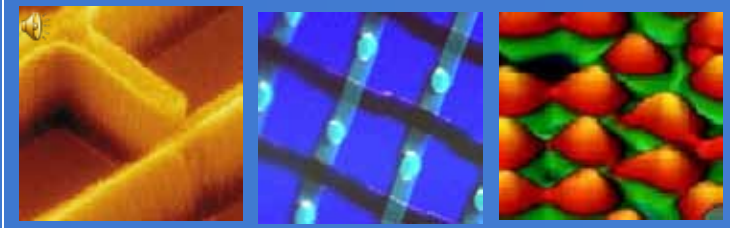

Assessing the Risks of Emerging Nanomaterials

nanoTox®
Safety in a Small World

Bridging NanoEHS Research Efforts

"US Industry Considerations"

Donald Ewert; Director, Field Services
Corporate EH&S Manager; OSO BioPharmaceuticals Manufacturing
Past-Chair; AIHA-Nanotechnology Working Group

Joint US-EU Workshop; Washington, DC; March 10-11, 2011

nanoTox, Inc. Service Capabilities

- Global Provider of 3rd Party Safety Evaluations
- Regulatory Compliance - US, EU, Japan, Canada, China
- Workplace Safety - Industrial Hygiene, Occupational Health
- Medical Management - Health Surveillance, Registries
- Fast-Track Site & Occupational Health Assessments
  - Ø **Fundamental OEHS Program Elements** *(24 Elements)*
  - Ø **Hazard Identification & Development** *(25 Elements)*
  - Ø **Exposure Control** *(30 Elements)*
  - Ø **Communication, Education & Training** *(14 Elements)*

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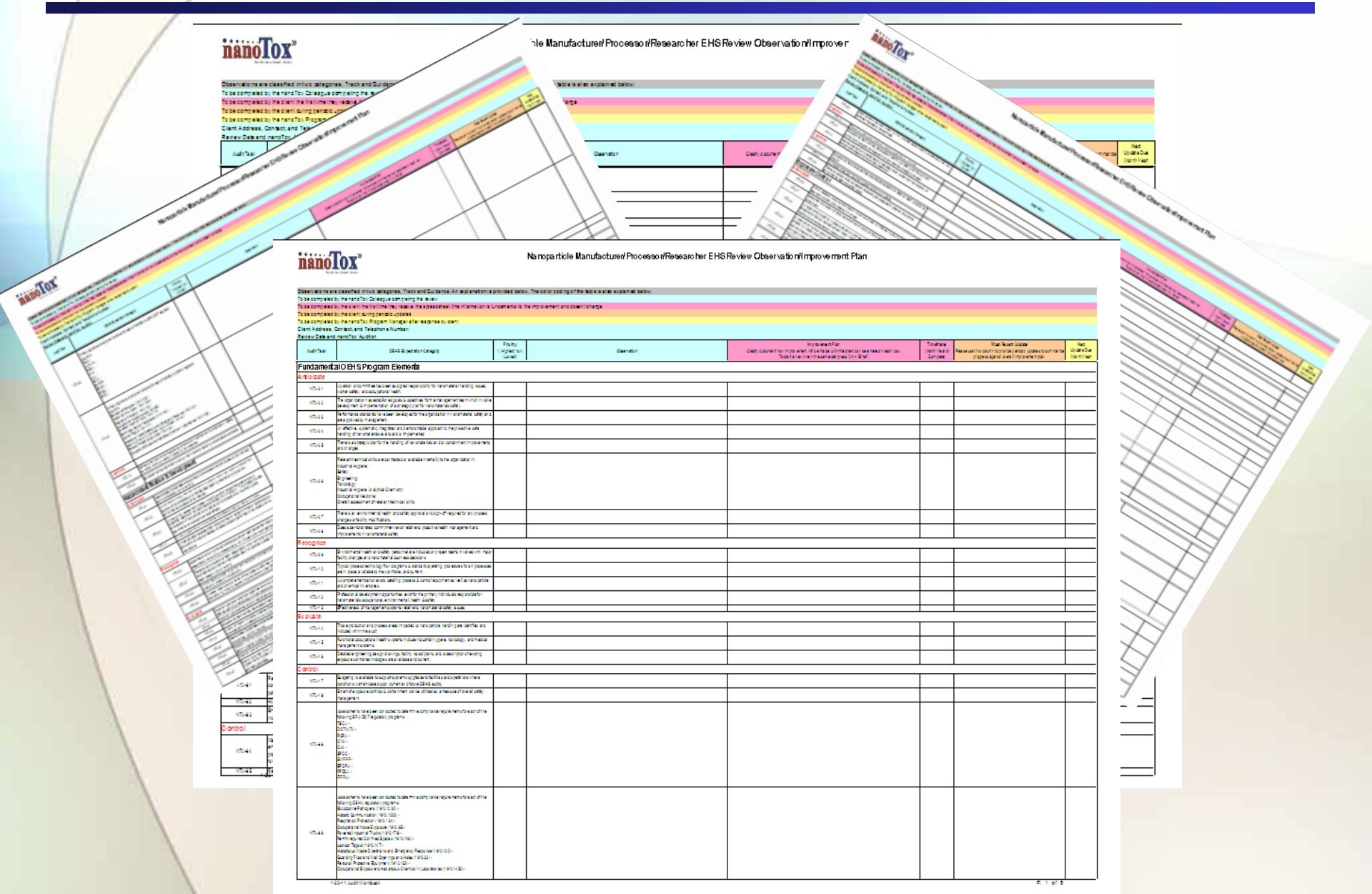


Industry Insights & Considerations

"Setting a Standard in Exposure Assessment"

Occupational, Environmental, Health & Safety

Major Regulatory Risks *(US-OSHA)*

Employer's General Duty Clause

- The employer has an obligation to protect workers from serious and recognized workplace hazards even where there is no standard**.**
- Employers must take whatever abatement actions are feasible to eliminate hazards.
- Examples (Ergonomics, Indoor Air Quality, Workplace Violence, Occupational Exposure, etc.)

Major Regulatory Risks *(US-OSHA)*

Right-To-Know; Material Safety Data Sheets

- MSDS's are the most basic and widespread component of our right-to-know about chemical health hazards in the workplace.
- The information contained in the MSDS helps workers know how to handle chemicals appropriately, assists firefighters, hazardous materials teams, and health care professionals in the event of a facility emergency or disaster, and helps citizens to learn about chemicals that are used and stored in their communities.

Major Regulatory Risks *(US-EPA)*

1) TSCA – Materials Management

- Pre-Manufacturing Notice & Significant New Use Rules

2) NEPA – Manufacturing Management

- Clean Water Act
- Clean Air Act
- Hazardous Waste Management
- Community Right-to-Know

Issues Affecting EH&S Integration

- *Most nanoscale materials undergo one to two physico-chemical changes before being forwarded to market. As a result, any data that exists may fail to accurately reflect the final hazard.*
- *The use of nanomaterial characterization data from manufacturers to catalog and inventory nanoscale materials will not provide the toxicology data needed to advance occupational health. Manufacturer data is designed to provide the end customer with material performance and is generally meaningless as a useful tool in evaluating health & safety characteristics associated with each chemical substance.*

Issues Affecting EH&S Integration

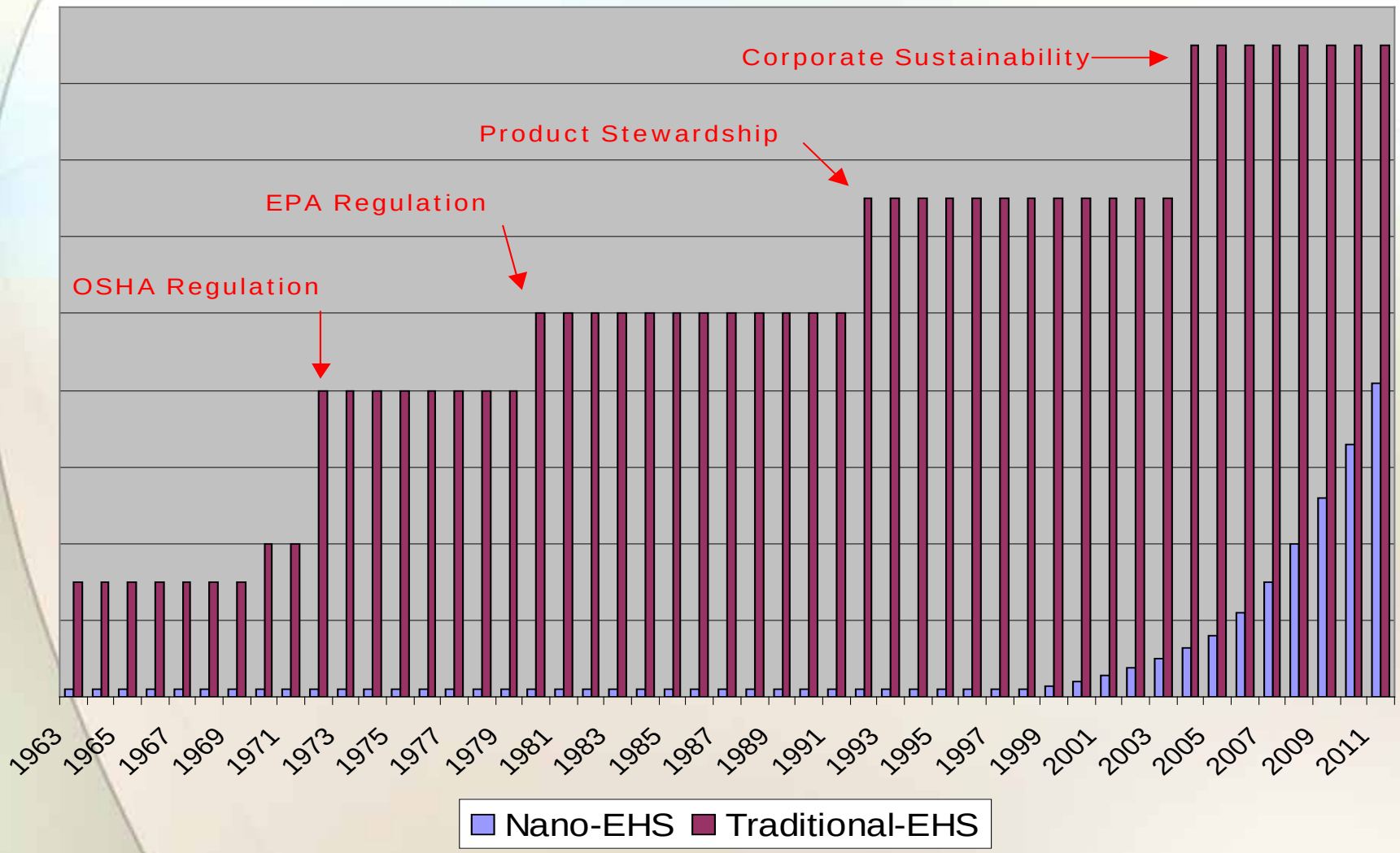
- *Current regulation is generally focused on hazardous materials while nanoscale materials cover a much broader spectrum of characteristics. We must find a way to keep from overwhelming the existing inventory system with irrelevant information on materials that have no health & safety impact on society. We must also find a means of rapidly identifying and characterizing those nanoscale materials that do possess acute or latent toxicities.*

- *Manufacturers, importers, and processors will ultimately bear the burden for any efforts involving development of nanoscale material inventories and characterization.*

Issues Affecting EH&S Integration

- *As we complete nanoscale materials characterization, each nanoparticle will ultimately be assigned risk. We must find a means of balancing rapid assessment processes with the tremendous volumes of characterization data that already exists in this decision making tree. If not, serious conflicts in hazard classification could result in an ultra-conservative approach with much greater burdens on the manufacturing community.*

40 Years of Growth in EH&S Spending



Compound Characteristics that Affect Exposure

Low	Risk	High
Wet	Physical Form	Dry
Large	Particle Size	Small
Dense	Density	Light
Spherical	Particle Shape	Feathery
No	Electrostatic	Yes
Limited	Routes of Ingestion	Unlimited
Low	Bio Availability	High
Fast/ Reversible	Acute / Chronic	Slow / Irreversible
None	'gens	All

Process Characteristics that Affect Exposure

Less	Action	More
Closed	Operation	Open
Low Energy / Velocity	Process	High Energy / Velocity
Low D p/ Temp	Pressure	High Dp/Temp
None	Transfers	Multiple
Well	Training	Poorly
None Required	Operator Skill	Highly Dependent
Routine	Task Type	Non Routine
Short	Duration	Long
One Operation	Frequency	Multiple Operation

Facility Characteristics that Affect Exposure

Better	Feature	Worse
- Ve to Corridor	Pressure	+ Ve to Corridor
Two stage + Ve buffer	Airlock	Single stage no buffer
Isolator	ECM	LEV
HEPA Terminals	Filtration	No HEPA
Away from Access	Airflow	Towards Access

Environmental Health & Safety - The 21st Century

Nanoproduct manufacturing has now moved beyond hype and into active commercialization. A report by the National Center for Manufacturing Sciences reveals that within the next 3 years, 58% of all manufacturers will have some form of nanomanufactured product available in the market. Given this rapid penetration, worker and public health are a major consideration. **To minimize potential exposures to unbound nanoparticles, historically validated pharmaceutical control methods such as process safety, chemical hygiene, product stewardship, and control banding are available and effective. Thus, manufacturers and public health professionals who are familiar with and apply these techniques can generally assure an anxious public that nano risks are manageable, health and safety considerations are defined, and controls have been implemented.**

The Pharma Industry Lead

"Setting a Standard in Exposure Assessment"

Occupational, Environmental, Health & Safety

"If an overall manufacturing facility consists of three components – pharmaceutical material, personnel, and the environment surrounding them – containment is the isolation of the first of these components from the other two."

International Society for Pharmaceutical Engineering

nanoToxicology Categorization System

Criteria	Categorization Code				
	A	B	C	D	E
OEL	>1 mg/m^3	0.10 to <1 mg/m^3	10 to <100 µg/m^3	1 to < 10 µg/m^3	< 1 µg/m^3
Potency (mg/day)	> 100 low	100 - 10 low/mod	10 – 0.1 moderate	0.1- 0.01 mod/high	< 0.01 high
Acute Toxicity	Slightly toxic	Moderately toxic	Highly toxic	Extremely toxic	Super toxic
Severity of acute effects	Low	Low/Moderate	Moderate	Moderate high	High
Chronic Toxicity	None	None	Slight-moderate	Moderate	Severe
Absorption by inhalation/skin	Minimal inhalation or skin adsorption	Moderate inhalation or skin absorption	Significant inhalation or skin absorption	Significant inhalation or skin absorption	Significant inhalation or skin absorption
Irritation Potential: Skin Eye	None Mild to moderate	Mild to moderate Mild to moderate	Moderate to severe Severe	Severe to extreme Severe to extreme	Extreme Extreme
Sensitization	Not a sensitizer	Mild sensitizer	Moderate sensitizer	Strong sensitizer	Extreme sensitizer
Mutagenicity	None	Yes	Yes	Severe	Severe
Carcinogenicity	Negative	Suspected	Suspected-confirmed animal	Defined medical case studies	Defined medical case studies
Reproductive Disorders	None	None	Slight	Moderate	Known
Teratogenicity	None	None	Yes	Severe	Severe
Neurotoxicity	Minimal	Minimal to moderate	Moderate – immediate and delayed	Life threatening	Life threatening
Epidemiology	Confirmed – no effect	Case studies/ongoing definitive data	Defined medical case studies	Defined medical case studies	Defined medical case studies
Genotoxicity	None	None – (+) Ames test	(+) in a battery of genotox studies	(+) in a battery of genotox studies	(+) in a battery of genotox studies
Warning Properties	Good	Fair	Fair/Poor	Poor	None

Surrogate Containment Testing and Bulk Powder Dustiness

By:
Matthew J. Meiners, CIH
Division Manager

BUREAU VERITAS

Move Forward with Confidence

The “Containment Challenge”

- “**Dustiness**” - defined as the propensity of a material to emit dust during manufacturing: may be considered analogous to vapor pressure on a molecular scale.
- Determined by a complex interrelationship of factors. Can not be predicted reliably by theory and must be measured empirically.
- A standardized measure of “dustiness” has not been established.
- A variety of individual particle characteristics effect relative dustiness.

Medical Management

"Setting a Standard in Exposure Assessment"

Occupational, Environmental, Health & Safety

Biomonitoring as an Exposure Metric

- Reduces the uncertainty inherent in traditional exposure and risk assessments.
- Eliminates or reduces much of the uncertainty in estimating risk because internal dose and response is directly available.
- A valuable tool for assessing human exposure to chemical contaminants with testing divided into biomarkers of exposure, effect, and susceptibility.
- Provides unequivocal evidence of exposure when utilized as part of an occupational exposure assessment.

Medical Surveillance as a Critical Tool

- Integrates information from the employee's exposure history and relevant industrial hygiene measurements
- Data on individual employees can be analyzed cross-sectionally and longitudinally to qualify changes
- Analysis for trends in health and exposure data can be aggregated from multiple workers which allows for detection of changes within the normal range
  - Example: Small changes in the white blood cell count that are insignificant in any one employee may signal an important workplace exposure effect if they occur in group data. *Why do employees working with product X have a 5% lower wbc than other workers?*

Registries & Surveillance Databases

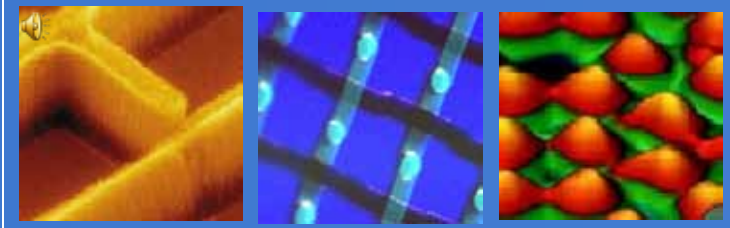
- Using a secure portal, data can be entered and accessed from any computer with internet access
- Algorithms can match specific laboratory tests and questionnaires to relevant job tasks and exposures
- "Smart forms" used in questionnaires and data collection portals avoid incomplete data collection or missing items
- Electronic collection of data facilitates tracking of individual and group trends.
- Abnormal results can be flagged and immediately reported to supervising health professionals.

A Comprehensive Stewardship Standard

- Toxicological Assessment of Engineered Nanomaterials
- nanoToxicology Categorization of Health Risk
- Site Survey and Process Inventories
- Utilization of Control Banding
- Occupational Health Training Programs
- Routine Physical & Biomedical Exposure Assessments
- Medical Health Surveillance & Monitoring Programs
- Integration Into Local & National Exposure Registries

Position Statement on Nanomaterial Product Sustainability

As an enabling technology applicable to diverse fields, including alternative energy, medicine, and electronics, among many others, nanotechnology offers tremendous value to society**. As with any emerging technology, nanotechnology and nanoscale materials must be managed in a responsible way to identify and minimize any potential adverse effect on human health or the environment. The Alliance is committed** to fostering the responsible and sustainable development of nanotechnology, to working with governmental and related nanotechnology stakeholders to develop appropriate scientific testing tools, methodologies, and data to characterize nanoscale materials, and **to developing informed, science-based governance policies, laws, standards, practices, and regulations pertinent to nanoscale materials.**



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Thank You For Participating

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