Risk and Occupational Health and Safety of Nanomaterials

Professor Hilary Godwin, UCLA

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Nanorisk: Advances, Challenges & Opportunities

• How we assess risk depends on the decision that needs to be made & by whom
• There are (still) data gaps, so tools for risk evaluation must include explicitly include methods for addressing & evaluating uncertainty
• Challenges to nanorisk evaluation are not unique; our advances will likely provide a path forward for evaluation of conventional chemicals as well
Challenges to Evaluating the Risks of Nanomaterials

• Decisions about risk need to be made by a wide range of stakeholders in the absence of comprehensive data
• Many of those decisions need to be made in real time (i.e., formal risk assessment would not be the solution even if there were comprehensive data)
• Greater alignment of decision-making tools with needs of specific stakeholders is required

- Adapted from Igor Linkov, NNI R3 workshop
“Humans are quite bad at making complex, unaided decisions”

- Slovic et al, 1977 (quoted from Igor Linkov)
<table>
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<tr>
<th>Challenge</th>
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<td>Need rigorous methodologies for exposure assessment so that we can ensure that current nanoworkers are not being exposed to undue risk; hard to distinguish</td>
<td>• Development of rigorous and practical methodologies (Tsai and Ellenbecker; NIOSH) for exposure assessment for high volume and carbonaceous NPs</td>
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<td>• NIOSH field site team’s approach to working hand-in-hand with nano industry to decrease potential for exposure</td>
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Big Update from NIOSH this year: lower REL for CNTs lowered to 1 μg/m³

NIOSH Guidance on Nano Safety

- Current Intelligence Bulletin 63: Occupational Exposure to Titanium Dioxide
  DHHS (NIOSH) Publication 2011-160
- Approaches to Safe Nanotechnology: Managing the Health and Safety Concerns Associated with Engineered Nanomaterials
  DHHS (NIOSH) Publication 2009-125
- Interim Guidance for Medical Screening and Hazard Surveillance for Workers Potentially Exposed to Engineered Nanoparticles
  DHHS (NIOSH) Publication No. 2009-116
- Safe Nanotechnology in the Workplace
  DHHS (NIOSH) Publication No. 2008-112
- NIOSH Nanotechnology Field Research Effort Fact Sheet
  DHHS (NIOSH) Publication No. 2008-121

http://www.cdc.gov/niosh/topics/nanotech/pubs.html
Resource for Academic Research Laboratories:
http://www.cein.ucla.edu/

Includes:
• Quick tool
• Guidance for handling spills and waste
• SOP template
Major Advances Made in the Last Five Years in Rapid Hazard Identification and Hazard Prediction

**Materials of interest**

*OECD-WPMN (2008)*

- SWCNTs
- MWCNTs
- Ag nanoparticles
- Fe nanoparticles
- Ti dioxide
- Al oxide
- Ce oxide
- Zn oxide
- Si dioxide
- Nanoclays
- Dendrimers
- Au nanoparticles
- Fullerenes (C60)

**Appropriate Physicochemical Characterization**

- Intrinsic: Material as acquired or synthesized
- Extrinsic: Altered properties in biological medium
- Tox SAR: Properties proximately associated with injury

**Groupings:**

- Properties/SARS
- Toxicological mechanisms
- Usage/exposure

**High Throughput DLS**

- TEM
- SEC
- MALLS
- DLS/ ZetaSizer
- etc

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**Figure:**

- **X-axis:** Time (h)
- **Y-axis:** Various media types
- **Legend:**
  - No Agent
  - BSA 2 mg/mL
  - 1% FBS
  - 2% FBS
  - 5% FBS
- **Colors:** Heatmap indicating varying conditions over time.

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**Table:**

- | Time (h) | H2O | BEGM | DMEM | LB | TSB | SD | YPD |
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Advances in Risk-Based Decision Making

• Open and effective forums for communication between those who need to make the decisions and those who are developing tools
  – Alternative Testing Strategies Workshop in Los Angeles in January 2013
  – NNI R3 Workshop in Washington, DC in Sept 2013
  – Health Canada Workshop in October 2013
  – SRA Workshop in Washington, DC planned for April 2014
  – OECD Workshop in Washington, DC planned for April 2014
  – Multistakeholder Workshop on Categorization in Washington, DC planned for May 2014
Stakeholders Engaged in January 2013
Alternative Testing Strategy Workshop @ UCLA

- Brown Univ
- NCSU
- Rochester Univ
- UCLA & UCSB (UC CEIN)
- UC Davis
- BASF
- Dow
- Lockheed Martin
- Penn Bio Nano Systems
- Promega
- AFRL
- CA DTSC
- EPA
- NIOSH
- OSHA
- Berguson & Campbell
- Hamner Institute
- Intertox
- Porter Wright
- Tox Horizons
- Vireo Advisors
Process for Stakeholder Engagement at Alternative Testing Strategy Workshop

**Definition of Questions & Goals**
Conference calls with representatives from diverse stakeholder groups to define the focus and agenda for the workshop and solicit input on participants in advance.

**Advance Preparatory Work**
Workshop statements solicited from range of stakeholders and distributed to all of the participants in advance.

**2-Day Roundtable Workshop**
Presentations on relevant work and stakeholder perspectives; moderated discussions on specific agenda topics; minutes from workshop distributed to all immediately after workshop for input.

**Follow-up**
Development of group publication (with 30 co-authors from diverse stakeholder groups) summarizing workshop discussions and conclusions; planning calls for follow-on activities.

Provisional Consensus about ATS Use for Nano EHS from January Workshop

- ATS widely accepted to prioritize ENM hazard assessment but not yet ready for quantitative risk assessment or regulation.

- Hazard ranking and grouping of ENMs could assist regulatory and occupational decision making.

- ATS and predictive toxicological paradigms can be used to establish hazard categories and material grouping as a 1st tier of testing, which is used to prioritize more costly and elaborate animal studies.

- Any framework that considers ATS for regulatory purposes needs to be transparent, participatory and engage a broad stakeholder community.

Nel et al. *ACS Nano* 2013, 7(8), 6422-6433.
A predictive toxicological approach for CNT is potentially helpful for hazard ranking, prioritizing animal experiments, and grouping of materials.

The development of hazard ranking, material grouping and SARs can become an integral part of new product development.

It is important to consider dose-response extrapolation and exposure scenarios that link mechanistic and predictive toxicological assessment to risk assessment.

Nel et al. *ACS Nano* 2013, 7(8), 6422-6433.
A Multi-Stakeholder Perspective on the Use of Alternative Test Strategies for Nanomaterial Safety Assessment

Andre E. Nel,†,‡,§,∥,∗ Elina Nasser,†,¶, ∗hilary Godwin,†,§,∥ David Avery,†,¶ Tina Bahadori,∥ Lynn Bergeson,∥ Elizabeth Beryt,†,‡,∥ James C. Bonner,∥ Darrell Boverhof,∥ Janet Carter,∥ Vince Castranova,∥ J. R. DeShazo,†,∥ Saber M. Hussain,※ Agnes B. Kane,⊥ Frederick Klaessig,‡,⊥ Eileen Kuempel,∥ Mark Lafranconi,⊥ Robert Landsiedel,⊥ Timothy Malloy,∥⊥ Mary Beth Miller,⊥⊥ Jeffery Morris,∥⊥ Kenneth Moss,∥⊥ Gunter Oberdorster,∥√ Kent Pinkerton,⊥⊥⊥ Richard C. Pleus,⊥⊥⊥ Jo Anne Shatkin,⊥⊥⊥ Russell Thomas,⊥⊥⊥ Thabet Tolaymat,∥∥∥ Amy Wang,∥∥∥ and Jeffrey Wong

†Department of Medicine, Division of NanoMedicine, ‡University of California Center for Environmental Implications of Nanotechnology, §Center for Nanobiology and Predictive Toxicology, †California NanoSystems Institute, and §Fielding School of Public Health, University of California, Los Angeles, California 90095, United States, ¶U.S. Environmental Protection Agency, Washington, D.C. 20460, United States, ¶¶Bergeson & Campbell, P.C., Washington, D.C. 20037, United States, ⊥North Carolina State University, Raleigh, North Carolina 27695, United States, ∥The Dow Chemical Company, Midland, Michigan 48674, United States, ∥∥Occupational Safety and Health Administration, Washington, D.C. 20210, United States, ⊥⊥National Institute of Occupational Safety and Health, Morgantown, West Virginia 26505, United States, ⊥⊥⊥Luskin School of Public Affairs, University of California, Los Angeles, California 90095, United States, •Air Force Research Laboratory, Dayton, Ohio 45431, United States, ※Brown University, Providence, Rhode Island 02912, United States, ••Pennsylvania Bio Nano Systems, Doylestown, Pennsylvania 18901, United States, •••Tox Horizons, LLC, Maineville, Ohio 45039, United States, •••BASF Product Safety, Ludwigshafen, DE 67056, Germany, •••Los Angeles School of Law, University of California, Los Angeles, California 90095, United States, •••Lockheed Martin Company, Applied NanoStructured Solutions, LLC, Baltimore, Maryland 21220, United States, •••University of Rochester, Rochester, New York 14627, United States, •••⊥⊥⊥University of California, Davis, California 95616, United States, ⊥⊥⊥⊥Intertox, Seattle, Washington 98101, United States, ⊥⊥⊥⊥⊥Vireo Advisors, Boston, Massachusetts 02205, United States, ⊥⊥⊥⊥⊥Hammer Institutes for Health Sciences, Research Triangle Park, North Carolina 27709, United States, ⊥⊥⊥⊥⊥⊥U.S. Environmental Protection Agency, Cincinnati, Ohio 45268, United States, ⊥⊥⊥⊥⊥⊥⊥U.S. Environmental Protection Agency, Research Triangle Park, North Carolina 27711, United States, and ⊥⊥⊥⊥⊥úsqueda Department of Toxic Substances Control, Sacramento, California 95812, United States
Increasing availability of tools to help bridge the knowledge gaps available online

http://www.mendnano.com/
Good compilations/summaries of gaps exist and point to priorities as we move forward.
Continuing challenges

• Decisions about risk need to be made by a wide range of stakeholders in the absence of comprehensive data
• Many of those decisions need to be made in real time (i.e., formal risk assessment would not be the solution even if there were comprehensive data)
• Greater alignment of decision-making tools with needs of specific stakeholders is required

BUT THESE ISSUES ARE NOT UNIQUE TO NANO

Current: One material at a time descriptive animal testing


- Wide coverage of toxicants
- Robust scientific platform for screening
- Predictive tests utilizing toxicity mechanisms
- High throughput discovery
- Connectivity to in vivo

Proposed: Rapid mechanism-based predictive testing

Meng et al. ACS Nano. 2009
http://www.nap.edu/catalog.php?record_id=11970
http://www.epa.gov/ncct/toxcast
Today’s Presentations:

• Laura Hodson (NIOSH) “Tools for risk management of engineered NPs in the workplace”
• Candace Tsai (Purdue) “Potential inhalation exposure and containment efficacy when using hoods for handling nanoparticles”
• Yanjun Ma (Virginia Tech) “Effects of nanomaterial disposal on wastewater microbial communities and toxicity implications”
• Erik Muller (UCSB) “Exposure time independent assessment of CuO ENP toxicity on zebrafish egg hatching”
• Jie Hong (UTEP) “Toxicity effects of seven Cu compounds/nanoparticles in lettuce (Lactuca sativa) and alfalfa (Medicago sativa)”
• Arnab Mukherjee (UTEP) “Effects of bare ZnO nanoparticles on green pea plants in soil”