Adopting a Life Cycle Approach to Risk Analysis for Novel Forest Products

Jo Anne Shatkin, Ph.D.
CLF Ventures, Inc.

Unlocking the Potential of Nano-Enabled Biomaterials

Edmonton, Alberta
June 24, 2009

Note: The views presented here are those of the presenter only, and do not represent the views of CLF Ventures, or CLF.
Topics

- Key concerns about engineered nanomaterials
- Evaluating risks to access benefits
- Addressing issues across the product life cycle
- Overview of life cycle/risk frameworks
CLF Ventures, Inc.

- We work at the intersection where organizations meet their stakeholders and the environment.
- We help organizations implement projects with economic and environmental benefits.
What CLFV Does
"JUST ANOTHER COUPLE OF PAGES."
Why Be Concerned about Nanomaterial Impacts?

- Novel properties
- History dictates action
- Technology advancing quickly
- Paucity of information
- Potential for wide dispersion in the environment amidst uncertainty
- Significant NGO activity and low consumer knowledge
- Few standards or guidelines - yet!
Key Concerns about Nanotechnology Risks

- Avoiding a “nano” legacy
- Uncertainty about health and environmental risks
- Lack of standards
- Hype – it’s unclear which issues are real, perceptions a risk, too
Issues

• Lack of information on potential effects of NM on human health and the environment

• Toxicological uncertainties for NM
  – Large surface area relative to size
  – Reactivity and catalytic potential
  – Possible translocation within organism
  – Potential for bioaccumulation

• Concerns about life cycle issues
Challenges Present Opportunities

- Can be proactive about identifying and reducing risk
  - Promotes environmentally sustainable technology development
  - If EHS concerns, need to develop approaches for assessment and management

- Engineering materials provides flexibility to address EHS concerns up-front, if identified

- Understanding risks provides a competitive edge in efficiently managing them
  - When risks are anticipated, can plan for them, rather than reacting
Understanding risks allows efficient management of them

- **Risk Assessment:**
  - Is increasingly part of regulatory structures
  - Allows decision making under uncertainty
  - Can address potential concerns throughout the life cycle of a product
  - Prioritizes research directions
  - Identifies areas for product innovation
  - Reduces potential for unforeseen impacts
  - Provides a tool box of approaches
Advantages of a Risk-based Approach

- Practical
  - Can inform decision making

- Efficient
  - Early screen for liabilities, required testing

- Proactive
  - Considers technical, societal, market and regulatory
Differentiating Hazards from Risks

- All materials are toxic at some concentration
- Risk = hazard * exposure probability
- There must be an exposure for there to be a risk
Key Elements of a Risk-based Analysis Framework for Nanomaterials

- **Tiered – Start with Screening Tools**
  - Use early in the product development cycle to identify potential concerns

- **Address Life Cycle Concerns**
  - Consider worker, consumer, and environmental issues

- **Focus on Exposure**
  - Indicators, not Perfect Data
  - Hazard, Exposure and Toxicity Dimensions

- **Adapt Products to Findings (Evaluative)**
  - Incorporate findings into actions
Screening for Potential NANO Risks across the Product Life Cycle

- Raw materials
  - novel structures, material combinations, ↑ reactivity
- Manufactured Forest Products
  - New potential exposures, applications, waste generation
- Packaging and distribution
  - Customer knowledge, communication, labeling
- Product Usage
  - Novel behavior in matrix, potential consumer exposure
- End of Life
  - Environmental dispersion; recycling/disposal impacts
In the product life cycle, environmental exposures are less easily assessed and managed.
Proposed Risk Frameworks for Nano

- Life Cycle Approaches to Risk incorporate biological and environmental exposures in the framework
  - CEA Comprehensive Environmental Assessment (Davis 2007)

- Screening Approaches can still be data intensive
  - Nano Risk Framework (EDF/DuPont 2007)
  - ILSI RF Risk Screening Framework (toxicology only)
International Life Sciences Institute – Risk Sciences Institute Screening Approach

**Physical Chemical Properties**
- particle size and size distribution;
- shape;
- surface area;
- chemical composition;
- surface chemistry;
- surface contamination;
- surface charge (in suspension, solution, and in powder form);
- crystal structure;
- particle physicochemical structure;
- agglomeration state;
- porosity;
- method of production;
- preparation process;
- heterogeneity;
- prior storage of material; and
- concentration.

**In vitro assays**
- **Cellular**
  - lung;
  - skin;
  - mucosal membrane;
  - endothelium, blood;
  - spleen;
  - liver;
  - nervous system;
  - heart; and
  - kidney studies.

- **Non-cellular**
  - nanoparticle durability;
  - protein interactions;
  - complement activation;
  - pro-oxidant activity.

**In vivo assays**
- Tier 1 evaluations for
  - pulmonary, oral, dermal and injection exposures;
  - inflammation;
  - oxidant stress; and
  - cell proliferation in select organs.

- Tier 2 evaluations for
  - pulmonary exposure;
  - deposition; translocation;
  - toxicokinetics/biopersistence studies;
  - multiple exposure effects;
  - reproductive effects;
  - alternative model studies;
  - mechanistic studies.

Oberdörster, G. et al. 2005. Particle and Fibre Toxicology 2005, 2:8
http://www.particleandfibretoxicology.com/content/2/1/8
Comprehensive Environmental Assessment (CEA)

CEA ≈ LC + RA

LC = Product Life Cycle framework
RA = Risk Assessment paradigm

### Comprehensive Environmental Assessment (CEA)

<table>
<thead>
<tr>
<th>Life Cycle Stages</th>
<th>Environmental Pathways</th>
<th>Fate &amp; Transport</th>
<th>Exposure</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feedstocks</td>
<td>Air</td>
<td>Primary contaminants</td>
<td>Biota</td>
<td>Eco-systems</td>
</tr>
<tr>
<td>Manufacture</td>
<td>Water</td>
<td>Secondary contaminants</td>
<td>Human populations</td>
<td>Human Health</td>
</tr>
<tr>
<td>Distribution</td>
<td>Soil</td>
<td></td>
<td></td>
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<tr>
<td>Storage</td>
<td>Food chain</td>
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<td>Use</td>
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<tr>
<td>Disposal</td>
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</tbody>
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NANO SLCRA
**NANO SLCRA**

**Case Example**
Nanocrystalline Cellulose for Packaging Application

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**Analysis**

**Hazard Identification**
- No nanomaterials in raw materials
- Extract released during isolation process
- Uncontained disposal practices for Nano-containing wastes
- Product contains unbound crystalline particles
- Post application recycling distributes nanoparticles

**Exposure Assessment**
- Material production process not enclosed
- Packaging process is very dusty
- Use exposes consumers to nanoparticles
- Disposal practices create secondary human exposure pathways

**Recommendations**

**Toxicity Assessment**
- Material characterization
- Design protocol to assess toxicity of packaging product in vivo and in vitro

**Inhalation and Dermal Exposures**
- Develop tracking system
- Work with solutions not particles
- Contain process releases
- Provide PPE/training for handling production materials
- Conduct training
- Develop MSDS
- Assess use/disposal exposures

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**CLF Ventures, Inc.**
NANO SLCRA Streamlined Framework

- Use as a screening tool to identify and prioritize health and environmental/ process issues
- Complement with regulatory/ market competition/ societal concern analysis
- Analysis identifies key uncertainties – can inform product development
- Revisits early decisions with new information
NANO SLCRA Features

• Proactive, early stage, affordable, easily implementable process even with few available data.

• Develops risk management practices based on minimizing exposure and potential human health effects and environmental impacts.

• Applicable for NM research and development, product manufacturing, consumer applications, and evaluation of NM fate in the environment.

• Prioritizes future data needs.
Summary

• Innovation is inherently risky

• The environmental, safety and health aspects of innovative materials are not well understood

• Companies, workers, customers and the environment benefit from a proactive approach to identify and address potential risks early in the innovation cycle

• Screening Level Risk Assessment is a useful tool for identifying and managing amidst uncertainty
"Look, I'd like to avoid overkill, but not at the risk of underkill."

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Thank You Very Much!

Jo Anne Shatkin, Ph.D.

CLF Ventures
jashatkin@clf.org

+1 617-850 1715
Managing the Health and Environmental Risks of Nanotechnology in the Forest Products Industry

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Findings: Council of Canadian Academies Expert Panel on Nanotechnology about Engineered Nanomaterial Risks

3.1 Nanomaterials can pose particular challenges to risk assessment, and hence to regulation, because they exhibit properties based on their physical structure and their chemistry.

3.2 The diversity of possible nanomaterials is vast and the tolerances of a biological system to changes in the physicochemical properties of nanomaterials that determine their behaviour are poorly understood.

3.3 To date, there are no unique biological effects associated with exposure to nanomaterials, but there is still a poor understanding of how specific nanomaterials lead to specific endpoints.
3.4 Prevailing *human and ecological risk assessment frameworks are robust*, but their application to nanomaterials requires new ways of measuring exposure, dose and response.

3.5 *Changes in the potential for nanomaterials to cause harm at different stages in their life-cycle imply a need for a life-cycle approach to risk assessment.*

3.6 There are *inadequate data to inform quantitative risk assessments* on current and emerging nanomaterials. At most, only qualitative risk assessments are feasible, given the current state of knowledge.

3.7 Systematically-targeted *research is needed* to fill the knowledge gaps and reduce uncertainty.
Risk Analysis:

**Advancing the Science for Nanomaterial Risk Management Sept 2008, Washington DC**

- Public expert workshop organized by the Society for Risk Analysis *Emerging Nanoscale Materials Specialty Group*

- Brought together risk analysts with nano-experts in to advance our understanding and build new networks

- A deliberative workshop to address:
  - What is “nano” about risk assessment for nanoscale materials?
  - What tools in the field of risk analysis can be used for managing nanomaterials?
  - What are the needs for communicating about risks?
  - How to consider nanotechnology benefits for risk reduction?
Risk Analysis: Advancing the Science for Nanomaterial Risk Management

Workshop Co-Sponsors
Repeated themes

- Considerable uncertainty in understanding of nano-specific attributes and relevance to biological and environmental effects
- Size matters, but it's not clear there is a bright line, e.g. at 100 nm
- Regulatory approaches are likely to be case-by-case in the near term
- Perceptions outside of industry and the government are critical, and proactive measures to communicate with the public are critical to ensuring the development of nano-products
Key Issues Identified

- Many previously identified concerns are not specific to nanomaterials or nanotechnologies
- Can address some concerns “by design”
  - Engage risk analysts to work with product designers
- Need for a long term plan/framework to answer questions with pending data
- Conduct case-by-case evaluations to elicit key concerns
- Conduct expert workshops more broadly to identify issues
- Test/compare adaptive approaches to risk analysis that incorporate the product life cycle
Project on Emerging Nanotechnologies/Grocery Manufacturers Association Regulatory Case Study

- Examined scientific and regulatory challenges for emerging nanoscale materials in food packaging
- Identified technical challenges
  - Characterizing the material
  - Adequacy of safety testing
- Identified regulatory challenges
  - Data needs for regulatory review
  - Definitions
  - Thresholds are based on mass
- Recommends Industry Stewardship, and adopting a life cycle approach to risk analysis for ENM

(Taylor 2008 Assessing the Safety of Nanomaterials in Food Packaging)
Consider Life Cycle Approaches to Risk Assessment and Risk Management

- Provides a framework for assessing biological and environmental exposure - a significant advance
- How to implement these approaches – not part of the current risk management paradigm
- A variety of frameworks exist/proposed
  - Comprehensive Environmental Assessment (Davis 2007)
  - Nano Risk Framework (EDF/DuPont 2007)
NANO SLCRA
Conceptual Exposure Model- Nano Clay

Gas barrier layer includes nanoclay composite in food or beverage package

**USE**
- discard

**DISPOSAL**
- land disposal
- incineration

**REUSE**
- refill
- alternate use
- recycle

**PATHWAY**
- LEACH TO GW
- AIR RELEASE
- SECONDARY -SURFACE WATER
- SECONDARY -SOIL

**RECEPTOR**
- HUMAN
- HUMAN/ECO

**PATHWAY**
- OCCUPATIONAL
- SECONDARY USER
- RAW MATERIAL TO NEW PRODUCT
- INCIDENTAL

**RECEPTOR**
- HUMAN
- HUMAN/ECO
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Environmental Defense – DuPont Nano Risk Framework

- Describe Material & Application
  - Properties
  - Hazards
  - Exposure
- Evaluate Risks
- Assess Risk Mgmt
- Decide, Document & Act
- Review & Adapt

Iterate

Assess, prioritize & generate data
Regulatory Implications from the State of the Science

• Lack of tools for measurement (and lack of data) prohibit exposure measurements; limit ability to conduct risk assessments; and prevent monitoring

• Safe levels for existing nanomaterials are unknown and prohibit standard setting

• Significant research is required to understand whether nanomaterials pose novel risks

• Slow pace of scientific research could slow the regulatory process and create greater risk for nanotech entries to market – case law may prevail, or consumers may reject it
Nanoscale particles vs. Nanotechnology

- Long history of using physical and chemical methods to create small molecules
- Emerging nanoscale materials are novel
  - E.g. nanocrystalline cellulose
- Is this a reasonable distinction?
- Why focus on size—is there a scientific rationale
  - No biological basis for 100 nm cutoff
- Is there a need for regulatory distinction
  - Are existing nanoparticles demonstrated to be safe?
- Can the public discern the difference?
Consumer and NGO Perspectives
Consumer Research Suggests Benefits Recognized

- 46% of respondents in the U.S. and 39% in Canada thought nanotechnology “will improve our quality of life in the next twenty years,” and 6% in the U.S. and 5% in Canada thought it will “make things worse.” Significantly, fully 35% of those in the U.S. and 43% of Canadians did not know or declined to answer (Priest 2006).

- 60% of the 3909 U.S respondents agreed to the statement “human beings will benefit greatly from nanotechnology” versus only 9% that agreed nanotechnology is “threatening to make humans an endangered species” (Bainbridge 2002).
Public perceptions limited by lack of knowledge

- **Low public understanding of nanotechnology**
  - 7 in 10 U.S. adults have heard little or nothing about nanotechnology – Canada is similar
  - Only 6% say they have heard a lot about, whereas two in five (42%) of adults have heard nothing about it

- …poses challenges for consumer acceptance
  - “There are significant challenges to portray the nanometer scale world to the general public. [The public’s] foundation is not sufficient to allow them to fully embrace the scale” (Batt et al. 2008: 8).
  - Where there is little manifest social benefit (as has been the case, arguably, with GM food), small risks may become powerful dissuaders” (Priest 2006).
Broader Societal Risks of nanotechnology

- Consumers may not perceive the benefits of nanotechnology and may therefore not purchase associated products
- One bad incident may irreversibly undermine public confidence in nanotechnology
- Lack of regulation could prove to be a liability for industry when it comes to nanotechnology
- Some types of product processing may generate nanoparticles, and some groups may perceive or want to promote this as nanotechnology, even if they are not engineered nanomaterials
### Pivotal non-governmental organization (NGO) reports, collaborations and alliances

<table>
<thead>
<tr>
<th>Organization</th>
<th>Report/Action</th>
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<tbody>
<tr>
<td>ETC Group **</td>
<td><em>Down on the Farm: The Impact of Nano-scale Technologies on Food and Agriculture</em> (2004)</td>
</tr>
<tr>
<td>ICTA, FoE and coalition of groups</td>
<td><em>Citizens Petition to the US FDA on cosmetics</em> (May 2006)</td>
</tr>
<tr>
<td>60 International NGO - coalition</td>
<td><em>2007 Joint Statement of Principles for the Oversight of Nanotechnologies and Nanomaterials</em></td>
</tr>
<tr>
<td>Environmental Defense Fund and DuPont (USA)</td>
<td><em>“Nano Risk Framework”</em> (July 2007)</td>
</tr>
<tr>
<td>NRDC</td>
<td><em>EHS nanotechnology framework</em> (May 2007)</td>
</tr>
<tr>
<td>The Soil Association (UK)</td>
<td><em>Ban on nanomaterials from the organic cosmetics, foods and textiles that it certifies</em> (Jan 2008)</td>
</tr>
<tr>
<td>Friends of the Earth (FoE) Australia</td>
<td><em>Out of the laboratory and on to our plates: Nanotechnology in food and agriculture</em> (March 2008)</td>
</tr>
<tr>
<td>ICTA-led coalition</td>
<td><em>Sues US EPA for failure to regulate NanoSilver</em> (May 2008)</td>
</tr>
</tbody>
</table>
Most common Advocacy NGO appeals

<table>
<thead>
<tr>
<th>Consumer/labor groups</th>
<th>Environmental NGOs</th>
<th>Ethical science and technology groups</th>
<th>Bio/Ag oriented groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Open public dialogue on nanotechnology</td>
<td>• Regulation</td>
<td>• Regulation</td>
<td>• Regulation</td>
</tr>
<tr>
<td>• Worker protection</td>
<td>• Public dialogue</td>
<td>• Moratorium</td>
<td>• Moratorium</td>
</tr>
<tr>
<td>• Labeling</td>
<td>• Increased research on nanotechnology</td>
<td>• Equity in costs and benefits</td>
<td>• Labeling</td>
</tr>
<tr>
<td></td>
<td>• Precaution</td>
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</tbody>
</table>
News Item: Scientists undecided about the need for nanoparticle regulation.

"I'm looking for a loophole!"
Opportunities

Develop Industry-wide Product Stewardship Initiative

- Agree on standards for testing nanomaterials and assuring safety
- Increasing the transparency of industry-led science to improve credibility
- Use risk analysis to put risks and benefits in context
- Proactive communication about processes to test the safety of nanomaterials can influence consumer confidence (e.g. ILSI NA work on nanosilver)
- Educate consumers about the benefits of nanotechnology, e.g. for food safety, to improve perceptions
Summary

- The environmental, safety and health aspects of innovative materials are not well understood and are perceived as risky.

- A proactive approach, using Streamlined LC Risk Assessment to identify and address potential risks early in the innovation cycle is a useful tool for identifying and managing amidst uncertainty.

- There is an opportunity for industry and the government, in partnership to address the risks, and realize the benefits.
Thank You Very Much!

Jo Anne Shatkin, Ph.D.

CLF Ventures

jashatkin@clf.org

+1 617-850 1715
NANO SLCRA Adaptive Screening Risk Assessment Framework for NM

IDENTIFY AND CHARACTERIZE HAZARDS

ASSESS EXPOSURE

EVALUATE TOXICITY

RAW MATERIALS  Process  PRODUCT  Packaging  USE/REUSE/DISPOSAL

CHARACTERIZE RISK

RISK MANAGEMENT

ITERATE
Framing the Issues for Health/Environmental Risk Assessment

1. Hazard Identification
2. Toxicity Assessment
3. Exposure Assessment
4. Risk Characterization

(NRC 1983)
Framing the Issues:
Hazard characterization for nanotechnology

- How to define nanomaterials
  - Distinguish engineered from other nanoparticles?
  - Are agglomerated or aggregated particles nano?
  - Is a composite material containing nanoparticles “nano”?
- Do we characterize the particle, or the product?
- What are the appropriate measurement units?
- How to characterize variability, uncertainty?
Framing the Issues: Exposure Assessment for Nanotechnology

• Need new ways to characterize exposure
  – Mass may not be most useful measure
  – When does size trigger new measures?
  – How does the matrix affect exposure?
• Limitations of available analytical techniques
• Methods require low detection limits
• Also need to characterize “background” exposures
• Limited data on transport and fate
Framing the Issues: Dose Response for Nanotechnology

• Uncertainty in defining dose
• Different behavior of nanoparticles
  – Are there new effects?
• Difficulty in measuring responses- data are equivocal
• ADME
• Diversity of materials and characteristics
  – When are particle distributions different?
  – What are the tolerances?
Summary of “Nano” Toxicology

• Limited data available from well designed studies
  – most is in vitro or inhalation studies

• Reactive oxygen formation (ROS) is a commonly observed mechanism of toxicity
  – Leads to inflammation

• Study conditions affect results

• Surface coating/particle size/surface charge/surface area/ contamination and aggregation may be important
Oral Toxicology of Nanoparticles

• Studies suggest nanoparticles may act as “Trojan horses” - may be particularly important in the GI tract, opening the door for increased exposure to immunoactive molecules

• Similar to most existing research on nanoparticles, studies evaluating the potential relationship between microparticles and initiation of Crohn’s disease and inflammation generally, are equivocal
Framing the Issues: Characterizing Risks of Nanomaterials

- Current frameworks adequate and appropriate, but significant model and parameter uncertainty
- Still much research to be done to quantify risks
- Need to address uncertainty and variability
- Available studies are comparative, e.g.
  - Brunner et al. (2006) (comparative in vitro toxicity)
  - Sayes et al. (2004; 2006) (cytotoxicity of variously substituted C60 fullerenes)
  - Robichaud et al. (2005) (comparative risks of nanomanufacturing)

- New Metrics and Endpoints for Risk?