Risk Analysis for Nanotechnology: State of the Science and Implications

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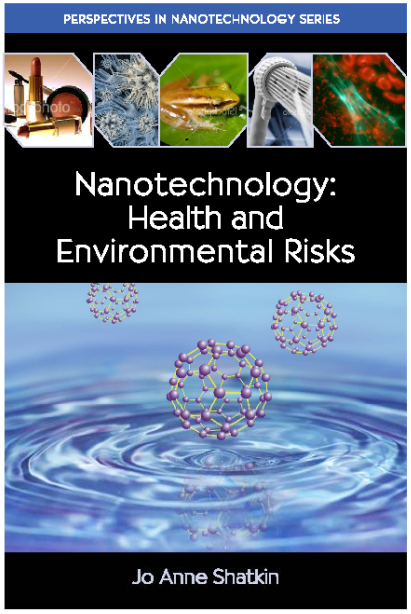


USDA
Washington, DC

CLF Ventures, Inc.

Overview

- Framing the issues
  - Need to consider risks in the context of benefits
  - Nano challenges to risk assessment
- Adopting a life cycle approach in risk assessment
- Society for Risk Analysis Expert Workshop Findings
- Regulatory perspectives

Some Agricultural Applications of Nanotechnology

- High value biomaterials
  - Nano crystalline cellulose
  - Enzymes
- Biofuels
- Sensor technology
- Nanoscale pest management
- Smart packaging

Promoting Sustainable Technology Development

- Can be proactive about identifying and reducing risk
  - Promotes environmentally sustainable technology development
  - If Environmental, Health and Safety (EHS) concerns, need to develop approaches for assessment and management
- Engineering materials provides flexibility to address EHS concerns up-front, if identified
- Understanding impacts provides advantages in efficiently managing them
  - When risks are anticipated, can plan for them, rather than reacting
  - Early stage analysis informs sound decision making

"JUST ANOTHER COUPLE OF PAGES."

Maximizing Benefits

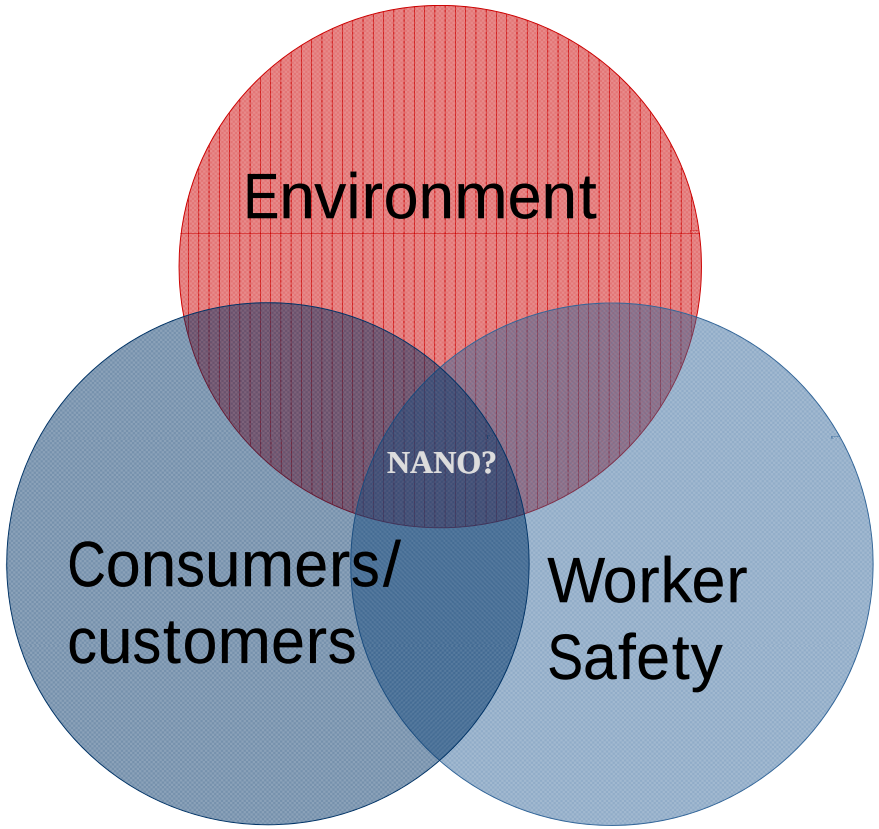
- Framing the issues
  - The need to be proactive about impacts
- Life Cycle Assessment
  - Applicability to new technology development
- Risk Assessment
  - Challenges for nanomaterials and nanotechnologies
- Screening Tools

Why Be Concerned about Nanomaterial Impacts?

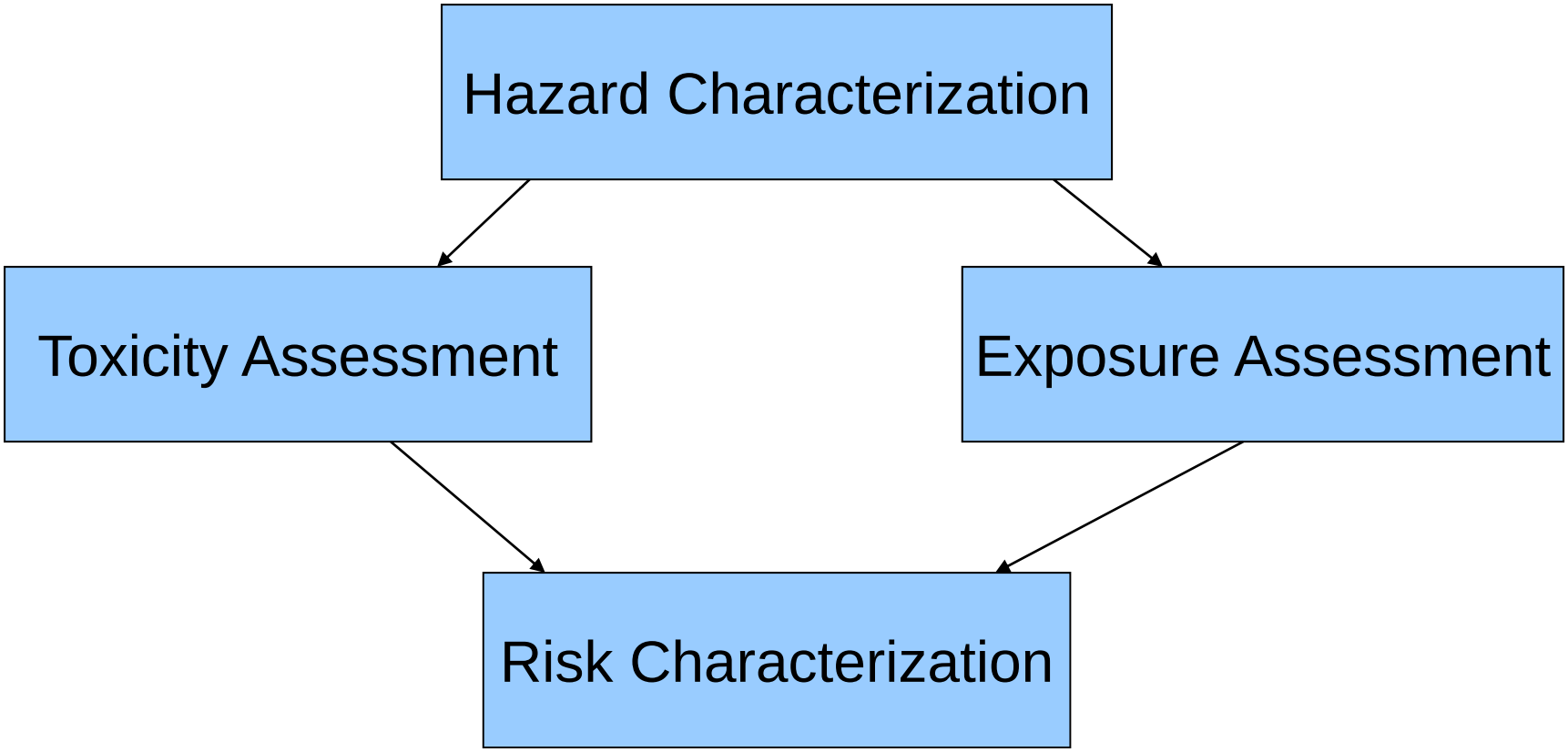
- Novel properties
- History dictates action
- Technology advancing quickly
- Paucity of information
- Potential for wide dispersion in the environment amidst uncertainty
- Significant NGO activity and low consumer knowledge
- Few standards or guidelines - yet!

Key Concerns about Nanotechnology Risks

- Avoiding a "nano" legacy
- Uncertainty about health and environmental risks
- Hype – its unclear which issues are real, perceptions a risk, too



Framing the Issues for Health/ Environmental Risk Assessment of Engineered Nanoscale Materials



(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 novel effects?
- Difficulty in measuring responses
  - data are equivocal
- Absorption, Distribution, Metabolism, Excretion
- Diversity of materials and characteristics
  - When are particle distributions different?
  - What are the tolerances?

Framing the Issues:
Dose Response for Nanotechnology

- Limited data available from well designed studies
  - most is in vitro or inhalation studies to particles
- Reactive oxygen formation (ROS) is a commonly observed mechanism of toxicity; physical effect on cells
  - Leads to inflammation
- Study conditions affect results
- Surface coating/particle size/surface charge/ surface area/ contamination and aggregation may be important

Framing the Issues: Characterizing Risks of Nanomaterials

- Several deliberations conclude that 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
- Still a limited ability to conduct quantitative assessments
- New metrics and endpoints for risk?

Framing the Issues: Uncertainty Analysis *Haven't we been here before?*

- Foodborne vs. Nosocomial antimicrobial resistance
- Chemical mixtures
- Climate change impacts
- Cellular phones and non-ionizing radiation
- Nutrient requirements
- Vitamin and mineral fortification of food
- Fish consumption advisories

Risk Analysis is a robust approach for assessing and managing uncertain hazards and risks

Society for Risk Analysis

In December 2006 formed the **Emerging Nanoscale Materials Specialty Group (EMNMS)** with 75 founding members.

- 135 Current Members from 22 Countries
- Diverse interests and expertise
- Affiliations
  - Academia
  - Government
  - Non-profits
  - Trade organizations
  - Industry
  - Students
  - Others

The Emerging Nanoscale Materials Specialty Group (EMNMS) aims to:

- Facilitate the exchange of ideas and knowledge among practitioners, researchers, scholars, teachers, and others interested in risk analysis and emerging nanoscale materials.
- Encourage collaborative research on risk analysis and emerging nanoscale materials.
- Provide leadership and play an active role in advancing issues related to risk analysis and emerging nanoscale materials.

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 the benefits of nanotechnology for risk reduction?

Workshop Co-Sponsors

Panel Discussion on Data Gaps


SRA
Nano
dvancing the Science for Nanomaterial Risk
Dose Response White Paper
Nanotoxicology and Is It More
My Computer

Repeated themes

- Considerable uncertainty in understanding of nano-specific attributes and relevance to biological and environmental effects
- Size matters, but its 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 successful development of nano-products

Key Issues Identified

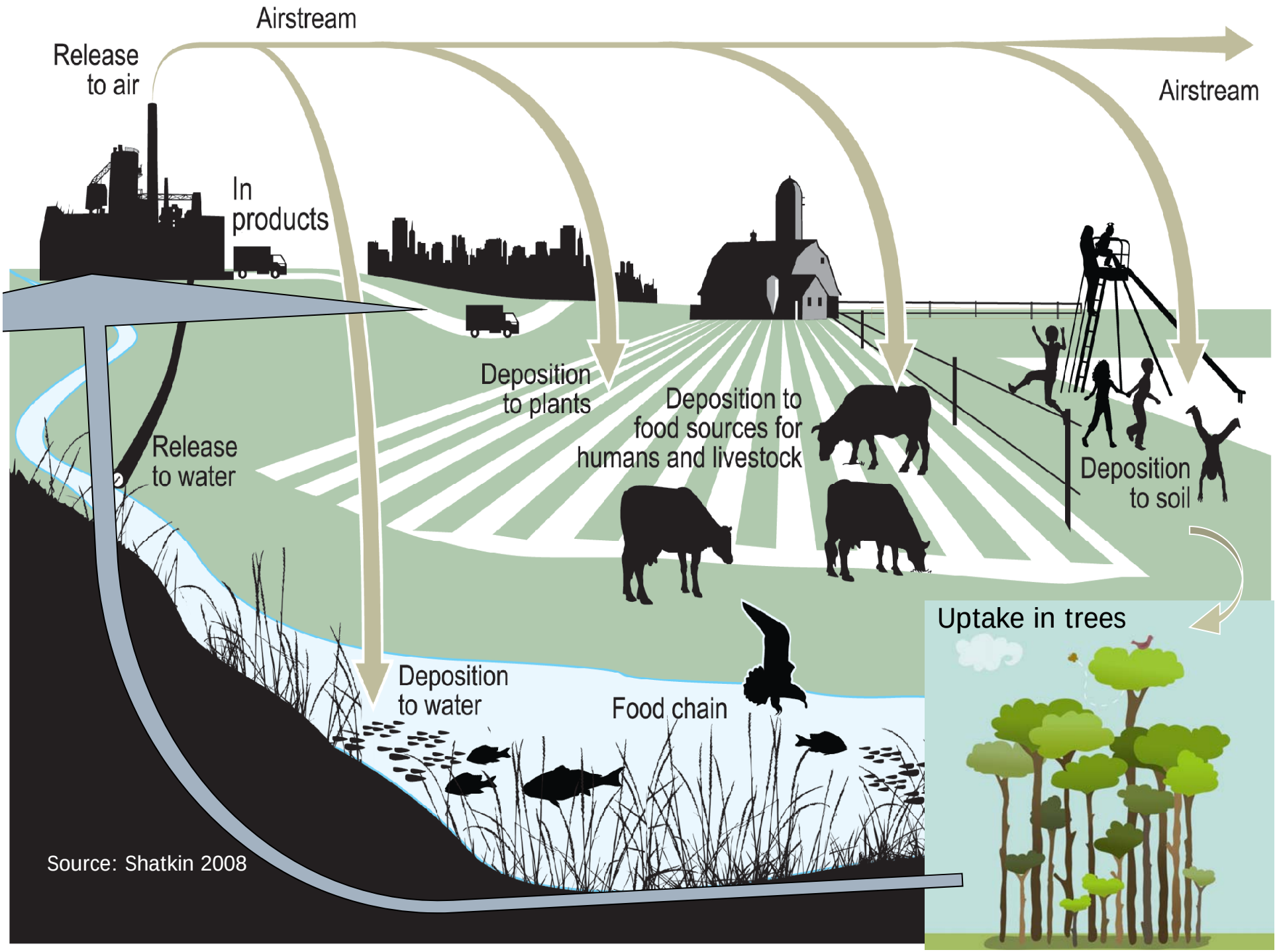
- Many previously identified concerns are not specific to nanomaterials or nanotechnologies
- Can address some concerns "by design"
  - Engage risk analysts to work with product designers
- Need for a long term plan/framework to answer questions with pending data
- Conduct case-by-case evaluations to elicit key concerns
- Also conduct expert workshops more broadly to raise overarching issues
- Test/compare adaptive approaches to risk analysis that incorporate the product life cycle

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

Key Elements of a Risk-based Analysis Framework for Nanomaterials

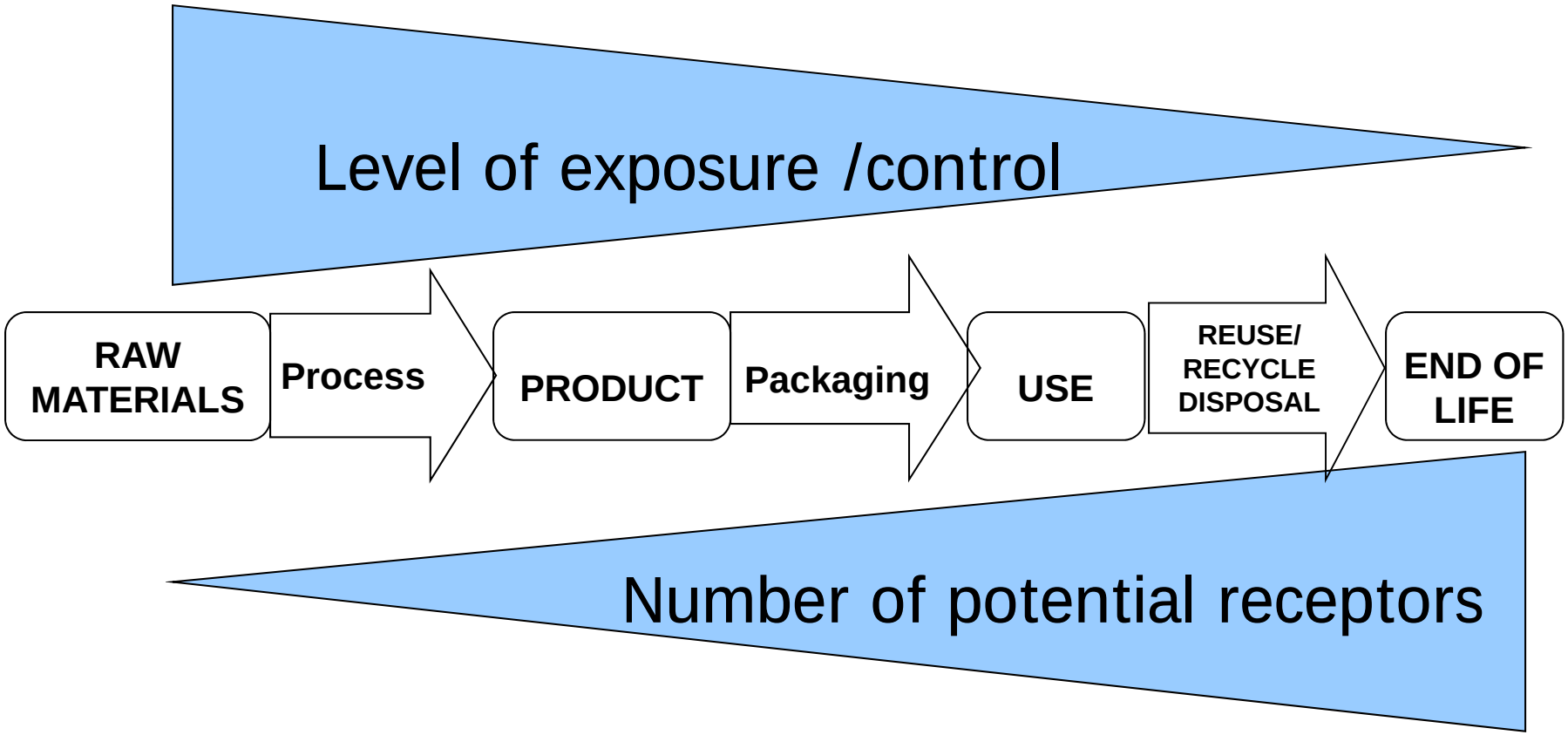
- Tiered – Start with Screening Tools
  - Use early in the product development cycle to identify potential concerns
- Address Life Cycle Concerns
  - Consider worker, consumer, and environmental issues
- Focus on Exposure
  - Indicators, not Perfect Data
  - Hazard, Exposure and Toxicity Dimensions
- Adapt Products to Findings (Evaluative)
  - Incorporate findings into actions


Airstream
Release to air
Airstream
In products
Deposition to plants
Deposition to food sources for humans and livestock
Release to water
Deposition to soil
Uptake in trees
Deposition to water
Food chain
Source: Shatkin 2008

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
  - **Nano SLCRA** (Shatkin 2008. *Nanotechnology Health and Environmental Risks* CRC Press)
  - **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**

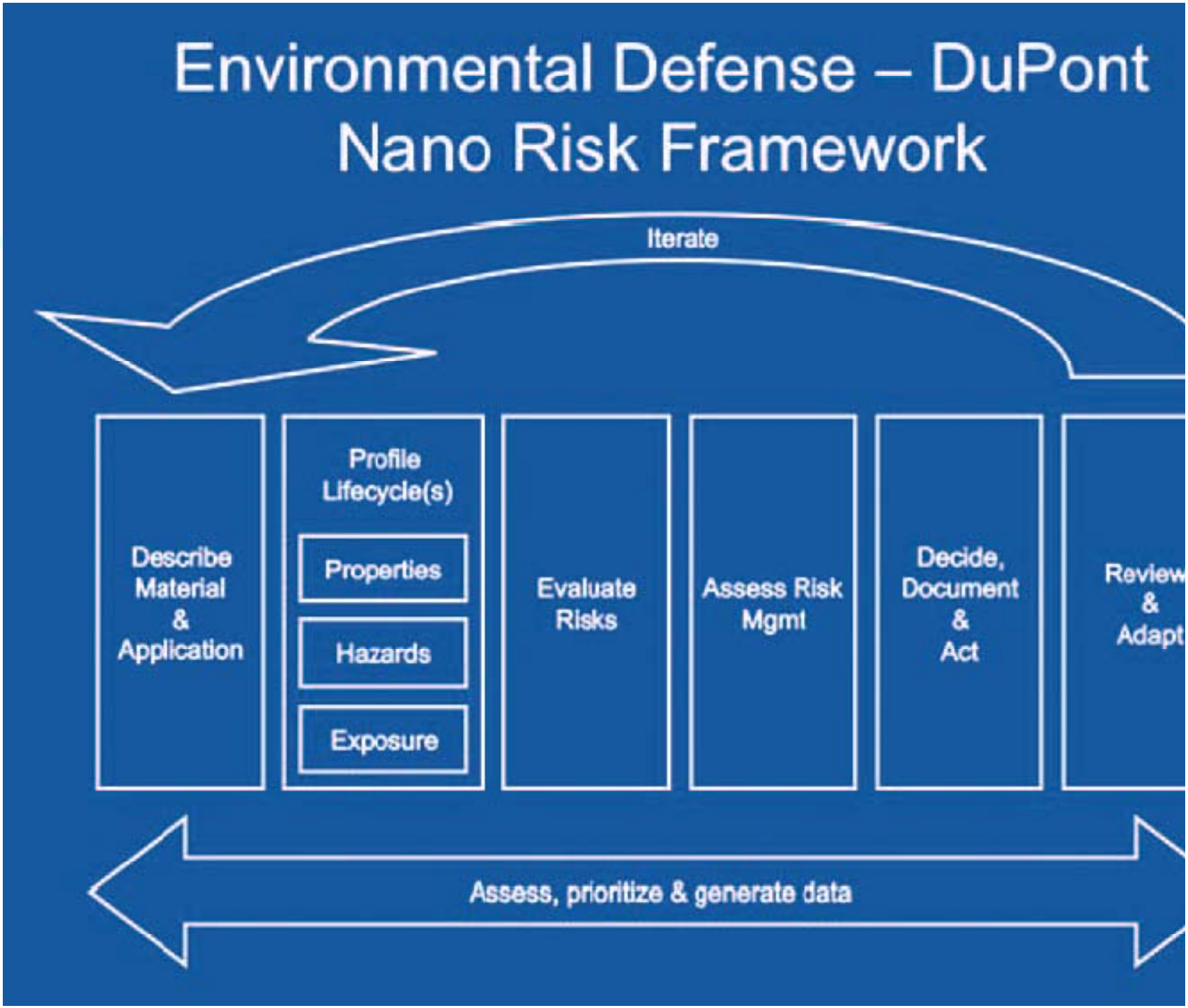
Tier 1 evaluations for

- 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

Oberdöerster, G. et al. 2005. *Particle and Fibre Toxicology* 2005, **2**:8
http://www.particleandfibretoxicology.com/content/2/1/8


Environmental Defense – DuPont
Nano Risk Framework
Iterate
Describe Material & Application
Profile Lifecycle(s)
Properties
Hazards
Exposure
Evaluate Risks
Assess Risk Mgmt
Decide, Document & Act
Review & Adapt
Assess, prioritize & generate data

Comprehensive Environmental Assessment (CEA)

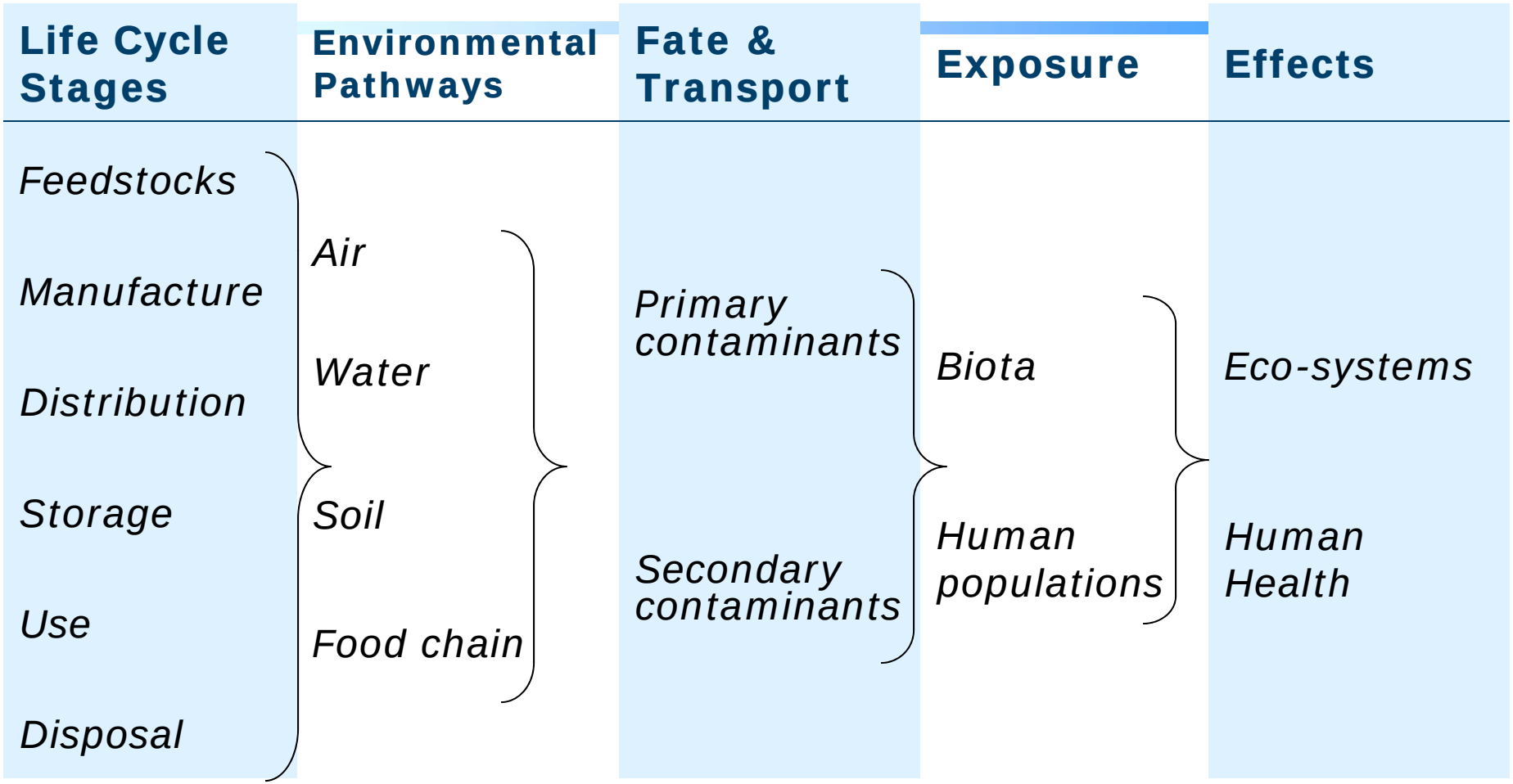
$$CEA \approx LC + RA$$

LC = Product Life Cycle framework

RA = Risk Assessment paradigm

See: Davis, J. M. "How to assess the risks of nanotechnology: learning from past experience" *J. Nanosci. Nanotechnol.* 7(2): 402-409, 2007

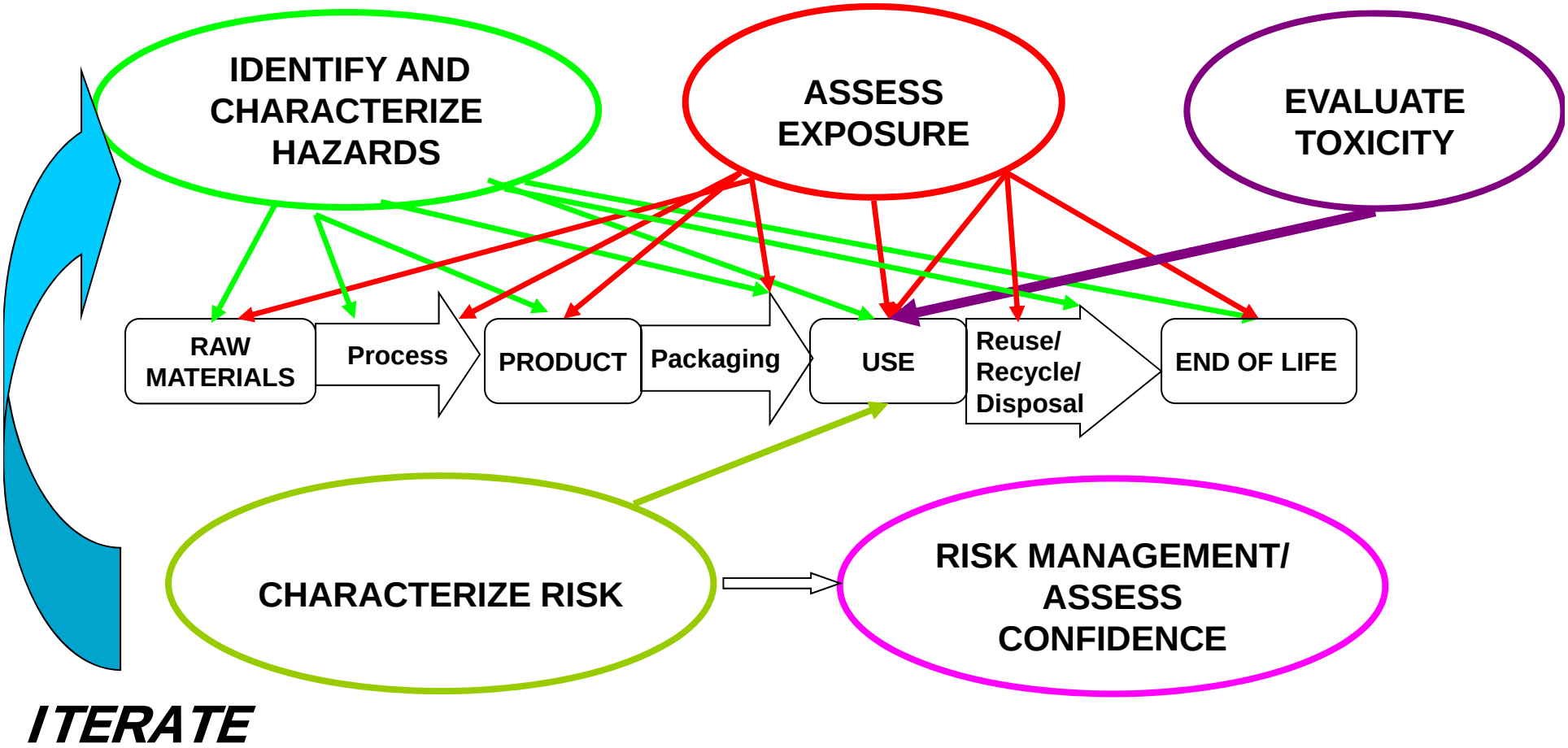
Comprehensive Environmental Assessment (CEA)



Source: adapted from Davis, J. M. and Thomas, V.M. *Annals N.Y. Academy of Science* 1076: 498-515, 2006

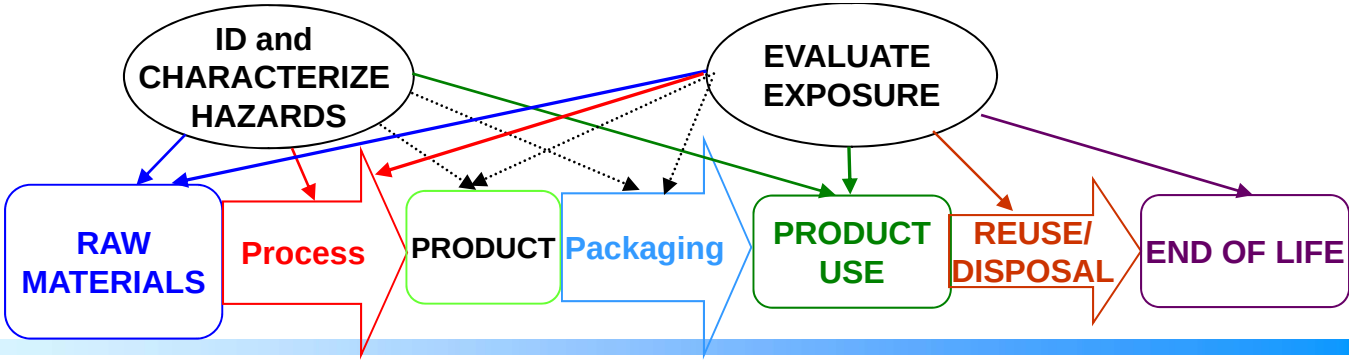
NANO SLCRA

Adaptive Streamlined Life Cycle/ Risk Assessment Framework for Nano Materials (Shatkin 2008)



NANO SLCRA

Case Example Nanocrystalline Cellulose for Packaging Application



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

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 and are perceived as risky
- Everyone benefits 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."

Source: K. Thompson, 2004.


News Item: Scientists undecided about the need for nanoparticle regulation.
NANO · PARTICLE SAFETY TEST
"I'm looking for a loophole!"
ETC 2004

Thank You Very Much!

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