A Small (nano) Dose of Nanotoxicology

An Introduction to the Effects of Nanomaterials – Nanoparticles - Small Size - Big Problems?

CHE-WA Children's Environmental Health Working Group Thursday morning, September 12, 2013



Steven G. Gilbert, PhD, DABT www.asmalldoseof.org www.toxipedia.org

A Cobalt nanoparticle coated with layers of graphene

A Small Dose of Toxicology 2nd Edition



Free e-book Healthy World Press

PowerPoint slides for each chapter Nanotox

See: www.asmalldoseof.org -- <u>smdose</u>

Nanomaterials

Very Small > Very disruptive (electricity, telephone, birth control ...) Huge benefits Potential for huge harm

Nanotechnology

Latin from Greek nanos 'dwarf'

"Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications." http://www.nano.gov/

Multiple disciplines, including science, engineering, technology, toxicology, biomedical, government, materials science (manufacture / characterization)

4th C: The Lycurgus Cup (Rome) - dichroic glass; colloidal gold and silver in the glass allow it to look opaque green when lit from outside but translucent red when light shines through the inside.'





http://www.nano.gov/timeline



13th-18th C: "Damascus" saber blades contained carbon nanotubes and cementite nanowires—an ultrahigh-carbon steel formulation that gave them strength, resilience, the ability to hold a keen edge





http://www.nano.gov/timeline



1857: Michael Faraday discovered colloidal "ruby" gold, demonstrating that nanostructured gold under certain lighting conditions produces different-colored solutions.



http://www.nano.gov/timeline



1936: Erwin Müller, working at Siemens Research Laboratory, invented the field emission microscope, allowing near-atomic-resolution images of materials.



http://www.nano.gov/timeline



1981: Russia's Alexei Ekimov discovered nanocrystalline, semiconducting quantum dots in a glass matrix and conducted pioneering studies of their electronic and optical properties.

1985: Rice University researchers Harold Kroto, Sean O'Brien, Robert Curl, and Richard Smalley discovered the Buckminsterfullerene (C60), more commonly known as the buckyball, which is a molecule resembling a soccerball in shape and composed entirely of carbon, as are graphite and diamond.



1991: Sumio Iijima of NEC is credited with discovering the carbon nanotube (CNT). Iijima shared the Kavli Prize in Nanoscience in 2008 for this advance and other advances in the field.



http://www.nano.gov/timeline



1999–early 2000's: Consumer products making use of nanotechnology began appearing in the marketplace



http://www.nano.gov/timeline



2004: Britain's Royal Society and the Royal Academy of Engineering published Nanoscience and Nanotechnologies: Opportunities and Uncertainties advocating the need to address potential health, environmental, social, ethical, and regulatory issues associated with nanotechnology.

2008: The first official National Nanotechnology Initiative (NNI) Strategy for Nanotechnology-Related Environmental, Health, and Safety (EHS) Research was published, based on a two-year process of NNI-sponsored investigations and public dialogs.

2011: The NSET Subcommittee updated both the NNI Strategic Plan and the NNI Environmental, Health, and Safety Research Strategy, drawing on extensive input from public workshops and online dialog with stakeholders from Government, academia, NGOs, and the public, and others.

Promises of Nanotechnology

Clean Energy

Clean, secure affordable energy Solar panels more efficient. Fuel cell development

Clean Water

Nanomaterials - detection of impurities (pollutants, microbes, etc), as well as removal of them, catalysts reduce waste water

How big is a nanometer (nm)?

- Sheet of paper is about 100,000 nm thick.
- A strand of human DNA is 2.5 nanometers in diameter
- A human hair is approximately 80,000-100,000 nanometers wide
- > There are 25,400,000 nm in an inch.
- A single gold atom is about a third of a nanometer in diameter
- A nanometer is a millionth of a millimeter (10-9)

Common engineered nanomaterials

Amorphous silica





TiO2 (nanotubes)



Nanosilver









Nanogold



Nano New Chemical Entity?

Nanomaterials can exhibit different fundamental physical, biological, and chemical properties than their larger counterparts.

Consequences?

Classes of nanomaterials

- Engineered nanomaterials: Manufactured materials with engineered structure between 1 - 100 nm.
- Incidental nanomaterials: Materials with a structure between 1 - 100 nm produced as a by-product of a process. Examples: welding fume and diesel emission particulates.
- Natural nanomaterials: Materials with a structure between 1 - 100 nm that are a result of natural processes. Example: volcanic emissions, sea spray, and atmospheric gas-to-particle conversion.
- Mimic of natural nanomaterials create engineered nanomaterials. Example: Metallic Organic Frameworks (MOFs) similar structure and characteristics of volcanic ash

Nanomaterial New Properties?

- Unusual physical, chemical, and biological characteristics at nanoscale
- Individual nanoparticles have different properties than bulk solutions
- Greater surface area/volumepotentially more reactive
- Ability to manipulate individual particles
- Surface chemicals

Consequences?

Nano Products Growing

March 2011, consumer products inventory contains 1317 products or product lines



http://www.nanotechproject.org/inventories/consumer/analysis_draft/



US NanoMetro Map

goods based on nanotechnology is predicted to grow from \$147 billion in 2007 to \$3.1 trillion in 2015



Seattle NanoMetro Map

WA 35 companies / universities working with nano



http://www.nanotechproject.org/inventories/map/

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Seattle NanoMetro Map

Examples

 Hummingbird Scientific Analytical instruments http://www.hummingbirdscientific.com/home/ Lacey, WA 98516

Nordstrom

3LAB 'Super h' Age-Defying Serum

An advanced treatment serum that contains Nano-Claire GY[™] the world's first cosmetic grade synthetic growth hormone \$320 http://shop.nordstrom.com/sr?keyword=nanotechnology&origin=keywordsearch

<u>APEX NANOTECH, LLC</u>
<u>Gasoline additive (secret technology)</u>
http://www.apexnanotech.com/

http://www.nanotechproject.org/inventories/map/

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Take Precautions

Prey -- novel by Michael Crichton



Baby Bear - With the additive of Silver Nanoparticles, our product has been <u>clinically proven</u> to fight against harmful bacteria, molds and mites.



Baby Blanket - The fabric is made using so-called 'nano technology' and allows the naturally occurring metal silver to be incorporated into the material.



http://www.nanotechproject.org/inventories/consumer/browse/categories/goods_for_children/

- Antibacterial Silver Athletic and Lounging Socks: Sharper Image®PRODUCT "Cushioned, fitted, quarter-length sports socks knitted with a cotton material containing millions of invisible silver nanoparticles. Innovative socks are <u>naturally</u> antibacterial and antifungal."
- 3XDRY® ESSEX SHIRT: Simms Fishing Products -- "UPF 30 offers all day sun protection Fabric features a <u>special silver-based</u> nanotechnology -





http://www.nanotechproject.org/inventories/consumer/browse/categories/health_fitness/clothing/

Antibacterial Kitchenware: Nano Care Technology, Ltd. -- Our Antibacterial tableware with nano silver coating could kill the attached bacteria and microbial in ten minutes and the effect can last for a long time even permanently and keep the surface always clean.



Nano-in Natural Environmental Cleaning Agent: Nano-Infinity Nanotech Co., Ltd. -- "this Nano micelle product containing <u>natural glycerin can</u> completely remove any pesticide residues on fruits/vegetable, and all the oil/dirt on cutlery. Its efficient and safe cleaning power is a must for your healthy life."



http://www.nanotechproject.org/inventories/consumer/browse/categories/food_beverage/cooking/

Behr® PREMIUM PLUS® Exterior Paint: Behr® Process Corporation --"...Nanophase's proprietary nanoparticles are now being used in Behr's Premium Plus Ultra paint. Nanophase's nanoparticles not only lend the paint improved adhesion and anti-mildew properties."



 Samsonite® Silhouette® 11
Collection: Samsonite – "Tricore Nylon with DuPont Nano Technology fabric protection



http://www.nanotechproject.org/inventories/consumer/browse/categories/food_beverage/cooking/



Case Study – Titanium dioxide (TiO2)

- > white pigment
- Many uses paints, coatings, plastics, papers, inks, foods, medicines, toothpastes



 cosmetic and skin care products strong UV light absorbing capabilities coated with silica or alumina
NANO – clear instead of white

Case Study – Titanium dioxide (TiO2)

- titanium dioxide (TiO2) and zinc oxide (ZnO) rub on clear instead of white.
- "The U.S. Food and Drug Administration's newly released sunscreen rules fail to meaningfully consider the risks posed by nanoscale ingredients, according to public interest groups including Friends of the Earth, The International Center for Technology Assessment and Consumers Union." June 23, 2011

(http://www.foe.org/news/archives/2011-06-new-fda-sunscreen-rules-called-blind-to-nanotechnolo)

Case Study – Silver Nanoparticles

History –

- Hippocrates, noted beneficial healing and antidisease properties
- Silver coins in milk (1900s)
- regulatory approval as an antimicrobial agent
- Use declined in 1940s with antibiotics



- Silver sulfadiazine antibacterial wound treatment – burns, external infections
- colloidal silver as an alternative medicine treatment – no data, claims unsupported

Case Study – Silver Nanoparticles

- Silver nanoparticles of between 1-100 nm in size
- Uses catalysis, optics, electronics, medical, water treatment, textiles, consumer products



Silver nanoparticles are now replacing silver sulfadiazine – wound dressing

US EPA State of the Science Literature Review: Everything Nanosilver and More – August 2010 - http://www.epa.gov/nanoscience/files/NanoPaper1.pdf

Case Study – Silver Nanoparticles

More than 200 products -including odor-resistant socks, baby bottles and clothes-washing machines -are laced with specks of nanosilver



- Harms aquatic organisms
- Regulate the chemical as a pesticide
- Harms bacteria in wastewater treatment plants
- Health allergic reaction, accumulation in liver, brain?, Argyria and staining

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Case Study - Quantum Dots

- Semiconductor Nanocrystals
 - Ranging in size from approximately
 - 2 150 nm
 - Metalloid crystalline core

 - & Cadmium (Cd)
 - Cap or shell covering core
 - ✤ Selenium (Se)
 - ✤ Tellurium (Te)
 - Coating
 - Biocompatible coating
 - Functional groups
 - Green Dots (no heavy metals)
 - Nanoco Group PLC http://www.nanocotechnologies.com/
 - Functional groups
 - Market size \$7.5 billion 2022
 - Nanoco http://betanews.com/newswire/2012/05/18/marketsandmarkets-global-quantum-dots-qd-

market-worth-of-7480-25-million-by-2022//





Case Study - Quantum Dots

Quantum Dots and You

- Medical imaging
 - Cancer
 - Diagnostics
 - Therapeutics
- Biological imaging agent
 - "Tag" proteins
 - Monitor cellular uptake



Figure 7. Sensitivity and multicolor capability of QD imaging in live animals. Approximately 12 million QD-beads in green, yellow, and red were injected sub-cutaneously at three adjacent locations on a host animal.


Dose / Response



Individual Sensitivity

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Nanotoxicology Issues

Occupational Health > Workers Human Health Consumers Vulnerable – kids / elderly Environmental Health Eco-system --- Aquatic life, **Terrestrial life, Plant, Wildlife**

Nanotoxicology Practical Issues

- How to properly take field (environment / work place) samples, detect, characterize, quantify
- Standard testing procedures, protocols
- > Incorporating into laws, regulations
- Air quality and sediments standards as examples?

Nanotoxicologoy Issues



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Environmental, Health, and Safety research

Who is responsible?

- National Institute for Standards and Technology (NIST)
 - Instrumentation, metrology, and analytical methods
- National Institutes of Health (NIH)
 - Nanomaterials and human health
- Environmental Protection Agency (EPA)
 - Nanomaterials and the environment
- National Institutes of Occupational Safety and Health (NIOSH)
 - Human and environmental exposure assessment
- Food and Drug Administration (FDA)
 - Risk management (also EPA)
- Consumer Product Safety Commission (CPSC)
 - xx?

Consumer Product Safety Commission

Evaluation of Consumer Products

The potential safety and health risks of nanomaterials, as with other compounds that are incorporated into consumer products, can be assessed under existing CPSC statutes, regulations and guidelines. Neither the Consumer Product Safety Act (CPSA) nor the Federal Hazardous Substances Act (FHSA) requires the premarket registration or approval of products. Thus, it is usually not until a product has been distributed in commerce that the CPSC would evaluate a product's potential risk to the public.

CPSC Nanomaterial Statement - http://www.cpsc.gov/LIBRARY/CPSCNanoStatement.pdf



Occupational Health

"The people that research, develop, manufacture, package, handle, transport, use and dispose of nanomaterials will be those most exposed and therefore most likely to suffer any potential human health harms. As such, worker protection should be paramount within any nanomaterial oversight regime."

WHO -- http://www.who.int/occupational_health/background_review_1.6.12.pdf

Occupational Health

> Is PPE adequate ? Individual sensitivity / vulnerability Are MSDS sheets informative ? EU and Canadian MSDS yes, not US Transparency about use ? Regulation adequate ? High concern – inhalation – carbon nano tubes, nano-silver

Human Health

Products

- Expanding products
- Absorption (sun screens)
- How much of what ? Right to know?
- Weak regulation CPSC
- Who regulates socks / washing machines ?

Medical

- Expanding products
- FDA regulating medical uses more of a precautionary approach
- Supplements not regulated (silver is natural)

A risk to human and environmental health?

- The physical and chemical characteristics of nanomaterials that give promise, also have the potential for peril.
- Effects are not well characterized.
- Ultrafine particles (UFPs) generally cause more toxicity in lung models
- Reactivity of some particles increases as surface area-volume ratio increases
- Surface coatings?
- Represents a very important need for research.

Environmental Health

- Persistence
- > Bioaccumulation
- Release to environment
- Water / Air
- Coating
- Surface area (not weight)



Carbon Nanotubes / Asbestos







Asbestos fibers

Carbon Nanotubes aligned

Carbon Nanotubes powder

Environmental Health

Cancer, Study Says

II. Macro Vs. Nano

said. Unfortunately, Maynard added, scientists have not even agreed on what the best method is for measuring airborne levels of nanotube dust.

Donaldson, K., Murphy, F., Schinwald, A., Duffin, R., & Poland, C. A. (2011). Identifying the pulmonary hazard of high aspect ratio nanoparticles to enable their safety-by-design. Nanomedicine (Lond), 6(1), 143-156.

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Nanomaterial challenges

Nanomaterials synthesis

- the control of physical properties obtaining uniform particle size distribution
- identical shape
- morphology
- chemical composition
- crystal structure.

Cradle to Grave challenges

- Manufacture many methods chemical coatings
- Use consumer to industry human / environmental exposure
- Disposal / Reuse / Recycle

One of The Problems

Thousands of nanoparticle types, each having unique chemical and physical characteristics, and potentially, unique biological reactivity.`





Methodological Needs

> developing methods to measure

- nanosilver concentration
- size
- shape
- surface charge
- crystal structure
- surface chemistry
- surface transformations Range of tools

Solutions

Hummingbird Scientific

http://www.hummingbirdscientific.com/home/ Analytical equipment - Lacey, WA 9851

Center for Nanotechnology at UW

The NanoTech User Facility (NTUF) established in 1998 to provide the nanotechnology community with access to advanced characterization and nanofabrication equipment https://depts.washington.edu/ntuf

Pacific Northwest National Laboratory Materials sciences -- http://www.pnnl.gov/

Regulation - FDA

June 2011, FDA - Draft Guidance for Industry entitled, "*Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology*"

The draft foods guidance The draft cosmetics guidance

http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ucm300914.htm?source=govdelivery

Regulation - FDA

The draft foods guidance

- > Affects the identity of the food substance;
- Affects the safety of the use of the food substance;
- Affects the regulatory status of the use of the food substance;
- > Warrants a regulatory submission to FDA.

http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ucm300914.htm?source=govdelivery

Regulation - FDA

The draft cosmetics guidance

safety assessment of nanomaterials when used in cosmetic products.

- Cosmetics are not subject to premarket approval; however, they must be safe for consumers under labeled or customary conditions use, and they must be properly labeled.
- Cosmetics manufactured using nanomaterials are subject to the same legal requirements as any other cosmetics. Companies and individuals who market cosmetics are legally responsible for the safety of their products.
- In general, the processes currently in use for assessing safety are appropriate for cosmetics containing nanomaterials. However, data needs and testing methods should be evaluated in light of the properties or functions that may be exhibited by nanomaterials used in cosmetic products

http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ucm300914.htm?source=govdelivery

Regulation - EPA

Nanoscale Materials

Many nanoscale materials are regarded as "chemical substances" under the Toxic Substances Control Act (TSCA). To ensure that nanoscale materials are manufactured and used in a manner that protects against unreasonable risks to human health and the environment, EPA is pursuing a comprehensive regulatory approach under TSCA. This four-pronged approach includes: Premanufacture notifications; a Significant New Use Rule; an information gathering rule; and a test rule.

Regulation - EPA

Nanosilver

"Currently, tracking products that contain nanosilver is getting to be difficult because the products are almost always packaged under numerous brand names, and current labeling regulations do not require that the nanomaterial be listed as an ingredient."

US EPA State of the Science Literature Review: Everything Nanosilver and More – August 2010 - http://www.epa.gov/nanoscience/files/NanoPaper1.pd

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Cradle to Grave - EPA

Assess the cradle to grave cost/risk associated with any given product

- Life Cycle Assessment (LCA)
- Comprehensive Environmental Assessment (CEA)

Risk assessment paradigm, which includes hazard identification, dose-response assessment, risk characterization and exposure assessment

US EPA State of the Science Literature Review: Everything Nanosilver and More – August 2010 - http://www.epa.gov/nanoscience/files/NanoPaper1.pdf

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European Union

European Union is implementing a new Classification, Labeling and Packaging (CLP)Regulation. CLP includes the requirement that if the form or physical state of a substance is changed, an evaluation must be done to determine if the hazard classification should be changed.

http://www.understandingnano.com/nanotechnology-regulation.html

Nike

Nike currently restricts the use of nanomaterials within apparel, footwear, and equipment product lines.



Products to which nanomaterials are applied must:

- Not leach or release chemicals (or particles) in order to be effective or as a result of wear , unless safety data are available and acceptable
- Meet legislative standards (globally)
- Be appropriately registered (e.g., EU Biocide Directive, if used as bacteriostatic agent)
- If registration not required: Manufacturer/supplier has made available an analysis of consumer safety
- Pass a corporate toxicity review (conducted thru the Considered Chemistry team)
- Be proven effective (for our product types)
- Comply with the Nike Corporate RSL (Restricted Substances List)

Nike Restricted Substances List (RSL) and Sustainable Chemistry Guidance

(SCG)



http://www.nikeresponsibility.com/rsl

Questions / Recommendations

- Are nanomaterials new substances?
 YES
- Transparency about use in industry and consumer products
- Research / Standards for sampling and assessment
- Fate and transport cradle to grave
- Human and Environmental health effects

Silent Spring I

"As crude a weapon as a cave man's club, the chemical barrage has been hurled against the fabric of life."

Rachel Carson – Silent Spring (1962)



Silent Spring II

"The "control of nature" is a phrase conceived in arrogance, born of the Neanderthal age of biology and the convenience of man."

Rachel Carson – Silent Spring (1962)

Resources

W UNIVERSITY of WASHINGTON



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http://depts.washington.edu/envdev/nanotox/

Precautionary Principle

"When an activity raises threats of harm to human health or the environment, precautionary measures should be take even if some cause and effect relationships are not fully established scientifically."

Wingspread Conference, 1998.

NIRT

Nanotechnology information, reporting and tracking (NIRT) review panel

Why a NIRT

Business in WA

Track the use of nanotechnology in WA Help encourage business opportunities Encourage Nanotech R&D, manufacturing

Human health

Many consumer product now use nanotechnology How much consumer exposure Individual vulnerability (children?) Worker health and safety

Environmental health Consumer and manufacture use Consequences of environmental exposure

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Additional Information

- > Web Sites
- Nanotechnology wikipedia http://en.wikipedia.org/wiki/Nanotechnology
- The National Nanotechnology Initiative (NNI) - <u>http://nano.gov/</u>
- The International Council on Nanotechnology (ICON) http://icon.rice.edu/
- Toxipedia Nanotoxicology http://www.toxipedia.org/display/toxipedia/ Nanotechnology

Authorship Information

This presentation is supplement to "A Small Dose of Toxicology"

For Additional Information Contact Steven G. Gilbert, PhD, DABT E-mail: sgilbert@innd.org Web: www.asmalldoseof.org www.toxipedia.org

NW Public Health

Public Health and the Precautionary Principle

By Steven G. Gilbert



See: http://healthlinks.washington.edu/nwcphp/nph/

nwph
Precautionary Principle

"When an activity raises threats of harm to human health or the environment, precautionary measures should be take even if some cause and effect relationships are not fully established scientifically."

Wingspread Conference, 1998.

Central components

- Setting goals (Health indicators)
- Taking preventive action in the face of uncertainty
- Shifting the burden of responsibility to the proponents of an activity (Who benefits?)
- Exploring a wide range of alternatives to possibly harmful actions (Is it necessary?)
- Increasing public participation in decision making (transparency of information & environmental justice)