size, morphology**

3 micron tall pyramidal tip with a 30 nm end radius



cantilever

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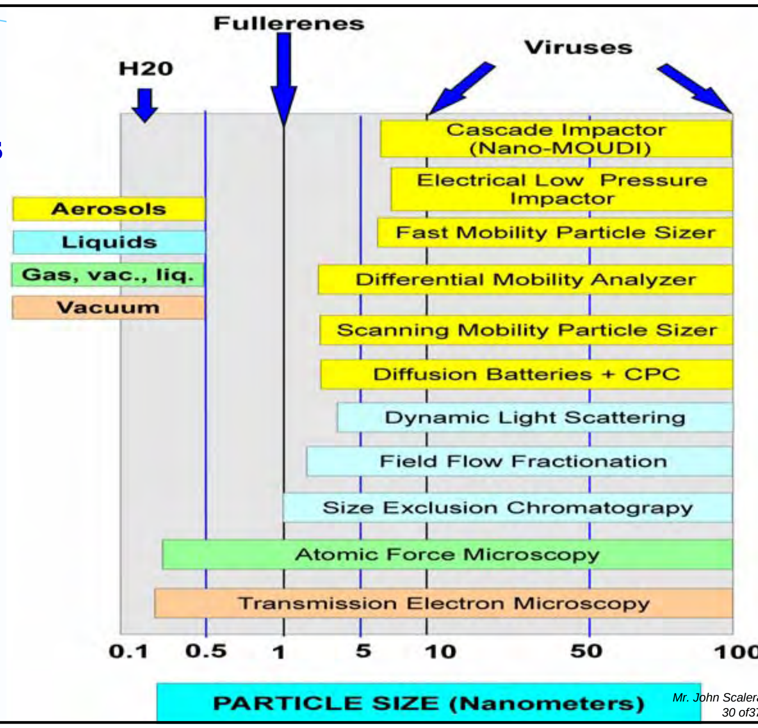
29 of37

Particle Sizing Methods



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30 of37

Surface Area Analysis

- Surface Area
- Epiphaniometer
  - Particles exposed to radiation (^{211}Pb),then passed through capillaries and collected onto filters for radiation level analysis (radiation level measure is proportional to particle surface area).
- BET-Method (Brunauer, Emmet, and Teller) *[Burtscher]*
  - Measures the amount of gas absorbed onto surface areas.
- TSI Model 3050 “Nanoparticle Surface Area Monitor”

www.TSI.com

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31 of37

Analytical Techniques: Chemical Composition

- X-ray Fluorescence (XRF)
- Mass Spectrometry (MS)
- Proton-Induced X-ray Emission (PIXE)
- Inductively Couple Plasma-Atomic Emission Spectroscopy (ICP-AES)
- ICP-Mass Spectroscopy (ICP-MS)

Mr. John Scalera
32 of37

Standards Development: ASTM

- Committee E56 on Nanotechnology
  - E56.02 Characterization: Physica Chemical, and Toxicological Properties
    - WK8705: Measurement of Particle Size Distri f Nanomaterials using Photon Correlation Spectros
    - WK9952: Standard Practice for Measuring Length a Thickness of Carbon Nanotubes Using AFM Methods
    - WK10417: Standard Practice for the Preparation of Nanomaterials Samples for Characterization

Mr. J
33 of37

Standards Development: International Organization for Standardization (ISO)

- ISO TC 229 Nanotechnologies
  - Nov. 2005 inaugural meeting
    - WG 1 Terminology and Nomenclature (Canada)
    - WG 2 Measurement and Characterization (Japan)
    - WG 3 Health, Safety and Environment (U.S.)

Mr. John Scalera
34 of37

Standards Development: American National Standards Institute (ANSI) & U.S. TAG to ISO TC 229

- ANSI Nanotechnology Standards Panel
  - ANSI-NSP formed in August 2004
  - U.S. Tech. Advisory Group (TAG) to ISO TC 229
    - ANSI accredited
    - July 2005 inaugural meeting
    - Workgroups: Terminology and Nomenclature, Measurement and Characterization, Health, Safety and Environment (U.S.)

Mr. John Scalera
35 of37

Standards Development: Institute of Electrical and Electronics Eng. (IEEE)

- **Standard Methods for the Characterization of Carbon Nanotubes Used as Additives in Bulk Materials (P1690TM) (In Progress)**
  - **This project will develop standard methods for the characterization of carbon nanotubes used as additives in bulk materials.**

Mr. John Scalera
36 of37

Additional Information Sources: Analysis Overviews

- "Overview of Methods for Analysis Single Ultrafine Particles," Andrew Maynard. Phil Trans. R. Soc. Lond. A(2000)358, pp 2593-2610.
- "Nanoparticles and the Environment," Pratim Biswas, Chang-Yu Wu. J. of Air & Waste Management Assoc., Vol. 55, June 2005.
- "A Review of Atmospheric Aerosol Measurements," Peter McMurry. Atmospheric Environment, Vol 34, Issues 12-14, 2000, pp 1959-1999.
- "Emerging Issues in Aerosol Nanoparticle Science and Technology" NSF Workshop Report. Workshop held at U.of CA, Los Angeles, June 27-28, 2003.
- "Chapter One: Exposure Measurements." Chow J., Johann P., et. al. Chemosphere, Vol. 49, Issue 9, Dec. 2002, pp 873-901
- "Research Strategies for Safety Evaluation of Nanomaterials. Part VI. Characterization of Nanoscale Particles for Toxicological Evaluation," Kevin Powers, Scott Brown, et al. Tox. Sciences 90(2), 296-3003 (2006)

Mr. John Scalera
37 of37

Dr. Anil K. Patri

National Cancer Institute at Frederick
Frederick, Maryland

Dr. Anil K. Patri is a Senior Scientist in the Nanotechnology Characterization Laboratory (NCL) at the National Cancer Institute at Frederick. His expertise is in the interface of chemistry and biology pertaining to nanomaterial. Dr. Patri directs a chemistry lab at NCL and collaborates with scientists from NIST and FDA for the physico-chemical characterization and assessment of nanomaterial intended for cancer therapeutic and diagnostic applications.

Prior to joining NCL, Dr. Patri served as a staff scientist at the Center for Biologic Nanotechnology (now MNIMBS) at the University of Michigan and developed nanomaterial for targeting, imaging, and drug delivery application to cancer. His graduate and post-doctoral training were on the synthesis, modification, and application of dendrimers to material and biomedical applications. He received his Ph.D. in Organic chemistry from the University of South Florida, M.Sc., in Organic Chemistry from Aligarh University, and B.Sc., in Biology and Chemistry from Osmania University, India.

Session 3: Detection and Characterization of Nanomaterials in the Environment

July 12, 2:00-3:00 PM

Preclinical Characterization of Nanomaterials

Dr. Anil K. Patri, National Cancer Institute at Frederick, Frederick, Maryland

Abstract

Preclinical Characterization of Nanomaterial

Engineered nanomaterial offers great potential to radically change the way we diagnose, treat, and prevent cancer. Their unique properties such as modifiable size and tunable surface functionality facilitate targeted delivery of embedded therapeutic and imaging agents to a disease site with unprecedented specificity. This approach minimizes dosage, which reduces toxicity and side effects, while increasing the therapeutic benefit. There is an urgent need to quickly transition these novel technologies to benefit those who are suffering from insidious diseases such as cancer, while being cautious of the impact of their production and their use on the environment and health.

The complex nature of nanomaterial poses challenges in their reproducible synthesis, scale-up, isolation, purification, characterization, along with their *in vitro* and *in vivo* safety and efficacy assessment. To address these challenges, developing methodologies and standards requires a multi-disciplinary group of scientists, expertise, team effort, appropriate instrumentation, and resources.

This presentation will focus on the mission and approach of NCL at NCI Frederick, in a formal scientific interaction and collaboration with the National Institute of Standards and Technology (NIST) and the U.S. Food and Drug Administration (FDA), to perform pre-clinical characterization and assessment of nanomaterial intended for cancer therapeutics and diagnostics. The research outcome will help the community-at-large. Several tools and techniques to evaluate the material properties will be discussed.

Session 3: Detection and Characterization of Nanomaterials in the Environment

July 12, 2:00-3:00 pm

Preclinical Characterization of Nanomaterials

Dr. Anil K. Patri, Nanotechnology Characterization Laboratory, National Cancer Institute at Frederick (SAIC Frederick), Frederick, Maryland

Highlights

The Nanotechnology Characterization Laboratory (NCL) is established by the National Cancer Institute (NCI) to serve as a national resource and knowledge base for cancer researchers by performing and standardizing the pre-clinical characterization of nanomaterials intended for cancer therapeutics and diagnostics. The activities of NCL represent a formal scientific interaction of three Federal agencies: NCI, US Food and Drug Administration (FDA) and National Institute of Standards and Technology (FDA). Through these collaborations, the NCL will develop data that will facilitate standards for nanotechnology strategies and lay a scientific foundation that will enable informed regulatory decisions concerning the testing and approval of nanoscale cancer diagnostics, imaging agents, and therapeutics.

There are several advantages of multifunctional nanomaterial. They can be used as vehicles for carrying targeting agents, therapeutics and imaging agents. Through targeted delivery, the efficacy of the drug at the disease site is increased, even at lower doses, while minimizing toxic side-effects. Nanomaterial imaging agents can enhance the disease detection capability.

Small molecule therapeutic physicochemical characterization methods have been well established to facilitate regulatory review. For nanomaterial, new parameters such as size, polydispersities, shape, surface characteristics, composition, purity, stability etc. need to be measured as these parameters influence their in vivo biological behavior such as ADME and toxicity. NCL characterization cascade captures the structure-activity relationship trends and includes physico-chemical, in vitro and in vivo assays. NCL conducts these tests to help cancer researchers in academia, government and industry and in the process of developing standards at ASTM E56 committee on nanotechnology.

Question-and-Answer Session

A question was asked regarding the practicality of developing reference materials and running them through the techniques mentioned during Mr. Scalera's presentation. Dr. Patri responded that reference materials are in the process of being developed by the National Institute of Standards and Technology (NIST). NIST will begin by fully characterizing two different sizes of nanomaterials. A NIST representative added that NIST is working with the National Cancer Institute (NCI) to create standard materials and is considering using them in international discussions. NIST is starting with size-based standards and working toward other parameters.

Preclinical Characterization of Nanomaterial

Anil K. Patri, Ph.D.
Nanotechnology Characterization Lab
(SAIC Frederick)
National Cancer Institute at Frederick

Nanotechnology and OSEWER: New Opportunities and Challenges
July 12, 2006

SAIC-Frederick, Inc.
A Subsidiary of Science Applications International Corporation
An Employee-Owned Company

Treatment Options for Cancer

- Surgery
- Radiotherapy
- Chemotherapy

} Limitations and side effects

Urgent need to utilize novel technologies and ideas

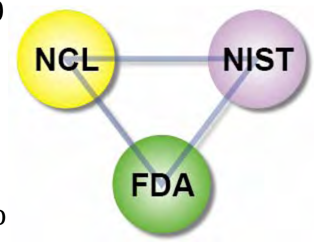
- Early diagnosis
- Targeted therapy
- Minimize side effects
- Monitor
- Provide better living standards

Dr. Anil K. Patri
2 of26

Nanotechnology at the National Cancer Institute

NANOTECHNOLOGY CHARACTERIZATION LABORATORY

- NCI has funded exploratory work since 1999 on integrating nanotechnology into biomedical research
- Unconventional Innovations Program (UIP)
  - Diagnostics (Imaging)
  - Therapeutics
- Priority is to now transition that research into the clinical realm.

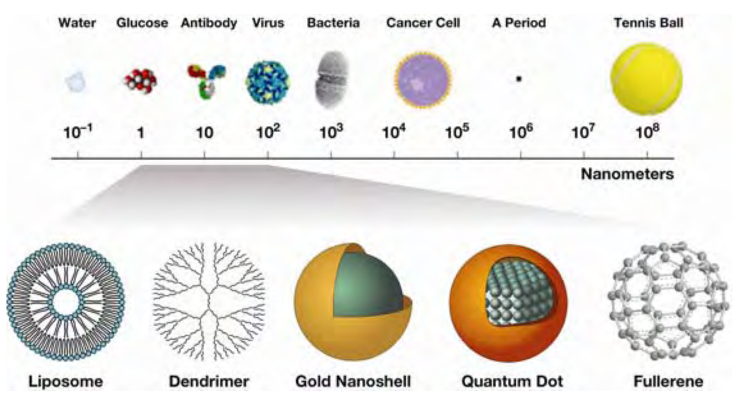


Dr. Anil K. Patri
3 of26

Nanotechnology Definition

NANOTECHNOLOGY CHARACTERIZATION LABORATORY

"Research and technology development at the atomic, molecular or macromolecular scale leading to the controlled creation and use of structures, devices and systems with a length scale of approximately 1 – 100 nanometers (nm)." **(Source: National Nanotech Initiative)**



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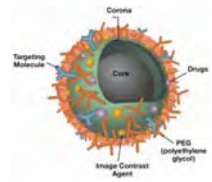
4 of26

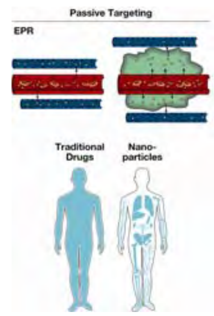
Why Nano?

Therapeutic Benefits

- Solubility
  - Carrier for hydrophobic, hydrophilic therapeutics
- Multifunctional capability
  - Targeting, Imaging, Drug payloads
- Change in pharmacokinetics and pharmacodynamics
- Active and passive targeting
  - Antibody and ligand conjugates
- Reduced systemic toxicity



McNeil, (2005), J. Leuk. Biol., 78:585-594



↑Solubility ↑Stability ↑Specificity = ↓Toxicity ↑Efficacy

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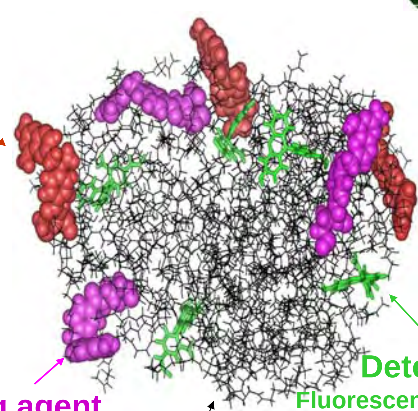
5 of26

Multifunctional platform

Therapeutic Agent (Methotrexate)



Detecting agent
Fluorescent probe or Gd chelate

Targeting agent
(Folic acid or Antibody)

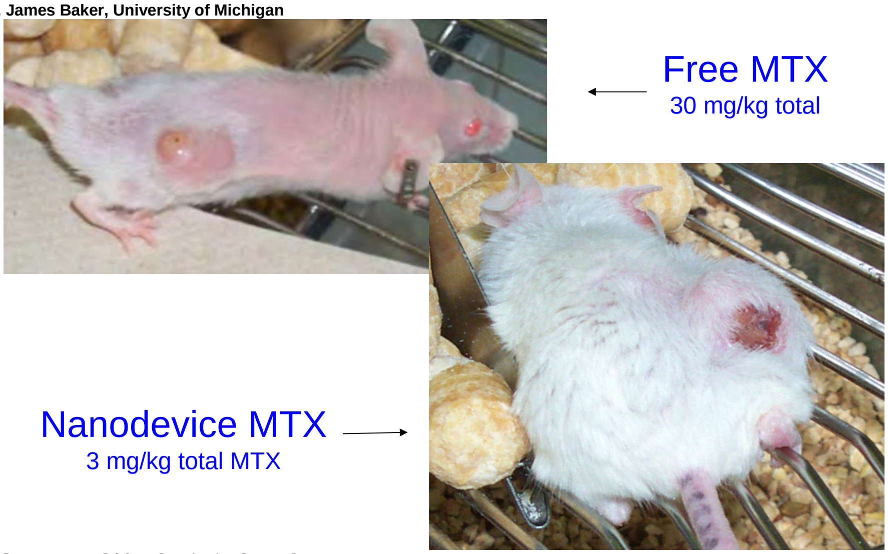
G5-polyamidoamine
(dendrimer platform)

Dr. James Baker, University of Michigan

Dr. Anil K. Patri
6 of26

Active Targeting

Dr. James Baker, University of Michigan



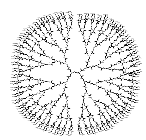
Free MTX
30 mg/kg total

Nanodevice MTX
3 mg/kg total MTX

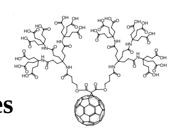
Cancer Res **2005**; 65: (12) 5317-5324

Dr. Anil K. Patri
7 of26

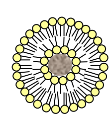
Nanoparticles by type for medical applications



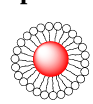
- **Organic Nanoparticles (e.g.: Polymers, Dendrimers, Functionalized fullerenes)**



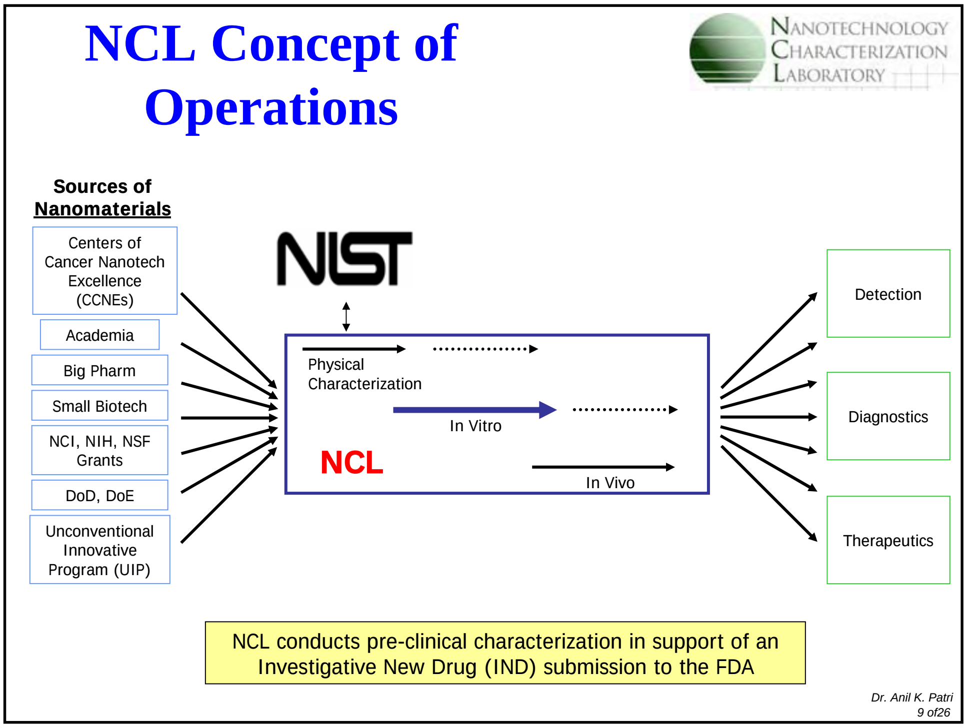
- **Organic/Inorganic hybrids (e.g.: Quantum dots, Nanocomposites, Gd-chelates)**
- **Liposomes (e.g.: Functionalized, inclusion complexes**

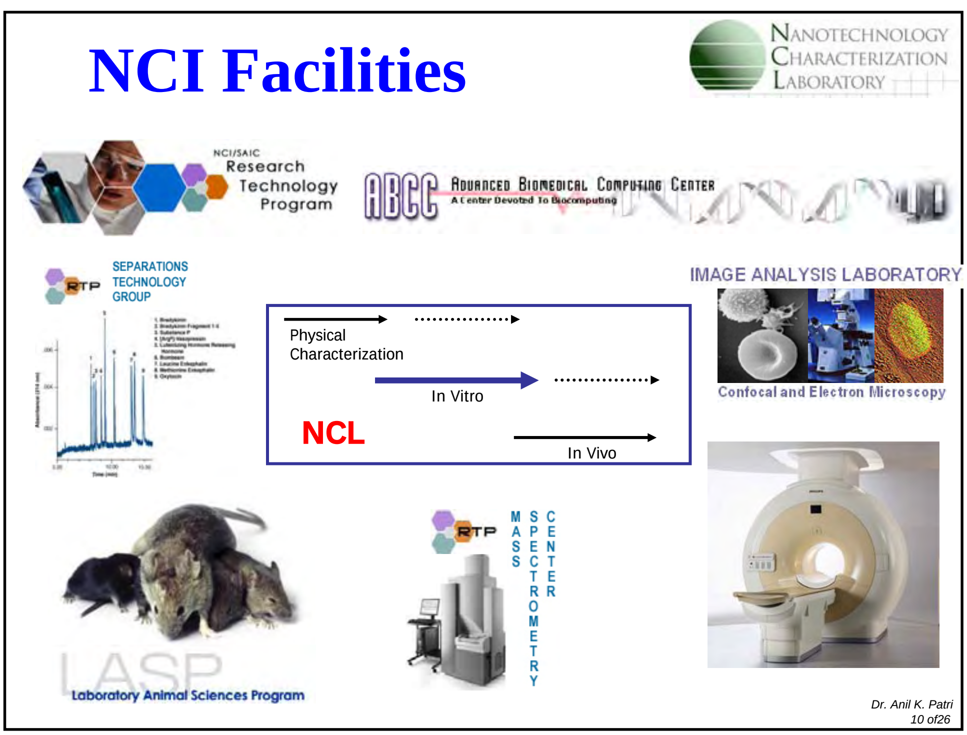


- **Nanoemulsions (e.g.: Oil-water-surfactant mixtures)**
- **Biological nanoparticles (e.g.: Protein and peptide based nanoparticles with other active components)**



Dr. Anil K. Patri
8 of26


NCL Concept of Operations
NANOTECHNOLOGY CHARACTERIZATION LABORATORY
Sources of Nanomaterials
Centers of Cancer Nanotech Excellence (CCNEs)
Academia
Big Pharm
Small Biotech
NCI, NIH, NSF Grants
DoD, DoE
Unconventional Innovative Program (UIP)
NIST
Physical Characterization
In Vitro
NCL
In Vivo
Detection
Diagnostics
Therapeutics
NCL conducts pre-clinical characterization in support of an Investigative New Drug (IND) submission to the FDA
Dr. Anil K. Patri
9 of26


NCI Facilities
NANOTECHNOLOGY CHARACTERIZATION LABORATORY
NCI/SAIC Research Technology Program
ABCC Advanced Biomedical Computing Center
A Center Devoted To Biocomputing
RTP SEPARATIONS TECHNOLOGY GROUP
IMAGE ANALYSIS LABORATORY
Confocal and Electron Microscopy
Physical Characterization
In Vitro
NCL
In Vivo
RTP MASS SPECTROMETRY CENTER
LASP
Laboratory Animal Sciences Program
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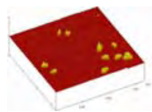
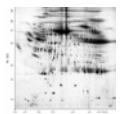
10 of26

NCL Assay Cascade



Physico-chemical Characterization:

- Size
- Shape
- Composition
- Solubility
- Molecular weight
- Surface chemistry
- Identity
- Purity
- Stability



In Vitro:

- Pharmacology
- Blood contact properties
- Effects on immune cell function
- Cytotoxicity
- Mechanistic toxicology
- Sterility

In Vivo:

- ADME
- Safety
- Efficacy

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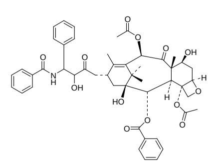
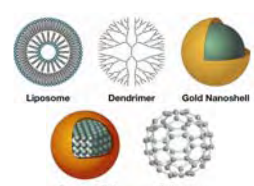
11 of26

Instrumentation for Physicochemical Characterization



Small molecules



Nanomaterial

- Elemental analysis
- Mass
- NMR
- UV-Vis
- IR
- HPLC
- GC
- Polarimetry

→

Physicochemical Parameters
- **Composition**
- **Physical properties**
- **Chemical properties**
- **Identification**
- **Quality**
- **Purity**
- **Stability**

←

- Microscopy (AFM, TEM, SEM)
- Scattering techniques (PCS, MALS, SAXS, SANS)
- SEC, AFFF
- Electrophoresis (CE, PAGE)
- Zeta potential
- Fluorimetry

Same parameters – different/additional characterization methods

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12 of26

Physico-chemical Characterization

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- Size, Size distribution
- Shape
- Molecular weight
- Surface characteristics
  - Net charge
  - Zeta potential
- Functionality

  Functional component
  - Identification
  - Quantitation
  - Functional and stability assessment
- Composition
  - Elemental
  - Core-shell
- Purity
  - Homogeneity/Inhomogeneity in Ligand distribution
  - Free components
- Stability
  - Thermal
  - pH
  - Photo
  - Aggregation
  - Freeze-thaw
  - Lyophilization
  - Centrifugation
  - Short-term storage
  - Long-term storage
  - Release kinetics
  - Stability of the 'coating'

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13 of26

In vitro Cascade

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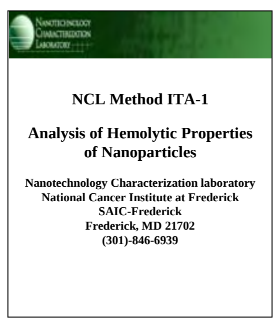
In Vitro

- Sterility
  - Bacterial/Viral/Mycoplasma
  - Endotoxin
- Targeting
  - Cell Binding/Internalization
- Blood Contact Properties
  - Plasma Protein Binding
  - Hemolysis →
  - Platelet Aggregation
  - Coagulation
  - Complement Activation
  - CFU-GM
  - Leukocyte Proliferation
  - Macrophage/Neutrophil Function
  - Cytotoxic Activity of NK Cells
- Toxicity
  - Phase I/II Enzyme Induction/Suppression
  - Oxidative Stress
  - Cytotoxicity (necrosis)
  - Cytotoxicity (apoptosis)
- Metabolic Stability


NCL Method ITA-1

Analysis of Hemolytic Properties of Nanoparticles

Nanotechnology Characterization laboratory
National Cancer Institute at Frederick
SAIC-Frederick
Frederick, MD 21702
(301)-846-6939

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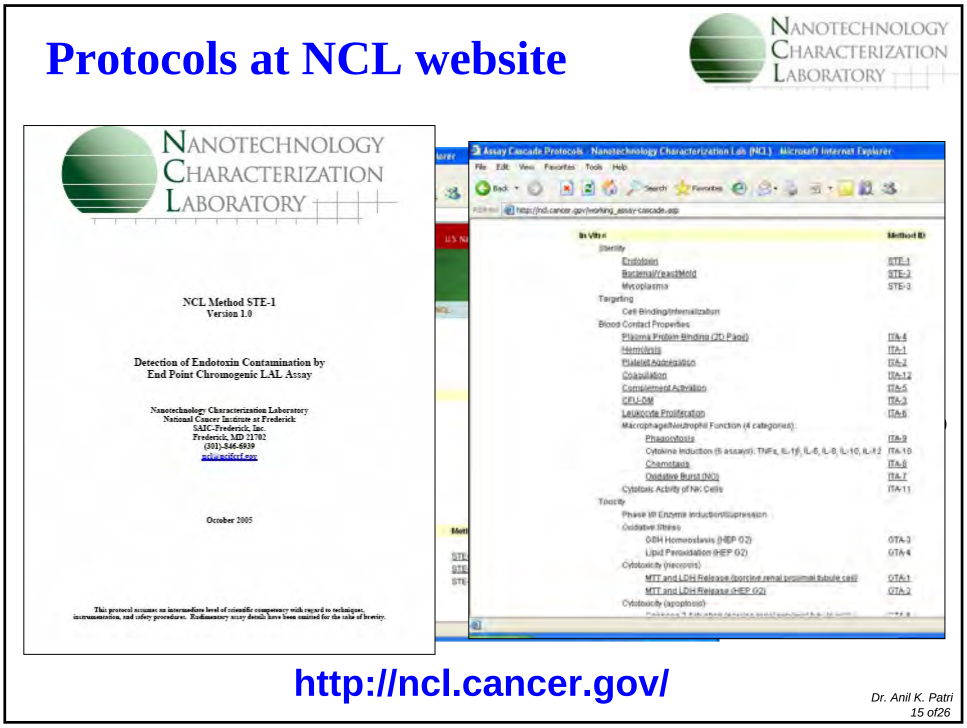
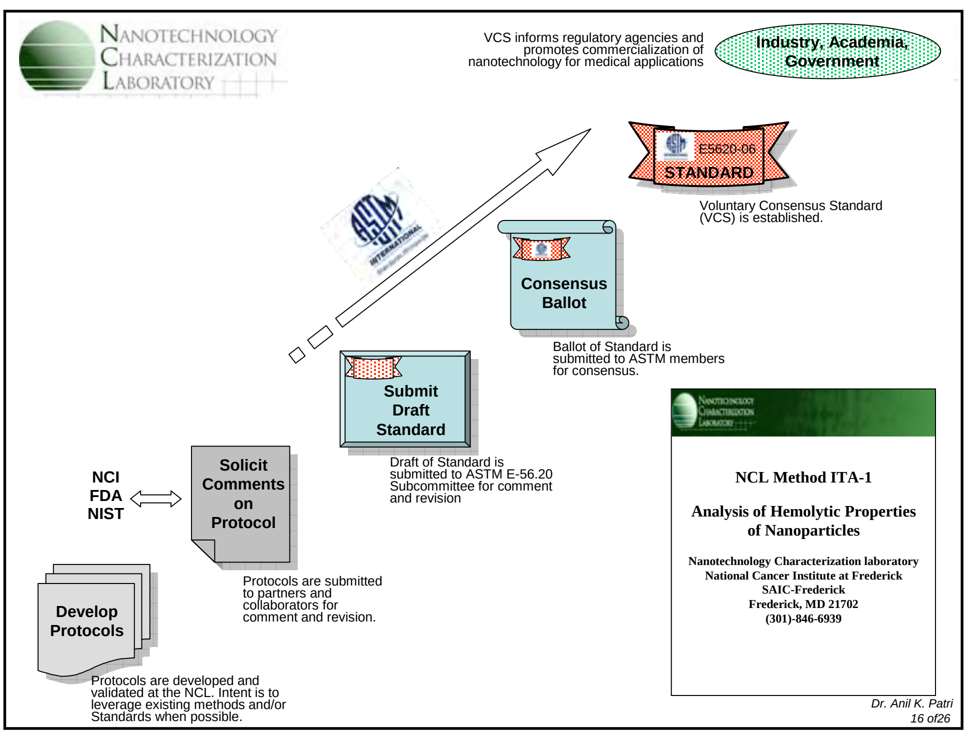
14 of26


Protocols at NCL website
NANOTECHNOLOGY CHARACTERIZATION LABORATORY
NCL Method STE-1
Version 1.0
Detection of Endotoxin Contamination by End Point Chromogenic LAL Assay
Nanotechnology Characterization Laboratory
National Cancer Institute at Frederick
SAIC-Frederick, Inc.
Frederick, MD 21702
(301)-846-6939
October 2005
http://ncl.cancer.gov/
Dr. Anil K. Patri
15 of26


NANOTECHNOLOGY CHARACTERIZATION LABORATORY
VCS informs regulatory agencies and promotes commercialization of nanotechnology for medical applications
Industry, Academia, Government
E5620-06
STANDARD
Voluntary Consensus Standard (VCS) is established.
Consensus Ballot
Ballot of Standard is submitted to ASTM members for consensus.
Submit Draft Standard
Draft of Standard is submitted to ASTM E-56.20 Subcommittee for comment and revision
NCI
FDA
NIST
Solicit Comments on Protocol
Protocols are submitted to partners and collaborators for comment and revision.
Develop Protocols
Protocols are developed and validated at the NCL. Intent is to leverage existing methods and/or Standards when possible.
NCL Method ITA-1
Analysis of Hemolytic Properties of Nanoparticles
Nanotechnology Characterization laboratory
National Cancer Institute at Frederick
SAIC-Frederick
Frederick, MD 21702
(301)-846-6939
Dr. Anil K. Patri
16 of26

Environmental Aspects

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Studies Applicable to Environmental Risk Assessment

- **General Cytotoxicity Assays**- determining concentration-response relationships, SAR studies
- **Mechanistic Studies**- Identifying apoptosis, oxidative stress and cytochrome P450 induction/suppression as potential mechanisms
- ***In Vivo* Toxicology Studies-** Identification of target organs
- **General ADME-** define t1/2, clearance mechanisms (i.e. metabolism, biliary excretion, renal clearance, etc.)

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17 of26

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DATA

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18 of26

Detection and Quantitation in Matrix

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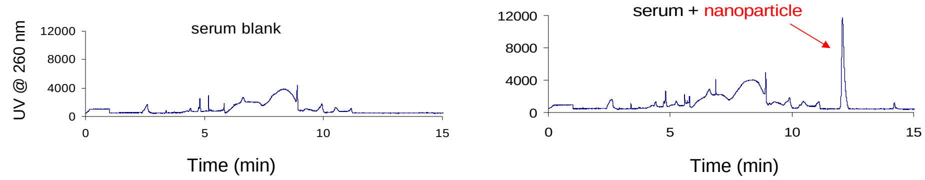
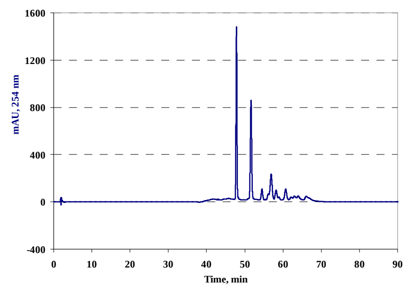
Capillary electrophoresis



HPLC (QC)



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19 of26

Metrology: Size

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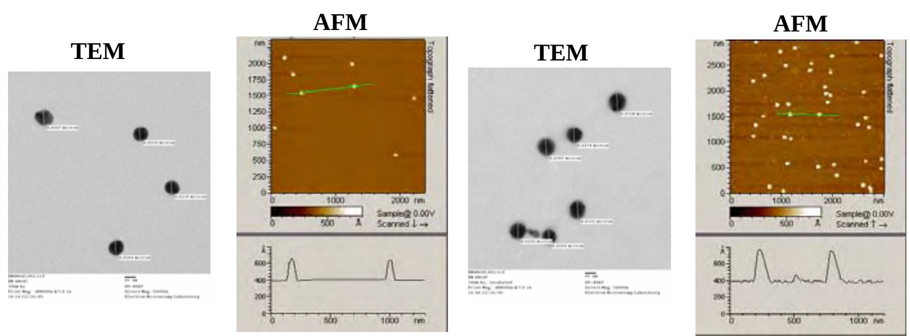
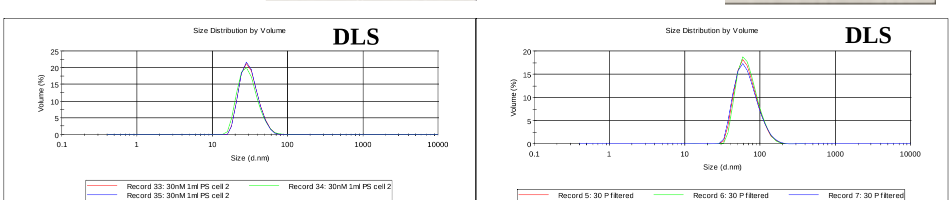
30 nm Gold colloids | **30 nm Gold colloids with protein**





31 nm **69 nm**

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20 of26

Stability: Liposomes

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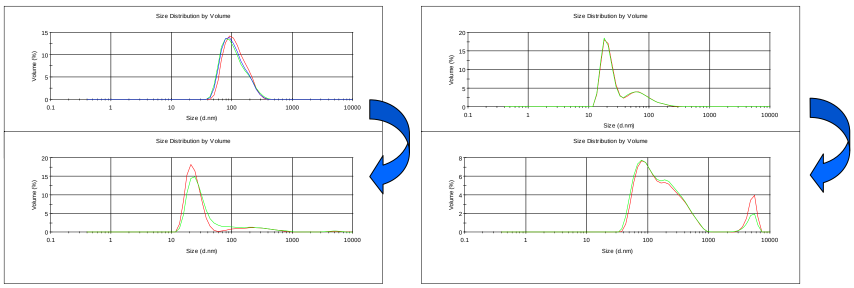
Shelf stability

Size immediately after preparation



Change in size after 3 months of storage

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21 of26

Structure Activity Relationships

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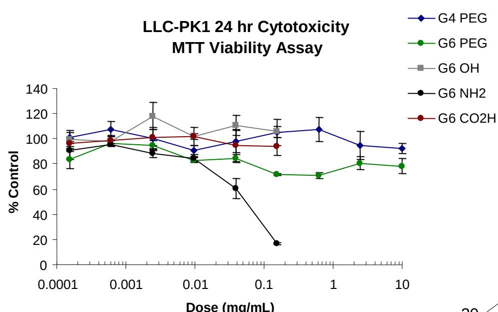
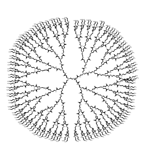
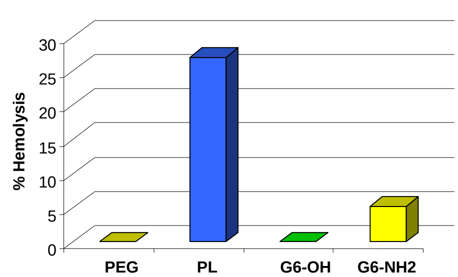


Effect of Surface Functional Group on cell viability



G6 Dendrimer

Hemolysis



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22 of26

Acknowledgements

NCL

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Anil Patri, Ph.D.
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Banu Zolnik, Ph.D.
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Barry Neun, B.S.

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King Chan, Ph.D.
Suzanne Specht, B.S.
Anu Puri, Ph.D.
Darue Prieto, M.S.
Jack Simpson, Ph.D.
Tad Guszczynski, Ph.D.
Kunio Nagashima

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23 of26

Questions/Comments

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Dr. Anil K. Patri
24 of26

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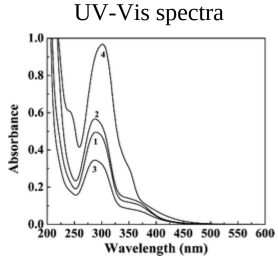
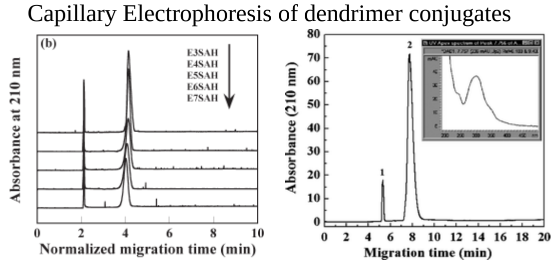
25 of26

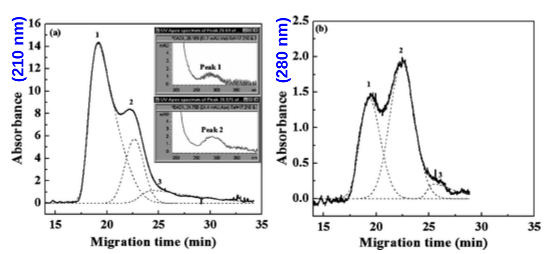
Multifunctional Nanoparticles: Characterization of ligand distribution

UV-Vis spectra



Capillary Electrophoresis of dendrimer conjugates





Multifunctional with Folic acid and Methotrexate

Shi, X.; et al. *Electrophoresis*, **2005**, 26, 2960-2967.
Shi,X; et al. *Analyst*, **2006**, 131, 374-381.

Dr. Anil K. Patri
26 of26

Dr. Gregory V. Lowry

Carnegie Mellon University
Associate Professor
Civil and Environmental Engineering
Pittsburgh, Pennsylvania

Dr. Gregory V. Lowry is an Associate Professor in the Department of Civil and Environmental Engineering at Carnegie Mellon University in Pittsburgh, PA. Dr. Lowry's expertise is nanoparticle characterization, including the reactions they promote and their fate and transport in the environment. Dr. Lowry's research group currently investigates the use of novel surface coatings to enhance the transport and reactivity of zerovalent iron and metal-oxide nanoparticles in the subsurface is enhanced, and promotes adsorption of nanoparticles to the NAPL-water interface. Dr. Lowry also has projects on sediment remediation and contaminant transport in porous media, including developing and evaluating "active" sediment caps that destroy and/or sequester PCBs.

Session 4: Fate and Transport of Nanomaterials

July 12, 3:30-4:30 PM

Dr. Gregory V. Lowry, Carnegie Mellon University, Associate Professor, Civil and Environmental Engineering, Pittsburgh Pennsylvania

Abstract

The most evident near-term element of nanotechnology is the rapidly developing nanomaterials industry. Commercial applications of nanomaterials currently or will soon include nanoengineered titania particles for sunscreens and paints, carbon nanotube composites in tires, silica nanoparticles as solid lubricants, reagents for groundwater remediation, and protein-based nanomaterials in soaps, shampoos, and detergents. The production, use, and disposal of nanomaterials will inevitably lead to their appearance in air, water, soils, or organisms. The potential toxicity of engineered nanomaterials to indigenous microorganisms, to aquatic organisms, and to humans remains uncertain. Responsible uses of manufactured nanomaterials in commercial products and environmental applications, as well as prudent management of the associated risks, require a better understanding of their mobility, bioavailability, and impacts to a wide variety of organisms.

The matter of determining whether or not a substance is “dangerous” involves determining any toxicity presented by the material, but also the degree to which the material will come into contact with organisms. A higher mobility of nanomaterials in the environment implies a greater potential for exposure as nanomaterials are dispersed over greater distances and their effective persistence in the environment increases. There is an urgent need to evaluate the fate and transport of nanomaterials in the environment and to consider the possible impacts of nanomaterial fabrication and the manner in which conventional chemical feedstocks and wastes will be handled.

Several processes will control the fate and transport of nanomaterials in the environment including redox processes, aggregation, and deposition onto particles. Redox transformations may decrease or increase the toxicity of a nanoparticle. The propensity to attach to surfaces or to form aggregates will limit the mobility of nanomaterials in the environment. Natural and synthetic polymers or surfactants adsorbed onto nanoparticles, however, can dramatically increase their mobility. Environmental geochemical conditions, e.g. pH, ionic strength, and ionic composition can greatly affect the rate and extent of each of the processes controlling the fate and transport of engineered nanomaterials in the environment. The effect of each of these geochemical conditions on the fate and mobility of engineered nanomaterials in the environment is discussed. Implications of these findings on the environmental risks that engineered nanomaterials may pose and on the proper disposal and treatment of engineered nanomaterials.

Session 4: Fate and Transport of Nanomaterials

July 12, 3:30-4:30 pm

Dr. Gregory V. Lowry, Carnegie Mellon University, Associate Professor, Civil and Environmental Engineering, Pittsburgh Pennsylvania

Highlights

The two general types of sources are point sources (manufacturing effluent, landfills) and non-point sources (stormwater runoff, tire wear, wet deposition).

Aggregation: nanoparticles can aggregate in water through Van der Waals interactions, chemical bonding, hydrophobic effects, and magnetic attraction. High diffusion coefficients lead to many collisions, and frequent contact between particles promotes aggregation. Coating nanoparticles decreases aggregation by two mechanisms: charge stabilization, or steric stabilization. Nano-sized iron in aqueous suspension readily aggregates. Particle concentration can affect the stable size of aggregates formed and the speed of aggregation. As concentration increases, aggregation is more rapid and aggregates may become large enough to settle out via gravity.

Attachment of nanoparticles to surfaces limits mobility and bioavailability, and may affect transformation/degradation. Attachment is a function of the particle and its surface properties. Bare nano-sized iron particles stick to sand grains and then begin to stick to each other (they have a higher affinity for each other than for silica).

Some important questions include: How long do nanoparticles last, and what do they become once transformed? What kinds of reactions take place (redox, photolysis, biotransformations)?

Redox transformations change the surface characteristics of nanoparticles. Processes that may alter the surface properties on nanomaterials include oxidation, hydroxylation, and sorption of organic matter. Biotransformations are likely but have not yet been demonstrated. Surface modifications that could affect particle toxicity and/or mobility include surface functionalization (either by redox reactions at the surface, through engineered coatings, or by sorption of dissolved organic materials to nanoparticles), and loss of engineered surface coatings on nanoparticles (coatings could be biodegraded or desorbed depending on their makeup).

Factors that limit nanoparticle mobility in porous media (e.g., aquifer) include aggregation, straining (particles or aggregates exceed pore size), and attachment (particles stick to soil).

Physical and chemical factors that need to be considered when assessing mobility include pH, particle surface chemistry, velocity, grain size, heterogeneity, particle size, particle concentration, and ionic strength.

At low concentrations, bare iron particles have limited mobility; at high concentration, the particles have no mobility. A surface coating increases mobility. Coating materials produce either electrostatic repulsion between particles or steric repulsion. With these coatings, stable suspensions are possible and particles do not attach to aquifer grains.

The relative mobility of particle types can be estimated using a standard formula which includes a sticking parameter (designated as alpha). From alpha, one can estimate the travel length for a specified tolerance under conditions specific to the experiment. A smaller negative alpha value indicates that a chemical sticks more. For particles with surface coatings designed specifically to enhance mobility,

transport distances are anticipated to be on the order of meters to 10's of meters under normal groundwater conditions. These are rough estimates as they are highly specific to the conditions of the laboratory tests and should be used cautiously. Overall, mobilty in porous media is low under typical groundwater conditions. Surface modification may enhance mobility.
Mobility of nanomaterials in surface waters is unknown. Dilution in receiving water may limit aggregation or promote disaggregation. Attachment to other suspended solids and/or photolysis from surface waters is also possible.

It appears that nanoparticles can be cycled in organisms. In a study in which single-walled nanotubes were ingested by copepods, nanotube aggregates were detected in the copepods' digestive tracts and feces. Nano-sized iron has been observed in Medaka fish gills.

Questions regarding the fate and transport of nanomaterials include:

- Will they bioaccumulate or facilitate the bioaccumulation of other contaminants?
- How significant are biotransformations?
- Is photolysis significant?
- What role does heterogeneity play in particle mobility?
- Is incineration effective in destroying nanomaterials?
- What is the fate of surface coatings on nanomaterials?

Questions regarding the potential toxicity of nanoparticles include:

- What are the environmentally relevant concentrations of nanomaterials?
- Despite aggregation is the low population of single particles responsible for toxicity? There are bound to be some single particles present – do these cause the bulk of toxicity?
- Do surface coatings enhance or mitigate the toxicity of the particles?

Question-and-Answer Session

When asked about the basis for low mobility of landfill leachate, Dr. Lowry indicated that calcium and magnesium promote aggregation, and landfill leachate contains Ca and Mg. Clay is less porous than sand, and nanomaterials should be less mobile in clay. Therefore, transfer through the clay barrier in landfill leachate containing high concentrations of divalent cations would be expected to be limited.
When asked about mobility of coated particles, Dr. Lowry answered that particles must be able to attach to dense non-aqueous phase liquid (DNAPL). Coated particles have been shown to move tens of meters in bench-top experiments. It is an engineering challenge to get nanoparticles to move a certain distance and then stop.

A questioner asked about the difference between aggregation and agglomeration. Dr. Lowry indicated that aggregation implies strong attractive forces and is irreversible; agglomeration is not as strong as aggregation and is more readily reversible, i.e. they are easier to break apart into smaller agglomerates or individual particles. Bare particles aggregate strongly. Surface-coated particles agglomerate eventually, but can be broken up readily.

A commenter noted that development of nanoparticles passes through stages. In stage 1, particles are passive; research then progresses to create dual functional particles, then to interconnected or intelligent systems. We need to consider not only passive nanomaterials but also polyfunctional materials. When asked whether a drug delivery molecule could get delivered to some unintended site in the body, Dr. Lowry answered that this is possible.

When asked whether the ability of agglomerates to penetrate crevasses would depend on the flow of water, Dr. Lowry answered that effectiveness does depend on flow. One hundred meters down is too far to treat effectively. If particles sit at interface, DNAPL can be destroyed as it flows out of crevasses.

When asked whether the model for bioaccumulation of nanomaterials was similar to that of PCBs, Dr. Lowry responded that it is tempting to think that traditional models might apply, but there is enough difference between nanoparticles and regular chemicals to suggest that their bioaccumulation might differ.

Environmental Transport and Fate of Nanomaterials

Gregory V. Lowry

Associate Professor of Environmental Engineering
Carnegie Mellon University, Pittsburgh, PA 15213-3890, USA

The research is funded by U.S. EPA - Science To Achieve Results (STAR) Program
Grant # R830898

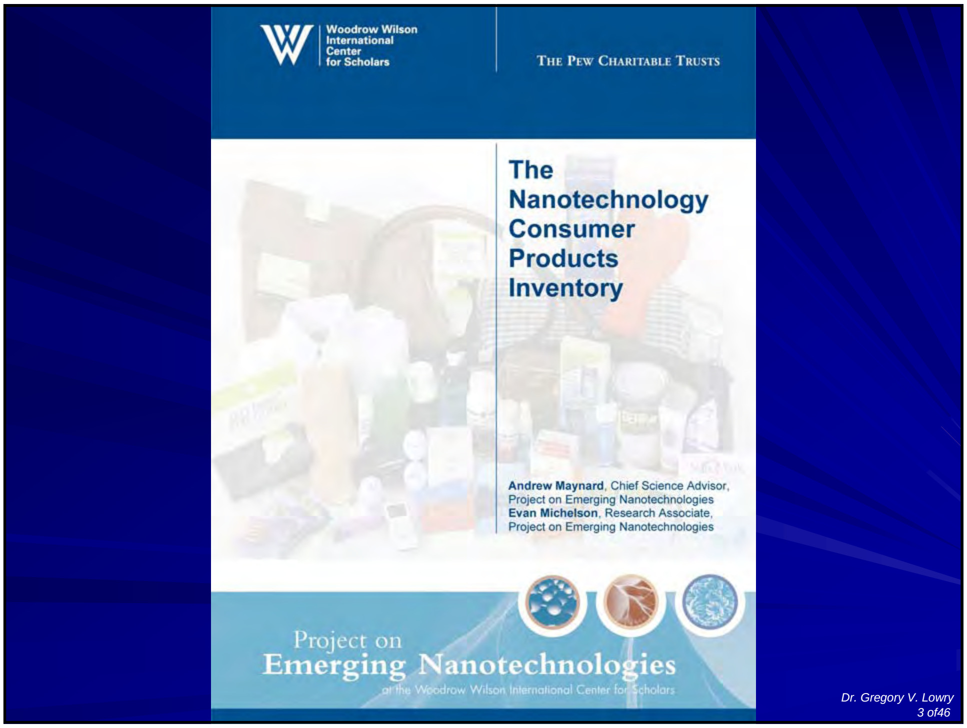
Civil and Environmental ENGINEERING
Carnegie Mellon

Nanomaterials

- Most active area of nanotechnology research
- Current or near term applications:
  - nano-engineered TiO_2 for sunscreens and paints
  - carbon nanotube composites in tires
  - silica nanoparticles as solid lubricants
  - reagents for groundwater remediation
  - protein-based nanomaterials in soaps, shampoos, and detergents.

M. R. Wiesner, G. V. Lowry, P. Alvarez, D. Dionysiou, and P. Biswas. *Environ. Sci. Technol.* (in press)

Dr. Gregory V. Lowry
2 of46



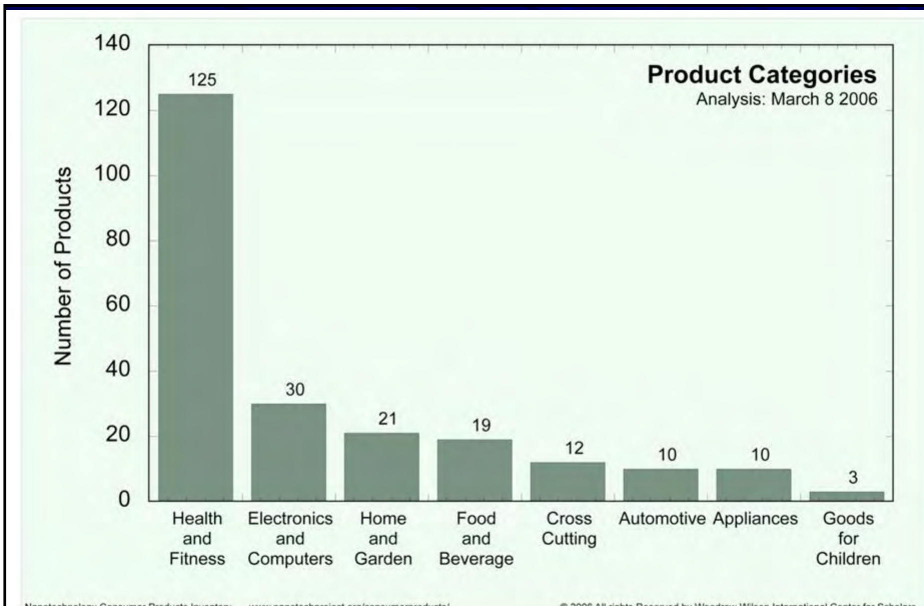


Figure 1. Number of products, according to category. Because some products are grouped into multiple categories, the total number of products in this chart exceeds 212.

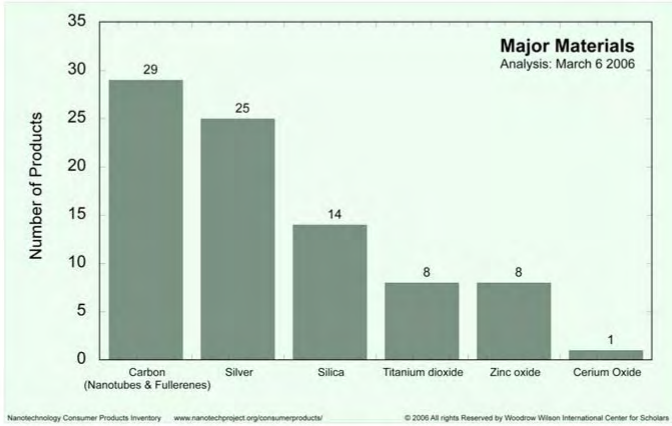


Figure 4. Numbers of products associated with specific materials.

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5 of46

Potential Risks

- Nanotechnology risks are largely unknown
- Risk is a function of both exposure *and* toxicity
- Need to monitor
  - – Exposure pathways
  - – Fate and transport in the environment
  - – Toxicity

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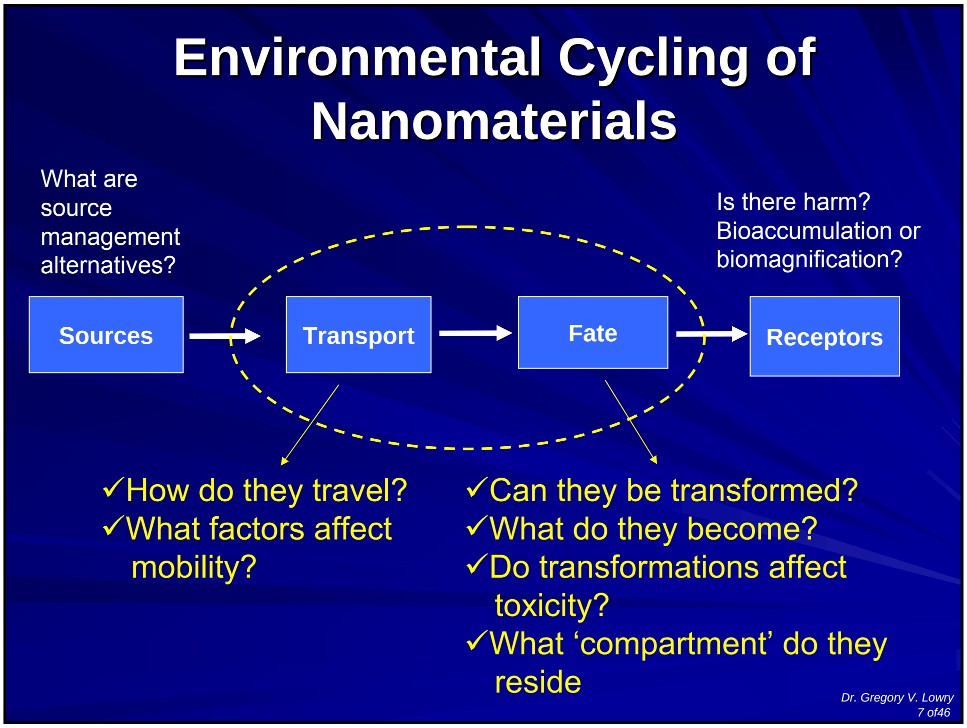
6 of46



Environmental Cycling of Nanomaterials
What are source management alternatives?
Is there harm? Bioaccumulation or biomagnification?
Sources
Transport
Fate
Receptors
✓How do they travel?
✓What factors affect mobility?
✓Can they be transformed?
✓What do they become?
✓Do transformations affect toxicity?
✓What 'compartment' do they reside
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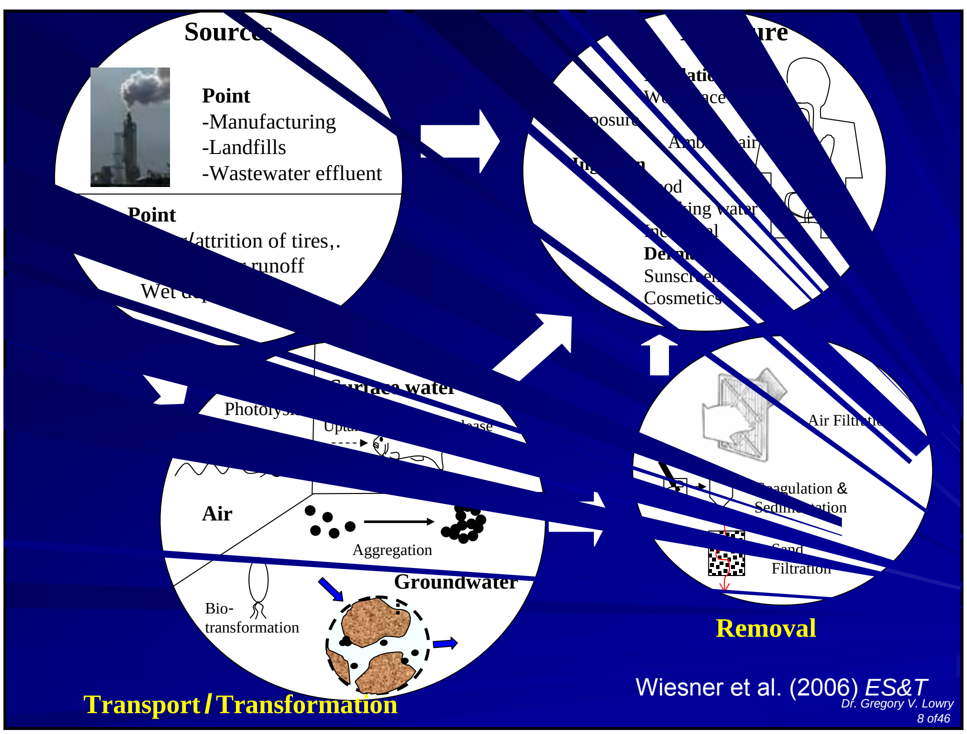
7 of46



Point
-Manufacturing
-Landfills
-Wastewater effluent
Air
Aggregation
Groundwater
Bio-transformation
Cosmetics
Removal
Transport / Transformation
Wiesner et al. (2006) ES&T
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8 of46

Outline

- Fate processes affecting the mobility of nanomaterials in the environment
  - Aggregation
  - Attachment/filtration
- Transformations
  - Abiotic (redox transformations, photolysis)
  - Biotransformation
- Mobility in the environment
  - Groundwater
  - Surface water

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9 of46

Nanoparticle Aggregation

- Particles aggregate in water:
  - High Hamaker constant-i.e. attractive van der Waals forces
  - Chemical bonding
  - Hydrophobicity
  - Magnetic attraction
- Small particles have high diffusion coefficients and many collisions between particles

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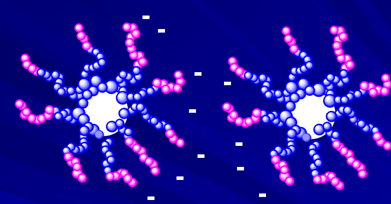
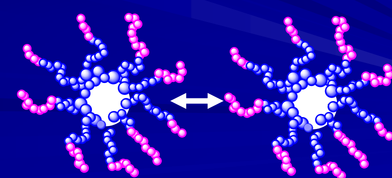
10 of46

Nanoparticle Stabilization

- Charge Stabilization



- Steric Stabilization



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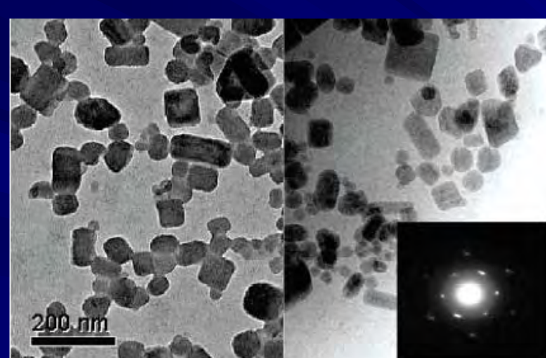
11 of46

Fullerene Aggregation in Water



✓Cluster dimensions ranged from 25-500 nm

✓Stable suspensions ≤ 0.05M (NaCl)

✓No surface coatings

Fortner, et al. (2005). C60 in Water: Nanocrystal Formation and Microbial Response. *Environ. Sci. Technol.* 39(11); 4307-4316.

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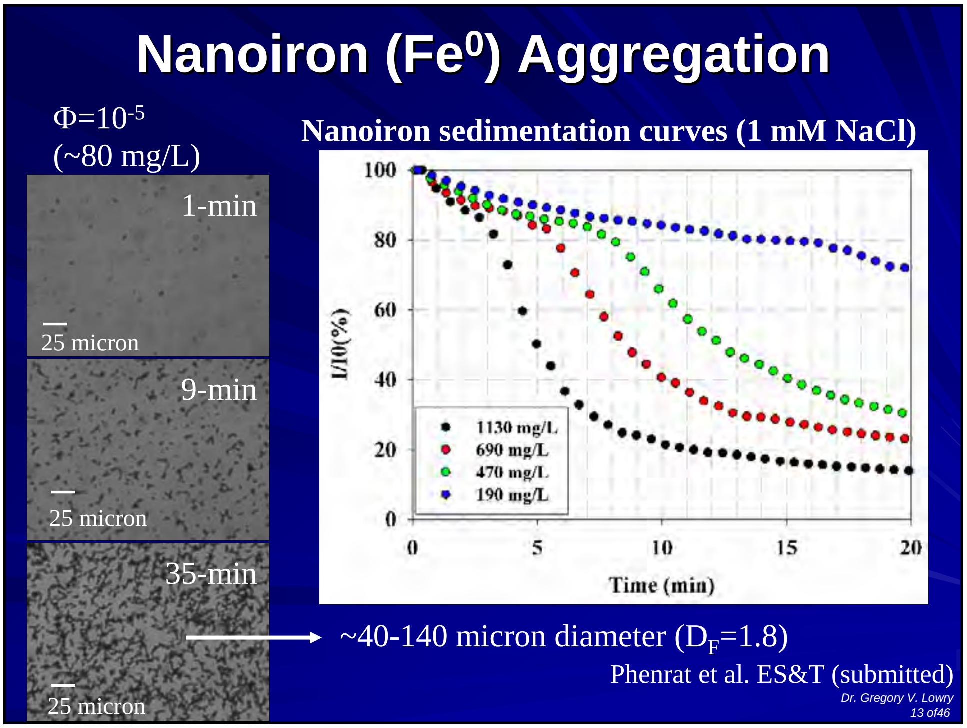
12 of46


Nanoiron (Fe0) Aggregation
Φ=10-5
(~80 mg/L)
1-min
25 micron
9-min
25 micron
35-min
25 micron
Nanoiron sedimentation curves (1 mM NaCl)
I/I0(%)
Time (min)
1130 mg/L
690 mg/L
470 mg/L
190 mg/L
~40-140 micron diameter (DF=1.8)
Phenrat et al. ES&T (submitted)
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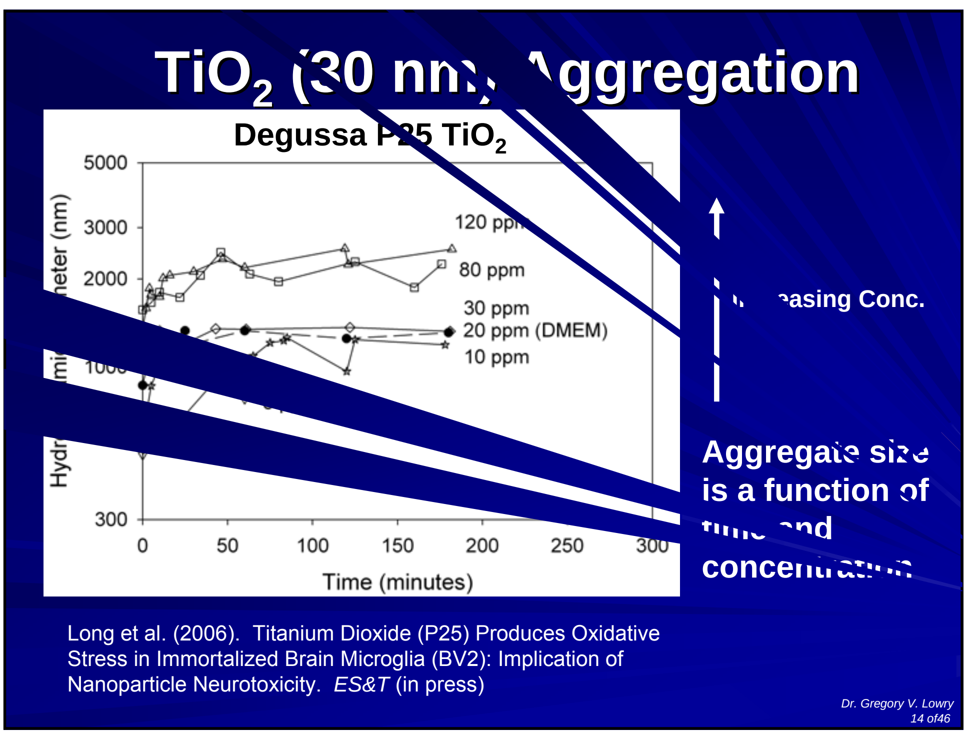
13 of46


Degussa P25 TiO2
Time (minutes)
80 ppm
30 ppm
20 ppm (DMEM)
10 ppm
Long et al. (2006). Titanium Dioxide (P25) Produces Oxidative Stress in Immortalized Brain Microglia (BV2): Implication of Nanoparticle Neurotoxicity. ES&T (in press)
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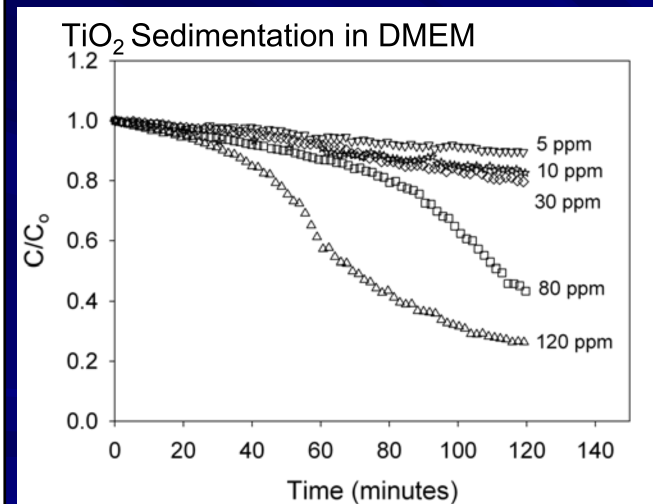
14 of46

Nanoparticle Size and Sedimentation



Particle concentration affects:

1. Size of aggregates formed
2. Stability of suspensions
3. Fate of the particles

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15 of46

Attachment to Surfaces

- Attachment is an important fate process
  - Limits mobility in porous media
  - May affect bioavailability
  - ... transformation/degradation
- ... (Hamaker Constant) and its surface properties
  - Differences between NPs

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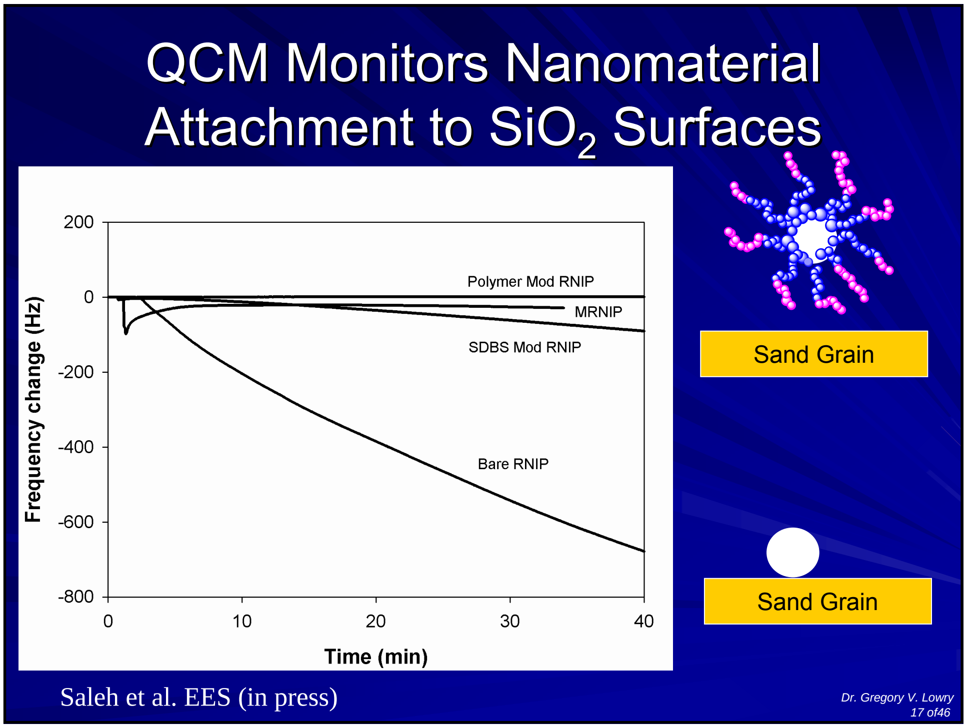
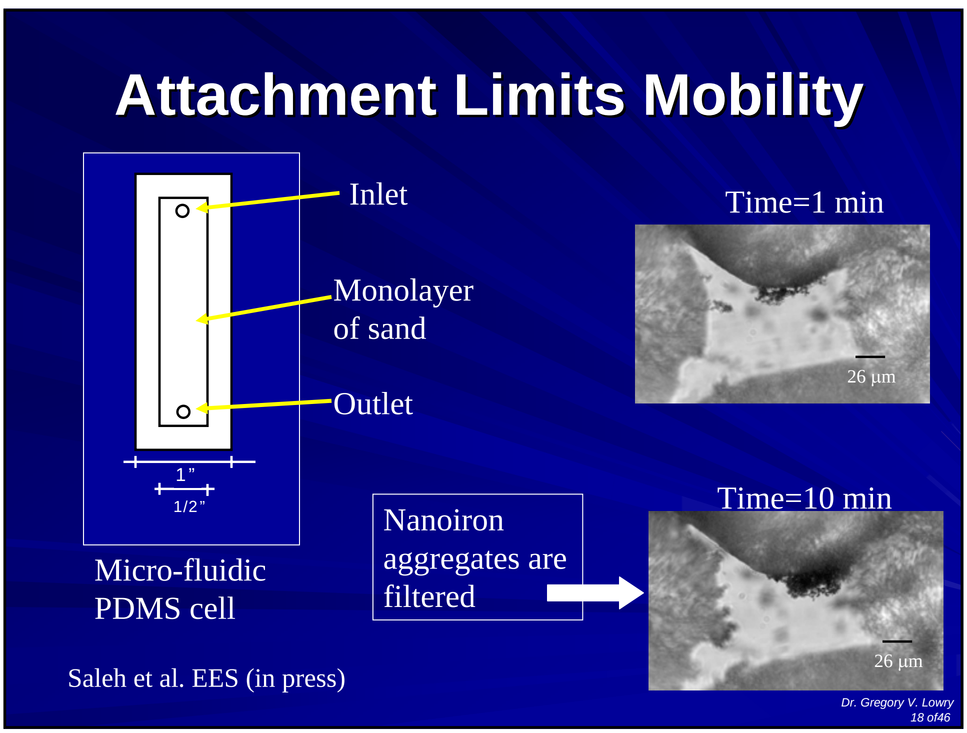
16 of46


QCM Monitors Nanomaterial Attachment to SiO_2 Surfaces
Frequency change (Hz)
200
0
-200
-400
-600
-800
0
10
20
30
40
Time (min)
Polymer Mod RNIP
MRNIP
SDBS Mod RNIP
Bare RNIP
Sand Grain
Sand Grain
Saleh et al. EES (in press)
Dr. Gregory V. Lowry
17 of46


Attachment Limits Mobility
Inlet
Monolayer of sand
Outlet
1"
1/2"
Micro-fluidic PDMS cell
Time=1 min
26 µm
Time=10 min
26 µm
Nanoiron aggregates are filtered
Saleh et al. EES (in press)
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18 of46

Nanomaterial Transformations

- Fundamental Questions
  - How long do the particles last?
  - What do they become?
- Abiotic transformations
  - Redox reactions
  - Photolysis (not in groundwater)
- Biotransformations
  - Aerobic oxidations
  - Anaerobic reductions

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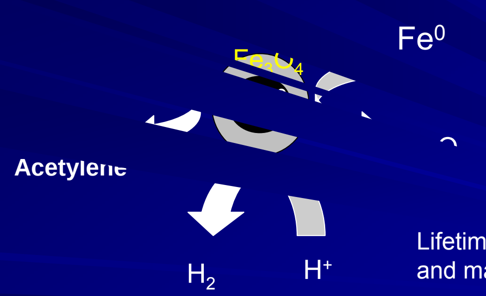
19 of46

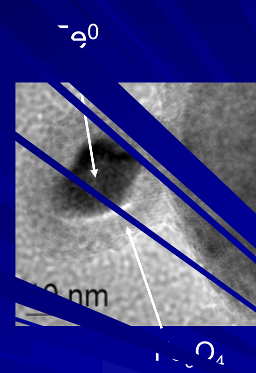
Reactive Fe^0 Nanoparticles

Contaminants reduced

Nano Fe^0 is oxidized



H+ is reduced



Lifetime depe... ...ding, pH, and maybe microbial activity

Liu et al, (2005) *ES&T 39*, 1338

Liu and Lowry, (2006) *ES&T (submitted)*

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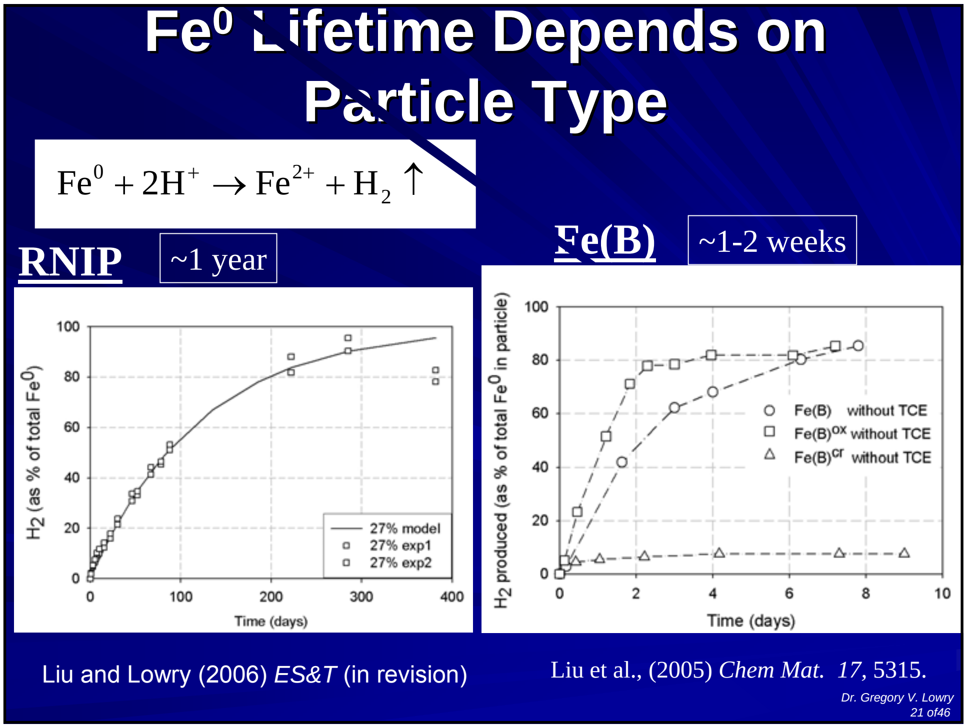
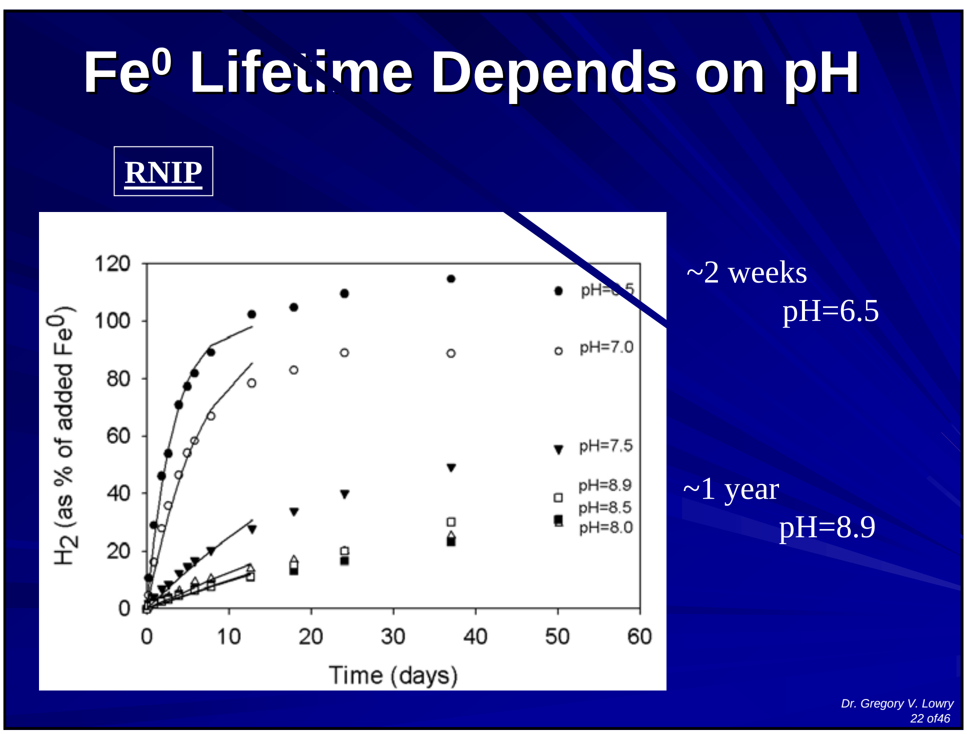
20 of46


Fe0 Lifetime Depends on Particle Type
Fe0 + 2H+ → Fe2+ + H2 ↑
RNIP
~1 year
Fe(B)
~1-2 weeks
H2 (as % of total Fe0)
Time (days)
27% model
27% exp1
27% exp2
H2 produced (as % of total Fe0 in particle)
Fe(B) without TCE
Fe(B)ox without TCE
Fe(B)cr without TCE
Liu and Lowry (2006) ES&T (in revision)
Liu et al., (2005) Chem Mat. 17, 5315.
Dr. Gregory V. Lowry
21 of46


Fe0 Lifetime Depends on pH
RNIP
H2 (as % of added Fe0)
Time (days)
pH=6.5
pH=7.0
pH=7.5
pH=8.9
pH=8.5
pH=8.0
~2 weeks
pH=6.5
~1 year
pH=8.9
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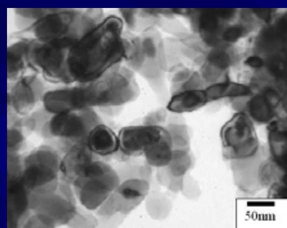
22 of46

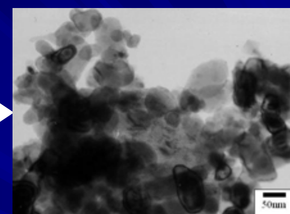
Nanoparticle Fate: Reaction with TCE in Water

RNIP (Fe^0/Fe_3O_4)

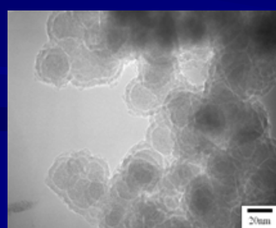


+ TCE/H_2O →

(Fe_3O_4/Fe_2O_3)

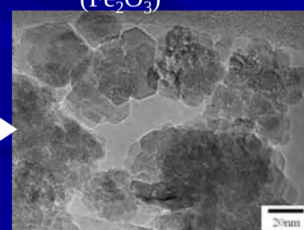


Fe(B) ($Fe^0/FeB_x/Na_2B_4O_7$)



+ TCE/H_2O →

(Fe_2O_3)



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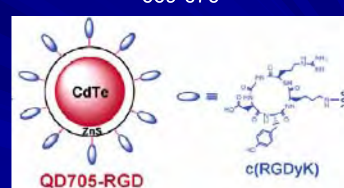
23 of46

Other transformations that could affect particle toxicity or mobility

- Surface functionalization
  - E.g. hydroxylation of fullerene to fullerol
  - Sorption of DOM or alginates
- Oxidation of NPs in the atmospheric
  - E.g. oxidation of diesel soot
- Loss of surface coatings on NP
  - Biodegradation of coatings
  - Desorption of coatings
- Biotransformations
  - Microbially induced redox transformations
    - Direct or indirect through release of reactive oxygen species or reductants (e.g. Fe^{2+})

Cai et al., 2006
Nanoletters 6 (4)
669-676



Wiesner et al. (2006) *ES&T*

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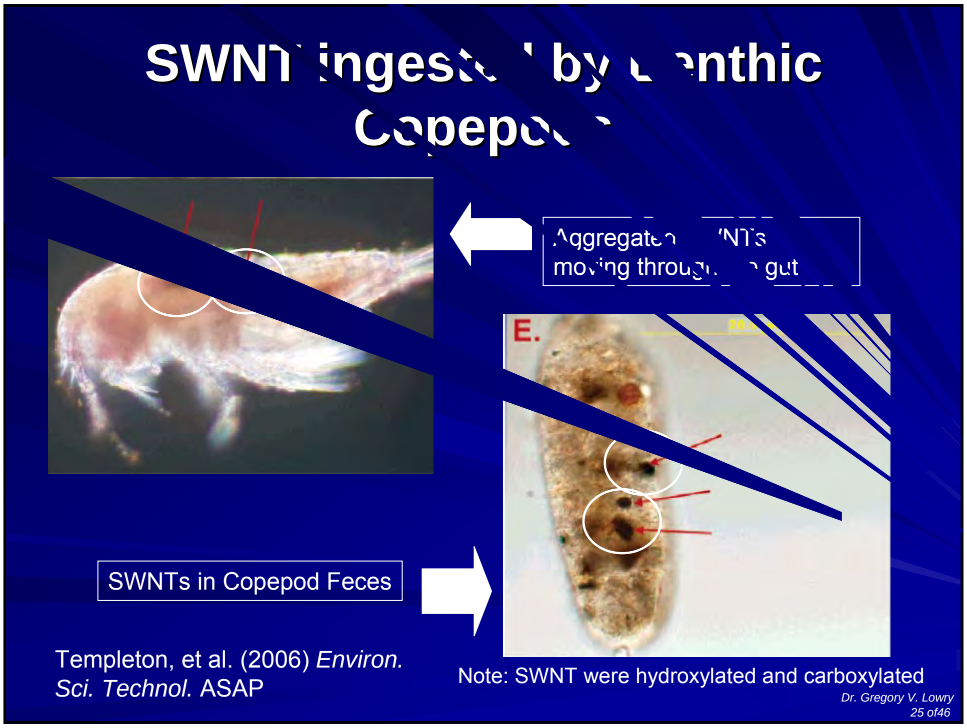
24 of46


SWNTs in Copepod Feces
E.
Templeton, et al. (2006) Environ. Sci. Technol. ASAP
Note: SWNT were hydroxylated and carboxylated
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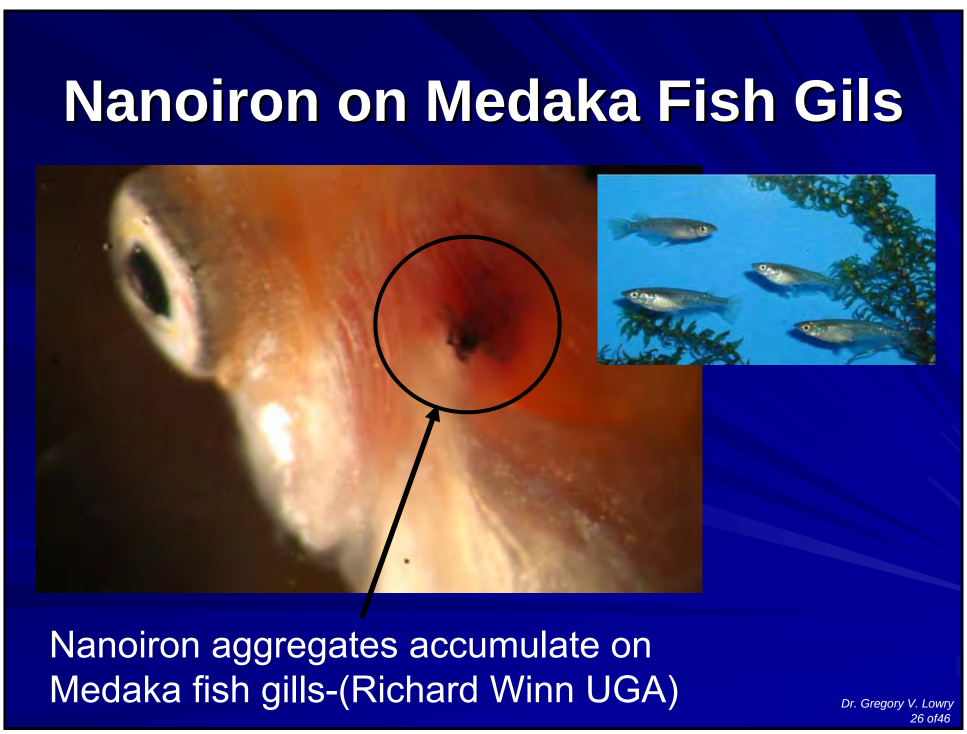
25 of46


Nanoiron on Medaka Fish Gils
Nanoiron aggregates accumulate on Medaka fish gills-(Richard Winn UGA)
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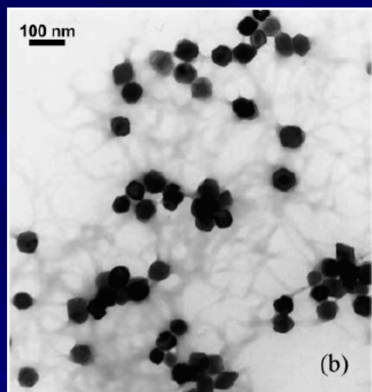
26 of46

Nanoparticle Functionalization in Natural Waters (Sorption of DOM)



Hematite-Alginate Aggregates
10^9 particles/mL; 784 μg/L alginate

- Alginates- biopolymers produced by brown seaweed
- Natural Organic Matter

Chen et al., 2006 *ES&T* 40 1516-1523

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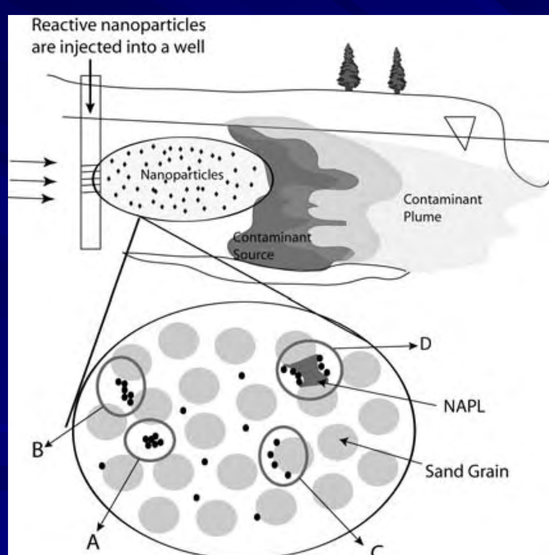
27 of46

Nanomaterial Mobility in Porous Media



- A---Aggregation
- B---Straining
- C---Attachment
- D---NAPL Targeting

Lowry, *Env. Nanotech.* (in press).

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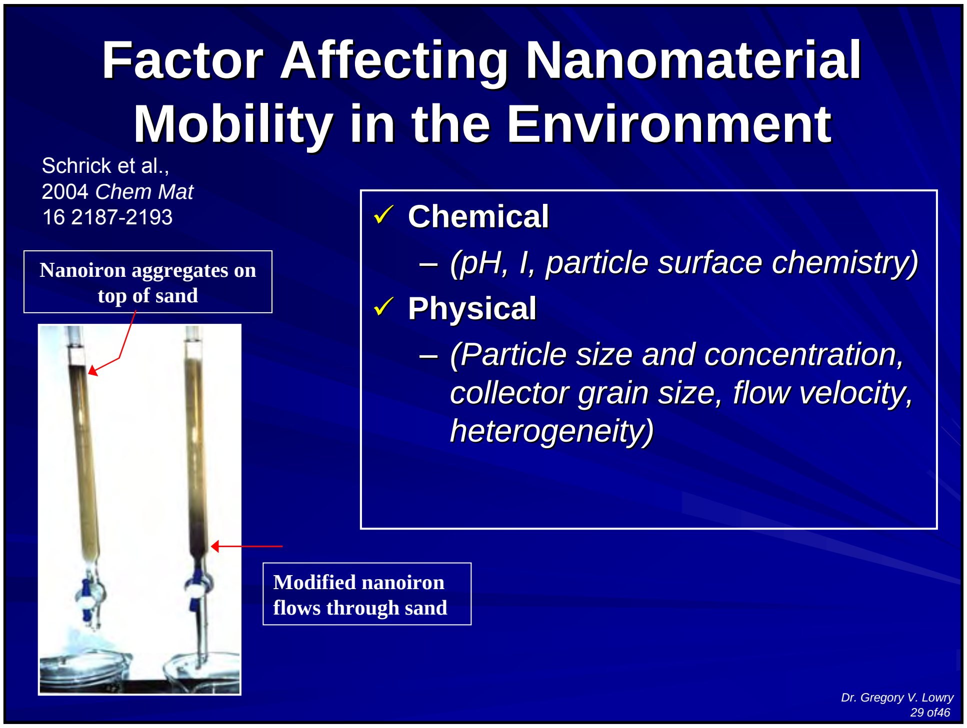
28 of46


Factor Affecting Nanomaterial Mobility in the Environment
Schrick et al., 2004 Chem Mat 16 2187-2193
Nanoiron aggregates on top of sand
Modified nanoiron flows through sand
✓ Chemical
– (pH, I, particle surface chemistry)
✓ Physical
– (Particle size and concentration, collector grain size, flow velocity, heterogeneity)
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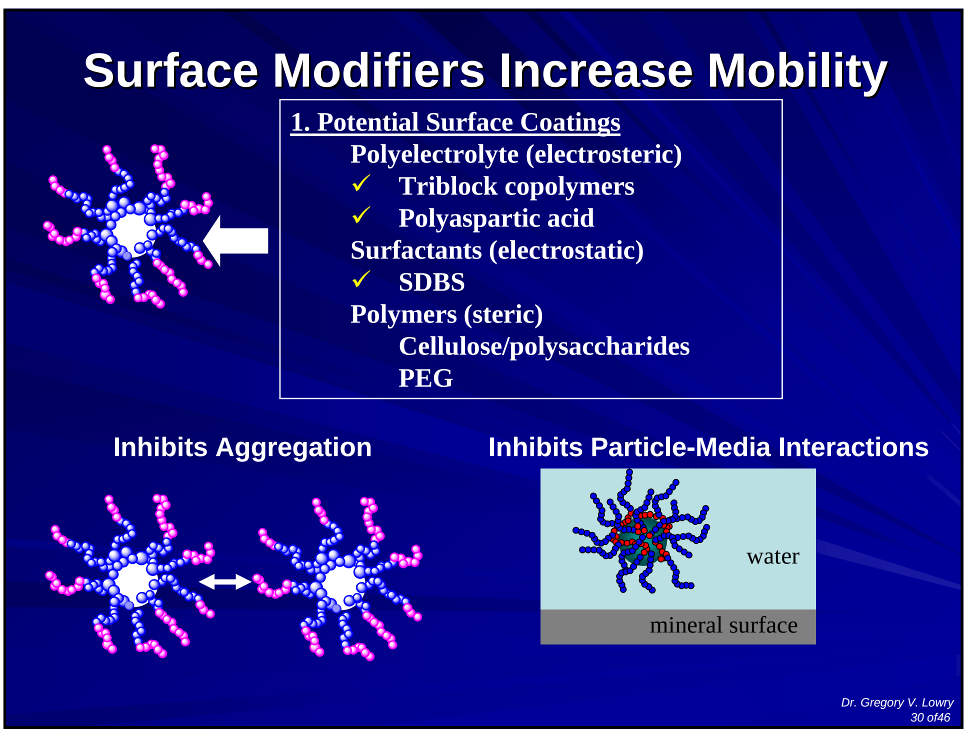
29 of46


Surface Modifiers Increase Mobility
1. Potential Surface Coatings
Polyelectrolyte (electrosteric)
✓ Triblock copolymers
✓ Polyaspartic acid
Surfactants (electrostatic)
✓ SDBS
Polymers (steric)
Cellulose/polysaccharides
PEG
Inhibits Aggregation
Inhibits Particle-Media Interactions
water
mineral surface
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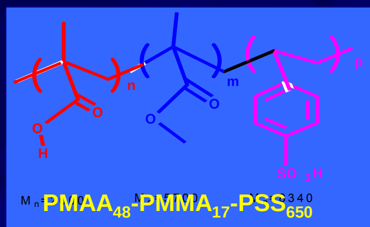
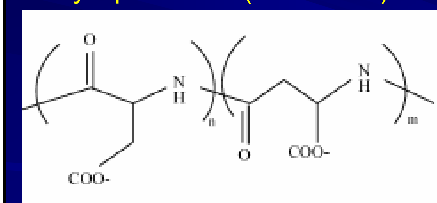
30 of46

Modifiers Evaluated

Copolymer (MW=40k to 60k)



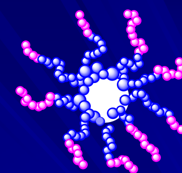
Polyaspartic acid (MW=2k-3k)



SDBS (MW=350)

$C_{12}H_{25}(C_6H_4)SO_3^-$

Increasing MW



Polyelectrolytes

Surfactant

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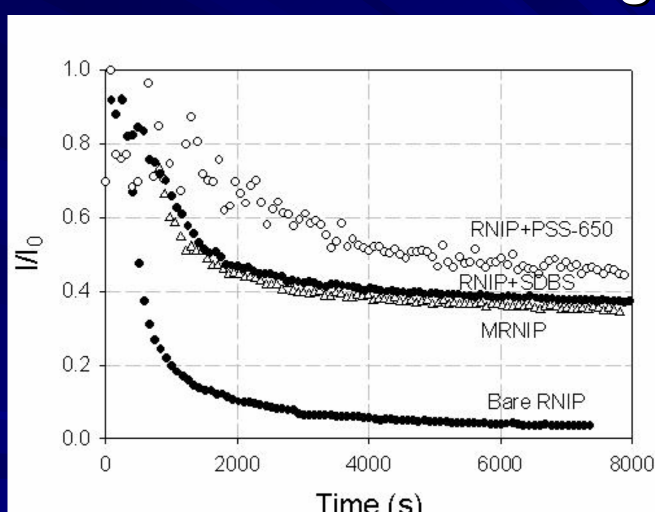
31 of46

Modifiers Inhibit Agg/Sed

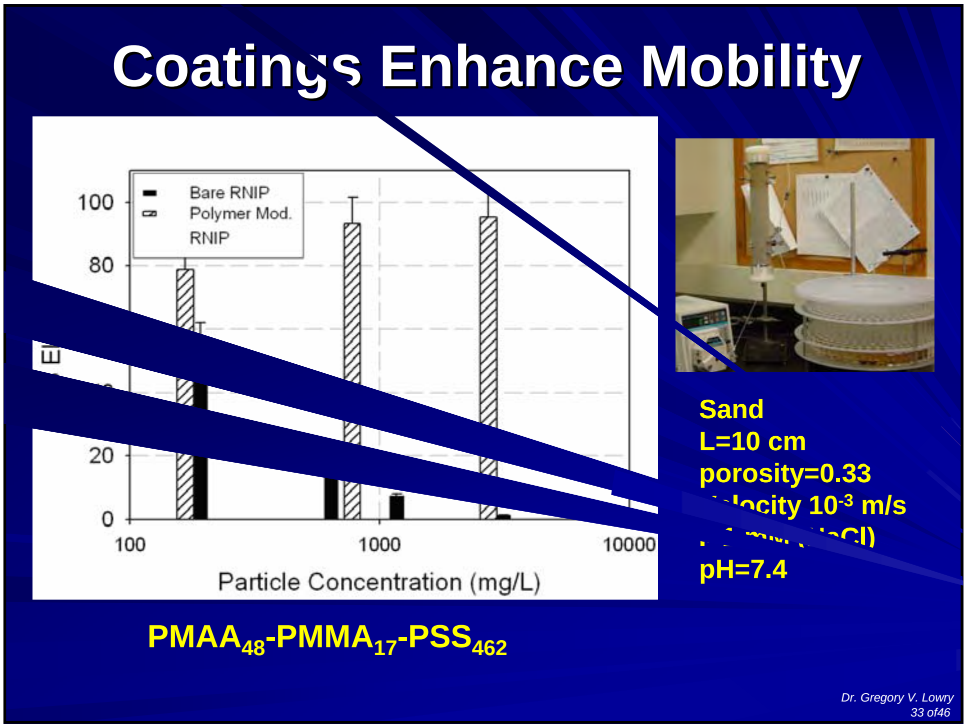


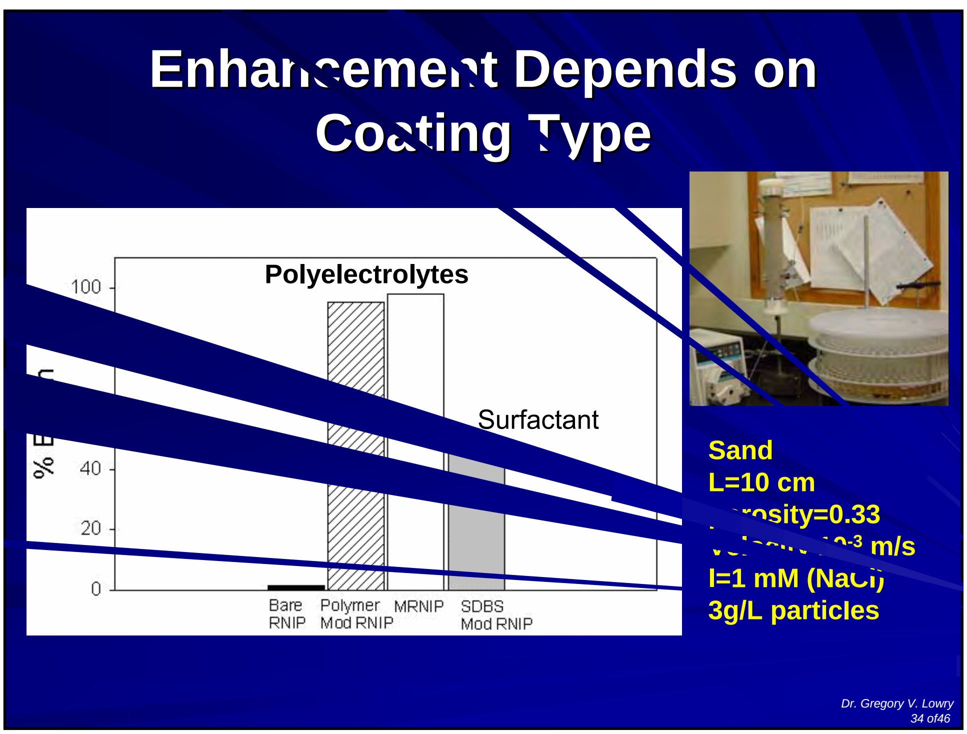
Largest Polymer
Least aggregation

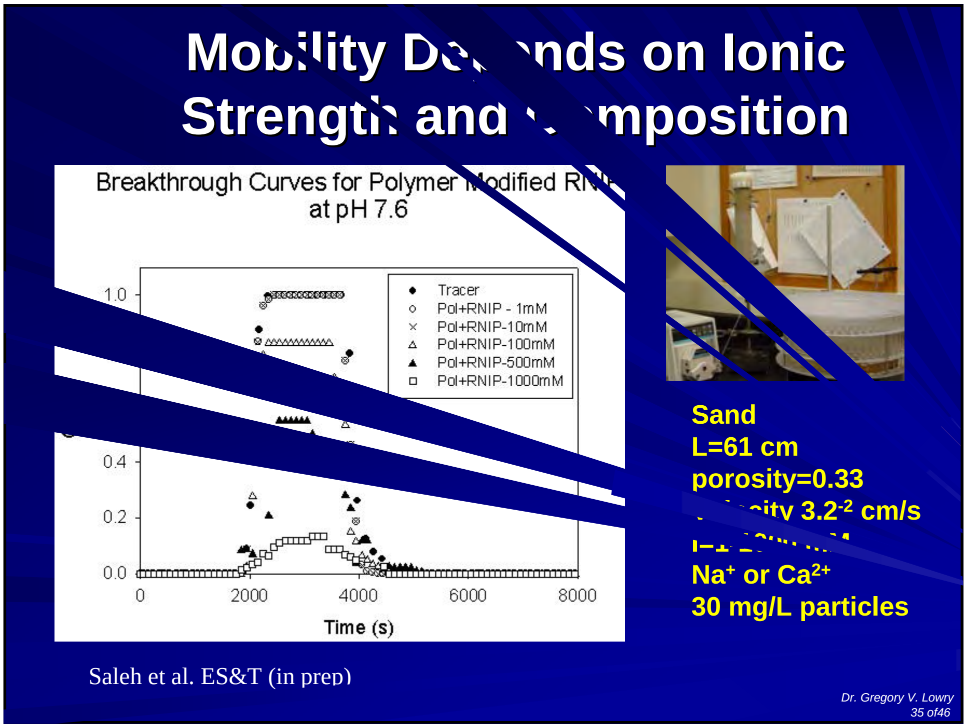
No Polymer
Most aggregation

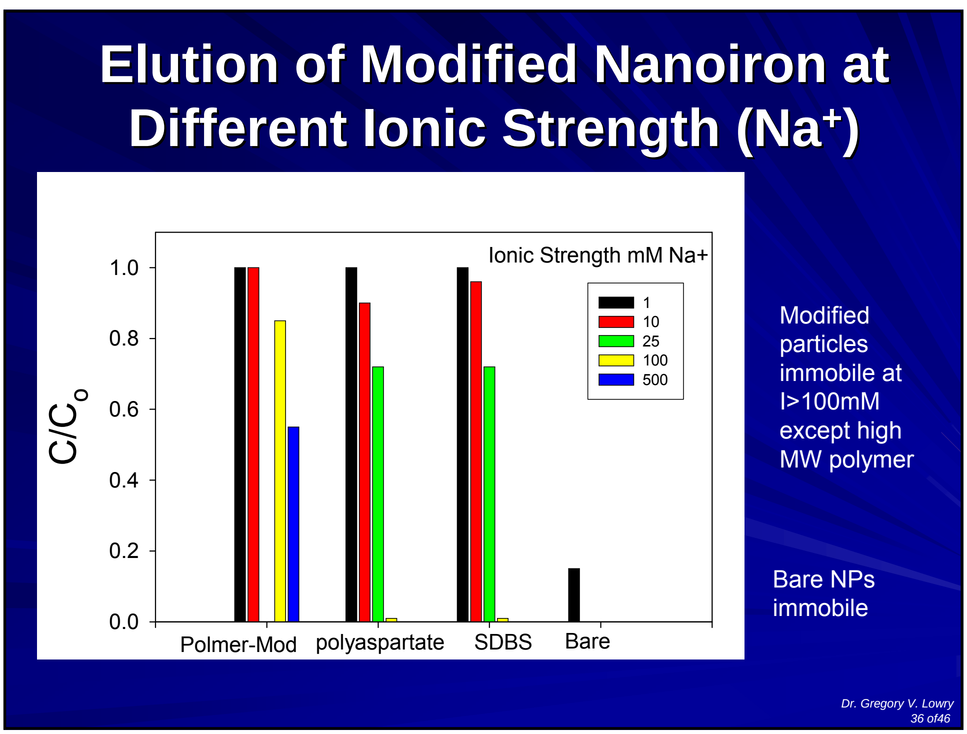
Saleh, N., et al. **(2005)**. "*Nano Lett.* 5 (12) 2489-2494.

Dr. Gregory V. Lowry
32 of46

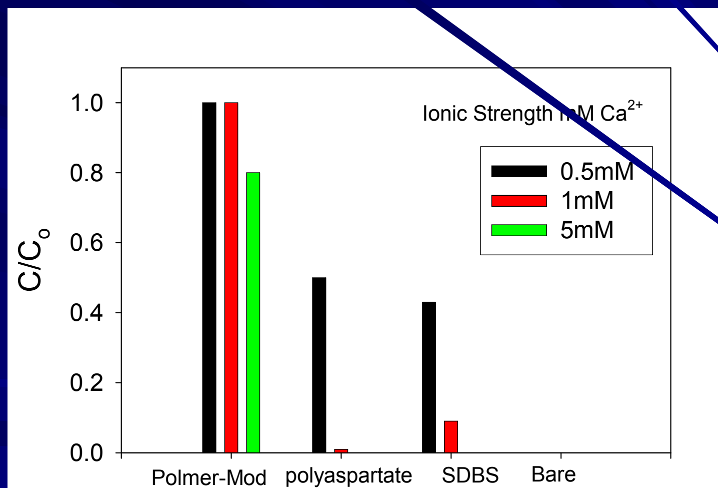

Coatings Enhance Mobility
Bare RNIP
Polymer Mod. RNIP
100
80
20
0
100
1000
10000
Particle Concentration (mg/L)
Sand
L=10 cm
porosity=0.33
pH=7.4
PMAA48-PMMA17-PSS462
Dr. Gregory V. Lowry
33 of46


Enhancement Depends on Coating Type
Polyelectrolytes
Surfactant
100
40
20
0
Bare RNIP
Polymer Mod RNIP
MRNIP
SDBS Mod RNIP
Sand
L=10 cm
3g/L particles
Dr. Gregory V. Lowry
34 of46


Mob lity De nds on Ionic
Strengt and mposition
Breakthrough Curves for Polymer odified R
at pH 7.6
1.0
0.4
0.2
0.0
0
2000
4000
6000
8000
Time (s)
Tracer
Pol+RNIP - 1mM
Pol+RNIP-10mM
Pol+RNIP-100mM
Pol+RNIP-500mM
Pol+RNIP-1000mM
Sand
L=61 cm
porosity=0.33
city 3.2-2 cm/s
Na+ or Ca2+
30 mg/L particles
Saleh et al. ES&T (in prep)
Dr. Gregory V. Lowry
35 of46


Elution of Modified Nanoiron at
Different Ionic Strength (Na+)
C/Co
1.0
0.8
0.6
0.4
0.2
0.0
Ionic Strength mM Na+
1
10
25
100
500
Polmer-Mod
polyaspartate
SDBS
Bare
Modified
particles
immobile at
I>100mM
except high
MW polymer
Bare NPs
immobile
Dr. Gregory V. Lowry
36 of46

Elution of Modified Nanoiron at Different Ionic Strength (Ca^{2+})



Particles immobile at I>1 mM Ca^{2+} except high MW polymer

Dr. Gregory V. Lowry
37 of46

Relative Mobility and Estimated Transport Distances

- Calculate the sticking coefficient from breakthrough data

Column Length **Breakthrough**

$$L_T = -\ln\left(\frac{C_L}{C_o}\right)\left(\frac{4a_c}{3(1-n)\alpha\eta_o}\right)$$

Travel Length **Tolerance level**

- Estimate Travel Distance for given tolerance (C/C_o)

a_c=media grain radius; n=porosity
η_o=single collector efficiency
α=sticking coefficient (function of I)

Dr. Gregory V. Lowry
38 of46

Estimated Transport Distance for (C/C_o=0.01)

Mod	Na^+ (mM)	Log α (--)	Dist. (m)	Ca^{2+} (mM)	Log α (--)	Dist. (m)
Polymer	10	--	--	0.5	--	--
(MW=60k)	100	-2	33	5	-1.89	25
Aspartate	10	-2.5	45	0.5	-1.77	8
(MW=3k)	100	-0.96	1.2	1	-0.96	1.2
SDBS	10	-2.7	150	0.5	-1.33	6.6
(MW=350)	100	-0.6	1.2	1	-0.89	2.4

Dr. Gregory V. Lowry
39 of46

Mobility of Carbon and Metal-oxide Nanomaterials

TABLE 1. Characteristics of Nanomaterials Used for Filtration Experiments and Calculated Particle Mobility in a System Resembling a Sandy Groundwater Aquifer[a]

nanomaterial	size (nm)	electrophoretic mobility (10^{-8} $m^2 s^{-1} V^{-1}$)	C/C_0 ± 2 SD	α ± 2 SD	log α	distance to reduce C/C_0 to 0.1% (m)[b]
fullerol	1.2, M	not detectable	0.99 ± 0.01	(0.0001 ± 0.0001)	−3.98	14
SWNT	0.7−1.1[c] × 80−200, P (d_h = 21 nm[d])	−3.98	0.94 ± 0.01	(0.001 ± 0.0004)	−2.89	10
silica	57, M	−1.95	0.97 ± 0.01	0.008 ± 0.003	−2.10	2.4
alumoxane	74, P	−2.45	0.85 ± 0.02	0.039 ± 0.001	−1.32	0.6
silica	135, M	−2.58	0.68 ± 0.01	0.169 ± 0.004	−0.77	0.2
n-C_{60}	168, M	−1.99	0.56 ± 0.06	0.298 ± 0.013	−0.52	0.1
anatase	198, P	−0.27	0.56 ± 0.01	0.336 ± 0.005	−0.47	0.1
ferroxane	303, P	−0.43	0.30 ± 0.03	0.895 ± 0.023	−0.05	0.1

[a] M, monodisperse suspensions; P, polydisperse suspensions. [b] Conditions assumed for calculations: T = 15 °C, H = 10^{-20} J, Darcy velocity = 0.003 cm/s, porosity = 0.30, mean sand grain diameter = 350 μm. [c] According to the model cross-section of an individual fullerene nanotube encased in a close-packed cylindrical surfactant micelle (*16*), the outer diameter of this nanomaterial is close to 4 nm with a specific gravity of approximately 1.0. [d] Average hydrodynamic diameter.

I= 10 mM, pH=7, v=0.003 cm/s

Lecoanet, et al. (2004). Laboratory Assessment of the Mobility of Nanomaterials in Porous Media. *Environ. Sci. Technol.* 38(19); 5164-5169.

Dr. Gregory V. Lowry
40 of46

Mobility of Nanomaterials from Landfills

- Mobility from landfills could be limited considering leachate properties*
  - Calcium 200-3000 mg/L (<5mM)
  - Magnesium 50-1500 mg/L
  - Sodium 100-200 mg/L
  - Clay liners and leachate collection

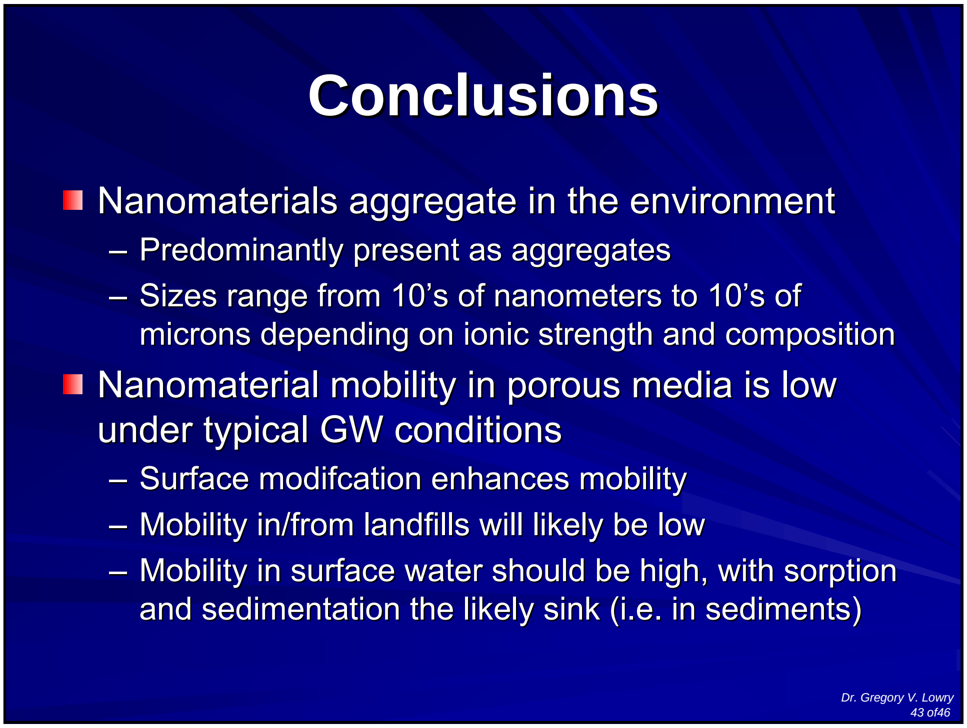
*Davis and Masten, *Principles of Environmental Engineering and Science*, McGraw Hill, 2004

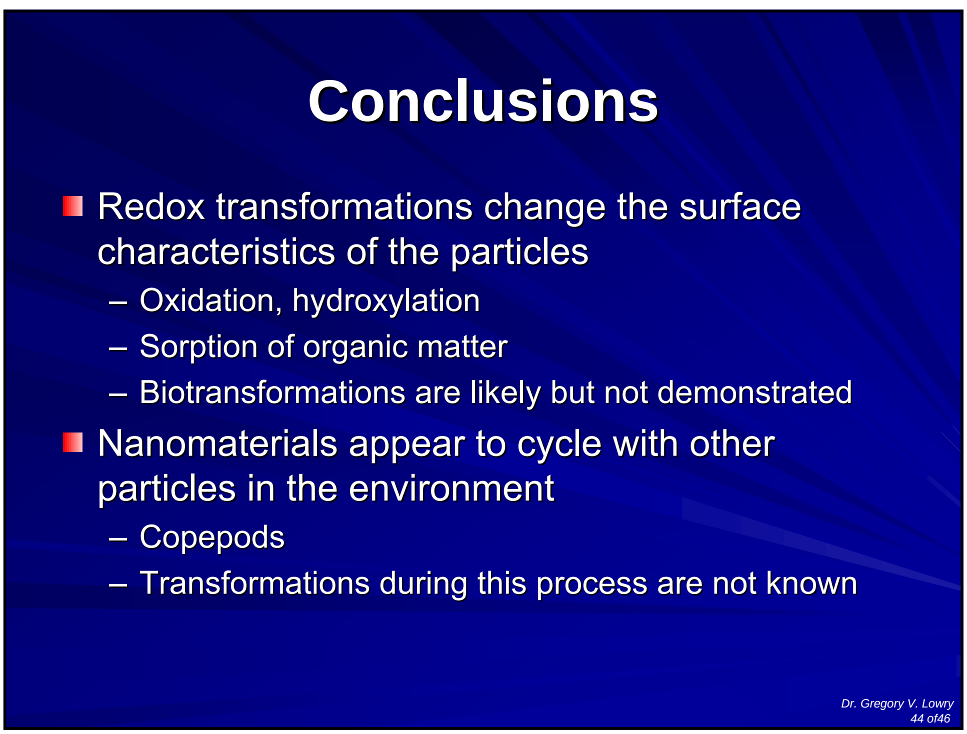
Dr. Gregory V. Lowry
41 of46

Mobility in Su[illegible]ce [illegible]aters

- [illegible]obility in surface waters is [illegible]
  - [illegible] in receiving waters may [illegible] aggreg[illegible] or promote disaggregati[illegible]
  - [illegible] surface [illegible] in surface water[illegible] [illegible]ot know[illegible]
  - Attach[illegible] other su[illegible] solids is possible and my resu[illegible] sedimentation and partitioning to solids
  - Photolysis in surface waters is possible

Dr. Gregory V. Lowry
42 of46


Conclusions
Nanomaterials aggregate in the environment
– Predominantly present as aggregates
– Sizes range from 10's of nanometers to 10's of microns depending on ionic strength and composition
Nanomaterial mobility in porous media is low under typical GW conditions
– Surface modifcation enhances mobility
– Mobility in/from landfills will likely be low
– Mobility in surface water should be high, with sorption and sedimentation the likely sink (i.e. in sediments)
Dr. Gregory V. Lowry
43 of46


Conclusions
Redox transformations change the surface characteristics of the particles
– Oxidation, hydroxylation
– Sorption of organic matter
– Biotransformations are likely but not demonstrated
Nanomaterials appear to cycle with other particles in the environment
– Copepods
– Transformations during this process are not known
Dr. Gregory V. Lowry
44 of46

Open Questions

- Fate and Transport
  - Will NMs bioaccumulate or facilitate the bioaccumulation of other contaminants?
  - How significant are biotransformations of NMs?
  - Is photolysis significant?
  - What role does heterogeneity play in particle mobility?
  - Is incineration effective at destroying NMs?
  - What is the fate of surface coatings on nanomaterials?
- Toxicity
  - What are "environmentally relevant" concentrations of NMs?
  - Despite aggregation, is the low population of single particles responsible for toxicity?
  - Do surface coatings enhance or mitigate the toxicity of the particles?

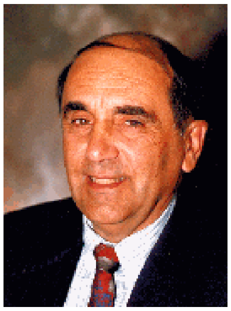
Dr. Gregory V. Lowry
45 of46

Acknowledgement

- Toda Koygo Corp. and Degussa Inc.
- U.S. EPA-STAR (R830898)
  - Barb Karn and Nora Savage
- US DOE EMSP Program (DE-FG07-02ER63507)

This research is funded by
U.S. EPA - Science To Achieve Results (STAR) Program
Grant # R830898

Dr. Gregory V. Lowry
46 of46



Dr. Lou Theodore

Professor, Graduate Program Director
Manhattan College, Department of Chemical Engineering
Riverdale, New York

B. Ch.E. The Cooper Union
M.S., Eng.Sc.D. New York University

Louis Theodore is Professor of Chemical Engineering at Manhattan College, Riverdale, New York. He received the degrees of B.Ch.E. from the Cooper Union and the degrees of M.Ch.E and Eng.Sc.D. from New York University. Over the past 46 years, Dr. Theodore has been a successful educator, researcher, professional innovator, and communicator in the engineering field. At Manhattan College he has taught courses in Environmental Management, Waste Incineration, Accident and Emergency Management, Pollution Prevention, Thermodynamics, Reaction Kinetics, and Air Pollution and Its Control.

Dr. Theodore is an internationally recognized lecturer who has provided nearly 200 courses to industry, government and technical associations, and has served as an after-dinner or luncheon speaker on numerous occasions. More recently, Dr. Theodore has developed and served as the principal moderator/lecturer for USEPA courses on hazardous waste incineration and air pollution control equipment. He has also consulted for several industrial companies in the field of pollution prevention and environmental management, and is presently a consultant/expert witness for the USEPA and US Department of Justice.

Included in Dr. Theodore's 92 text/reference books are: Pollution Prevention (Van Nostrand Reinhold), Engineering and Environmental Ethics (Wiley-Interscience), Air Pollution Control Equipment (Prentice-Hall), Introduction to Hazardous Waste Incineration (Wiley-Interscience), and section author/editor in Perry's Handbook of Chemical Engineering (McGraw-Hill). He is also the co-founder of Theodore Tutorials, a company specializing in providing training needs to industry, government and academia.

Dr. Theodore is the recipient of the International Air and Waste Management Association's (IAWMA) prestigious Ripperton award that is "presented to an outstanding educator who through example, dedication and innovation has so inspired students to achieve excellence in their professional endeavors." He was also the recipient of the American Society for Engineering Education (ASEE) AT&T Foundation award for "excellence in the instruction of engineering students."

Dr. Theodore is a member of IAABO (International Association of Approved Basketball Officials) and certified to referee scholastic basketball games. He previously served on a Presidential Crime Commission under Gerald Ford and provided testimony as a representative of the parimutuel wagerer (horseplayer). His column AS I SEE IT, a monthly feature of the Williston Times, addresses social, economic, political, technical and sports issues.

Professional Interest:
Development of tutorial workbooks; continuing education courses in the environmental management area; waste incineration calculations; air pollution control equipment design; pollution prevention. Dr. Theodore recently presented a continuing education course titled "Nanotechnology" at the IAWMA meeting in Minneapolis in June, 2005.

Recent Selected Publications:

L. Theodore, "Ask the Expert/Engineering Calculations," 5 articles: Adsorbeers, Absorbers, Afterburners, Baghouses, and Cyclones. *CEP*, March, April, June, July, August, respectively, 2005.

L. Theodore and R. Kunz, *Nanotechnology: Environmental Implications and Solutions*, John Wiley and Sons, Hoboken, NJ, 2005.

J. Reynolds, J. Jeris, L. Theodore, *Handbook of Chemical and Environmental Engineering Calculations*, Wiley-Interscience, NYC, 2002.

A. M. Flynn, J. Reynolds, L. Theodore, "A Course on Health, Safety, and Accident Prevention," ASEE meeting, Albuquerque, NM, 2001.

A. M. Flynn, L. Theodore, "An Air Pollution Control Equipment Design Course for Chemical and Environmental Engineering Students Using an Open-Ended Problems Approach," ASEE meeting, Rowan College, 2001.

J. Santoleri, J. Reynolds, L. Theodore, *Introduction to Hazardous Waste Incineration*, 2nd edition, Wiley-Interscience, NYC, 2001.

G. Burke, R. Singh, L.Theodore, *Handbook of Environmental Management and Technology*, 2nd edition, Wiley-Interscience, NYC, 2000.

R. Dupont, K. Ganesan. L. Theodore, *Pollution Prevention: The Waste Management Approach for the 21st Century*, Lewis Publishers, Boca Raton, FL 2000.

M.K. Theodore, J. Reynolds, L. Theodore, "A Pollution Prevention Calendar," *Proceedings of the 93rd Annual AWMA Meeting*, Salt Lake City, 2000.

J. Spero, B. DeVito, L. Theodore, *Regulatory Chemicals Handbook*, Marcel Dekker, NYC, 2000.

A. Leone, J. Reynolds, L. Theodore, *Fundamentals of Engineering for Chemical Engineers -- Afternoon Exam*, for PE licensing, a Theodore Tutorial, Air and Waste Management Association (AWMA Bookstore), Pittsburgh, PA, 1999.

W. Matystik, L. Theodore, R. Diaz, *State Environmental Agencies on the Internet*, Government Institutes, Rockville, MD, 1999.

C. Hellwege, Z. Kahn-Jetter, R. Borrmann, J. Reynolds, L. Theodore, *Fundamentals of Engineering for Chemical Engineers -- Morning Exam*, for PE licensing, a Theodore Tutorial, Air and Waste Management Association (AWMA Bookstore), Pittsburgh, PA, 1999.

Co-author of sections on "Environmental Management" and "Pollution Prevention" in *Perry's Chemical Engineering Handbook*, seventh edition, McGraw-Hill, New York, NY, 1998.

H. Beim, J. Spero, L. Theodore, *Reference Guide for Hazardous Air Pollutants*, Van Nostrand Reinhold, NYC, 1998.

J. Wilcox, L. Theodore, *Engineering and Environmental Ethics*, Wiley-Interscience, NYC, 1998.

L. Theodore, J. Reynolds, K. Morris, *The Complete Dictionary of Environmental Terms*, Gordon and Breach, Newark, NJ 1997.

L. Theodore, K. Nueser, *Engineering Economics and Finance, A Theodore Tutorial*, ETS International Inc., Roanoke, VA, 1996.

J. Wilcox, J. Reynolds, L. Theodore "United States Federal Sentencing Guidelines and the Development of Ethics Education Programs in the Environmental Industry," *Proceedings of the Annual AWMA Meeting*, Nashville, TN, 1996.

M.K. Theodore, L. Theodore, *Major Environmental Issues Facing the 21st Century*, Prentice-Hall, Saddle Brook, NJ, 1996.

K. Ganesan, R. DuPont, L. Theodore, *Air Toxics: Problems and Solutions*, Gordon and Breach, Newark, NJ, 1996.

M. Budin, L. Theodore, "Sources and Control of Industrial Gas Emissions," *Proceedings of the Mid-Atlantic States Section of AWMA Meeting*, Atlantic City, NJ, 1995.

L. Theodore, J. Mycock, J. Reynolds, "The Theodore Tutorial: A Unique Approach to the Academic and Professional Training of Engineers," *Proceedings of the World Conference on Engineering Education*, St. Paul, MN, 1995.

L. Theodore, "Dissolve the USEPA ... Now," *Environmental Manager*, Volume 1, November 1995.

J. McKenna, J. Mycock, L. Theodore, *Handbook of Air Pollution Control and Technology*, CRC Press/Lewis Publishers, Boca Raton, FL, 1995.

Recent External Grants:
"Environmental Management," National Science Foundation, Undergraduate Faculty Enhancement Program, with Utah State University, 1996-1997.

Grant from U.S. Environmental Protection Agency to further develop software for a hazardous waste incinerator, Manhattan College, with J. Reynolds, 1995-1996.

"Air Toxics," National Science Foundation, Undergraduate Faculty Enhancement Program, with Montana Tech, 1994-1995.

Grant from U.S. Environmental Protection Agency to develop problems and author a self-instructional workbook for the use of PRO/II, a process flowsheet simulator, Manhattan College, 1994-1995.

"Undergraduate Faculty Seminar: Pollution Prevention," National Science Foundation, Undergraduate Faculty Enhancement Program, with J. Reynolds, Manhattan College, 1992.

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Session 5: Waste Management of Nanomaterials

July 13, 9:00-10:00 AM

Dr. Lou Theodore, Manhattan College, Department of Chemical Engineering, Riverdale, NY

Abstract

Nanotechnology is the second coming of the industrial revolution. It promises to make that nation (hopefully ours) that seizes the nanotechnology initiative the technology capital of the world. One of the main obstacles to achieving the goal will be to control, reduce, and ultimately eliminate environmental and environmental related problems associated with this technology; the success or failure of this new use may well depend on the ability to effectively and efficiently address these environmental issues.

The environmental health and hazard risk associated with both nanomaterials and the applications of nanotechnology for industrial uses are not fully known. Some early studies indicate that nanoparticles can serve as environmental poisons that accumulate in organs.

Although these risks may prove to be either minor, or negligible, or both, the engineer and scientist is duty bound to determine if there are in fact any health, safety, and environmental impacts associated with nanotechnology. This presentation will address these issues. Much of the material is drawn from the John Wiley & Sons texts *Nanotechnology: Environmental Implications and Solutions* by Theodore and Kunz (2005) and *Nanotechnology: Basic Calculations for Engineers and Scientists* by Theodore (2006).

Specific topics include:
1. Introduction to Waste Management
2. Treatment/Control
3. Multi-media Concerns
4. Pollution Prevention
5. Environmental Concerns
6. Environmental Regulations
7. Conclusions

Session 5: Waste Management of Nanomaterials

July 13, 9:00-10:00 AM

Dr. Lou Theodore, Manhattan College Department of Chemical Engineering Riverdale, NY

Highlights

Nanoscale particles have unique properties, which lead to infinite possible uses. Quality control is an issue in the development of nanoparticles because of the unique chemical and physical properties of particles (of the same chemical composition) of different size.

Nanoparticle emissions from incineration may have environmental effects. Incineration can be kept at a high level of efficiency -- it depends on what control devices are used. Baghouses can be especially effective. The diffusion properties of small particles can be exploited in this context.

There are two necessary elements of hazard assessment: (1) probability; and (2) consequences. From this information, one can estimate risk.

Assessment of health risks to workers would fall under EPA and OSHA. Hazard risks would fall under OSHA. Risks to civilians will fall under the domain of EPA. There are no existing regulations.
A cost-benefit analysis is needed for any new regulation.

Professionals are obligated to do everything in their power to prevent health and hazard problems. The obligation is on the regulator to gather as much data as possible; EPA should try to learn as much as possible about nanotechnology. However, it should not impose regulations/restraints on industrial development. Companies need to address potential liability for all products. A non-regulatory procedure should be implemented.

EPA has a vehicle in TSCA for evaluating new chemical substances. The question is, “what is a new chemical substance?” How do we handle all of the new substances? There are so many differences possible based on size, charge, method of manufacture, etc.

Question-and-Answer Session

When asked about new regulations, Dr. Theodore said that chemical engineers, physicists, someone from ASTM, etc. should be consulted regarding what regulations should be in place. EPA will have to develop models that will describe the whole gamut of properties. The number of chemicals is going to complicate regulations. A commenter notes that one problem with TSCA is the issue of confidential business information (CBI) (e.g., a way to share information, yet still maintain confidentiality to protect competitive advantage). Regarding TSCA CBI, companies provide information about structure, but they are not obligated to say whether the material is nano-sized. Dr. Theodore indicated that EPA can change its interpretation of the (TSCA) rule.

NANOTECHNOLOGY:

ENVIRONMENTAL IMPLICATIONS AND SOLUTIONS

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NANOTECHNOLOGY–WHAT IS IT??????

AMBIGUITIES INHERENT IN DEFINITION

Nanoparticle:
Collection of 100+ atoms in 1-100 nm diameter range

1. Research at 1-100 nm level
2. Create uses and applications at nanosizes

3a. Molecular manufacturing via molecular assembly

Centuries vs. Decades
New vs. "Old" laws
Intuition vs. Facts

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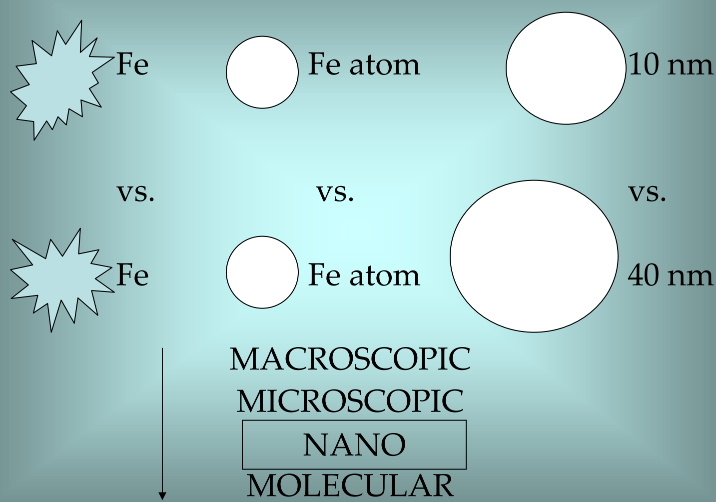
3b. Building atomically-precise products

3c. Quality control difficult, if not, impossible



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ARISTOTLE: EARTH, FIRE, WATER, AND AIR

BOYLE: TINY MATTER COMBINES IN VARIOUS WAYS TO FORM CORPUSCLES

1. "What would happen if we could arrange the atoms one by one the way we want them (within reason, of course; you could not put them so that they are chemically unstable, for example)?"
2. "So it should be possible to see the individual atoms."
3. "What would the properties of the materials be, if we could really arrange the atoms the way we want them?"
4. "But i can hardly doubt that when we have some control of the arrangement of things on a small scale, we will get an enormously greater range of possible properties that substances can have, and of different things that we can do."
5. "Atoms on a small scale behave like nothing on a large scale, for they satisfy the laws of quantum mechanics. At the atomic level, we have new kinds of possibilities, new kinds of effects."
6. "The principles of physics, as far as i can see, do not speak against the possibility of maneuvering things atom by atom. It is not an attempt to violate any laws. It is something in principle, that can be done, but in practice, it has not been done because we are too big."

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7. “I am, as I said, inspired by the biological phenomenon in which chemical forces are used in repetitious fashion to produce all kinds of weird effects (one of which is the author).”
8. “If you could swallow the surgeon, you put the mechanical surgeon inside the blood vessel, it goes into the heart, and looks around.”
9. “So I want to build a billion tiny factories, models of each other, that manufacture simultaneously.”

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EDUCATION – MAD SCRAMBLE

1. Nano program – major (under)
2. Eng/Sci major with nano minor
3. Eng/Sci major with nano integration
4. Nano program – major (graduate)

How to best teach it

- Science
- Applied science
- Engineering fundamentals
- Engineering

Nano involves the application of previously learned material except

1…………………
2…………………

Most have yet to realize nano role

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Attempt to apply present day environmental management to nanotechnology

Emphasis will be key on engineering approach and problem solving

4 parts

1. Chemistry fundamentals
2. Particle technology
3. Applications
4. Environmental concerns

CHEMISTRY FUNDAMENTALS – (PART 1)

1. Units, conversion constants and dimensional analysis
2. Atoms, elements, and the periodic table
3. Molecular rearrangements
4. Concentration terms
5. Particle surface area and volume
6. Material science principles
7. Physical and chemical property estimation

PARTICLE TECHNOLOGY – (PART 2)

1. Nature of particles
2. Particle size distribution
3. Particle sizing and measurement methods
4. Fluid particle dynamics
5. Particle collection mechanisms
6. Particle collection efficiencies

APPLICATIONS – (PART 3)

1. Patents
2. Size reduction
3. Prime materials
4. Production/manufacturing routes
5. Ventilation
6. Dispersion
7. Ethics

ENVIRONMENTAL CONCERNS – (PART 4)

1. Environmental regulations
2. Toxicology
3. Non-carcinogens
4. Carcinogens
5. Health risk assessment
6. Hazard risk assessment
7. Epidemiology

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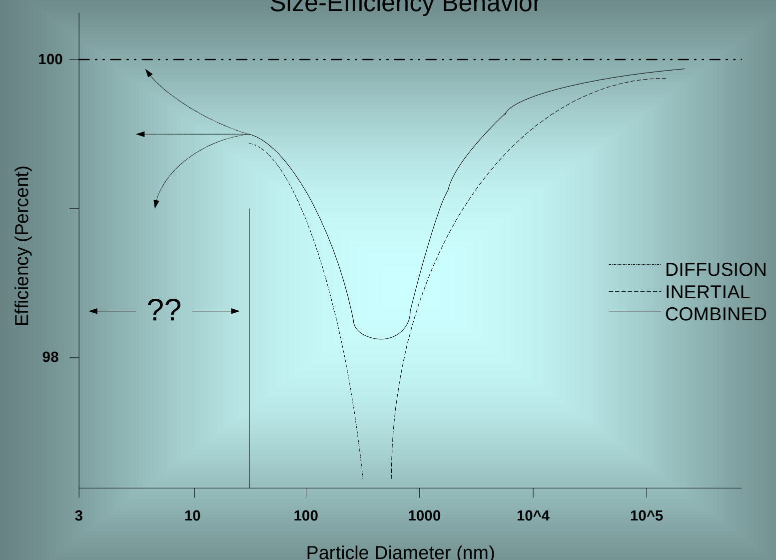
Size-Efficiency Behavior



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ENVIRONMENTAL CONCERNS – (PART 4)

1. Environment regulations
   - Standard stuff (?)
   - Work of Bergeson

   Public perception
   - Need only one incident
   - Short- and long-term health effects
   - Zero risk???
   - Calls for more funding

2. Toxicology
   - Science of poisons
   - Boom area in nanofield
   - TLV PEL
   - IDHL Ceiling values

3. Non-carcinogens – threshold value

4. Carcinogens – ? threshold value

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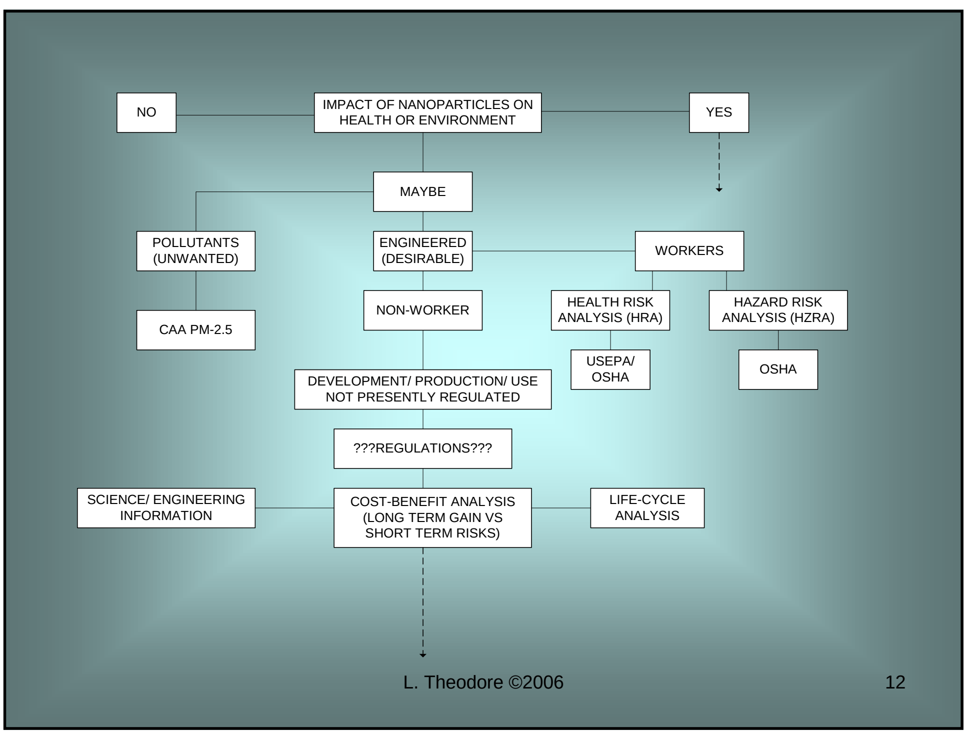

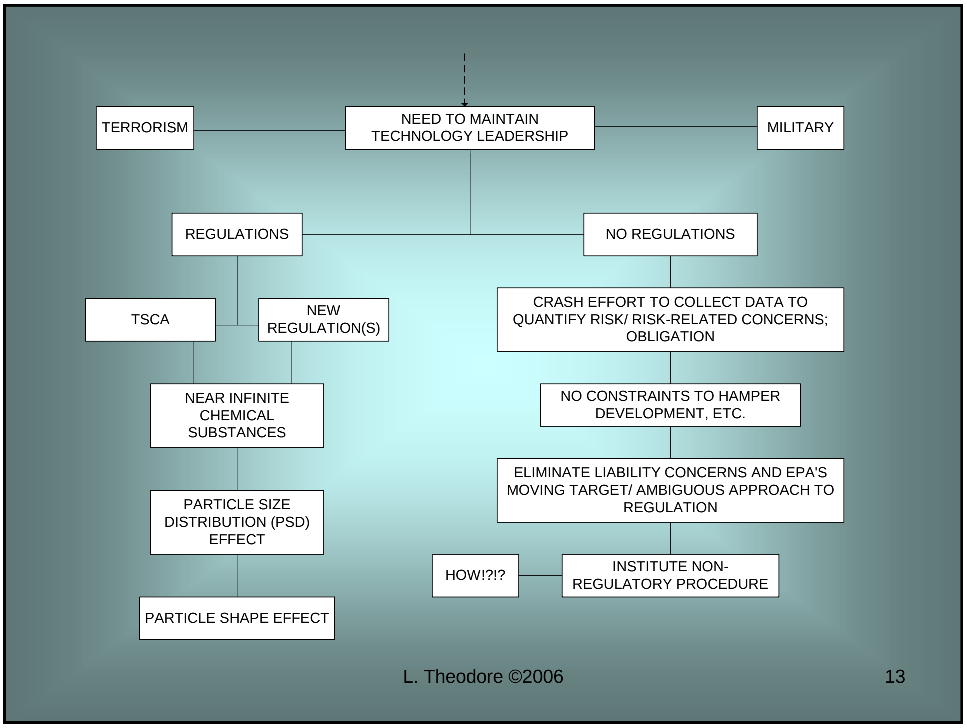

5. Health risk assessment

   Health vs. Hazard

6. Hazard risk assessment more important than health?

7. Epidemiology

   Study of frequency/occurrences

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EPILOGUE

Probably no need to worry, but need near-absolute assurances ala global warming

Need a cost-effective product analysis

Cost
- Impact on existing markets
- Return (on investment)
- Patent concerns

Effectiveness
- Enjoyable life
- Healthier life
- In effect: Risk vs. Reward

Monster success story

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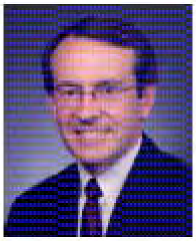

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Practice
Mark Greenwood is a Partner in the Washington DC office of Ropes & Gray, where he practices environmental law.

Professional Experience
Mark advises clients on a wide range of environmental regulatory and enforcement matters, arising under chemical, pesticide, air, hazardous waste and reporting statutes. He has special expertise in helping clients face environmental challenges to existing commercial products and in helping clients navigate regulatory reviews necessary to bring new technologies to market. He also has developed a national reputation in matters involving public disclosure of environmental information. Before joining Ropes & Gray in 1994, Mark worked for the U.S. Environmental Protection Agency for over 16 years. He held a variety of senior positions in the Office of General Counsel, managing legal issues in areas as diverse as pesticides, toxic chemicals, hazardous waste management, Superfund, and environmental reporting. From 1990-94, he was Director of the Office of Pollution Prevention and Toxics, the arm of EPA concerned with regulation of chemicals in commerce, biotechnology, public "right to know" programs and pollution prevention.

Honors & Awards
- *Best Lawyers in America*

Bar Admissions
- Washington, D.C., 1978

Education
- 1978, J.D., University of Michigan Law School
- 1978, M.S. (Public Policy), University of Michigan
- 1974, B.A., University of Michigan

Session 6: Review of Regulations, Positions, Policies, Guidance, and Actions for Nanomaterials

July 13, 10:15 AM-12:00 PM

Responding to Public Concerns about Nanotechnology

Mr. Mark Greenwood, Ropes and Gray, Washington, DC

Abstract

Much of the current discussion about how government should address the potential risks of nanotechnology focuses on regulatory oversight for new products containing nanoscale materials. As the public awareness of nanotechnology grows, it can be expected that the citizens will ask regulatory agencies responsible for air, water, and waste management to address their questions and concerns. Are these agencies really prepared to address such questions? This presentation identifies the key environmental protection policy issues related to nanotechnology from the perspective of managers of air, water, and waste programs. It will suggest areas where these program managers must develop greater understanding of the nanotechnology issues as well as potential actions to consider in anticipation of public concerns.

Session 6: Review of Regulations, Positions, Policies, Guidance, and Actions for Nanomaterials

July 13, 10:15 AM -12:00 PM

Responding to Public Concerns about Nanotechnology

Mr. Mark Greenwood, Ropes and Gray, Washington DC

Highlights

The nanotechnology industry is not really an industry; rather, it is a set of technologies that can be applied to various industries. However, it may be treated as an industry for policy and regulatory purposes.

The general public has a positive reaction to medical improvement and improved consumer products. There is little support for a ban on nanotechnology development; a Woodrow Wilson Center survey revealed that 70% of respondents would not support such a ban. However, the public has concerns with adequate testing and movement to other routes of exposure (e.g., getting into food).

Applicability of TSCA regulation of new chemicals is uncertain. There is uncertainty about when a nanomaterial is a "new material." The difficult issue is assessing novel properties. How do properties relate to hazard? At what point do the nature of the material and the nature of the hazard get changed? How much of the macromolecule properties are relevant at the nanoscale? The form of use is also important. Nanoparticles are often part of a more complex mixture, and can agglomerate. Sometimes agglomeration increases toxicity; sometimes agglomerated particles are no longer nanoscale. Regulation of new products is often done by analogy to known existing products; however, structure activity relationships (SAR) might not work for assessing nanotechnology.

There is uncertainty about fate and transport, and about interactions between engineered and naturally-occurring nanomaterials. We do not currently have widespread technology to monitor for nanoparticles.

For risk management, occupational control and production design to reduce exposure are important. What control strategies can be used to limit release and exposure? Also, labeling will be a contentious issue. There will be some pressure to have labels that say only "contains nano," but what are the implications of this?

It will be important for OSWER to define its role in nanotechnology. Some of the questions that OSWER will face include: how much nanomaterial is in the environment? Where is it, where does it go, and how much is there? Without effective monitoring, how will you estimate "how much?"

There is a need to develop capabilities in responding to spills, managing workplace exposure, and determining risks. There is also a need to prepare information for the public (for general dissemination and in response to questions). Existing regulatory programs will collect varying amounts of data on new nanomaterials, including data on the following: chemical and physical characteristics; production processes; occupational risk; and exposure. Existing programs will probably not gather information on monitoring data, fate and transport, or risk management for wastes. The level of information available will depend on the use (e.g., drugs and pesticides will be data-rich, whereas cosmetics will not).

Question-and-Answer Session

Mr. Greenwood indicated that manufacturers must provide regulators with information on what is in nanowaste. A questioner asked what we know about imports that contain nanoscale materials. Mr. Greenwood answered that, depending on the interpretation of TSCA, imports are regulated but compliance can be an issue. When asked about the potential to underestimate risk associated with nanomaterials, Mr. Greenwood answered that it is important to distinguish engineered nanomaterials from naturally-occurring ones (i.e., how do we regulate based on size alone when many natural nanomaterials also exist?). Regarding protective gear to prevent worker exposure to nanoscale materials, Mr. Greenwood indicated that this is a front-burner issue for NIOSH, OSHA, and industry. When asked how to distinguish nanotechnology as a legislative context, Mr. Greenwood indicated that Congress sees nanotechnology as a great opportunity, not as a problem. The Agency is in the best position to propose new legislation for nanotechnology. A questioner asked, Do you have concerns with the NNI's definition of nanotechnology? Mr. Greenwood responded that the NNI definition is science-based; he wondered about how to translate this into the policy framework.

Considerations for Government Oversight of Nanotechnology

Mark Greenwood

ROPES & GRAY

ROPES & GRAY LLP   BOSTON   NEW YORK   PALO ALTO   SAN FRANCISCO   WASHINGTON, DC

Agenda

- Who is the “industry”?
- Public perceptions
- Challenges facing product oversight programs
- Challenges facing waste management programs
- Potential collaboration?

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2 of18
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Nature of the "Industry"

- Nanotechnology is not really a single industry
  - It is a technology applicable in multiple contexts
  - It is sweeping across many industries
  - 10-15 years: it will not be distinct from "technology"
- Yet it may be treated as an "industry" for policy and political purposes, at least initially
  - Separate interest groups, policies, programs
  - Over time this may not make sense
  - Beware efforts to separate it from ongoing risk assessment and management activities

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3 of18
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Nature of "Industry" (con.)

- Defining it as a separate industry is confounded by the "nanotechnology" definition
- National Nanotechnology Initiative definition
  - Technology manipulating materials that have at least one dimension below 100 nanometers
  - Creating structures with novel properties and functions
- What constitutes a "novel property"?
  - What is "novel" can vary with commercial context
  - This could occur in many industries
  - Uncertainty of definition leads to unclear scope

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4 of18
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Public Perceptions

- Initial surveys of public perceptions
- Low general awareness of what nano is
- When explained, mostly positive reaction
  - Medical applications draw greatest interest
  - Then better consumer products
  - Little support for a ban pending more information
- Concerns about the unknowns
  - Affected by perception of past failures in policy
  - Need for adequate testing
  - Will it go where it should not (e.g., food)?

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5 of18
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Public Perceptions (con.)

- Confused about existing structure of oversight
  - Roles of EPA, FDA, OSHA, CPSC
- Perceptions of government actors
  - Highest trust in CDC, EPA, CPSC, OSHA, FDA
  - Lower for White House; lowest for Congress
- Government oversight perceived as needed
  - Voluntary not enough; but many undecided
- Key actions to build public trust
  - Increased safety testing
  - Good public information to inform choices

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6 of18
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Product Oversight Challenges

- Key agencies in product oversight
  - EPA: TSCA (program has begun); FIFRA (developing); CAA (first fuel additive under review)
  - FDA (sunscreen petition, October public meeting)
  - OSHA/NIOSH (testing of protective clothing, HEPA filters)
- Difficult jurisdictional issues
  - TSCA: Are nanomaterials "new" chemicals?
    - Chemical formula vs. unique physical structures
  - FDA: When is a product a "new" drug?

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7 of18
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Product Oversight (con.)

- Defining the potential hazards
  - Is "nano size" inherently dangerous?
    - Probably not; but it affects exposure (e.g., migration to brain)
  - How to assess effect of "novel" properties on hazard
    - What is the novel property? Is it a sliding scale?
    - Ex: electrical charge vs. surface area?
    - Understanding cellular chemistry and mechanism of action
  - How to factor in what is known about macro-molecule
  - Form in use and in the environment
    - Ex: coatings; mixtures with other materials
  - Agglomeration potential can affect likely hazard

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8 of18
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Product Oversight (con.)

- Considerations for exposure potential
  - Uncertainty of fate, transport in environment
    - What happens to a small particle with an "active" surface
  - Context: other nanoparticles in environment
    - Engineered nanomaterials vs. environmental nanoparticles
    - Ex: wood smoke, auto exhaust
    - How to define unique risk of engineered nanomaterial?
  - Challenges of monitoring
    - Not possible for specific engineered nanomaterials
    - Product oversight will rely on models, surrogates, mass balance calculations; very limited exposure data

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9 of18
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Product Oversight (con.)

- What are the data needs?
  - Probably more extensive than for regular chemicals
    - Translocation of nanomaterials in body
    - Need to understand physical structure and attributes
  - Ultimately it is impractical to test every material for every potential concern; what are priorities?
  - May trade off data requirements for risk management measures
  - Will be guided by analogies drawn from existing data to answer questions and guide data requests

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10 of18
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Product Oversight (con.)

- What forms of risk management make sense?
  - Protecting workers
    - Testing of gloves, masks now under way
  - Product design to reduce exposure
    - Focus on use only? What about disposal scenarios?
  - Performance of measures to control particles
    - Can high performance filters work at nanoscale?
    - Conflicting claims in marketplace
  - Effectiveness of treatment, destruction technologies
  - Labeling: notice, warnings, instructions?

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11 of18
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Waste Management Challenges

- Do waste management agencies need a "nano program"?
  - Some actions (e.g., spill) will trigger responsibility
  - Logical program to respond to public concerns
  - Less a "program"; more a "capability"
- Key questions
  - Am I ready for likely public questions?
  - Can I take effective remedial action if needed?
  - Can I estimate nanomaterials in the environment?
  - Can I identify effective control strategies?

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12 of18
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Waste Management (con.)

- Answering public questions
  - Basics of nanotechnology
  - Government responsibilities for oversight
  - Hazard potential: what concerns have arisen?
    - Ex: specific chemistry matters
  - Exposure potential: what is the likelihood that I could be exposed to dangerous levels?
    - Potential loadings from particular sources
    - Comparisons to other things (e.g., other nanoparticles)
  - What actions can the government take?
  - What actions can I take to reduce concerns?

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13 of18
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Waste Programs (con.)

- Effective remedial action
  - Spill control measures
  - Management of uncontrolled particles
    - Ex: asbestos abatement measures?
  - Opportunity to use nanomaterials in treatment and remediation: What are the contingency plans?
- Estimation of nanomaterials in the environment
  - Know the primary sources in your jurisdiction
  - Determine estimation techniques
    - Surrogate monitoring vs. mass balance estimation

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14 of18
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Waste Programs (con.)

- Identification of effective control strategies
  - Effectiveness of particle control measures
    - Ex: what air filters control nanoscale particles?
    - Ex: application of ultra-filtration process equipment to wastes
  - Protective measures for individual
    - Analogies to occupational exposure
  - Disposal, treatment measures
    - Ex: destruction capabilities of typical waste treatment
- Public engagement is key to risk communication
  - It is a process, not a one-way message

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15 of18
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Potential Collaboration

- What you can expect from product programs
  - Chemical, material characterizations
    - Available physical-chemical, toxicity data
    - Analogs to help identify, narrow potential hazards
  - Production processes, product formulations
    - Ex: pesticide Confidential Statements of Formula
  - Occupational risk measures
    - Potential analogies to consumers using particular products
  - Exposure models
    - May be question about relevance to nanoscale material

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16 of18
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Potential Collaboration (con.)

- What not to expect from product programs
  - Monitoring data
    - They probably did not need it to do their job
  - Risk management measures for waste
    - Likely to be borrowing from waste programs, if at all
  - Fate, transport testing data
    - Accepted methods probably not tailored to nanomaterials
    - More likely that models were used
- Great program variation based on product use
  - Ex: FDA drug, EPA pesticide vs. FDA cosmetic

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17 of18
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Conclusion

- Nanotechnology presents a unique challenge for the design of government programs
  - Technology offers great social, economic benefit
  - It will spread broadly throughout society before health and environmental implications are fully understood
  - Potential "Wow to Yuck" response by public
  - Some hazards are present, but difficult to define
  - Hard to calibrate government oversight to real concerns
  - Life cycle effects mean that all programs are relevant
- Important for OSWER to define its role

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18 of18
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Mr. Tracy D. Hester

Bracewell and Giuliani, LLP
Houston, Texas

Tracy D. Hester heads the environmental law section in the Bracewell & Giuliani's Houston office. Mr. Hester has assisted clients in regulatory counseling with an emphasis on enforcement defense, environmental permitting and cost recovery litigation. His practice also focuses on the innovative application of environmental laws to emerging technologies and novel compliance strategies.

Mr. Hester has represented clients from diverse industrial sectors, including petrochemical manufacturers, petroleum and natural gas pipelines, petroleum refineries, utilities, nanoscale materials manufacturers, cement kilns, newspaper printers, hazardous waste disposal operations, and financial institutions. Mr. Hester has represented companies and local governments in litigation or compliance negotiations on ozone regulatory policy and total maximum daily load water quality projects. He also assists companies with emergency response planning and security assurance legal requirements.

Mr. Hester has also taught advanced seminars on Environmental Enforcement, Practice of Environmental Law and Hazardous Waste Law as an Adjunct Professor at the University of Houston Law Center.

Session 6: Review of Regulations, Positions, Policies, Guidance, and Actions for Nanomaterials

July 13, 10:15 AM-12:00 PM

Applying RCRA and CERCLA Requirements to Nanoscale Materials and Wastes

Mr. Tracy D. Hester, Bracewell and Giuliani, LLP, Houston, Texas

Abstract

As nanomaterials appear in more products and production processes, they will inevitably begin to appear as well in discarded products, production wastes and unintentional releases to the environment. Because nanomaterials may display unusual or unique qualities, they may also pose challenges to existing RCRA and CERCLA regulations designed to control releases of regularly-sized versions of the same materials. This presentation will briefly outline some potential areas for investigation to identify potential environmental issues by the release or disposal of nanoscale waste materials, and it will provide a brief overview of some possible strategies to address these concerns.

Session 6: Review of Regulations, Positions, Policies, Guidance, and Actions for Nanomaterials

July 13, 10:15 AM -12:00 PM

Applying RCRA and CERCLA Requirements to Nanoscale Materials and Wastes

Mr. Tracy D. Hester, Bracewell and Giuliani, LLP, Houston, Texas

Highlights

There are over 270 consumer products marketed as containing nanomaterials and a projected market of over $9 billion for carbon nanotubes by 2020. Some nano-containing products are not adequately labeled; truth in labeling will be an issue, especially for consumer products.

There is growing interest in management standards for nanomaterials: there have been several petitions to EPA and at least one call for a moratorium on the commercial use of nanomaterials.

Material Safety Data Sheets (MSDS) may not adequately identify hazards or protections needed for nanoparticles. For example, one MSDS drawn from a cursory Internet search describes a tin oxide nanopowder and states that "no data exist on the effects of fine particles" that would reflect a hazard, but it then advises that "care should be taken to avoid ingestion, inhalation, and skin or eye contact." The data sheet adds that the tin oxide is not considered to a hazardous product, but it then warns that there are no data on first aid response and urges readers to "seek medical advice immediately upon exposure." These conflicting statements reflect a growing need for consistent disclosure practices in MSDSs for nanoparticles.

How are nanoparticles to be disposed of? In many cases, the value of nanomaterials is high - for example, several nanoscale products use nanoscale precious metals such as gold, silver and platinum. Certain configurations of carbon nanotubes are extremely difficult to fabricate and are extremely valuable in small quantities. Generators of wastes containing these materials therefore can have a strong incentive to recapture nanoscale materials as recovered product rather than discard them in waste streams.

As the volume of nanoscale materials in commerce and consumer products grows, we will inevitably have to face situations where nanoscale materials have been spilled or released into the environment or workplace. For example, a facility operator who suffers a spilled drum of nanoscale material will immediately face several novel issues: how do you handle spills of nanomaterials that pose different properties from conventional versions of the same materials? How do you notify workers about such a release and assure their safety? How do you code waste as containing nanomaterials when the material does not appear on any hazardous materials lists? Given the current lack of readily available technology to detect many nanoscale materials in the environment, how do you measure/demonstrate the amount of nanoparticles in waste media to show that it is not hazardous? Ambiguities exist in CERCLA, EPCRA, and state laws on virtually all of these issues.

For example, nanoscale silver in a waste stream might appear in extracts in a TCLP test that would render the waste characteristically hazardous. It is unclear, however, whether the current design of the TCLP properly reflects the actual levels of nanoscale silver released from the waste when disposed into the environment.   Changes to the mobility of a waste constituent when it is nanoscale in size may also affect the true degree of risk, if any, that it would pose upon improper co-disposal.

Environmental permitting for facilities that manage nanoscale materials will also need to be addressed. For example, a facility that manufactures a product that uses nanoscale materials may produce hazardous waste streams that contain nanomaterials. Many current facilities produce nanomaterials in small quantities, and as a result they may qualify for exemptions from full-scale hazardous waste permitting requirements for treatment, storage and disposal facilities. For example, small lots of nanoscale waste could easily fall under exemptions for satellite accumulation areas, conditionally exempt small quantity generators, or product reuse exemptions. As facilities grow in size and the volumes of nanoscale wastes increase, however, EPA will need to assess how to review and issue waste, water and air permits for these types of facilities. This path may require EPA to wrestle ultimately with novel questions about corrective action, land ban treatment standards, and innovative treatment technologies.

Nanoscale materials can be used to treat spills (nanoremediation), but data are still needed to demonstrate long-term effectiveness. Nanoscale iron has been used in several field tests for ground water remediation and costs 30 -50% less than pump-and-treat technology; it degrades without long-term groundwater impacts, and can be effective against TCE, PCBs, PCE.   The intentional release of nanoscale iron into the environment, however, poses exactly the type of concerns which have led some scientific advisory groups and environmental organizations to urge application of the precautionary principle. Given the reluctance of some environmental agencies to use novel remediation technologies, it will take some outreach to get acceptance.

Thoughts for the future: This is a difficult challenge due to differences in activities and toxicities of nanoparticles. States will also be developing guidance and regulations.

Question-and-Answer Session

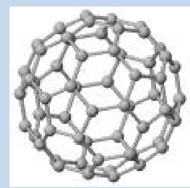
When asked how to distinguish nanotechnology as a legislative context, Mr. Hester added that Congress' concern is not solely regulation, but also to strongly promote the economic benefits and opportunities of nanotechnology. This attitude may change, however, following a significant spill or injury caused by nanomaterials.

New World of Nanowaste:

Review of Regulations, Positions, Policies
and Action Related to Nanotechnology

Tracy Hester
Bracewell & Giuliani, LLP

Environmental Impact of Nanotechnology
EPA OSWER Conference
Washington, DC
July 13, 2006



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1 of27

New World of Nanowastes

Here and Now

- Over 270 consumer products marketed as containing nanomaterials
- Projected market of $9 billion for carbon nanotubes alone by 2020
- Concerns emerging about unintended effects
  - Environmental fate and transport
  - Toxicological effects
  - Bioaccumulation

Mr. Tracy D. Hester
2 of27

New World of Nanowaste

Growing Concerns About Nanotech

- **Growing interest in management standards for nanomaterials**
  - EPA TSCA Pilot Registration Program
  - Petition to FDA for regulation of cosmetics and sunscreens containing nanomaterials
  - Petition to EPA for registration of nanosilver from Samsung products
  - Calls for moratorium

- **Coalescing national and international standards, but none yet final**

Mr. Tracy D. Hester
3 of27

New World of Nanowastes

Nanowaste Scenarios

- Scenario 1: How to respond to a spill of nanoscale materials?
- Scenario 2: How does a RCRA TSDF permit reflect management of nanoscale wastes?
- Scenario 3: Any regulatory issues for using advanced nanoscale materials in a remediation project?

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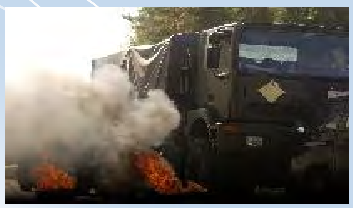
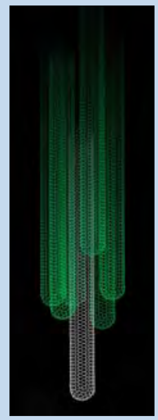
4 of27

New World of Nanowastes

Scenario 1: Big Spill of Little Stuff

- The scene: an overturned truck spills several drums into a ditch at the entrance to the facility.
- Potential materials: titanium dioxide, aluminum or carbon nanotubes.





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5 of27

New World of Nanowastes

Scenario 1: Big Spill of Little Stuff

- Reporting the spill
- Determining what emergency actions to undertake
- Disposing of the wastes from the response action

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6 of27

New World of Nanowastes

Scenario 1: Big Spill of Little Stuff

Emergency Response Information

- Spill containment and response notification to NRC and LEPC
  - Reporting under CERCLA: which "hazardous substance" is it?
  - If it is one, what RQ does it have?
  - Is it reportable under EPCRA or state law?
- MSDS – describes bulk or nanoscale materials?

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7 of27

New World of Nanowastes

RAW SINGLE-WALL CARBON NANOTUBES (SWNT)
Material Safety Data Sheet

Nanothinx
P.O. Box 1405
Panepistimioupolis
(University Campus)
Rio-Patras 26500 GREECE

Tel: +30-2610-965208
Fax: +30-2610-990987
info@nanothinx.com
http://www.nanothinx.com

1. Product Composition and Specifications

Raw SWNTs		Characterization method
Production method	CCVD	
Available form	Black powder	
Diameter	0.8-1.2 nm	TEM, Raman
Length	≥ 5 μm	SEM, TEM
Bundles	15-30 nm	SEM, TEM
Nanotubes purity	<70%	TGA, SEM
Metal particles	>30%	TGA
Amorphous carbon (in the predetermined Nanotubes purity)	< 5 %	TGA, Raman
Odor	Odorless	


2. Hazards Identification

Indications of Hazards to Humans and the Environment Irritating to eyes and respiratory system.

Date Created: 23/03/2005 Date Revised: 10/05/2006

Mr. Tracy D. Hester
8 of27

New World of Nanowastes

PRODUCT AND COMPANY IDENTIFICATION

DATE: October 03

1.1 Product Name - Tin Oxide Nanopowder

1.2 Chemical Symbol - Tin (IV) oxide SnO_2 Synonyms: Stannic oxide, tin dioxide

Special care should be taken to avoid ingestion, inhalation, skin contact or eye contact

1.3 **This powder is an experimental sample, comprised of loosely aggregated ultrafine nanometer particles. No data yet exists on the effects of such fine particles on the body.**

Special care should be taken to avoid ingestion, inhalation, skin contact or eye

2. COMPOSITION / INFORMATION ON INGREDIENTS

Supplied in the following purities

2.1 Tin Oxide Nanopowder **CAS No: 18282-10-5**

EINECS: 2421590

3. HAZARDS IDENTIFICATION

Tin oxide is not considered to be a hazardous product as specified in Directive 67/548/EEC

4. FIRST AID MEASURES

4.1 Ingestion **No data available but seek medical advice immediately.**

4.2 Skin Contact -

Mr. Tracy D. Hester
9 of27

New World of Nanowastes

Scenario 1: Big Spill of Little Stuff

Handling the spilled materials

- Designating nanoscale materials as "discarded"
- Waste coding
- Spill removal standards

Mr. Tracy D. Hester
10 of27

New World of Nanowastes

Scenario 1: Big Spill of Little Stuff

Follow-up, if any, for nanomaterial spills

- Notice to exposed workers
- TSCA notifications

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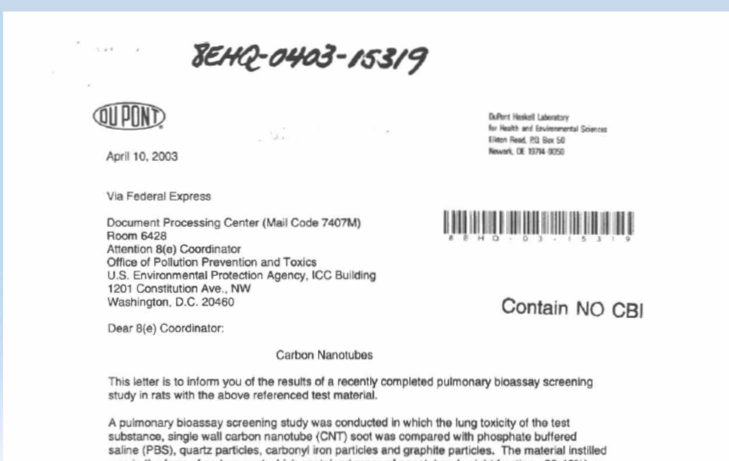
11 of27

New World of Nanowastes

TSCA Reporting



8EHQ-0403-15319

DU PONT

DuPont Haskell Laboratory
for Health and Environmental Sciences
Elkton Road, P.O. Box 50
Newark, DE 19714-0050

April 10, 2003

Via Federal Express

8EHQ-03-15319

Document Processing Center (Mail Code 7407M)
Room 6428
Attention 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency, ICC Building
1201 Constitution Ave., NW
Washington, D.C. 20460

Contain NO CBI

Dear 8(e) Coordinator:

Carbon Nanotubes

This letter is to inform you of the results of a recently completed pulmonary bioassay screening study in rats with the above referenced test material.

A pulmonary bioassay screening study was conducted in which the lung toxicity of the test substance, single wall carbon nanotube (CNT) soot was compared with phosphate buffered saline (PBS), quartz particles, carbonyl iron particles and graphite particles. The material instilled was in the form of carbon soot which contained ropes of nanotubes (weight fraction ~30-40%) as

TSCA 8(e) Notice for CNT health Effects, Du Pont, April 10, 2003

Mr. Tracy D. Hester
12 of27

New World of Nanowastes

Scenario 2: Nano-Permitting

- An existing facility begins to produce a product that incorporates nanoscale silver

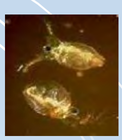
- The production process will generate off-specification nanosilver product and solid wastes

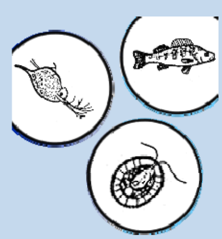
Mr. Tracy D. Hester
13 of27

New World of Nanowastes

Scenario 2: Nano-Permitting

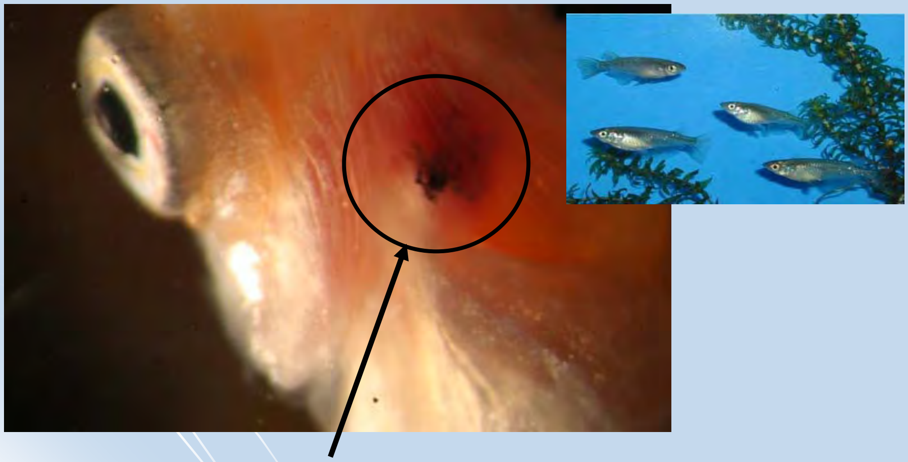
- Wastewater permitting:
  - Aquatic toxicity of nanoscale silver
  - Pending TriTAC petition on nanoscale silver discharges to water





Mr. Tracy D. Hester
14 of27

Nanoiron on Medaka Fish Gils



Nanoiron aggregates accumulate on Medaka fish gills-(Richard Winn UGA)

Mr. Tracy D. Hester
15 of27

New World of Nanowastes

Scenario 2: Nano-Permitting

- Solid wastes containing nanoscale silver
  - Production wastes
    - D011 (silver)
    - Effect of nanoscale on Method 1311
  - Off-specification products – waste?
    - Precious metals recovery and recycling
    - Speculative accumulation
    - Potential RCRA exemptions (in-process reuse, closed-loop recycling, etc)

Mr. Tracy D. Hester
16 of27

New World of Nanowastes

Scenario 2: Nano-Permitting

- Management of nanoscale wastes in RCRA units
  - 90-day storage tanks and containers
  - Exempt units and wastes – TETFs, WWTUs, ENUs, product tank bottoms
  - Satellite accumulation areas
  - Small quantity generators/CESQGs

Mr. Tracy D. Hester
17 of27

New World of Nanowastes

Scenario 2: Nano-Permitting

- Hazardous wastes and nanomaterials
  - Corrective action
  - Land ban treatment standards
  - Omnibus permitting authority
  - Imminent hazard abatement authority

Mr. Tracy D. Hester
18 of27

New World of Nanowastes

Scenario 2: Nano-Permitting

Public participation and notice for permit issuance and modifications


Berkeley Daily Planet

Bus Lane Plans Provoke Telegraph Neighborhood

Telegraph Avenue neighbors and merchants packed a Planning Commission meeting Wednesday to protest proposals to speed up buses from downtown Berkeley all the way to San Leandro by eliminating some traffic lanes for motorists on Telegraph Avenue and turning the three northernmost blocks of the street into a car-free, bus-only pedestrian mall.

"This would be the end of the world as we know it. Telegraph would look like a Greyhound Station," said Ken Sarachan, owner of Rasputin Music, who along with other leading Telegraph merchants—including the owners of Cody's Books, Moe's Books and Amoeba Music—opposed banishing cars from Telegraph north of Haste Street.

Matthew Artz: Protestors gathered at the entrance to the Lawrence Berkeley Naitonal Laboratory Thursday to protest today's planned groundbreaking for the Molecular Foundry.

Molecular Foundry Foes Protest Groundbreaking

About 30 protesters withstood steady drizzle early Thursday morning, worried that once Lawrence Berkeley National Laboratory (LBNL) completes its newest laboratory complex, far smaller, more dangerous particles could rain down on them. FULL STORY

Mr. Tracy D. Hester
19 of27

New World of Nanowastes

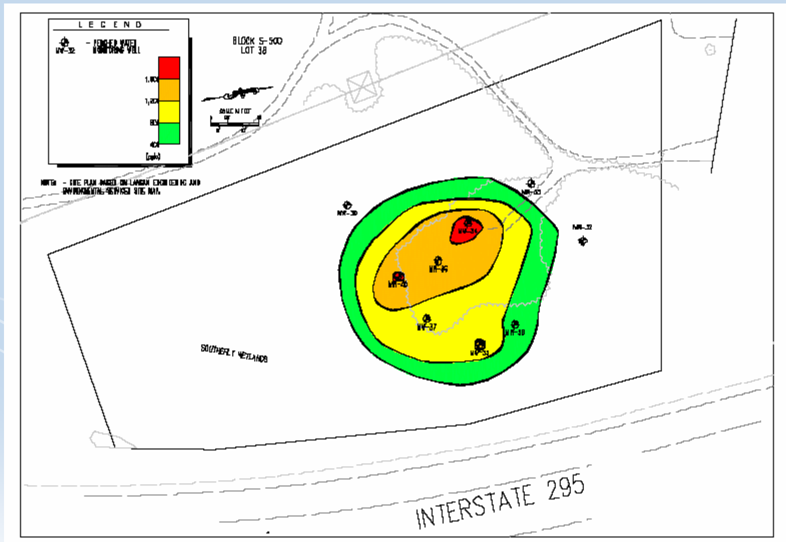
Scenario 3: Nano-Remediation

- Nanoscale materials pose great opportunities as well as challenges
- One rapidly emerging technology: groundwater remediation
  - Nanoscale iron
  - Used in several field tests with generally positive results

Mr. Tracy D. Hester
20 of27

New World of Nanowastes

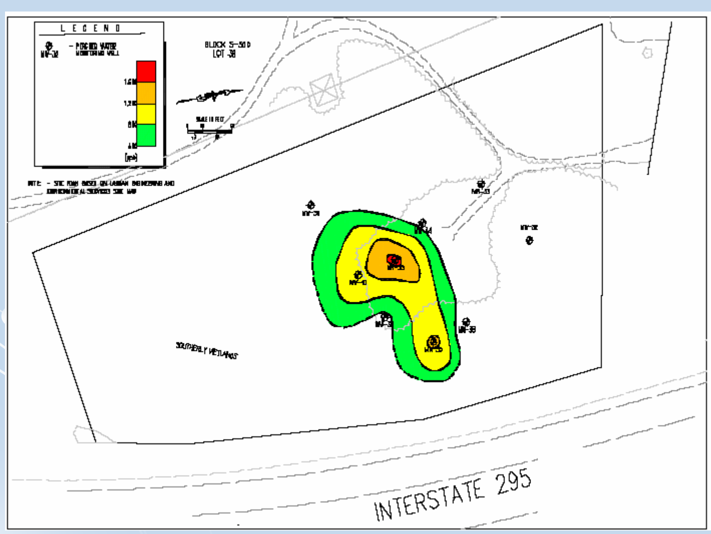
Scenario 3: Nano-Remediation



Mr. Tracy D. Hester
21 of27

New World of Nanowastes

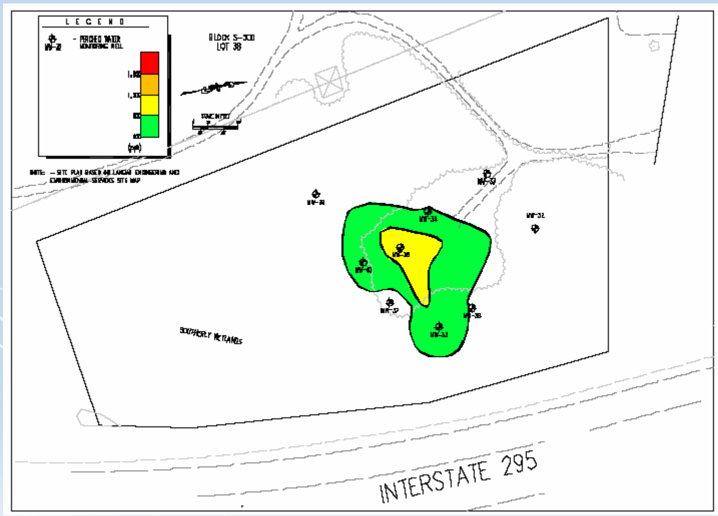
Scenario 3: Nano-Remediation



Mr. Tracy D. Hester
22 of27

New World of Nanowastes

Scenario 3: Nano-Remediation



Mr. Tracy D. Hester
23 of27

New World of Nanowastes

Scenario 3: Nano-Remediation

- Key results:
  - Nanoscale iron treatment can cost 30 to 50 percent less than pump-and-treat technology
  - Iron apparently degrades without long-term groundwater impacts
  - Effective against difficult contaminants (PCE, TCE, PCBs, halogenated aromatics)

Mr. Tracy D. Hester
24 of27

New World of Nanowastes

Scenario 3: Nano-Remediation

- **Key issues:**
  - State agencies may be cautious about use
  - Long-term groundwater impacts
  - Regulatory status of nanoscale iron used in treatment
    - Naturally occurring element
    - TSCA status as "new chemical"
  - Response action contractor liability protection

Mr. Tracy D. Hester
25 of27

New World of Nanowastes

Thoughts for the Future

- Not all nanoscale materials are the same

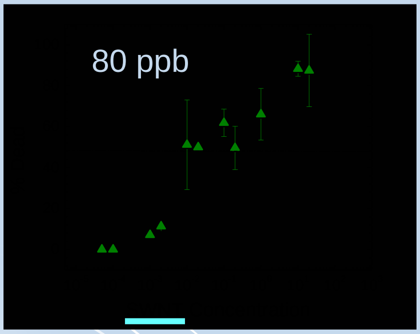
- State laws and regulations will play a major role
- Current federal laws and regulations are mostly sufficient for now, but likely to need adjustment

HOU Doc. No. 1970500

Mr. Tracy D. Hester
26 of27

NanoX: Not Toxicology As Usual

Are single-walled carbon nanotubes toxic?



- 20 major types of SWNT
- 4 manufacturing types (trace impurities)
- Lengths ranging from 5 – 300 nm
- 5 methods of purification
- 10 possible surface coatings

> 50,000 SWNT samples

Basic structure-function relationships for nanomaterials and biological impacts are necessary

Mr. Tracy D. Hester
27 of27

Session 7: Panel Discussion (EPA Presentations)

Prior to the panel discussion, the following representatives from various EPA offices gave brief presentations highlighting their offices' activities with respect to nanotechnology:

Mr. Jim Willis, US EPA OPPT

Dr. Barbara Karn, US EPA ORD, Woodrow Wilson International Center for Scholars/Emerging Nanotechnologies Project

Dr. Nora Savage, US EPA ORD, National Center for Environmental Research/Environmental Engineering Research Division

Ms. Marti Otto, US EPA OSRTI

Mr. Jim Willis, US EPA OPPT

Frequently there are public concerns voiced over new technologies, and EPA needs to appropriately balance risks and benefits and communicate to stakeholders in an open and transparent way. EPA needs to continue to implement TSCA to apply sound science to assess and, where appropriate, manage possible risks of nanomaterials. TSCA authorities are adequate for nanomaterials that are industrial chemicals.

EPA is reviewing new chemical nanomaterials. EPA held a public meeting last year to seek the views of stakeholders on approaches for oversight over nanomaterials. The Agency sought the views of a FACA advisory body, the National Pollution Prevention and Toxics Advisory Committee (NPPTAC), and has established an Agency-wide workgroup to consider the Agency's next course of action. EPA is also working to promote pollution prevention in the nanotechnology field and a conference on this is planned for the winter.

The Science Policy Council (SPC) established a workgroup to develop a white paper on EPA science and research needs for nanotechnology. All program offices and five regional offices were involved. Publication is expected in the fall. The white paper recommended areas for further research and detailed clear Agency needs in the area of nanotechnology.

Broader cooperation both Agency-wide and government-wide was encouraged. None of the offices alone has the internal resources and infrastructure needed to deal with all aspects of nanotechnology. The US agencies cooperate under the National Nanotechnology Initiative, and countries cooperate internationally through the OECD Working Party on Manufactured Nanomaterials. There is also the need to cooperate within the Agency, for example under the workgroup recommended in the SPC white paper.

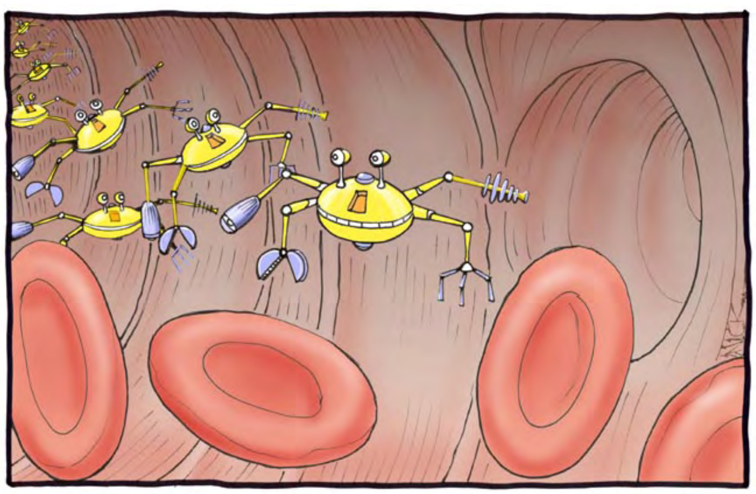
OPPT Activities regarding Nanotechnology

Jim Willis

Office of Pollution Prevention and Toxics

Nanotechnology and OSWER Symposium – July 12-13, 2006

Why it is important to get nano right the first time



"Okay nanobots, our primary mission is to clean out this guy's arteries. But while we're here I can't see any harm in also building him a nice pair of man-breasts..."

Mr. Jim Willis
2 of 7

TSCA Program Goal

Continue to implement TSCA in a way that enables the responsible development of nanotechnology and realizes its potential environmental benefits, while applying sound science to assess and, where appropriate, manage any potential risks to human health and the environment presented by nanoscale materials.

Mr. Jim Willis
3 of 7
Office of Pollution Prevention and Toxics, U.S. EPA

OPPT Activities

- Authorities under TSCA appear to be adequate but there is a fundamental need for a better understanding of potential risks
- Reviewing nanoscale materials that are new chemicals
- Developing possible Stewardship Program
- Developing policy guidance on new/existing
- Promoting Pollution Prevention benefits (conference anticipated in Washington this October)

Mr. Jim Willis
4 of 7
Office of Pollution Prevention and Toxics, U.S. EPA

SPC: White Paper

- Science Policy Council (SPC): EPA's venue for discussion and management of cross-agency science issues
- Intra-agency Nanotechnology Workgroup convened by SPC (December 2004) to develop a white paper to examine the applications and implications of nanotechnology for the consideration of Agency managers – 80+ workgroup members from across the Agency
- Peer review complete (19-20 April 2006); next draft expected to go to workgroup in July, SPC in August, publication in September

Mr. Jim Willis
5 of 7
Office of Pollution Prevention and Toxics, U.S. EPA

White Paper Recommendation Areas

- Pollution Prevention and Stewardship
- Research
  - Chemical identification and characterization
  - Environmental fate
  - Environmental detection and analysis
  - Potential releases and human exposures
  - Human health effects assessment
  - Ecological effects assessment
- Risk Assessment
- Cross-Agency Workgroup
- Collaboration
- Training

Mr. Jim Willis
6 of 7
Office of Pollution Prevention and Toxics, U.S. EPA

Need to ensure Broader Cooperation

- Agency-Wide, e.g., ORD, OSWER, OPP, OAR, OW, etc.
- Government Wide
  - Through NNI
  - Traditional inter-agency work groups to address common issues (e.g., occupational, consumer)
- Internationally
  - OECD (Working Party on Manufactured Nanomaterials)
  - Individual countries, such as the UK, Australia, who are developing and implementing programs
- Industry, NGOs, academia

Mr. Jim Willis
7 of 7
Office of Pollution Prevention and Toxics, U.S. EPA

Ms. Marti Otto, US EPA OSRTI

Nanotechnology has promising applications for site remediation. Research indicates that nanoscale zero valent iron (nZVI) may be able to address contamination by chlorinated hydrocarbons, metals, and pesticides. There are approximately 20 to 25 sites were nZVI has been field-tested or is being considered. A workshop on nanotechnology for site remediation was held in October 2005. The latest research results were discussed, and breakout sessions were held to discuss issues and develop recommendations. Proceedings from this conference are posted on the following website: http://es.epa.gov/ncer/publications/workshop/10_20_05_agenda.html.

OSWER's Superfund office is compiling information on field tests of nZVI and is also preparing a factsheet for project managers on the use of nanotechnology for site remediation. The Emergency Response T eam is evaluating personal protective equipment and other aspects of emergency response in case cleanup of a nanomaterial spill is required.

OSWER
Nanotechnology Activities

Nanotechnology and OSWER:
New Opportunities and Challenge
July 13, 2006

Marti Otto
Technology Information and Field Services Division
Office of Superfund Remediation and Technolog Innovation
U.S. Environmental Protection Agency
Otto.martha@epa.gov

OSWER Update

Potential implications of nanotechnology

Applications for site remediation

October 2005 Workshop

Outreach and Publications

Nanotechnology for Site Remediation

Potential applications include *in situ* injection of nanoscale zero-valent iron particles into source areas of groundwater contamination

Contaminants
- Chlorinated hydrocarbons
- Metals
- Pesticides

Over 15 field scale studies

Ms. Mart O o

3 of6

3

Nano Iron Slurry

Wei Xian Zhang, Lehigh University

Ms. Mart O o

4 of6

4

Workshop on Nanotechnology for Site Remediation

- Held October 20-21, 2005
- Purpose:
  - Present latest research results
  - Conduct breakout sessions to discuss issues and develop recommendations
  - Stimulate increased collaboration
- Proceedings and presentations:
- http://www.frtr.gov/hotnew.htm

Ms. Mart O o

5 of6

5

Outreach and Publications

- Issues area on CLU-IN website: http://clu-in.org/nano
- Workshop and Symposium proceedings
- Upcoming products on the use of nanotechnology for site remediation:
  - Database of site work
  - Fact sheet

Ms. Mart O o

6 of6

6

Dr. Nora Savage, US EPA ORD, National Center for Environmental Research/Environmental Engineering Research Division

Dr. Savage indicated that the Agency has many reasons to be interested in nanotechnology (e.g., opportunities, responsibilities, and potential hazards). Accordingly, the Agency has been a member of the National Nanotechnology Initiative (NNI) since 2001. The NNI does not provide funds to participating agencies; nanotechnology funds come from money allocated by the various agencies internally. However, the agencies investing larger amounts in nanotechnology provide funds to support the activities of the NNI.

The NNI has established several working groups including the Nanotechnology Environmental and Health Implications Working Group (NEHI WG). This workgroup will release a report titled "Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials" with assistance of several representatives from the Agency. Another working grop is the Nanotechnology Public Engagement Group (NPEG) which seeks to improve communication and dialogue with the public on nanotechnology.

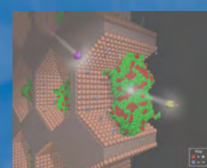
Dr. Savage is currently leading the effort to develop a nanotechnology research plan for ORD. The goal of this plan is to develop a research strategy that will best meet the regulatory and policy needs of the Agency in nanotechnology. ORD issues STAR grants and SBIR contracts in nanotechnology, and participates on various national and international consortia, symposia, and workshops on topics ranging from nomenclature to research strategies. ORD has also initiated an internal EPA-wide group, called NanoMeeters, that meets monthly to inform Agency personnel of recent events and news in nanotechnology. Members of this group are given a link to an intra-EPA database on nanotechnology that provides articles, presentations, information on upcoming events, etc.

Nanotechnology and EPA:

Goals, Initiatives, & Outreach

Nanotechnology and OSWER:

New Opportunities and Challenges



Nora Savage, PhD

US EPA,
Office of Research & Development
National Center for Environmental Research
Environmental Engineering Research Division

Why is EPA interested in nanotechnology?

- **Potential for Environmental Improvement**
  - **Cleaning up past environmental pollution**
  - **Improving present processes and systems**
  - **Preventing future environmental problems**
- **Possibility for harmful effects on human health/environment**
  - **Toxicity**
  - **Fate, Transport, transformation**
  - **Bioaccumulation, biotransformation, bioavailability**
- **EPA's regulatory responsibilities Toxicity**
  - **Toxic Substance Control Act**
  - **Clean Air Act**
  - **Clean Water Act**
  - **Comprehensive Environmental Response, Compensation and Liability Act/Superfund**

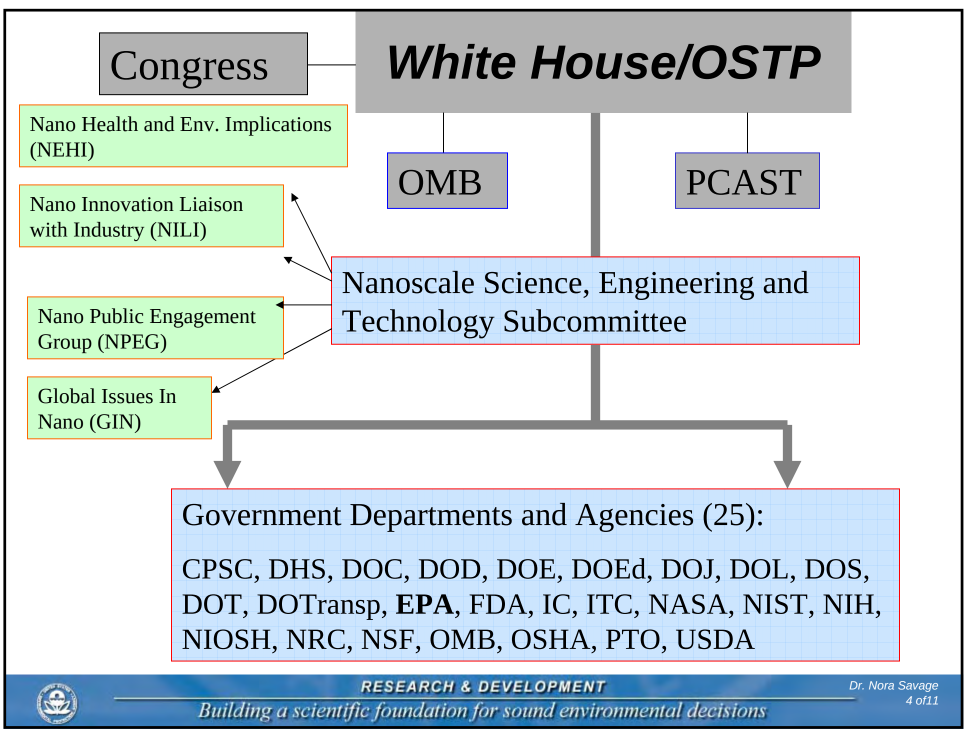
RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions

National Nanotechnology Initiative

EPA is a member of the subcommittee - Nanoscale Science, Engineering and Technology

- **Federal agencies and departments that participate in NNI**
- **Established in 2001**
- **Responsible for coordinating federal government's nanoscale research and development programs**
- **National Nanotechnology Coordinating Office (NNCO) – secretariat, point of contact**

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions
Dr. Nora Savage
3 of11



SPC White Paper

- Science Policy Council (**SPC**): venue for discussion and management of cross-agency science issues
- **Cross-agency Nanotechnology Workgroup** convened by SPC Dec. 2004
- Group charge: develop a white paper to examine the implications and applications of nanotechnology for the consideration of Agency managers
- Will serve as EPA's science and technology guide for nanotechnology
- You may obtain the draft white paper from www.regulations.gov or www.epa.gov/osa
- Anticipate **Final Document 2006**

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions
Dr. Nora Savage
5 of11

FY07: $8.6 million for Nano R&D

- Help advance nanotechnology's potential to create new and enhanced products in an environmentally sound manner, the President's Budget will strengthen EPA's ongoing efforts to:
  - (1) understand the potential human health and ecological impacts of manufactured nanomaterials, and
  - (2) investigate how nanotechnology can be used in environmental applications such as improved monitoring, pollution control, and site remediation
- FY 2007, a new in-house program will be integrated with ORD's existing STAR and SBIR extramural programs and coordinated with other federal environmental, health, and safety research conducted under the NNI, as well as with international organizations such as the OECD
- Developing an EPA nanotechnology research strategy

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions
Dr. Nora Savage
6 of11

EPA Nanotechnology STAR Grants

2001 **Environmental Applications of Nanotechnology**
- 16 awards, $5.6 million

2002 **Environmental Applications of Nanotechnology**
- 16 awards, $5 million\

2003 **Health and Environmental Effects of Manufactured Nanomaterials**
- 12 awards, $4 million

2004 **Environmental Applications of Nanomaterials**
- 7 awards, $2 million

2005 **Health and environmental effects of Nanoparticles**
- 19 awards, $7 million (joint with NSF, NIOSH)

2005/6 **Health and Environmental effects of Nanomaterials**
- $7 million, (joint with NSF, NIOSH, NIEHS)
- 156 received, 46 passed peer review

RESEARCH & DEVELOPMENT
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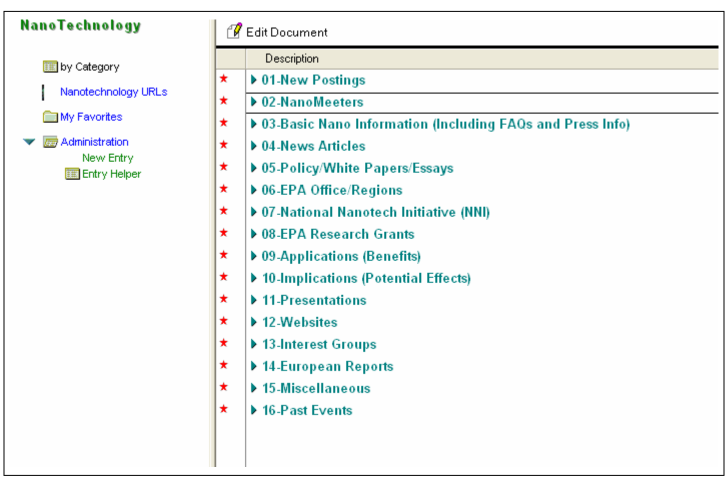
7 of11

NanoMeeters Notes Database



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Dr. Nora Savage
8 of11

Nanotechnology: ORD

- STAR grants ~ $25 million, 65 grants
- SBIR contracts ~ $4 million, Phase I and Phase II
- Co-Chair (with OPPTS) Agency White Paper workgroup
- $8.6 research budget request for 07
- ORD Research Strategy
- Cooperation with OPPT on: new chemical reviews, consideration of data elements for stewardship program, nanotech P2/DfE issues
- Participation in OECD nano Work Group
- Outreach to EPA Regions and Offices
- Outreach to national and international professional organizations

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions
Dr. Nora Savage
9 of11

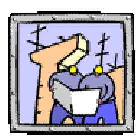
ORD Nanotechnology Activities

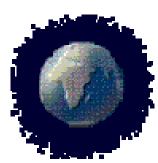
BUILDING A GREEN NANOTECH WORLD

Solicitations

Annual RFA since 2001

Annual SBIR since 2001





Meetings, Symposia, Workgroups

Interagency: Applications and Implications Conference w/ DOC, DOD, DOE, DOT, FDA, NIH, NSF, & USDA – September 2003

EPA Grantees' Workshops

ACS, AIChE, A&WMA, IEEE, ISEE/ISEA, MRS, SETAC, SOT,

Societal Implications II - Dec 2003

ANSI, ASTM, European Commission, ICON, ILSI, NAS, Woodrow Wilson Center, NAS, International organizations

NNI Nanotechnology Grand Challenge in the Environment – May 2003

RESEARCH & DEVELOPMENT
Building a scientific foundation for sound environmental decisions
Dr. Nora Savage
10 of11

Get Involved!

- Attend EPA NanoMeeters workgroup meetings
- Participate in writing RFA's
- Serve on relevancy reviews for nanotech grants
- Attend seminars and workshops on nanotech
- Present papers/chair sessions at professional meetings
- Think proactively regarding regulatory aspects of nanotech
- Assist in developing EPA-wide nano web page
- Use NanoMeeters database to keep current and communicate information to your colleagues

RESEARCH & DEVELOPMENT

Building a scientific foundation for sound environmental decisions

Dr. Nora Savage

11 of11

Dr. Barbara Karn, US EPA ORD, Woodrow Wilson International Center for Scholars/Emerging Nanotechnologies Project

EPA began a research grants program in nanotechnology applications for the environment in January, 2001 to help meet EPA's mission through this new technology.

ORD began to spread the word within the Agency, and encourage EPA offices to consider how nanotechnology may affect EPA's mission.

EPA must ensure that the environment and human health are taken into consideration in nanotechnology-related government research programs.

EPA has been able to get environmental health and safety issues discussed in NNI.

There is a joint research program on the implications of nanotechnology with the National Science Foundation, NIOSH, and NIEHS. There are plans to include the European Commission next year.

Global Issues in Nanotechnology (GIN) is working group of Nanoscale Science, Engineering and Technology (NSET). There have been recent discussions about issues of keeping trade secrets safe.

In addition to looking at nanoproducts themselves, OSWER needs to look at what products nanotechnology may be replacing. Large volumes of obsolete materials being replaced could end up in waste streams.

Nanotechnology and OSWER Meeting Panel

Barbara Karn, PhD
US EPA/Office of Research and Development
Woodrow Wilson International Center for Scholars/
Emerging Nanotechnologies Project

Washington, DC July 13, 2006

Dr. Barbara Karn
1 of8

6 Thrusts for EPA Nano research program

- Build and sustain a community of researchers in nanotech and the environment - both applications and implications.
- Promote nanotechnology within EPA and its mission.
- Assure consideration of the environment and human health in government research programs related to nanotechnology
- Work with industry to assure environmentally responsible development of nanotechnology and products containing nanomaterials.
- Provide leadership in international activities involving environment and human health and nanotech.
- Provide education and outreach to the public to promote understanding of nanotechnology with respect to environment and human health.

Dr. Barbara Karn
2 of8

International Activities

Proposed joint RFA with EC and US partners, NSF, NIOSH,NIEHS

International Dialogue for Responsible Nanotechnology

OECD IRGC GIN ICON

"Evidence" for reports

Invited talks:
Taiwan, Singapore, Thailand, India,
Hong Kong,
China, Japan, Belgium

Dr. Barbara Karn
3 of8

Green Nanotechnology Framework

1. Production of nanomaterials and products does not harm the environment

Making NanoX "greenly"

e.g., Green chemistry, Green engineering, DfE, Smart business practices

Using NanoX to "green" production

e.g., Nanomembranes, nanoscaled catalysts

Pollution Prevention Emphasis

2. Products of nano help the environment

Direct Environmental Applications e.g., environmental remediation, sensors

Indirect Environmental Applications e.g., saved energy, reduced waste

Anticipating full life cycle of nanomaterials and nanoproducts

NEXT STEPS: Policies that offer incentives for developing
green nanoproducts and manufacturing techniques

Dr. Barbara Karn
4 of8

Nanotechnology and the Environment
4th symposium sponsored by the Division of Industrial and Engineering Chemistry
At the 231st American Chemical Society National Meeting
Atlanta, Georgia March 26-30, 2006

The objectives of this symposium are to highlight the latest research results in nanotechnology that address pollution prevention at its source through greener synthesis of nanomaterials and products and use of nanotechnology to reduce pollutants in current processes

Session topics:
- Overview of nanotechnology programs and issues
- Environmentally benign synthesis of nanomaterials
- Bio-inspired nanotechnology
- Use of nanotechnology leading to cleaner production
- Nanotechnology for environmental clean-up
- Nanomaterials for use in energy applications
- Nanotechnology related to the hydrogen economy

Co-Chairs: Barbara Karn, U.S.EPA; James E. Hutchison, University of Oregon
Florian Schattenmann, General Electric; Nora Savage, U.S.EPA

Dr. Barbara Karn
5 of8

Be ready for waste streams caused by nanotechnology

Materials/substance flow analysis

A Back of the Envelope MFA calculation: Switching to nano

Each EPA employee has 1 computer with 1 CRT monitor

20,000 employees replace their CRTs with flat screen LCDs

0.45 kg Pb/17 inch CRT (DfE Report, US EPA)

9 tonnes of Lead to be disposed of from EPA monitors!

0.8 M^3 Lead ~ volume of 7 oil barrels

Can Nanotechnology change this waste picture?

Dr. Barbara Karn
6 of8

Nanotechnology and the Environment: Where we've come from and where we're going

Barbara Karn, PhD
US EPA/Office of Research and Development
Woodrow Wilson International Center for Scholars/
Emerging Nanotechnologies Project

American Chemical Society
4th Nano and the Environment Symposium
Atlanta, Georgia March 26, 2006

GET INVOLVED

Professional Associations
NanoMeeters
Agency & Academic Contacts

Use Expertise in Agency

Panel Discussion
A panel composed of the conference speakers and EPA personnel held a discussion during which they addressed the charged questions 1) Based on what is currently known in the nanotechnology area, what can be inferred about the properties and characteristics of a nanotechnology waste? and 2) How can nanotechnology impact current waste management practices for wastes?

Panel Members
Dr. Elizabeth Lee Hofmann, US EPA OSWER, Moderator

Mr. Jim Willis, US EPA OPPT

Dr. Barbara Karn, US EPA ORD, Woodrow Wilson International Center for Scholars/Emerging Nanotechnologies Project

Dr. Nora Savage, US EPA ORD, National Center for Environmental Research/Environmental Engineering Research Division

Ms. Marti Otto, US EPA OSRTI

Mr. Tracy D. Hester, Bracewell & Giuliani LLP, Houston TX

Mr. Mark Greenwood, Ropes & Gray, Washington DC

Dr. Stig Irving Olsen, Technical University of Denmark, Lyngby Denmark

Dr. Lou Theodore, Manhattan College, Department of Chemical Engineering

Mr. John Scalera, US EPA, Washington DC

Dr. Anil K. Patri, National Cancer Institute (SAIC Frederick) Frederick MD

Dr. Gregory V. Lowry, Carnegie Mellon University, Pittsburgh PA

Dr. David Warheit, E.I. DuPont de Nemours & Co., Inc Newark DE

Questions from OSWER to the Panel:

Based on what is currently known in the nanotechnology area, what can be inferred about the properties and characteristics of a nanotechnology waste?

Dr. Olsen: Nanotechnology is a horizontal technology, and will disperse into many types of products. Most waste streams will end up containing nanomaterials or nanotechnology products. One of the biggest issues is the depletion of scarce resources. We need to improve means of recovery of valuable materials from waste, possibly before it becomes waste.

Dr. Warheit: The issue of how to identify nanoparticles in waste is a very difficult problem. Even when we can control all of the variables in the lab, we can obtain different results depending on what we look for and what methods we use, even when working with the same material. Also, aggregation and agglomeration are issues when dealing with waste streams. We need to develop a life cycle assessment framework for product stewardship. DuPont, in collaboration with the Environmental Defense Fund, is attempting to do this. We should also carry out experimental simulations using one or two standardized materials, to determine which methods and which parameters to use (size, shape, charge, and surface characteristics).

Mr. Scalera: There are issues of complexity when dealing with environmental samples; some fundamental studies can be done before you reach that stage. We should start with fundamental studies to determine where to invest research funds (e.g., nanoparticles that are produced in significant volumes and are hazardous). First, we need to develop a feel for whether there is a hazard associated with the given nanoparticle. Then, you need to consider the production volume. If there is evidence of toxicity and large production volume, then you might want to consider its environmental fate and assess whether the nanomaterial is available in a toxic form and if other toxic forms are present. Instead of running a series of life cycle assessments (LCAs) to elucidate fate and transport, we may want to determine whether it aggregates in the environment. I am not aware of any standard methodologies to assess aggregation potential. Does the nanoparticle aggregate or agglomerate, and how easily? How toxic is the nanomaterial in each of its forms? Is there some way to disrupt the agglomeration? If it aggregates, can the aggregate be disrupted? There is a series of 4 to 5 more simplistic experiments that should be performed before LCA.

Dr. Patri: From the perspective of nanomaterial intended for medical application, this issue is difficult because of the diversity of materials involved, and the fact that most are in mixtures, are multifunctional, and/or are coated (to make them soluble or multifunctional with proteins attached, chemotherapeutics, heavy metals used for contrast agents, etc.). You generally may not see naked nanoparticles in the waste stream of nanomaterial.

Dr. Savage: Right now we test materials compound by compound, and we’re only just beginning to understand/consider synergistic effects of compounds in the environment. OSWER should understand stability and degradation of nanomaterials, and waste products of nanomaterials (do they get caught by scrubbers, do they move in leachate, accumulate in sludge, are they subject to biological activation, inactivation, breakdown, etc.). It’s important to know how nanomaterials could affect properties of leachate.

Mr. Willis: OSWER should consider whether it is possible to categorize nanomaterials or identify subsets of materials that are of greater or lesser concern (i.e., free nanoparticles, nanomaterials bound in a matrix, or one-dimensional nanomaterial coatings) as a way of setting priorities. OSWER should review the nanotechnology white paper, the ORD research framework, and the NNI research strategy to make sure that its needs get reflected in the research areas being considered.

Dr. Karn: The scientific literature may not contain reports of nanomaterials in which toxicity has not been observed, because negative results are not typically published. Scientists are expected to publish results; are researchers finding things to be toxic, just to get published? There is no journal of negative results; should there be a scientific journal or other mechanism devoted to negative findings (i.e., that a particular nanomaterial has no toxicity)?

Mr. Hester: While we may not have complete information about the properties of nanowastes, we need to understand which data will be important for decisions on whether and how to regulate nanoscale wastes. The ORD's strategy might serve as a mini-roadmap for research to identify these waste management regulatory issues. But more importantly, we should attempt to use an organized and cohesive approach to target the information that we need to handle discarded nanomaterials.

Dr. Lowry: The ongoing research to develop new nanoparticles makes it difficult to predict what the future will hold (i.e., what types of properties new nanomaterials may have). To date, colloid science explains the mobility of available nanomaterials; I've yet to come across a case where colloid science has not been able to explain nanoparticle mobility. There is a lot of research being done to develop new products with the expectation of revealing novel properties. It's not entirely clear yet where we need to apply more than standard colloid science to describe nanoparticle mobility.

Mr. Greenwood: Chemistry required for understanding nanowaste is typically not a part of traditional waste management. The chemistry required for understanding nanowaste is more than what is currently considered in waste stream considerations. We will need to know a lot more about what's in the waste stream, how it behaves in the environment, etc. We will need to reevaluate and revalidate our methods for waste treatment to see if they work with nanomaterials. We will need to consider how to control nanoparticles – does existing protective equipment work well enough? HEPA filters and new personal protective equipment (PPE) for handling nanowaste may need to be developed.

Mr. Hester: While we rightly have focused on some of the risk issues raised by nanomaterials, we shouldn't forget the beneficial pollution prevention aspects of nanotechnology. Nanotechnology has an enormous capacity to reduce the production of wastes in industrial processes, and it can remediate contamination and environmental releases in much more effective ways. For example, nanotechnology may allow for a new array of filtering technologies that could reduce wastes and/or the hazard posed by those wastes. Beyond these beneficial uses, we need to the time now to determine what uses of nanomaterials – including direct releases into the environment for remediation – might pose the vector of greatest impact. This assessment might include important data such as identifying the most likely sources of nanoscale wastes, or determining the impact of household wastes that will contain nanomaterials

A commenter asked, Do you know which waste streams will be producing the most nanomaterial waste?

Mr. Hester: No, although some consumer products containing nanomaterials have already entered the market and are undoubtedly being discarded. But for now, we don't know which products or waste streams will generate the largest volume of discarded nanomaterials.

Dr. Theodore: A bottom-up approach involves little to no waste. From an environmental management perspective, this is a big advantage. This would be a positive development from a pollution prevention standpoint. A more advanced approach to nanotechnology will involve improved environmental management practices.

Dr. Olsen: Hopefully future production techniques will reduce waste. Consumer waste will be one of biggest areas of nanowaste. A possible benefit of nanotechnology could be the use of radio frequent identification tags (RFID) to improve identification and recovery of different materials.

Dr. Karn: Nanosensors could be used to monitor nanomaterials in waste streams -- "nano measuring nano."

Dr. Theodore: This can also enable us to measure terrorist threats.

Ms. Otto: We need to invest resources in evaluating and improving our measurement and monitoring techniques. An immediate concern is making sure that we're monitoring fate and transport at field testing sites.

A questioner asked how we can use bottom-up techniques to assess effects (quantum mechanics as an example).

Dr. Karn: Green nanotechnology is emphasizing a consideration of bottom-up technologies (e.g., can we use self-assembly to reduce waste and improve the efficiency of production).

Mr. Willis: It might be beneficial to look at programs like the Resource Conservation Challenge: are there waste problems out there that nanotechnology can be used to solve? OSWER could look downstream at products or processes where "macro" chemicals are being replaced by nanoscale materials being replaced by nano-enabled products to get a sense of what is likely to enter the waste streams as well as the implications of dispersive use of nanoparticles. (e.g., release of nanoscale zero valent iron for site remediation). Engaging in the planned case study work can help here. Also, is there some way of making nanoparticles benign once the intended use ends?

Mr. Greenwood: We should be very open to the public with respect to how waste streams are managed. We need to consider what kind of information companies should be required to provide. Tort liability is a concern here; companies will want to avoid liability.

Dr. Warheit: OSWER needs to be very specific in what it wants to know, and how it formulates questions. Questions need to be clearly defined.

The discussion was opened to the audience.

A questioner asked whether ultrafine particles need to be regulated and whether nanoparticles that can penetrate biological membranes should be described as macromolecules.

Dr. Warheit: Not all nanoparticles and not all ultrafine particles behave the same. Nanoparticles have different biological activities. They may be able to translocate to different parts of the body. Also, nanoparticles could aggregate and become larger particles.

Dr. Lowry: Some nanoparticles do aggregate in the environment but it's quite possible that in a biological system you have a small fraction of particles that remain unaggregated. Three- to 5-nm particles are not macromolecules. They are Rhinovirus-sized.

Dr. Patri: The size of C60 buckyballs is similar to that of small molecules. Depending on what is bound to the nanomaterial in the body, it may be larger. Smaller-sized nanomaterials can be characterized using the same methods used for small molecules.

Dr. Lowry: We will want to have classifications for the particles – we can't look at all possible individual chemicals. But we don't know what the classifications should be yet.

A questioner asked if there are any other ways to classify nanomaterials.

Mr. Scalera: We may need to experiment to identify nanoparticles of concern before generating fate studies and toxicity studies.

A commenter noted that we may want to conduct pharmacokinetics studies, starting with the most common nanoparticles. Maybe certain nanoparticles can be lumped with ultrafines for regulatory purposes.

The second question was posed to the Panel.

How can nanotechnology impact current waste management practices for wastes?

Dr. Lowry: The most near-term application is using nanomaterials that have reactive and physical properties that allow us to remediate things that we can't get to easily such as deep surface contamination. We know that we can utilize nanoparticles and get surface chemistries that did not previously exist. This can allow us to remediate recalcitrant chemicals (e.g., PCBs, dioxins, different radionuclides) and waste in hard-to-reach spaces.

Dr. Theodore: Nanoparticles have unique, novel properties that can be utilized for waste remediation (waste water, air pollutants, etc.). Adsorptive properties can clean up water and gas streams. In addition, they have catalytic properties and that too can lead to destruction of toxic gaseous materials. Since we have a near-infinite number of new chemicals at our disposal, we might look at this from a pollution prevention point of view: can we replace current chemicals with new nanomaterials that don't have toxicological issues?

A questioner asked whether there is a possibility that our current environmental management approach is not applicable to nanoparticles, because of the nature of these materials.

Dr. Theodore: Many traditional practices will still apply (e.g., recycling and waste reduction) but new practices will have to be developed. The traditional approaches (e.g., source management, control, P2 hierarchy) will generally apply. Not much will change in terms of control (e.g., disposal will still use landfills).

Mr. Scalera: In a waste stream, agglomeration may result, and regulating by mass (quantity) may no longer apply in instances where toxicity is reduced by agglomeration.

Also, bioavailability will need to be accounted for. We will need to determine what toxicity characteristics are important.

Dr. Karn: I agree that some management changes are needed. EPA could evolve into addressing three problem areas: 1) current -- what we do with current laws; 2) past -- what we could have done right, but we still have to fix; 3) future -- get ahead of the science and commercial aspects, and anticipate problems.

Mr. Greenwood: Nanotechnology is a good opportunity to look at the link between waste management and the time when a chemical comes into commerce. Management programs typically consider product development and waste separately. We need to align waste management and product programs and ask the right questions in the beginning.

A commenter noted that the Office of Water has developed a framework for identifying nanomaterials in pharmaceuticals and personal care products (including medical products). Wastewater streams will contain nanomaterials from such products.

Dr. Karn: The waste stream issues are important from the consumer disposal standpoint. Nanoscale drugs will enter wastewater after being excreted from the body. Also, disposal of unused drugs that have not been through the body (e.g., how do you dispose of old prescriptions?)

A questioner asked whether it is possible to engineer particles with a finite lifespan and/or activity (e.g., that only exist at a certain temperature or pressure).

Mr. Willis: There may be opportunities to design benign particles (hydroxylating buckyballs). It's not clear whether this changes performance of the nanoparticles.

Dr. Lowry: Certain polymers can be designed to breakdown; this may be useful. Krzysztof Matyjaszewskii at Carnegie Mellon University designs polymers with groups that hydrolyze at known rates that would then break up the polymer into biodegradable components and lose functionality. Polymer chemistry is probably leading to the ability to design particle coatings with finite lifetimes.

Dr. Patri: Dendrimers that hydrolyze to benign products are being produced. Once they deliver the drug, they can be destroyed, resulting in glycerol and lactic acid. However, this will not be possible with all types of nanomaterials.

Mr. Greenwood: We should steer clear of developing new stovepipe programs; rather, we should build capacity to consider nanotechnology issues in multiple existing programs. There needs to be coordination and communication between programs.

Dr. Patri: The common defining feature of these nanomaterials is size; however, we must standardize the characterization of nanosized particles. It is important to be able to compare particles from different laboratories. Otherwise, we are not sure we're talking about the same thing. NIST is developing standard reference materials (SRMs) that will be thoroughly characterized. The first SRM will be based on size, then we will develop other SRMs within that size range with additional characteristics. The NIST/NCL development and characteristics of these SRM will be made publicly available. Quantity is an issue—it is difficult to produce 0.5 grams of nanoparticles. Once there is a real commercial application, it is easy to scale up production.

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