United States Environmental Protection Agency

Regulatory Priorities and Information Needs Linked to Grouping of Nanomaterials (U.S. perspective)

Joint Scientific Workshop on Grouping of Nanomaterials: NanoReg2 and GRACIOUS projects
12-13 September 2018
Paris

Office of Chemical Safety and Pollution Prevention

Overview

- Background on TSCA
- New Chemicals Review Considerations
- New Chemical Categories
- Regulatory Determinations under TSCA
- Issues with Developing a Nanomaterials Category

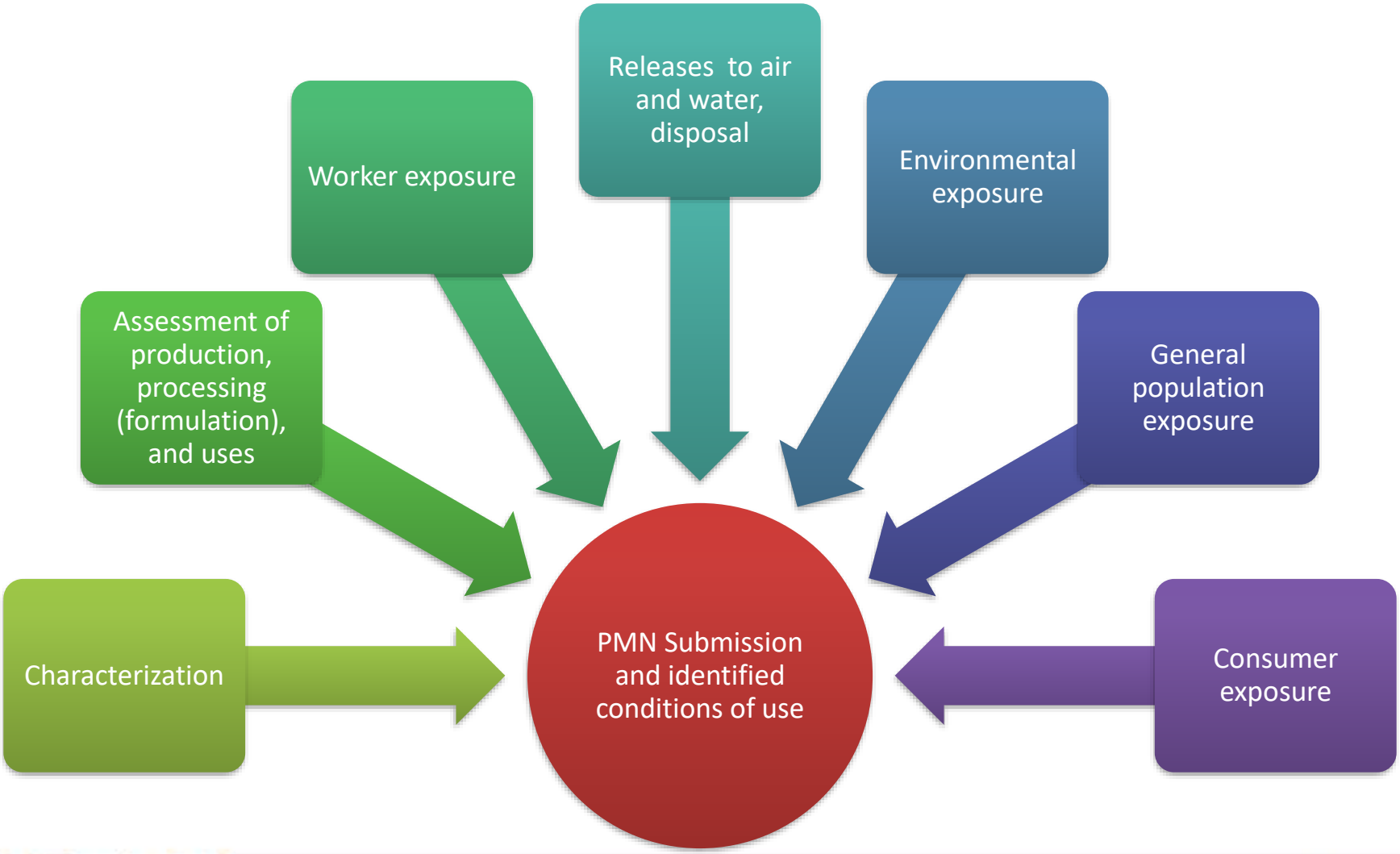
Toxic Substances Control Act (TSCA) - An Overview

- Provides basic authority for chemicals regulation in the U.S.
- TSCA requires EPA to:
  - Evaluate and, where appropriate, control unreasonable risk for new chemicals and new uses of certain existing chemicals
  - Prioritize, evaluate and address risk for existing chemicals that present unreasonable risk to health or the environment
  - Gather information on new and existing chemical substances and mixtures, including requiring testing where needed to fill data gaps
  - Coordinate with other Federal agencies
- Nanoscale materials are managed under TSCA; No U.S. legislation specific to nanoscale materials

TSCA – Information Required to be Submitted for New Chemicals via Premanufacture Notices (PMNs)

- Chemical Identity
  - Includes particle size and particle size range
  - Morphology or shape
- Byproducts and impurities
- Estimated production/import volume
- Proposed uses and amounts for each use
- Human exposure information
- Disposal methods and estimates of releases to the environment
- Existing test data in submitter's possession or control concerning human and environmental effects

TSCA New Chemical Review Considerations



Review of New Chemicals

- EPA reviews ~1000 new chemical submissions annually
- Statutory review period is short – 90 days
- Very few submissions include data (<15%)
- Reviews are typically based on structural analogues and categories

New Chemical Categories

- Chemical Categories are a practical way to extrapolate existing data to analyze related substances

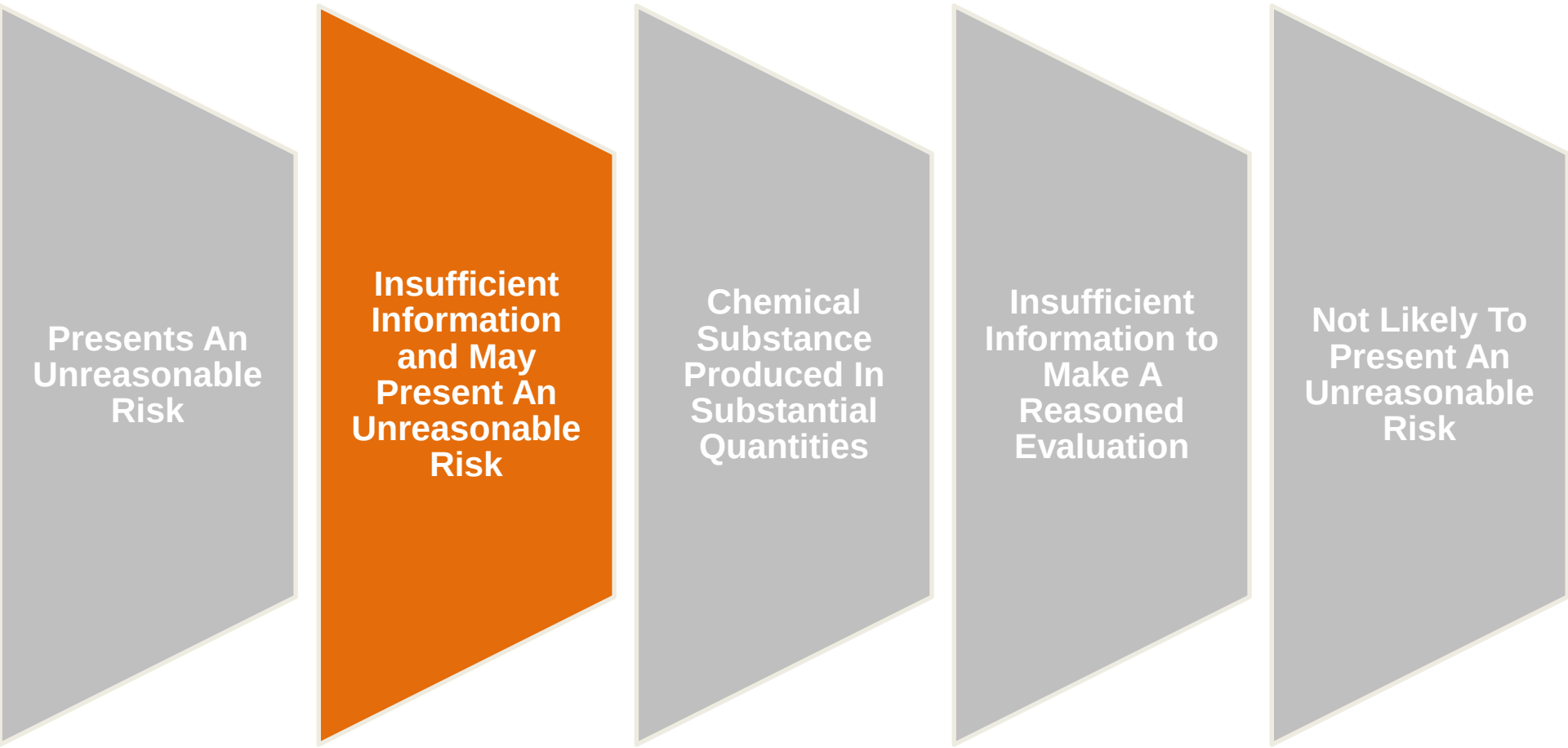
- Category evaluation supports:
  - Greater weight of evidence
  - Increased confidence in conclusions
  - Better basis for establishing biological plausibility

- Category analysis facilitates strategic testing to fill data gaps, where necessary
  - Weight of evidence used for deciding on additional testing
  - Defines the nature and scope of any potential testing needs

Categorization of Nanomaterials

- No category currently exists for nanomaterials specifically
- U.S. focus is on toxicity of components
  - For example, Cd
  - Functionalization of coatings
  - Persistence in the environment
- Nanomaterials may also fit into existing chemical categories, such as “Respirable, poorly-soluble particulates”:
  - Category is based on data for five different poorly-soluble particulates: silica, talc, titanium dioxide, a lithium manganese oxide, and carbon black
  - Use U.S. NIOSH REL for CNT/CNF (1 ug/m^3) for risk assessment
  - Physico-chemical properties testing and a 90-day inhalation toxicity test (OECD TG 413+ BAL) are often necessary to evaluate potential health and environmental impacts of nano substances

TSCA Determinations Under Section 5



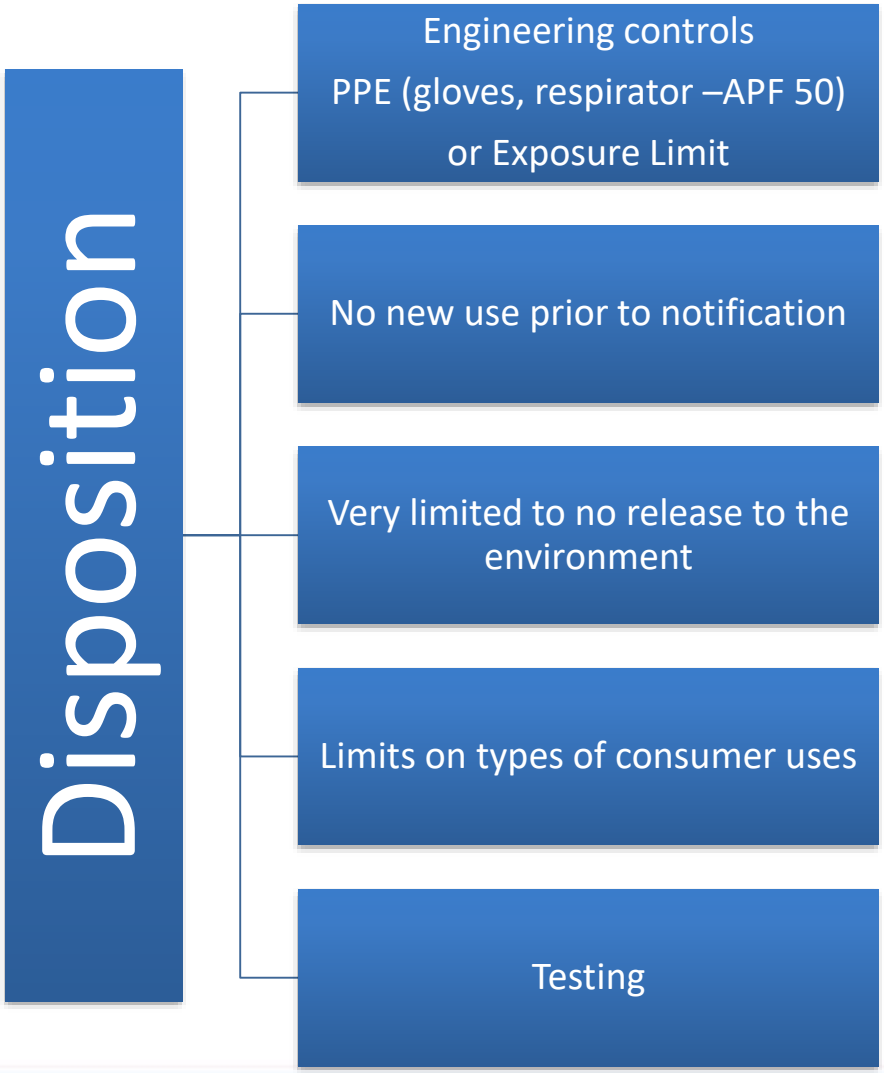
Section 5 Review and Determination

Insufficient Info and May Present An Unreasonable Risk

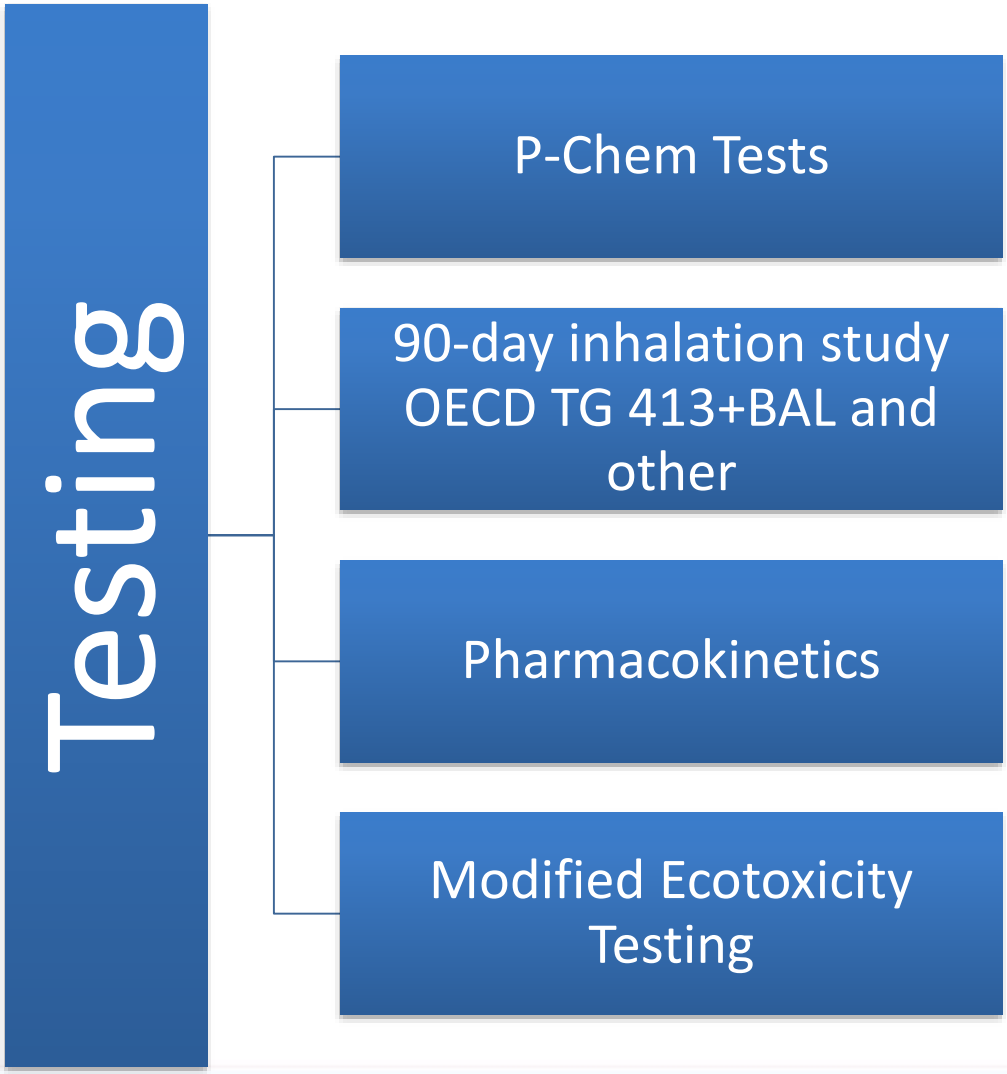
- As a result of the review, EPA determines that, in the absence of sufficient information to conduct a reasoned evaluation, the manufacture, processing, distribution in commerce, or use, may present an unreasonable risk of injury to health or the environment under the conditions of use.

- Regulation under section 5(e): Regulation Pending the Development of Information
  - Section 5(e) order
  - Testing or other potentially useful information may be required

Disposition



Testing


Testing
P-Chem Tests
90-day inhalation study OECD TG 413+BAL and other
Pharmacokinetics
Modified Ecotoxicity Testing

Nanomaterials under the TSCA New Chemicals Program

- More than 210 new chemical notices for nanomaterials have been received since 2005
- Most notices have completed EPA review, are regulated, but allowed in commerce
  - Requirements to prevent human and environmental exposure (PPE, certain end uses not allowed, no release to water, etc.)
  - Requirements to develop data for fate, ecotoxicity, and/or toxicity
- A limited number of 5-day, 28-day, 90-day, acute, irritation, sensitization, intratracheal instillation, and genetic toxicity studies have been conducted on nanomaterials (many of which have been on CNTs)

Carbon Nanotubes/Fibers

- EPA has received new chemical notices under TSCA on over **100 carbon nanotubes and fibers**

- Each CNT is considered a distinct chemical substance. Some key parameters:
  - # walls
  - inner diameter, outer diameter and length
  - functionalization
  - capped or open ended
  - straight, branched, or tree structure

- Production volumes have ranged from less than 100 kg scale to greater than 100,000 kg

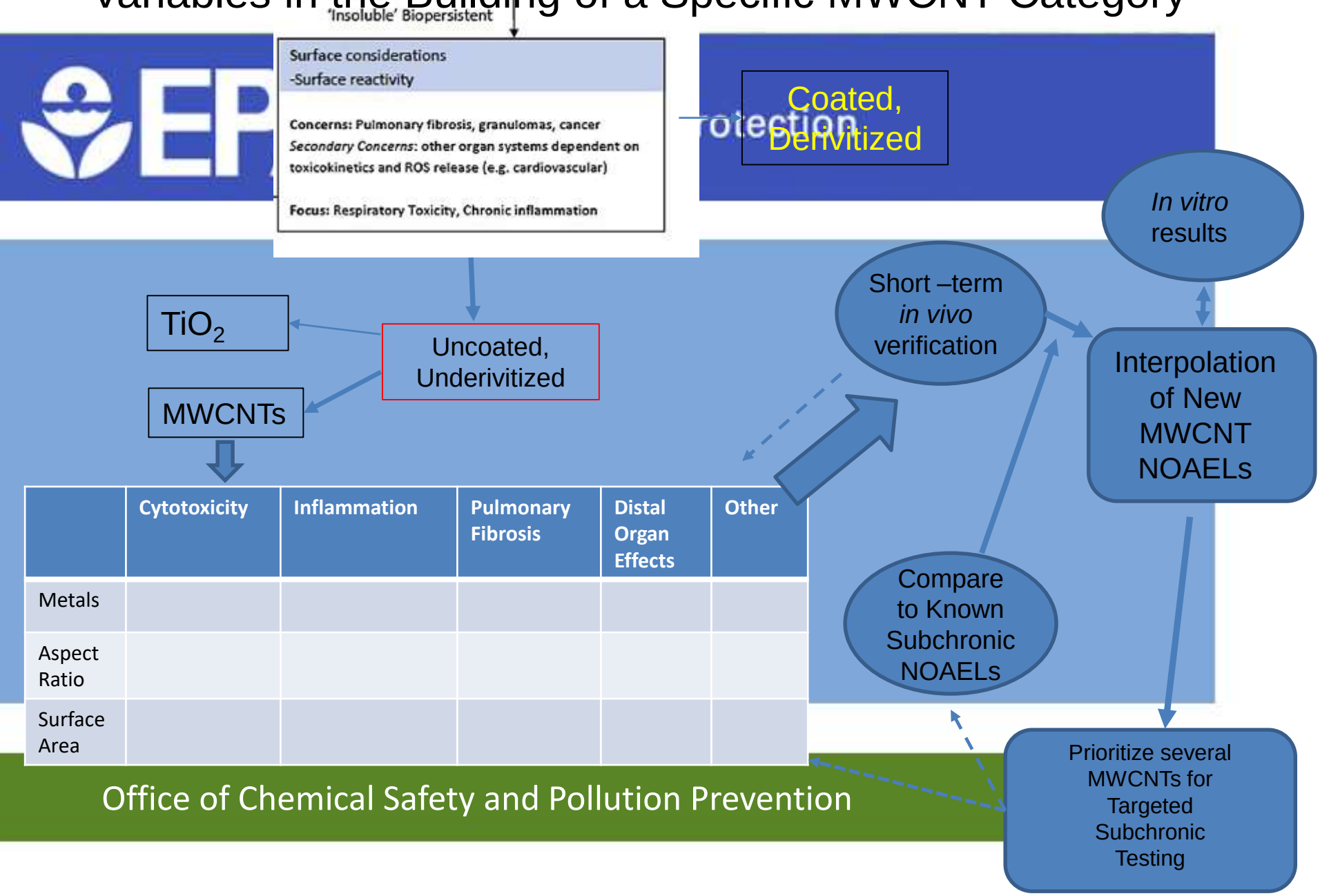
Challenges to Development of Chemical Category for CNTs

- Nanomaterials (and specifically CNTs) are engineered to have particular properties, which is different than functional group-based chemicals (aldehydes, ethers, etc.)
  - How do chemical-structural and material characterization properties correlate with physical-chemical properties?
  - CNTs often do not exist as distinct species; rather the populations of the materials can consist of distinct species and agglomerates and aggregates
  - A broad range of potential CNT forms may affect toxicology

- Insufficient data to identify relevant properties or identify properties key to establishment of a CNT category

- Unclear test methods/relevance of results

Variables in the Building of a Specific MWCNT Category



	Cytotoxicity	Inflammation	Pulmonary Fibrosis	Distal Organ Effects	Other
Metals					
Aspect Ratio					
Surface Area					

Two Examples of Characterization (Chemical Identity) Data Submitted on new CNTs

Property	MWCNT #1	SWCNT #2
Purity	Two levels of purity: 85% and >95% pure	Unspecified
Catalyst	Cobalt and nickel catalyst	Iron
Forms for sale	Sold as solid powder, liquid or liquid resin, solid resin	Sold as liquid ink dispersion

Two Examples of Characterization Data (Chemical Identity) Submitted on new CNTs (continued)

Property	MWCNT #1	SWCNT #2
Length	1.5 µm average	3 µm average
Width	ID: 3 nm OD: 15 nm	OD: 2 nm
Walls	3 – 14 walls	1
Agglomeration state	Forms agglomerates 300-400 µm in diameter	No information provided.

Two Examples of Characterization Data (Chemical Identity) Submitted on new CNTs (continued)

Property	MWCNT #1	SWCNT #2
Functionalization	Not functionalized	Functionalized w/ COOH
Branching	Not branched	Not branched
Capped or open-ended	Open-ended	Open-ended

Two Examples of Characterization (Physico-chemical properties) Data Submitted on new CNTs

Property	MWCNT #1	SWCNT #2
Solubility	< 1 ppb estimated	< 1 ppb estimated
Vapor pressure	Est. <0.000001 Torr @ 25 C	Est. <0.000001 Torr @ 25 C
Molecular weight	MW: 100000.00 g/mol	MW: 100000.00 g/mol
Bulk density	0.1 – 0.2 g/cm^3	0.1 – 0.2 g/cm^3 (from parent compound)
True density	2. g/cm^3	~2. g/cm^3 (from parent compound)

Environmental Fate of CNTs

- The Agency has insufficient information regarding the fate and transport of CNTs, and makes the following protective assumptions when assessing CNTs
  - 0% removal by a Publicly Owned Treatment Works (POTW) or a Waste Water Treatment (WWT) Plant from either biodegradation or sorption for assessing releases to surface waters
  - 0% removal via incineration
  - Rapid migration to groundwater from landfills
  - High persistence in the environment
  - Rapid transformation to highly dispersible chemical species via reaction with sunlight and natural organic matter

Ecotoxicology

- The Agency has not adopted a concentration of concern for CNTs
- CNT toxicity generally reported in the 10s to 100s ppm for both water- and sediment-borne material
  - Sublethal effects have been noted in rainbow trout at levels as low as 100 ppb.
- The solubility of CNTs is predicted < 1 ppb, but stable dispersions may be created in the presence of natural organic matter or via functionalization (environmentally feasible)
- Uptake studies in whole aquatic organisms indicate that CNT uptake is limited to ingested material
- CNT functionalization, length, capping, and purity may affect ecotoxicology

Environmental Risk Assessment

- Development of nanomaterial-specific test guidelines are needed for more appropriate environmental hazard assessment
- Furthermore, due to the transformation potential of CNTs, the Agency would likely require generation of additional data if a company wanted to release CNTs to the environment

Human Health Hazard Assessment

	Respiratory	Oral	Dermal
Absorption	Poor	Poor	Poor
Concerns	Lung overload Mutagenicity Immunotoxicity Lung cancer Effects from catalysts Effects from translocation	Effects from catalysts Systemic effects from translocation	Systemic effects from translocation Irritation - mild Sensitization – negative

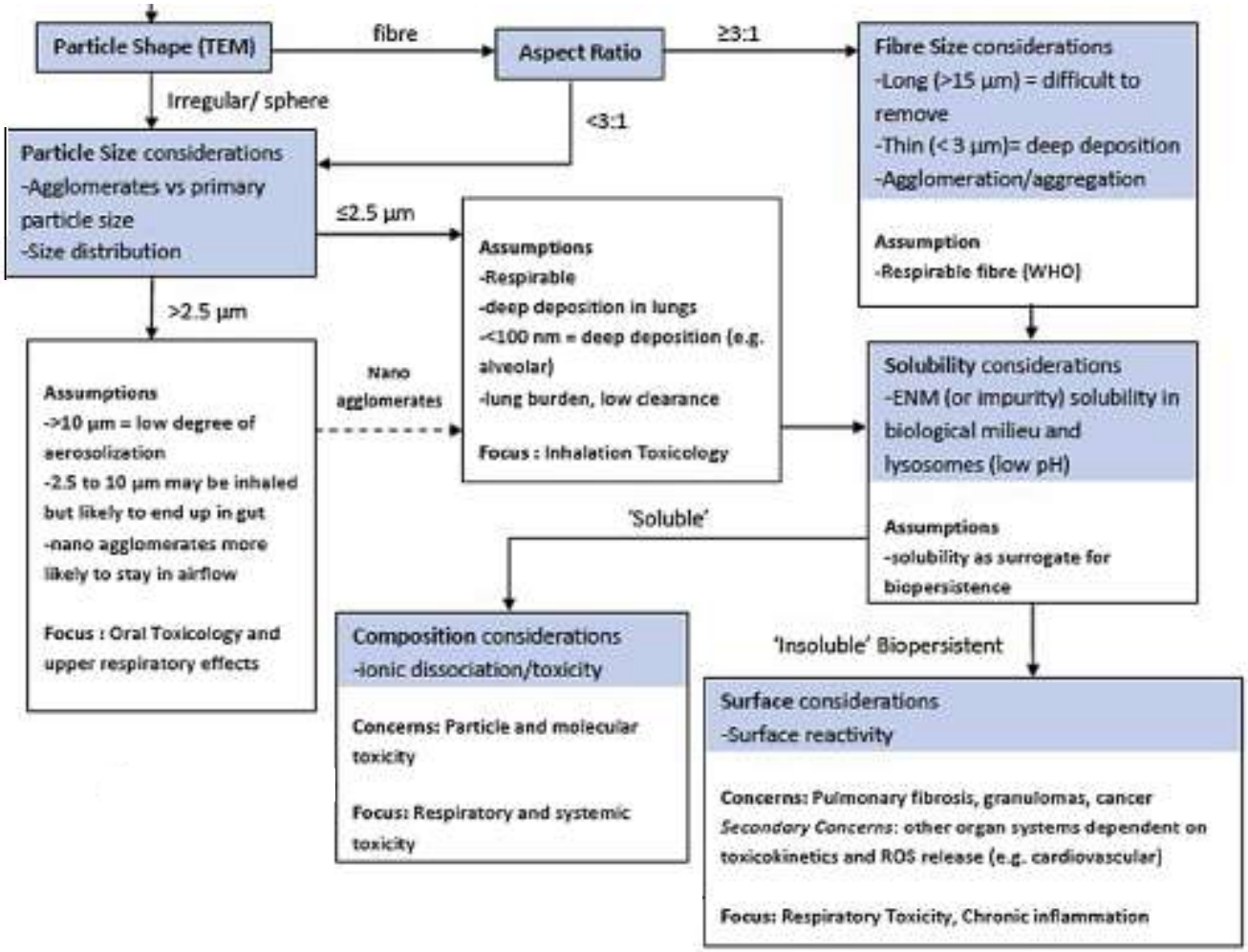
Occupational Exposure Challenges

- Large agglomerates – do these break down into respirable and inhalable particles that can reach the deep lung? What metric describes the propensity to break down?

- How do CNTs disperse in lung/other biological fluids? Is there relevance for measuring occupational exposures?

- Occupational inhalation exposures to respirable particles are a key concern
  - No consensus approach within EPA
  - Highly dependent on model and assumptions
  - Unclear how to interpret/utilize experimental data

Physicochemical Factors in Context of Inhalation Toxicity



Consumer Exposure Challenges

- The following forms of CNTs may be distributed to consumers:
  - completely reacted (cured);
  - incorporated or embedded into a polymer matrix that itself has been completely reacted (cured);
  - embedded in a permanent solid polymer form that is not intended to undergo further processing except for mechanical processing;

- Potentially useful information is testing to address the stability of CNTs in composites

For More Information

Reviewing New Chemicals Under TSCA:

https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca

Control of Nanoscale Materials Under TSCA:

https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/control-nanoscale-materials-under

Predictive Models and Tools for Assessing Chemicals Under TSCA

https://www.epa.gov/tsca-screening-tools

Thank you!

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