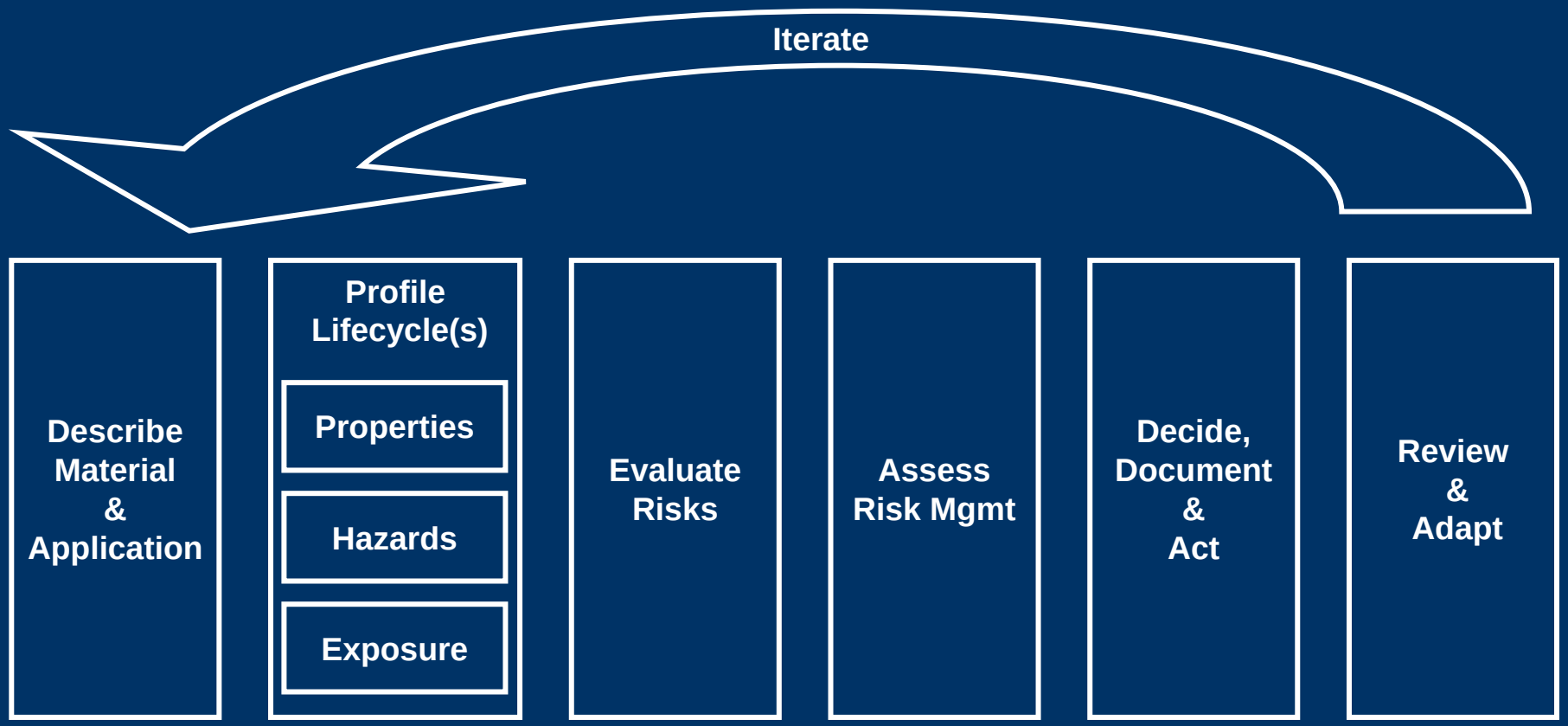
Nano Risk Framework



www.nanoriskframework.com

Richard Denison, Environmental Defense

Nanotechnology II, 3 October 2007

A Teamwork Approach

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THE WALL STREET JOURNAL.

TUESDAY, JUNE 14, 2005

MANAGER'S JOURNAL

Let's Get Nanotech Right

By FRED KRUPP and CHAD HOLLIDAY
June 14, 2005; Page B2

The science of the small is raising big expectations. New materials a tenth the size of a human cell, engineered atom by atom, promise to revolutionize everything from energy production to medicine. We've seen many extravagant predictions surrounding this new world called nanotechnology: A single slender cable built from nanoparticles might carry the world's total electrical supply. Environmental burdens might be lifted by nano-pores that desalinate water or nano-cages that trap bacteria. As with new "miracle" technologies in the past, there is much speculation regarding how "nanotech" can transform the world and national economies. Governments and private investors are rushing to make major investments in projects bearing the "nano" prefix.

What is nanotechnology really? Is it a fundamentally new science or just an extension of the technologies already used to create new materials and products? Could the novel properties that make nanoparticles so promising affect human health and ecosystems in a different way than more familiar larger particles? These and other questions must be answered. The hype surrounding nanotech drowns out the need for sound, disciplined research and commercialization guided by thoughtful regulatory standards.

We've been here before. A new technology is heralded as the "next big thing." Companies are created. R&D budgets expand, and investors' eyes gleam at the prospect of new markets. Then two or 10 or 20 years later, when the technology is in widespread use, other effects become evident.

For example, before 1929, the toxic gases ammonia, methyl chloride, and sulfur dioxide were used as refrigerants, but fatal accidents occurred because of leakage. In 1928, a new family of non-toxic chemicals, chlorofluorocarbons, was invented and became the standard for refrigerants. Only decades later did we recognize that the release of CFCs was dissolving the earth's ozone layer.

Unfortunately there are many similar examples, including DDT and leaded gasoline, where we later learned of various unintended consequences of initially promising technologies.

An early and open examination of the potential risks of a new product or technology is not just good common sense -- it's good business strategy. We need to make sure this assessment takes place now for today's "next big thing" -- nanotechnology. With the right mix of voluntary corporate leadership, coordinated research, and informed regulation, we can reap the benefits of this promising technology while reducing the likelihood of unintended consequences.

Given potential liability and market risks, industry, universities, government and public interest groups should collaborate to determine what testing is necessary for new nanoproducts. Businesses should conduct the needed testing before new products enter commercial use. Products that use nanomaterials are already in our stores. Good product stewardship requires a commitment to identifying and managing any potential risks. A collaborative effort could set interim standards for nanotechnology around the world while regulations are under development.

At the same time, our government also needs to invest more seriously in the research necessary to understand fully nanoparticle behavior. Funding to study health and environmental risk represents only 4% of the proposed federal investment in nanotech and becomes vanishingly small when you factor in private investment. Government spending on nanotechnology should be reprioritized so that approximately 10% goes to this purpose. Compared to the estimated $1 trillion market for nanotechnology, this would be a wise insurance policy on such a high-potential investment.

Lastly, both public and business interests will inevitably compel regulatory protection to ensure product safety and to create a level playing field for business. Current regulations, designed for a world before nanotechnology, should be reassessed and changed as needed to account for the novel properties of nanomaterials. Business and government may need new approaches to make sure workers, consumers, the public and the environment are adequately protected.

In the end, it all comes down to this: Can we reap the benefits while minimizing the risks? We believe we can. The key steps are identifying and addressing the risks. We encourage those with an interest and a stake in nanotech to collaborate in the development of responsible safety standards and to exercise great care in the launch of new materials. We urge the federal government to adequately fund the agencies that need to understand nanotechnology so they can create thoughtful and informed regulations for this exciting field of scientific discovery and commercial promise.

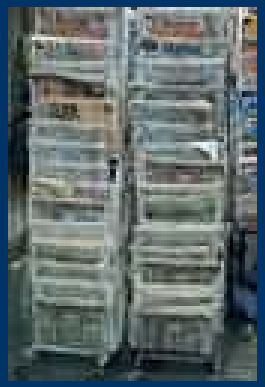
Mr. Krupp is president of Environmental Defense and Mr. Holliday is chairman and CEO of DuPont.

"An early and open examination of the potential risks of a new product or technology is not just good common sense -- it's good business strategy."

“In the Headlines”

“The guidelines are the most extensive effort yet to address a vexing issue surrounding the rapidly expanding field of nanotechnology; the lack of information about whether materials in such minute sizes can pose novel or unexpected hazards.”

New York Times
June 21, 2007



Elements of the Framework

- Comprehensive, practical and flexible system for evaluating and addressing potential environmental, health and safety risks across lifecycle
- Means to guide information development and update assumptions, decisions, and practices
- Tool to document and communicate basis for actions using output worksheet

A Mix of Old and New

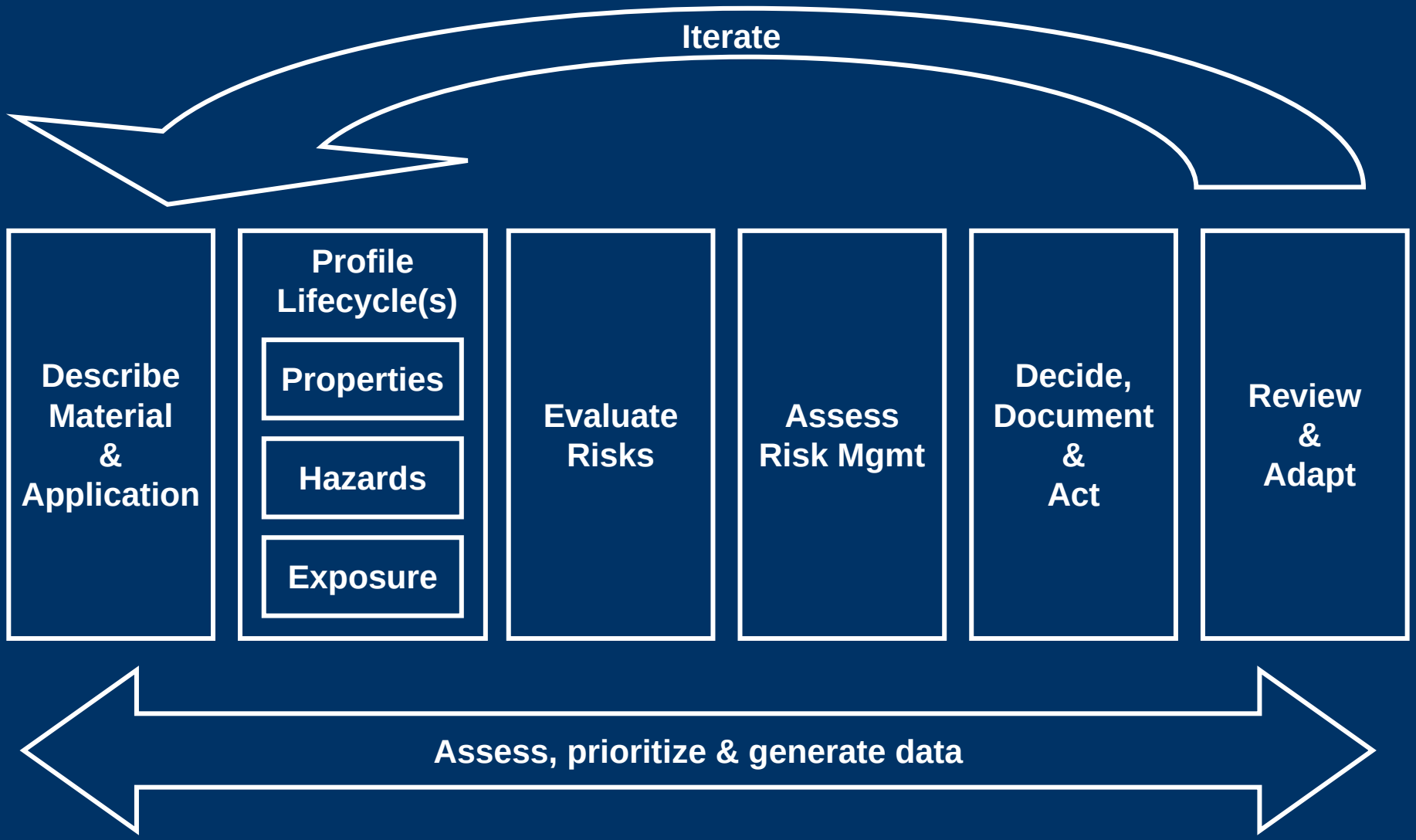
Familiar Elements

- Risk assessment
- Product development
- Lifecycle

New Elements

- Information-driven
- Base sets
- Iterative process
- Flexibility
- Transparency

Nano Risk Framework

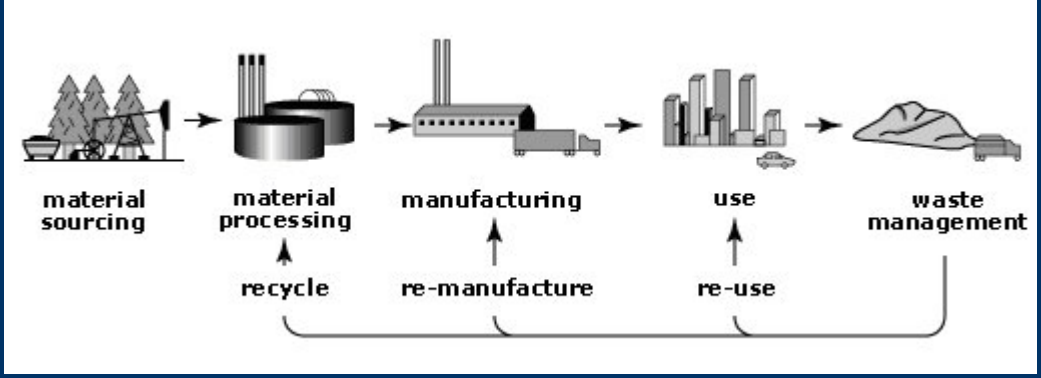


1. Describe Material & Application

- Identify source and manufacturing process
- Review literature
- Identify reference, incumbent and bulk material counterparts
- Describe material and expected applications, especially differences from incumbent and bulk materials

2. Profile Lifecycle(s)

- Consider full lifecycle



(adapted from www.ami.ac.uk/courses/topics/0109_lct/)

- Develop "base sets" of EHS information
  - Similar to other programs (SIDS, REACH)

2. Base Sets: Categories of Information

- Physical-chemical properties
- Hazards
  - Health hazard
  - Environmental hazard
  - Environmental fate and behavior
  - Safety hazard
- Exposure

“Base Sets” drive Lifecycle Profiles

- Benchmark information needed for informed risk decisions
  - Not basis for a full hazard/risk assessment
- Reference point for:
  - Factors to consider as early as possible in development
  - Type and amount of information expected by market launch
- Neither a ceiling nor a floor for info needs

2A. Base Set Physical & Chemical Properties

- Particle Size
- Size Distribution
- Surface-Area
- Particle Density
- Solubility
- Dispersability
- Bulk Density
- Agglomeration State
- Chemical Reactivity
- Surface Reactivity
- Porosity
- Surface Charge
- Technical Name
- Commercial Name
- Common Form
- Chemical Composition
- Molecular Structure
- Crystal Structure
- Physical Form

2B. Base Set Health Hazard Data

- Short-term Toxicity:

  One or more of the following, depending on conditions:
  - 28-day inhalation study
  - Single-dose instillation study
  - 28-day repeated-dose oral toxicity test
  - ➢ each with full histopathology, over a 90-day observation period

- Skin sensitization/irritation
- Skin penetration
- Genetic toxicity tests

2B. Base Set Environmental Hazard Data

- Acute Aquatic toxicity
  - Fish (fathead minnow or rainbow trout)
  - Invertebrates (*Daphnia)*
    (acute or chronic depending on conditions)
  - Aquatic plants (algae)

- Acute Terrestrial toxicity
  - Terrestrial invertebrates (earthworms)
  - Terrestrial plants

2B. Base Set Environmental Fate Data

- Environmental fate
  - Physical and chemical properties
  - Adsorption-desorption coefficients
  - Aggregation or disaggregation
- Persistence potential screen
  - Biodegradability test
  - Photodegradability / phototransformation
  - Stability in water (hydrolysis)
- Bioaccumulation potential screen

2B. Base Set Safety Hazard Data

- Flammability
- Explosivity
- Incompatibility
- Reactivity
- Corrosivity

2C. Base Set Exposure Data

- Manufacture
- Processing
- Use
- Distribution/storage
- Environmental releases
- Post-use management

Triggers for Additional Testing

- High exposure potential
- Significant changes, e.g., in production or use pattern
- Uncertain or high inherent hazard potential
- Results of base set studies
- Compensating for lack of data or uncertainty re: hazard or exposure

Additional Health Hazard Data

- Biological fate and behavior
- Chronic (≥1 year) inhalation/ingestion toxicity
- Chronic dermal irritation/sensitization studies
- Developmental and reproductive toxicity
- Neurotoxicity studies
- More extensive genotoxicity studies
- Focused toxicity studies, e.g.:
  - Susceptibility studies — animal models
  - Allergenicity and immunotoxicity
  - Organ function bioassays

Use of Default Values and Assumptions

Rationale

- Complete base sets may not be feasible at early stages of development
- Framework provides for the use of “reasonable worst-case” default values or assumptions
- Can be derived from several sources, e.g.:
  - analogous bulk materials (e.g., quartz particles), or
  - by assigning to highest tier in classification system
- Reasonable “worst-case” default assumptions particularly useful in absence of exposure data
  - allow risk assessment and communication

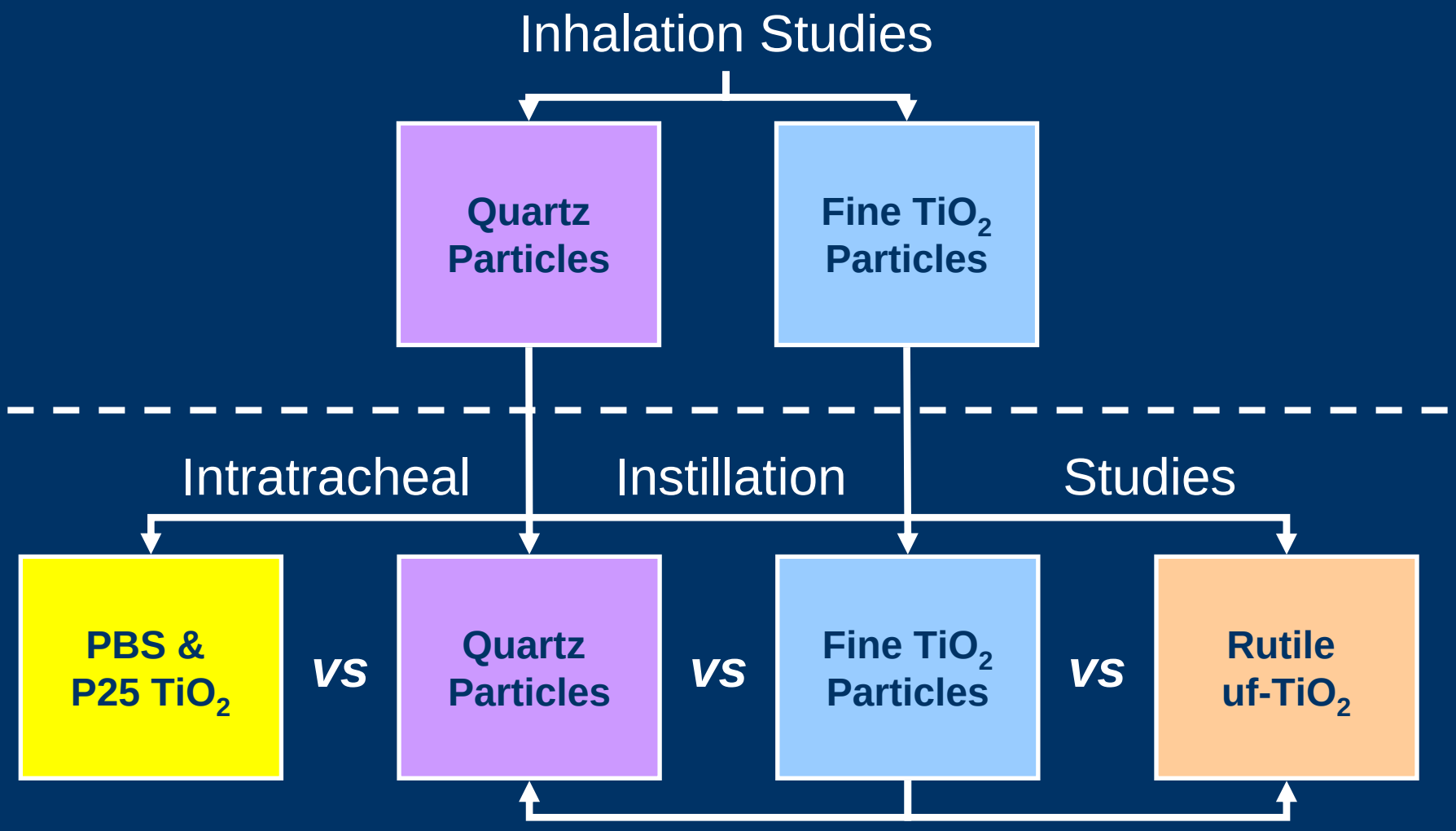
Use of Default Values and Assumptions (cont.)

- Not intended to substitute for toxicity or exposure data – but allow for a reasonable worst-case assessment in the absence of data
- Can be updated or replaced by the generation of pertinent hazard and exposure data
- Provides for a margin of safety to workers and other potentially exposed populations and environments
- Important for users of default values to share the assumptions made with key stakeholders

Use of Bridging Information

- When a NM has few specific hazard data, one way to inform decisions is to ”bridge” it to a material that has more robust data
- The two materials are entered into a hazard study, with the well-characterized material serving as a “control” for the material of interest
- The test is a shorter test than what would be needed for a more thorough understanding of toxicity of the material of interest
- The strength of the bridging strategy is dependent upon having robust data on the control material from more thorough toxicity tests
- Example: ultrafine TiO_2 pulmonary bioassay

Pulmonary Bioassay Bridging Studies



3. Evaluate Lifecycle Risks

- Considering stage of lifecycle, position in value chain:
  - Review hazard and exposure profiles
  - Evaluate (quantify where possible) nature, magnitude and likelihood of identified risks
  - Identify knowledge gaps
- Develop plan to fill data needs or develop “reasonable worst-case assumptions” for missing data elements

4. Assess Risk Management

- Determine needed level of protection to be achieved through risk management
- Assess adequacy of current management & engineering controls to address identified potential risks
- Determine best risk management options
- Develop plans for risk management, monitoring, compliance & reporting

5. Decide, Document & Act

- Review risk evaluation and risk management assessment
- Consider business, legal and stakeholder issues
- Decide whether and, if so, how to proceed
- Implement risk management, monitoring & compliance processes
- Determine & initiate additional data collection as needed
- Determine product review cycle
- Document and report decisions and actions

6. Review and Adapt

- Conduct reviews on a regular basis and as needed in response to significant changes in hazard and exposure information, production volume, and use profile:
  - Evaluate new data or changes
  - Review and revise as needed risk evaluation and risk management decisions
- Adapt risk management and collect additional information as appropriate
- Document and report any new decisions and actions

Output Worksheet

- Organize
- Record
- Share

OUTPUT WORKSHEET

An editable version of this Output Worksheet is available at www.NanoRiskFramework.com

Nanomaterial Risk Assessment Document — [nanomaterial]

Section 1: Describe Material and Its Applications
Develop basic descriptions — general overviews — of the nanoscale material and its intended uses.

General Overview: [a]

Material Description:
Material source or producer:
Manufacturing process:
Appearance:
Chemical composition:
Physical form/shape:
Concentration:
Size distribution:
Solubility:
State of aggregation or agglomeration:
Material CAS number (if applicable):

Material	CAS Number	Composition

Main applications (current or expected):

Stage of development:

General physical and mechanical properties of this material:

Past experience with this material or a similar material:

Potential benefits/positives of the material:

Potential risks/negatives of the material:
Health:
Environmental:

Sources of additional information:

[a] The general overview should contain descriptions sufficient to guide development of more detailed profiles of the material's properties related to hazard and exposure potential at various lifecycle stages (such as manufacture, use, and end-of-life). This overview should be developed from information in the possession of the user or available in the literature.

Case Studies

Material	TiO_2	CNTs	ZVI
Application	Light Stabilizer	Polymer Additive	Waste Remediation
Role	Producer	User	Customer
Stage	Commercial	R&D	Concept
Result	Proceed	Limit	Hold
Cost	125 hours $170 K	80 hours $5 K	40 hours $0

Desired Outcomes

- Comprehensive, practical, and flexible
- Evaluates and addresses the potential risks of nanoscale materials across the lifecycle
- Promotes responsible development of nanotechnology products
- Facilitates public acceptance
- Contribute to the development of government policy on nanotechnology safety

Environmental Defense – DuPont Nano Partnership

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Environmental Defense – DuPont

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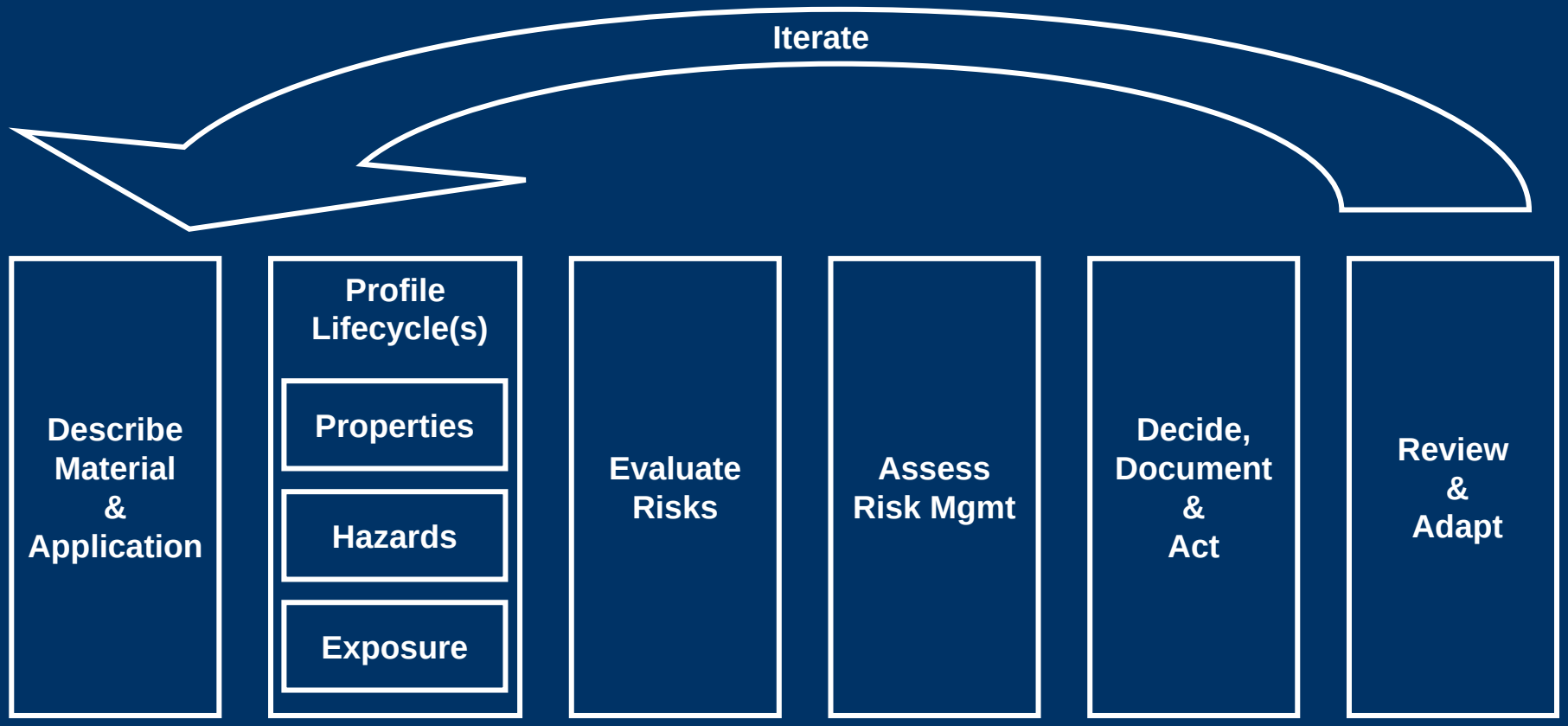

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includes Case Study summaries and worksheets!

Additional Environmental Hazard Data

- ADME studies on aquatic organisms
- Chronic toxicity to soil microorganisms and sediment- and soil-dwelling organisms
- Further testing for toxicity using additional terrestrial species
- Avian toxicity testing
- Population/ecosystem-level studies

Additional Environmental Fate Data

- Activated sludge respiration inhibition test
- Microorganism toxicity
- Persistence potential in relevant media
- “Inherent” biodegradability test
- Aerobic/anaerobic soil or sediment biodegradability
- Adsorption-desorption coefficient
- Potential for transformations via oxidation-reduction reactions

Additional Safety Hazard Data

- Stability
- Decomposition
- Polymerization
- Photoactivity