NanoEHS Landscape (mid 2016)

Greg Lowry
Walter J. Blenko, Sr. Professor of Civil & Environmental Engineering

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Key Questions to ask about Risk

Exposure
- Where do nanomaterials accumulate?
- Who is exposed?
- What form of the NM are we exposed to?
- What exposure concentration is expected?

Risk Characterization

Hazard
- What are the acute, chronic, and accumulative effects?
- What is the internal dose?
- How does transformation affect toxicity?
Exposure and Hazard are Inseparable

Exposure x Hazard = Risk
Nanomaterials are Dynamic

• Rates of processes are needed (not equilibrium)

\[ \frac{dn_{ki}}{dt} = \pm \alpha \beta n_i \gamma_j - k_{\text{dissolution}} n_k + k_{\text{formation}} n_k + k_{\text{transformation}} n_k + k_{\text{biouptake}} n_k + k_{\text{depuration}} n_k \]

- Settling
- Aggregation
- Deposition
- Precipitation
- Bioproduction
- Sulfdiation
- Complexation
- Hydroxylation
- Oxidation/Reduction …

• Transformation and aggregation affect reactivity, fate, toxicity and persistence
• System properties cannot be ignored
Evidence exists for particle-specific effects

Ag NP toxicity to *C. elegans*

Starnes et al., 2015, 2016, Env. Pollut.
Trophic transfer of nanoparticles occurs
Trophic Dilution → Bioaccumulation


We can identify and measure some nanomaterials in complex matrices

- Needed for regulatory purposes
- Needed for determining dose
- Improves mechanistic knowledge

Stegemeier et al., 2015 ES&T 49 (14) 8451
We have nanomaterial environmental fate and exposure models

- Determined key parameters describing ENM behaviors
- Second generation of models emerging
- Sign of maturing field


Dale et al. 2015 *ES&T* 49 (12), pp 7285
We can collect and share data for nanoEHS

• Important for read across

 QUERY 1

Citrate coated nanoAg particles
Between 40-50 nm in diameter
Dosed in in water column at 25ppm
Surrounding medium of 6.5 pH
Surface affinity
Accumulation in aquatic plant species

 QUERY 2

All nanoparticles
Between 40-50 nm in diameter
Measured in human & bovine serum
Surface affinity

Active projects throughout US & EU
Regulation of Nanomaterials is Advancing

• Adapting existing regulatory programs to include nanomaterials
  ○ TSCA New chemical review
  ○ REACH Registration
  ○ EU Cosmetics directive

• Labeling and Information Disclosure
  ○ Proposed TSCA reporting and recordkeeping rule
  ○ European registries

• International Cooperation
  ○ Canada-U.S. regulatory cooperation council
  ○ OECD Working party on manufactured nanomaterials
Where is nanoEHS Heading?

• “Realism”
  • Relevant exposure scenarios (functional assays)
  • Chronic low dose studies
  • Use of “transformed” materials in testing

• Optimizing Benefit-Risk Ratio (“Safe by design”)
  • Leveraging nanoEHS knowledge for effective and safe applications of nanomaterials
  • Environmental applications (water treatment, remediation)

• Categorization (groupings) of nanomaterials
“Realism”

- Incorporating “realism”
- Using relevant exposure scenarios/routes
- Chronic vs. acute exposures

Selck et al. 2016.
Functional Assays

- Measurement in **prescribed system**
- Quantifies a meaningful process for exposure, hazard or both
- Provides *rate constants* for exposure and hazard models

Hendren et al., 2015 *Sci. Tot. Env.* 536 p 1029
Optimizing Benefit-Risk Ratio ("Safe by Design")

Sotiriou et al 2014 *ES Nano* 1 144
Nanomaterial Categorization and Read-Across

ECETOC grouping
From Wendel Wohlleben

Arts et al 2015 Res. Tox. Pharm. 71 S1-S27
Some Important Gaps in Understanding

• No “accepted” testing protocols for nanoEHS
  • “translational roadmap” for exposure assessment
  • Validated bioassays for hazard and dosimetry metrics needed

• Models require further evolution
  • Lack of rate data to parameterize and validate models
  • Improve measurements in biological/environments media
  • Need sources of emissions

• Chronic low dose exposures not well studied

• Data and metadata standards needed for nanoinformatics

• Exposures during “use phase” are unknown

• Methods to quantify benefits of nanotechnology are lacking

• Effectiveness of public and private governance mechanisms

• “Next-generation” materials are not being addressed
Exposures along the Lifecycle

Manufacturing

Use Phase

End of Life

Workplace exposure

Exposure Potential??
NIOSH work produces results:

**Safe practices** protect workers and result in business success and public trust.

**Economic growth** will come from responsible advancements in manufacturing.

**Partnerships** with the private sector are key to the NIOSH success story. NIOSH is recognized by stakeholders as the “**most trusted and collaborative**” agency.

http://www.cdc.gov/niosh/topics/nanotech/
Dosimetry is Challenging

Dosimetry models

Cohen et al 2015, Nanomedicine 129
Harnessing and Quantifying the Benefits of Nanotechnology

- Energy
- Carbon sequestration
- Sustainable agriculture
- Clean water
- Restore/improve urban infrastructure
- Better medicines
From Nanomaterials to Nanomachines!

Fig. 3  Schematic showing the ever-expanding space of nanomaterial conjugation and the resulting permutations of nanomaterials.

Saleh et al., 2015 ES Nano 2 11-18
Questions to Consider in Breakouts

- Are there gaps in the draft goals and objectives? Are there objectives no longer needed?

- What will be the new/hot areas of research or challenges in the next 5-10 years?

- Outside of additional funding, what can the Federal Government do to support activities or address challenges in the areas above?

- How will we know when the nanotechnology enterprise is successful for NanoEHS? How do we measure this?

- What progress has been made in understanding the ethical, legal, and societal implications of nanotechnology? How has that progress been communicated?
NanoEHS Panel

• Brian Thrall
  • Pacific Northwest National Laboratory
  • nanomaterial cellular interactions

• Matt Hull
  • Virginia Tech (ICTAS, VTSuN, NanoSafe Inc.)
  • nanomaterial environmental fate/effects and nanoinformatics

• Debbie Kaiser
  • NIST
  • materials science, measurement and standards

• Timothy Malloy
  • UCLA
  • Environmental regulation and policy