Environmentally Realistic Exposures in Consumer Products

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Consumer Exposure Studies I: General Products

Vireo Advisors, LLC
Elements of Environmentally-relevant Exposure Assessment

**ELEMENTS**
- Realism
- “Reasonable worst case”
- Matrix effects
- Time
  - Aging
  - Frequency
- Dynamism

**FRAMEWORKS**
- Use category
- Complete exposure pathway
- Tiered approaches
- Life Cycle Stage

Vireo Advisors, LLC
Key dimensions of exposure

• Material characteristics – relevant metrics, predictive release properties
• Timing
• Receptor characteristics
• Magnitude
Approaches for Environmentally Relevant Exposure Assessment

- Nano LCRA
- Coating/textile standard methods (EPA nanosilver guidance)
- DF4nanoGrouping (ECETOC)
- NanoGRID/Collier et al 2015
- Sharma et al. 2015
NANO LCRA: Streamlined Life Cycle/ Risk Assessment Framework for Nanomaterials

ASSESS HAZARDS

EXPOSURE POTENTIAL

TOXICITY?

RISK ANALYSIS

RISK MANAGEMENT/
Prioritization/
Communication

ITERATE

Shatkin 2012
Key Attributes

- Screening level – Life cycle “thinking” – not a lengthy quantitative LCA study
- Consider range of relevant applications and use categories
- Consumer exposure can occur at any LC stage
- Also considers unintended uses
- Comparative - not necessarily quantitative data
- Flexible focus – highlighting differences from conventional substance
<table>
<thead>
<tr>
<th>Hazard</th>
<th>Magnitude</th>
<th>Likelihood</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>covalently bound particles in substrate</td>
<td>Exposure is to article where one component is &gt; 1% NM</td>
<td>Direct contact mitigated.</td>
</tr>
<tr>
<td></td>
<td>Exposure is to material &gt; 1% to &lt;10%</td>
<td>Unintentional - exposure possible based on activity.</td>
<td>Incidental - use 10-50 times per year</td>
</tr>
<tr>
<td>Med</td>
<td>particles potentially releaseable from substrate</td>
<td>Exposure to material is greater than 10% of mixture</td>
<td>Intentional - repeat exposure during normal use</td>
</tr>
<tr>
<td>High</td>
<td>dried particles in powder form</td>
<td>Exposure to material is greater than 10% of mixture</td>
<td>Intentional - repeat exposure during normal use</td>
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<tr>
<td></td>
<td>Intentional - repeat exposure during normal use</td>
<td>Regular - greater than 50 times per year</td>
<td>Regular - greater than 50 times per year</td>
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</tbody>
</table>
Example: Quantum Dots in a Coating Matrix
QD Vision – where color, power, and cost matter

• Founded 2004 out of MIT - 50+ employees (2009)
• Focus on displays & lighting markets
• First to market with quantum dot product for solid state lighting
• Thought leader in QD EH&S and technology
# Physical-Chemical Properties change during the product life cycle

<table>
<thead>
<tr>
<th>Life Cycle Stage</th>
<th>Stage of Product</th>
<th>Description</th>
<th>Agglomeration State/Aggregation</th>
<th>Composition</th>
<th>Crystal Structure</th>
<th>Particle Size/Size Distribution</th>
<th>Porosity</th>
<th>Purity</th>
<th>Shape</th>
<th>Solubility</th>
<th>Stability</th>
<th>Surface Area per particle (m²)</th>
<th>Surface Area total per batch (m²)</th>
<th>Surface Chemistry</th>
<th>Surface Charge</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Nano-material Reaction</td>
<td>Nanoparticles</td>
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<tr>
<td>2</td>
<td>Binding reaction</td>
<td>Micron size aggregate</td>
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<tr>
<td>3</td>
<td>Product formulation</td>
<td>Liquid Coating (in lab) with aggregate</td>
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<td>4</td>
<td>Storage and Transport</td>
<td>Liquid Coating (out of lab)</td>
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<tr>
<td>5</td>
<td>Application</td>
<td>Spray aerosol</td>
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<tr>
<td>6</td>
<td>Use</td>
<td>Dry Coated surface</td>
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<tr>
<td>7</td>
<td>Post Use (end of life)</td>
<td>Unknown</td>
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</table>
NANO LCRA Ex. 1
Hazard Identification for a nanoparticle in coating

IDENTIFY AND CHARACTERIZE HAZARDS

RAW MATERIALS → Process → PRODUCT → Packaging → APPLICATION/USE → disposal → REUSE/DISPOSAL

Nanoparticle and Binding Reactions (Stages 1&2) → Coating Formulation (Stage 3) → Storage and Transport (Stage 4) → Application and Use (Stages 5 & 6) → End-of-life (Stage 7)
NANO LCRA
Exposure Assessment Ex. 1

Event → Substrate → Pathway → Receptor Type

ASSESS EXPOSURE

RAW MATERIALS → Process → PRODUCT → Packaging → APPLICATION/USE → disposal → REUSE/DISPOSAL

Nanoparticle and Binding Reactions (Stages 1&2) → Coating Formulation (Stage 3) → Storage and Transport (Stage 4) → Application and Use (Stages 5 & 6) → End-of-life (Stage 7)
Potential Exposure – Stage 1
(In-lab example)

Event
- Spill
- Vaporize
- Direct Contact
- Transformation (oxidation/state change)

Substrate
- Indoor surface
- Air
- Clothing
- Skin
- Water
- Soil

Pathway
- Inhalation
- Dermal
- Ingestion/water
- Ingestion/soil
- Ingestion/biota

Receptor Type
- Human
- Environmental
Potential Exposure – Stage 6
(Out-of-lab example)

<table>
<thead>
<tr>
<th>Event</th>
<th>Spill</th>
<th>Vaporize</th>
<th>Direct Contact</th>
<th>Transformation (oxidation/state change)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substrate</td>
<td>Indoor surface</td>
<td>Air</td>
<td>Clothing</td>
<td>Skin</td>
</tr>
<tr>
<td>Pathway</td>
<td>Inhalation</td>
<td>Dermal</td>
<td>Ingestion</td>
<td>Water/soil/sediment</td>
</tr>
<tr>
<td>Receptor Type</td>
<td>Human</td>
<td>Environmental</td>
<td></td>
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</tr>
</tbody>
</table>
Application Phase

- Scenario 5.1
- Scenario 5.2
- Scenario 5.3
- Scenario 5.4
- Scenario 5.5
- Scenario 5.6
- Scenario 5.7
First Iteration Risk Characterization

• Exposure Assessment suggested only a few high concern scenarios

  • Lab/production stages are well controlled

• Designed and conducted product testing, to inform second iteration Exposure Assessment and Risk Characterization
Exposure Assessment
Initial Product Testing

• Tested highest concern exposure scenarios
  • Inhalation during coated product application
  • Wear testing of applied/dried coating product

• Prepared coated plaques
• 1 year accelerated aging simulation
• Specially designed test lab
• Real time and electron microscopy
Measured Background Levels of Nanoparticles
Nanoparticle counts - individual runs and average during spraying
Nanoparticle counts – sanding tests
Transmission Electron Micrograph of Sprayed Paint Sample
Second Iteration Risk Characterization

• Test results demonstrated very low exposure risk for application and use

• Risk Characterization updated – developed safe handling instructions

• Further review of recent literature lead to similar toxicity conclusions

• Overall product risk characterized as low
QDV LCRA Findings

• Life cycle exposure
  • Manufacturing and production phases well controlled
  • Exposure during application not distinguishable from background
  • Aggressive “wipe” testing produced no detectable exposure
  • End of life exposures uncontrolled

• Toxicity data extremely limited
  • recommendations for testing product as used

• Risk management focus on exposure prevention
Example: Tiered Research Needs for a Nano-Pesticide

Conditional Registration for Nanosilver Fabric Coating (EPA 2011)
DF4 nano Grouping (Arts et al 2015)

Fig. 2. The decision-making framework for the grouping and testing of nanomaterials (DF4nanoGrouping).
NanoGRID Framework

**TIER 1**
Screening Criteria
Based on material amount, size, properties, technology categories, and use

**TIER 2**
Release Potential
Conservatively assume 100% release, determine actual amount released

**TIER 3**
Environmental Persistence
Determine free particle persistence and dissolved fraction

**TIER 4**
Sustainability Testing
Biological testing for acute and chronic toxicity

**TIER 5**
In Depth Product Investigation
Material specific and site specific

Proceed through process until an informed decision is possible

Adequate Information for Decision

Source: Collier et al. 2015
Sharma et al. “Framework to evaluate exposure relevance and data needs for risk assessment of nanomaterials using *in vitro* testing strategies.”

*Risk Analysis* [Under Review].

Slides from:
Monita Sharma, Jo Anne Shatkin, Richard Canady, Carolyn Cairns, Amy J. Clippinger
presented at the

Society for Risk Analysis
Workshop on Alternative Testing Strategies for Nanomaterials

September, 2014 Washington, DC
Framework for assessment

Stage 1: Exposure assessment

Stage 2: Context-specific NM characterization

Stage 3: Tailor an in vitro testing strategy to exposure conditions

Stage 4: Evaluate strength of evidence for exposure

Sharma et al.
# Stage 1: Exposure assessment

<table>
<thead>
<tr>
<th>Determine likely route of exposure (inhalation, oral, dermal)</th>
<th>Determine likely exposure medium (e.g., water, air, dust, soil)</th>
<th>Exposure monitoring</th>
<th>Developement of exposure scenarios</th>
</tr>
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</table>

**Determine likely route of exposure:** Inhalation, oral, dermal.

**Determine likely exposure medium:** Water, air, dust, soil.
Stage 2: Context-specific NM characterization

- Evaluation of analytical methods
- Evaluation of phys-chem properties
- Grouping & read-across
Stage 3: Tailor an in vitro testing strategy to exposure conditions

Determine physiologically-relevant exposure conditions:
- cell types
- relevant matrix, such as stimulant or artificial fluids (e.g., lung surfactant, saliva, or gastric fluids)

Establish appropriate dose and dose metrics

Test using a realistic nanomaterial form e.g., appropriate life cycle stage when exposed (based on anticipated corona formation, dissolution, and aggregation)
## Stage 4: Evaluate strength of evidence for exposure

<p>| Evaluate existing data for its relevance to expected human exposure scenario | Use existing data to determine what additional testing is necessary, if any | Use results to further develop and optimize <em>in vitro</em> testing strategies |</p>
<table>
<thead>
<tr>
<th>Test</th>
<th>Exposure Source</th>
<th>Dose</th>
<th>Transformations</th>
<th>Biological Response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NM Characterization</strong></td>
<td>Has NM been adequately characterized in source matrix?</td>
<td>Is the NM introduced to the system in a form representative of the human situation?</td>
<td>Can administered NM be effectively differentiated from transformation by-products, conventional scale substances and other NMs endogenous to the biological system?</td>
<td>How do the identified NM features relate to biological responses of interest? How is response being related to NM dose measurements?</td>
</tr>
<tr>
<td></td>
<td>How is variability in NMs in source matrix evaluated and reported?</td>
<td>How completely are NMs characterized with biologically relevant criteria?</td>
<td>Are indirect indicators, radiolabeling or fluorescent tags needed to track NMs? Do they interfere with NM biological activity, detection or characterization?</td>
<td>What parameters of the biological system most influence NM activity and how are they being monitored?</td>
</tr>
<tr>
<td></td>
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<td>What, if any, impacts result from required sample prep processes?</td>
<td>What is the significance of possible bio-corona formation, dissolution, aggregation/agglomeration? How might such transformations affect NM measurements?</td>
<td>What is the significance of possible bio-corona formation, dissolution, aggregation/agglomeration? How might such transformations affect NM toxicity?</td>
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<td><strong>NM Detection</strong></td>
<td>Is analytical equipment compatible with NMs and source matrices of interest?</td>
<td>Is analytical equipment compatible with NMs and biological matrices of interest?</td>
<td>How will NM measurements be correlated with dose-response measures?</td>
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<td><strong>Dose-Response Correlates</strong></td>
<td>How can dose-response data be linked back to exposure source characterization and vice versa?</td>
<td>What, if any, impacts result from the required sample preparation processes?</td>
<td>How well are findings transferable to other cell types?</td>
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<td>What, if any, assumptions are inherent in the exposure and dose-response assessment?</td>
<td>How well does administered dose compare to delivered dose?</td>
<td>How well does delivered dose relate to cellular dose?</td>
<td>Are cells used in the test system the most vulnerable to or representative of NM exposure and its toxic effects?</td>
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<td>Does the test system simulate mechanical stresses important for physiological response?</td>
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<td>Does the test system contain microbial and other biological substances that are important mediators of NM toxicity?</td>
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<td>Does the test system simulate physiology in both diseased and healthy states? What is unique about NM behavior in these states?</td>
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<td>Biological Response</td>
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Sharma et al.
Key themes

• Tiered approaches are logical

• Address the 5 “W’s” (& How)

• Ensure testing is “environmentally relevant”

• Scenario ranking prioritizes key pathways for detailed evaluation.
Thank you

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