Objectives

• Approach - NANO Life Cycle Risk Framework
• Exposure: market analysis of nanocellulose
  – Methodology
  – Volume estimates
  – Implications for Exposure and Research Needs
• Toxicology
• Outline the roadmap to sustainable development
Dimensions of New Product Sustainability

Critical for Pre-commercial Assessment

Production

Life Cycle Impacts

Stewardship

SAFE/TRANSPARENT
APPLICATION/USE

END OF LIFE

RAW MATERIALS

PROCESS

PRODUCT

Packaging

APPLICATION/USE

Reuse/Recycle/Disposal

Production

Life Cycle Impacts

Stewardship

Critical for Pre-commercial Assessment
NANO LCRA for Nanocellulose
Iterative Risk Assessment

IDENTIFY AND CHARACTERIZE POTENTIAL HAZARDS

ASSESS EXPOSURE POTENTIAL & RISK

PRIORITIZE DATA GAPS

RISK MANAGEMENT/STRATEGY TO ADDRESS GAPS

END OF LIFE

APPLICATION/USE

Packaging

PRODUCT

Process

RAW MATERIALS

Reuse/Recycle/Disposal
# Environmental Market Drivers

<table>
<thead>
<tr>
<th>Retailer demand</th>
<th>Regulatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light-weighting to improve fuel efficiency</td>
<td>Café standards</td>
</tr>
<tr>
<td>Energy Efficiency</td>
<td>Stretch codes; building codes</td>
</tr>
<tr>
<td>Bio-based materials</td>
<td>Shopping bag/water bottle bans</td>
</tr>
<tr>
<td>Greener Consumer Products</td>
<td>EU Directive –vehicle recycling</td>
</tr>
<tr>
<td>Carbon Dioxide targets</td>
<td>Landfill bans/ recycling targets</td>
</tr>
<tr>
<td>Renewable/compostable</td>
<td></td>
</tr>
</tbody>
</table>
### Targeted Applications

<table>
<thead>
<tr>
<th>HIGH VOLUME</th>
<th>LOW VOLUME</th>
<th>NOVEL and Emerging APPLICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cement</td>
<td>Wallboard Facing</td>
<td>Sensors – medical, environmental, industrial</td>
</tr>
<tr>
<td>Automotive Body</td>
<td>Insulation</td>
<td>Reinforcement fiber - construction</td>
</tr>
<tr>
<td>Automotive Interior</td>
<td>Aerospace Structure</td>
<td>Water filtration</td>
</tr>
<tr>
<td>Packaging Coatings</td>
<td>Aerospace Interiors</td>
<td>Air filtration</td>
</tr>
<tr>
<td>Paper Coatings</td>
<td>Aerogels for the Oil and Gas Industry</td>
<td>Viscosity modifiers</td>
</tr>
<tr>
<td>Paper Filler</td>
<td>Paint-Architectural</td>
<td>Purification</td>
</tr>
<tr>
<td>Packaging Filler</td>
<td>Paint-Special Purpose</td>
<td>Cosmetics</td>
</tr>
<tr>
<td>Replacement -Plastic Packaging</td>
<td>Paint -OEM Applications</td>
<td>Excipients</td>
</tr>
<tr>
<td>Plastic Film Replacement</td>
<td></td>
<td>Organic LED</td>
</tr>
<tr>
<td>Hygiene and Absorbent Products</td>
<td></td>
<td>Flexible Electronics</td>
</tr>
<tr>
<td>Textiles for Clothing</td>
<td></td>
<td>Photovoltaics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recyclable Electronics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3D printing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Photonic Films</td>
</tr>
</tbody>
</table>
Volume Estimates

Vol = M * NC content * MP

M = recent market size
NC Content = % nanocellulose
MP = market penetration rate
Market Study Assumptions

• Recent research reports/expert network to identify target applications
• Current market size is maintained (no growth)
• Commercialization within the next 3-12 years
• Dry yield 40%
• Cost competitive with current alternatives
• Technical issues addressed
• No barrier to adoption
Adding Nanocellulose to Cement

• 0.5% adds 20% to strength; allows 17% less cement in concrete

• Global cement market volume is 3.3 Billion TPY
  – Weight addition of 0.5% CNC (Cao et al. 2013) >>> 16.5 million tonnes CNC

• This study – U.S. adoption for ultra-high performance structural cement market – pre-stressed and pre-treated only (5.7 M tonnes cement >> 21,000 tonnes CNC @75% market penetration)
Estimated Market Penetration Rates - High Volume Applications

- UHPS Cement
- Textiles for Clothing
- Hygiene and Absorbent Products
- Paper Filler
- Packaging Filler
- Packaging Coatings
- Automotive Body
- Paper Coatings
- Automotive Interior
- Plastic Film Replacement
- Replacement for Plastic Packaging

- Pessimistic
- Moderate
- Optimistic
Annual Tonnage Estimate by Forest Products Subsector

- Packaging
  - Film
  - Fiber/plastic replacement
  - Filler
  - Coatings

- Paper

- Wovens
Exposure Scenarios

• Worker
  – inhalation exposure to dry particles
  – Manipulating composites

• Consumer
  – Dermal
  – Food contact
  – Shredding/recycling

• Environmental
  – Water; waste; recycling
<table>
<thead>
<tr>
<th>Exposure Duration</th>
<th>Study</th>
<th>Material</th>
<th>Immunotoxicity</th>
<th>Cytotoxicity</th>
<th>Neurotoxicity</th>
<th>Genotoxicity</th>
<th>Carcinogenicity</th>
<th>Lethality</th>
<th>Systemic</th>
<th>Pulmonary</th>
<th>Cardiovascular</th>
<th>Dermal</th>
<th>Underlying</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CMF</td>
<td>▼</td>
<td>▼</td>
<td>▼</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Norppa (2012)</td>
<td>CNF</td>
<td>●</td>
<td>○</td>
<td>×</td>
<td>○</td>
<td>○</td>
<td></td>
<td></td>
<td>×</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ferraz, et al (2012)</td>
<td>CNF-PPy (as-is)</td>
<td>□</td>
<td>○</td>
<td>○</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNF-PPy (aged)</td>
<td>□</td>
<td>○</td>
<td>○</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNF</td>
<td>◆</td>
<td>◊</td>
<td>×</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SYMBOlS**

- ▼ Mouse macrophage
- ▼ Human macrophage
- ■ Human fibroblast
- □ Human monocyte
- ◆ Human keratinocyte
- ◊ Human cervix carcinoma cells
- ◊ Mouse hepatoma
- ● Human macrophage
- ○ Human cervix carcinoma cells & Boar sperm
- ○ Human bronchial epithelial cells
- ○ Human bronchial epithelial cells
- ◆ Human keratinocyte
- ◊ In vivo mouse
- ◊ Human bronchial epithelial cells
- ◊ In vivo mouse
- ◊ Nematode-C. elegans
<table>
<thead>
<tr>
<th>Pathway</th>
<th>Exposure Duration</th>
<th>Study</th>
<th>Material</th>
<th>Immunotoxicity</th>
<th>Cytotoxicity</th>
<th>Neurotoxicity</th>
<th>Genotoxicity</th>
<th>Carcinogenicity</th>
<th>Lethality</th>
<th>Systemic</th>
<th>Pulmonary</th>
<th>Cardiovascular</th>
<th>Dermal</th>
<th>Underlying</th>
</tr>
</thead>
<tbody>
<tr>
<td>INHALATION</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupational</td>
<td>Acute</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subchronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subchronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INGESTION/DERMAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupational</td>
<td>Acute</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subchronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Population</td>
<td>Acute</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subchronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INJECTION</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subchronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Symbol Table**

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Assay Organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>![□]</td>
<td>In vivo mouse</td>
</tr>
<tr>
<td>![X]</td>
<td>In vivo mouse</td>
</tr>
</tbody>
</table>
State of the Science on Safety

Weight-of-Evidence

• In general, several studies indicate CNC and CNF nanocelluloses *non-toxic* based on available data

• But, more complete data sets are needed
  – Longer term studies
  – More materials
  – Additional endpoints

Knowledge gaps

• Comparative data
  (Weight of Evidence)

• Functionalized or modified material data

• Data on composites/products

• Occupational inhalation data

• Consumer /environmental exposure data

• Nano-specific standards

• Standardized measurements

• Validated methods
EHS Priorities

- Safe Handling Processes
- International Safety Standards Development
- Sustainability Assessment and Certification

Source: Extremetech.com
Cellulosic Nanomaterial EHS Roadmap

1. Methods to assess occupational and environmental impacts

   a) Occupational safety guidelines
      1. Material handling; labeling; disposal; research
      2. Assess and build on existing wood dust/cellulose standards

   b) Develop exposure assessment & testing procedures
      1. Estimate exposure levels through modeling
      2. Assessment and measurement methods for air, water, other media
      3. Migration studies

   c) Verify/”validate” toxicology testing
      1. Confirm \textit{in vitro} tests valid for nanocellulose
      2. Assess additional exposure pathways/scenarios
      3. Criteria for new assessments (e.g. size distribution; functionalization)
Cellulosic Nanomaterial EHS Roadmap (2)

2. Develop/adopt **Standardized EHS Methods**

   a) **Sampling and Measurement Standards Development**
      1. Develop sampling protocols, including sample preparation
      2. Develop test approaches for different materials and applications

   b) **Occupational Exposure Standards**
      a) Guidance for sampling and worker protection

   c) **Environmental Impact Standards**
      1. Guidance for monitoring environmental impacts
      2. Measurement methods for air, water, other media
      3. Decision tree analysis

   d) **Consumer Product Standards**
      1. Guidance for testing nano-enabled products
3. Sustainability Measurements

a) Process impacts
   1. Chemical use and disposal
   2. Energy consumption
   3. Carbon impacts

b) Life cycle comparisons with alternatives
   1. Select applications
   2. Develop data for LCIA
   3. Build database and models

c) Establish certification standards
   1. Draft standards
   2. Convene stakeholders to vet and approve
   3. Publish standards
Thank you

Jo Anne Shatkin, Ph.D.
President

Vireo Advisors, LLC
jashatkin@vireoadvisors.com
Recent Analysis of Patent Applications for Wood-based Nanocelluloses

- 10% - Paper Coating
- 8% - Paper Furnish
- 22% - Composites
- 9% - Film

[Source Salmenkivi 2013]
## Alternative U.S. Acreage Estimates of Cellulose Needed*

<table>
<thead>
<tr>
<th></th>
<th>Green Tons/ Acre</th>
<th>Acres per Year</th>
<th>Hectares</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PLANTATION GROWN TREES</strong></td>
<td>470</td>
<td>183,000</td>
<td>72,000</td>
</tr>
<tr>
<td><strong>NATURAL FORESTS</strong></td>
<td>92</td>
<td>935,000</td>
<td>370,000</td>
</tr>
<tr>
<td><strong>FOREST RESTORATION “THINNINGS”</strong></td>
<td>22</td>
<td>3,900,000</td>
<td>1,500,000</td>
</tr>
</tbody>
</table>

*Assuming 100% from virgin wood pulp