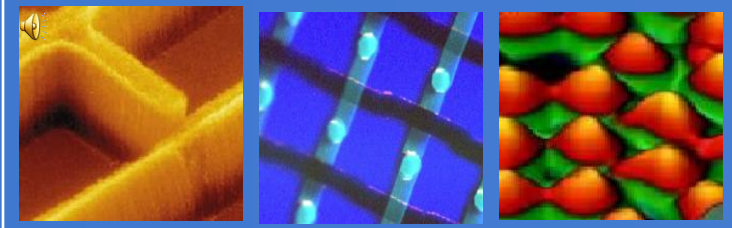


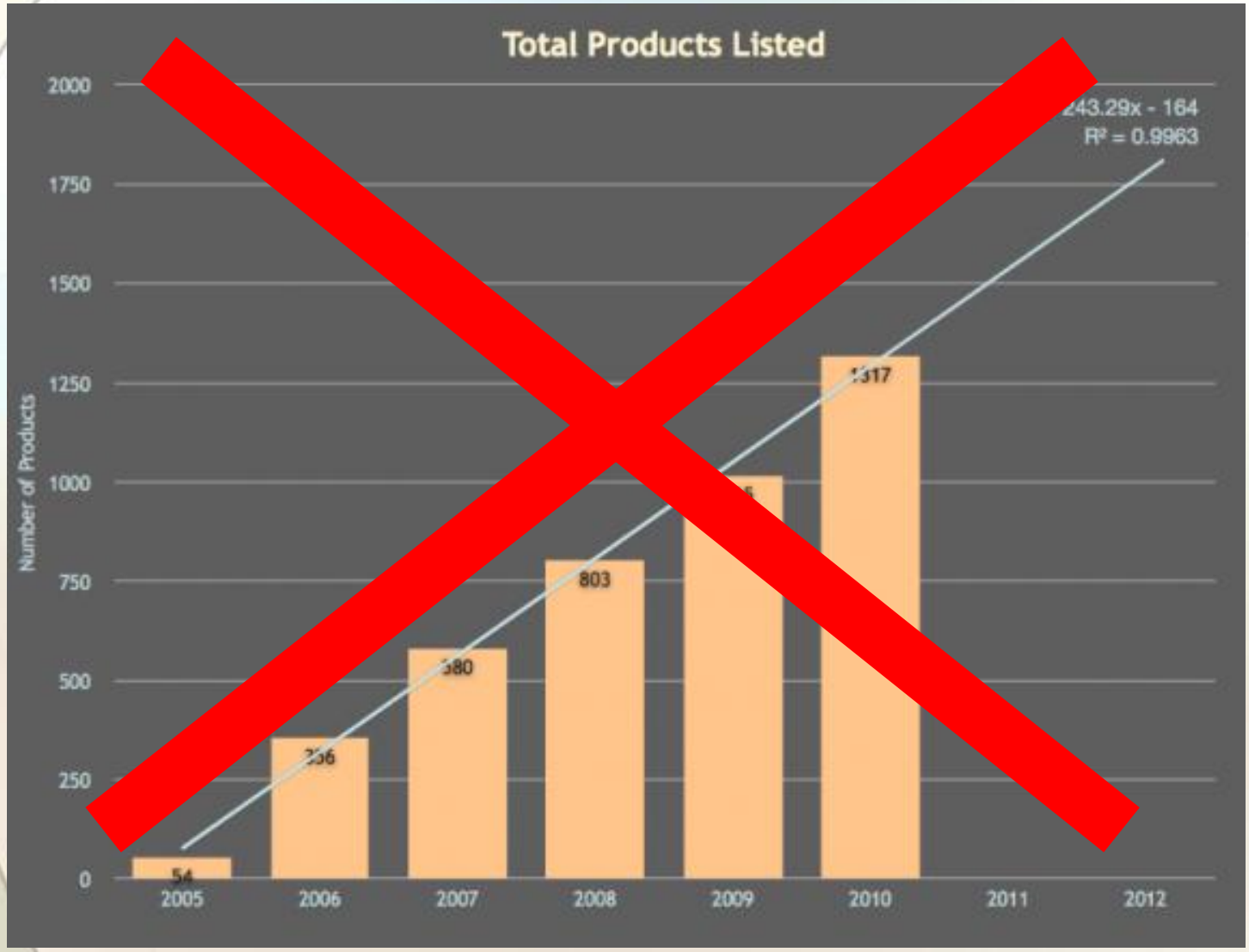
Assessing the Risks of Emerging Nanomaterials

Nanotechnology & OEHS Good Practices

"A Global Approach to Harmonization"

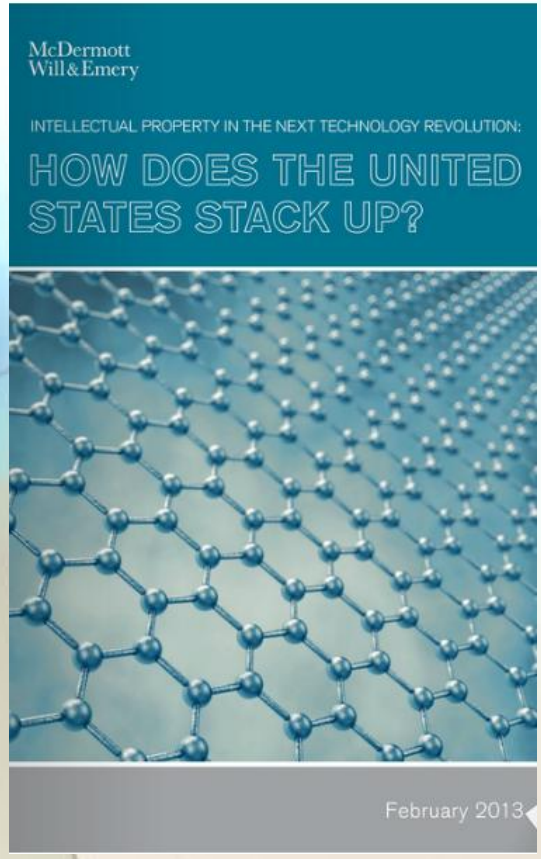
Donald Ewert, IH
Vice President – Field Services

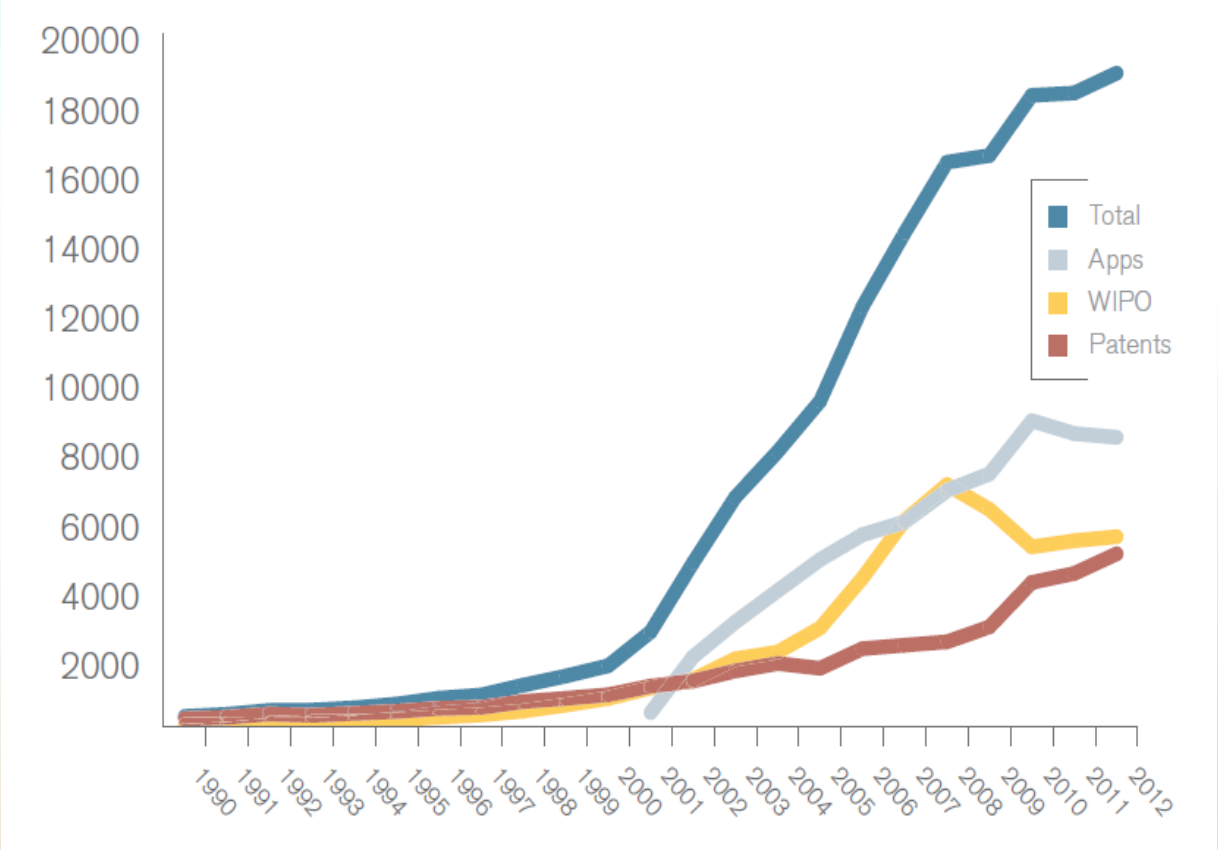
US-EU: Bridging NanoEHS Research Efforts - Joint Workshop
(Washington, DC; December 2-3, 2013)


Total Products Listed
Number of Products
2000
1750
1500
1250
1000
750
500
250
0
243.29x - 164
R² = 0.9963
54
803
1317
2005
2006
2007
2008
2009
2010
2011
2012


vitamins &
supplements

McDermott Will & Emery





"Nanotechnology patent literature" is defined as U.S. Published Patent Applications, U.S. Granted Patents and Published International Patent Applications having the term "nano*" in the claims, title or abstract. While the U.S. Patent Office (USPTO) has a nanotechnology class, specifically Class 977, the results of searching only Class 977 were found to be too narrow and did not apply to International Patent Applications. (WIPO - World Intellectual Property Organisation)

McDermott Will & Emery's 2012 "Nanotechnology: Who will be the leaders in the fifth technology revolution?"


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

Nanomaterials – A Fundamental Difference in Approach

While many definitions for nanotechnology exist, **the U.S. Environmental Protection Agency (EPA) uses the definition developed by the National Nanotechnology Initiative (NNI)** a U.S. Government research and development (R&D) program established to coordinate multi-agency efforts in nanoscale science, engineering, and technology.

The NNI (NNI 2007) requires nanotechnology to involve **all of the following**:

1. Research and technology development at the atomic, molecular, or macromolecular levels, **in the length scale of approximately 1-100 nanometer (nm) range in any direction**;
2. Creating and using structures, devices, and systems that have novel properties and functions as a result of their small and/or intermediate size; and
3. Ability to control or manipulate on the atomic scale.

Nanomaterials – A Fundamental Difference in Approach

Nanomaterials in REACH and in CLP

On 18 October 2011 the European Commission adopted the Recommendation on the definition of a nanomaterial. According to this Recommendation **a** "Nanomaterial" means:

1. A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and **where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 - 100 nm.**
2. In specific cases and **where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.**
3. By derogation from the above, fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm should be considered as nanomaterials.

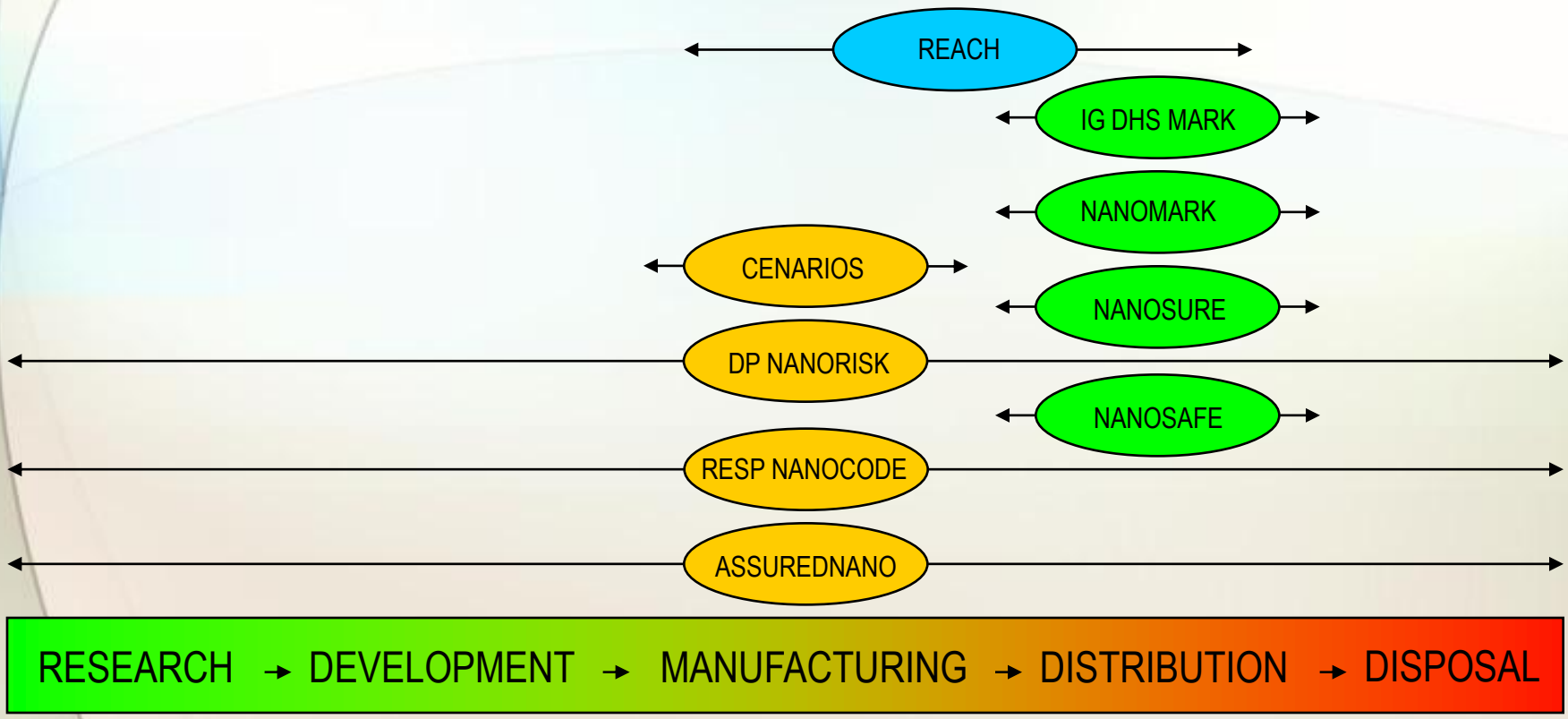
OEHS Management Systems

Existing Certification Programs

"Setting the Standard in Risk Management"

Measuring & Reporting OEHS Performance

Nanotechnology OEHS Schemes:



International Organization for Standardization

International Organization for Standardization (ISO)

OHSAS 18001 is the internationally recognized assessment specification for occupational health and safety management systems. It was developed by a selection of leading trade bodies, international standards and certification bodies to address a gap where no third-party certifiable international standard exists. OHSAS 18001 has been designed to be compatible with ISO 9001 and ISO 14001, to help your organization meet their health and safety obligations in an efficient manner.

Planning for hazard identification, risk assessment and risk control
OHSAS management program
Structure and responsibility
Training, awareness and competence
Consultation and communication
Operational control
Emergency preparedness and response
Performance measuring, monitoring and improvement

This standard does not establish OH&S performance criteria, nor does it provide detailed specifications for the design of an OHSAS management system

International Organization for Standardization

nanoTox

ISO/NP 45001

Occupational health and safety management systems -- Requirements

General information | Revisions | Corrigenda / Amendments

Edition: 1

ICS:

Status: Under development

Stage: 10.99 (2013-10-25)

TC/SC: ISO/PC 283

Number of Pages:

ISO 45001:2016 - New occupational health and safety management standard

ISO recently announced that ISO Committee ISO/PC 283 - Occupational Health & Safety Management Systems, has been formed with an objective to develop and publish an international standard for Occupational Health and Safety (OH&S) based on OHSAS 18001. The new standard will be known as ISO 45001.

At the first meeting of the committee ISO/PC 283, in October 2013, established an outline project plan for the development and publication of ISO 45001:

- ISO/CD 45001 (first committee draft) to be published by May 2014;
- ISO/DIS 45001 (first draft international standard) to be published by February 2015;
- ISO/FDIS 45001 (final draft international standard) to be published by March 2016;
- ISO 45001 to be published in October 2016.

ISO 45001:2016 - New occupational health and safety management standard

Annex SL defines a common high-level structure for all new and revised ISO management system standards - using common text in the standards. This will also have a significant impact on the revisions of ISO 9001 and ISO 14001 - currently being prepared.

The high level structure of the standard will be:

1. Scope
2. Normative references
3. Terms and definitions
4. **Context of the organization**
5. **Leadership**
6. Planning
7. Support
8. Operation
9. **Performance evaluation**
10. **Improvement**

nanOEHS Certification Program

What to We Need?

Certification Which is:

- Voluntary in Nature and Non-Regulatory in Character
- Specifically Based on Current Industry Standards in OEHS
- Capable of Rapidly Changing With Advances in Technology
- Able to Focus on Nanotechnology OEHS Program Tenets
- Based on Input From All Nanotechnology Stakeholders
- Not Based on the Performance of Executive Management
- Not Based on the Quality of the Products or Recall Criteria
- Inclusive of a Host of Yet to be Stated Considerations

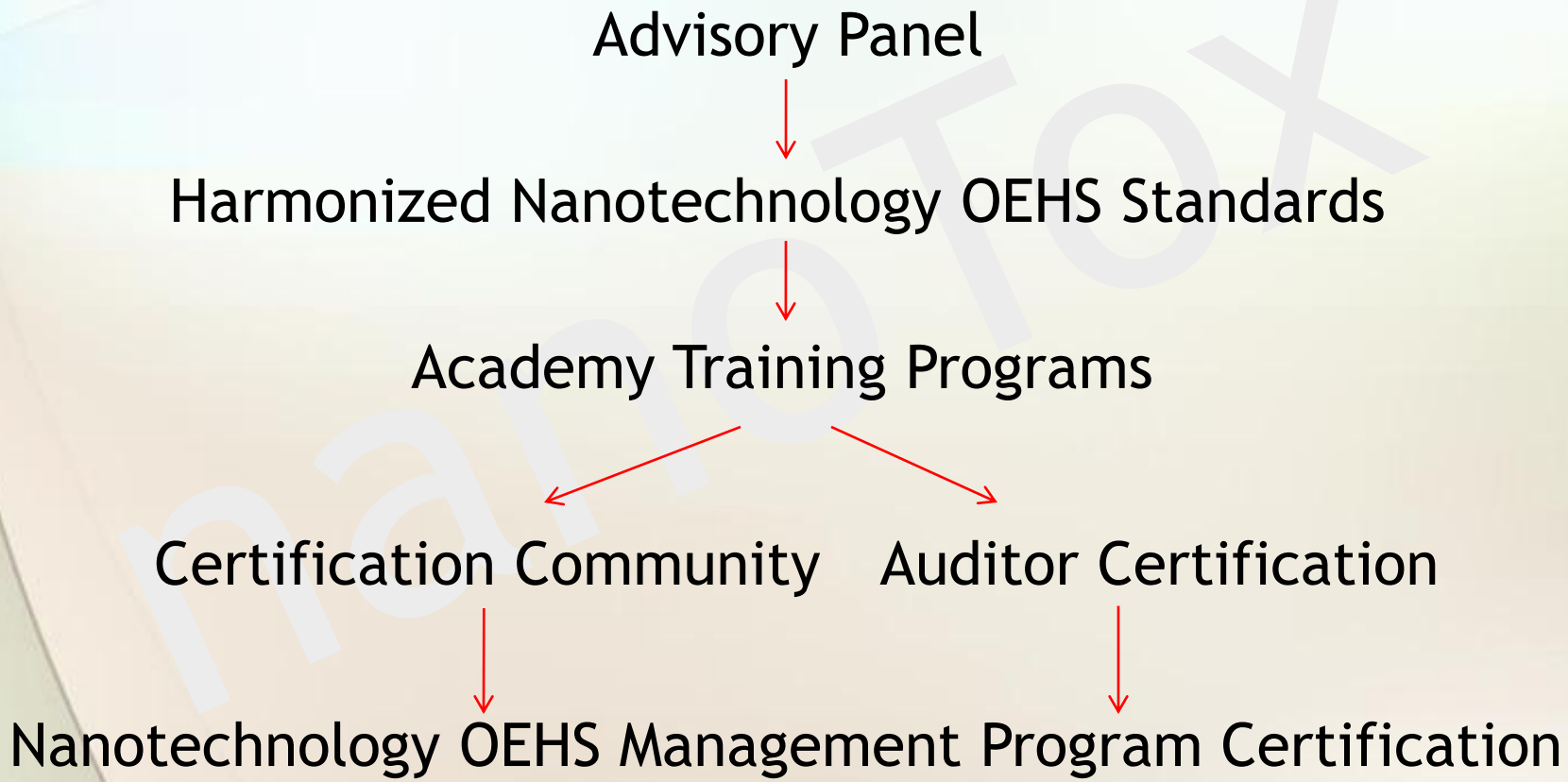
A Functional Model
(nOMS Certification)

"Setting the Standard in Risk Management"

Measuring & Reporting OEHS Performance

nOMS Certification Program

Executive Overview



nOMS Certification Program

Program Administrator

AP Member

AP Member

EU Co-Chair

Advisory Panel

US Co-Chair

AP Member

AP Member

AP Coordinator – Program Liaison

nOMS - Advisory Panel Model

Membership in the Advisory Panel is voluntary with members solicited based on their knowledge, experience and contribution to Nanotechnology OEHS. Contributing individuals represent a balance in perspectives from across commercial, institutional, scientific, medical, and worker points of view.

1. **Responsibilities:**
   a. Collection and collation of current Nanotechnology OEHS good practices from across international boundaries.
   b. Determination, selection and integration of currently available Nanotechnology OEHS good practices into a master program.
   c. Preparation of external guidance detailing the Nanotechnology OEHS good practices necessary to achieve industry standard.
   d. Development of audit systems and criteria, capable of fairly assessing Nanotechnology OEHS Programs against existing industry standard good practices.

nOMS - Advisory Panel Model (Cont'd)

2. Purpose:

a. To serve as the primary body in collating comprehensive standard(s) which serve to harmonize diverging and converging international approaches to Nanotechnology OEHS good practices.
b. To advocate for Certification of Nanotechnology OEHS Programs against harmonized good practice standards as created.
c. To establish clear and concise criteria by which Nanotechnology OEHS Programs can be audited for conformance to the current good practices is establishes.
d. To develop policies and procedures appropriate to the informatics and auditing processes involved with Certification of Nanotechnology OEHS Programs.
e. To facilitate any auditing complaints and assure fairness across all boundaries and applications.

nOMS - Advisory Panel Model (Cont'd)

3. Structure:

a. Voluntary membership status modeled after the American Industrial Hygiene Association – Nanotechnology Working Group.
b. All qualified individuals are invited to participate in the Advisory Panel at no cost to participants.
c. Members will be solicited for participation based upon their engagement in the Nanotechnology OEHS community of practice.
d. Membership within the Advisory Panel is separated according to the activity level of individual participants.

I. Individuals who actively contribute to the development of standards in Nanotechnology OEHS good practices retain full membership.
II. Members who wish to participate but, who are unable to actively contribute to the development of standards, retain corresponding membership.

nanOEHS Management System Certification

- Implementation of the Certification Program is typically scheduled over a six month time span beginning with issuance of the Nanotechnology OEHS Program Model and ending with successful completion of the audit.
- Level of customer resources necessary to achieve nOMS Certification depends on both the degree to which Nanotechnology OEHS has been integrated into business practices and the size/type of organization.
- Only those records and/or processes needed to demonstrate nOMS Certification are required. **The audit does not evaluate quality.**
- Biannual recertification is required following the initial on-site compliance audit to ensure adherence to continuous improvement and globally harmonized Nanotechnology OEHS Program tenets.
- During years in which the on-site audit is not conducted, the organization is required to conduct a self-audit and to self-certify the results.

US-EU bridging nanoEHS research efforts – CoR Chairs

Government of the Netherlands

Tom van Teunenbroek;
Ministry of Infrastructure and Environment

STANFORD UNIVERSITY

Lawrence Gibbs;
Stanford University

RUC Roskilde Universitet

Henriette Selck;
Roskilde University

ihcp Institute for Health and Consumer Protection

Dr. Hubert Rauscher;
European Commission

Pacific Northwest NATIONAL LABORATORY

Nathan A. Baker
Pacific Northwest National Laboratory

CLEMSON UNIVERSITY

Steve Klaine,
Clemson University

TNO innovation for life

Dr Derk Brouwer
TNO, The Netherlands

CEINT Center for the Environmental Implications of NanoTechnology

Mark R. Wiesner;
Duke University

ILSI Risk Science Innovation and Application

Richard Canady, ILSI Research Foundation

IOM

Martie van Tongeren, Institute of Occupational Medicine

Karolinska Institutet

Bengt Fadeel;
Karolinska Institutet

KANSAS STATE UNIVERSITY

Jim E. Reviere;
Kansas State University

nanOEHS Certification Program

OEHS Industry Standards?

OEHS Program Components Which:

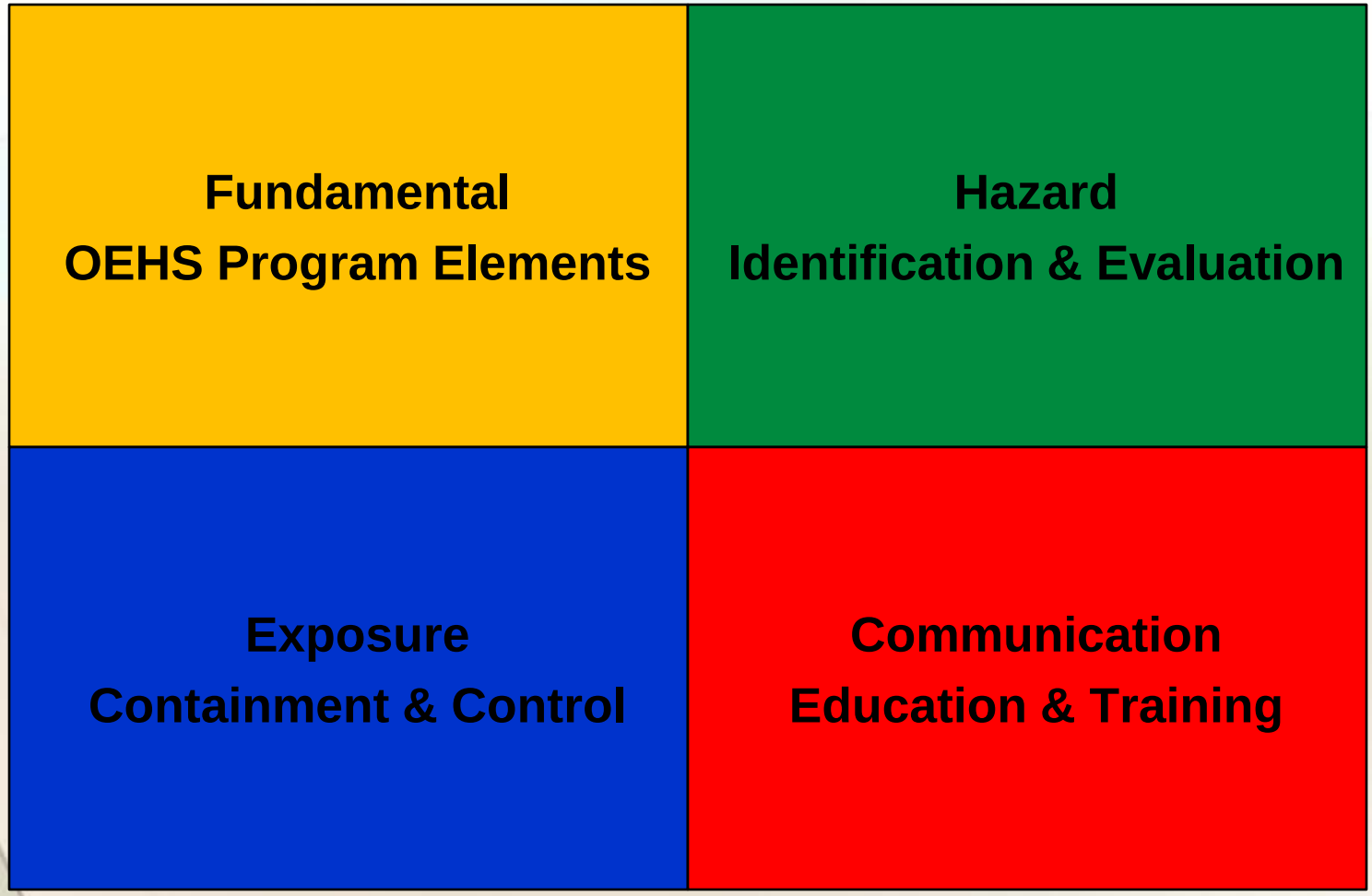
- Engages all Employment Levels From Technician to CEO
- Consistently Offers the Appropriate Level of Training
- Assures that Employees are Protected Using Good Practices
- Properly Investigates Material Hazards in Advance of Handling
- Measures the Performance of Containment & Control
- Provides Substantiation of TWA Exposure Levels for Employees
- Accounts for Life Cycle Effects of Hazardous Material Components
- Is Inclusive of a Host of Yet to be Stated Considerations

A Nanotechnology OEHS Model
(nOMS Certification)

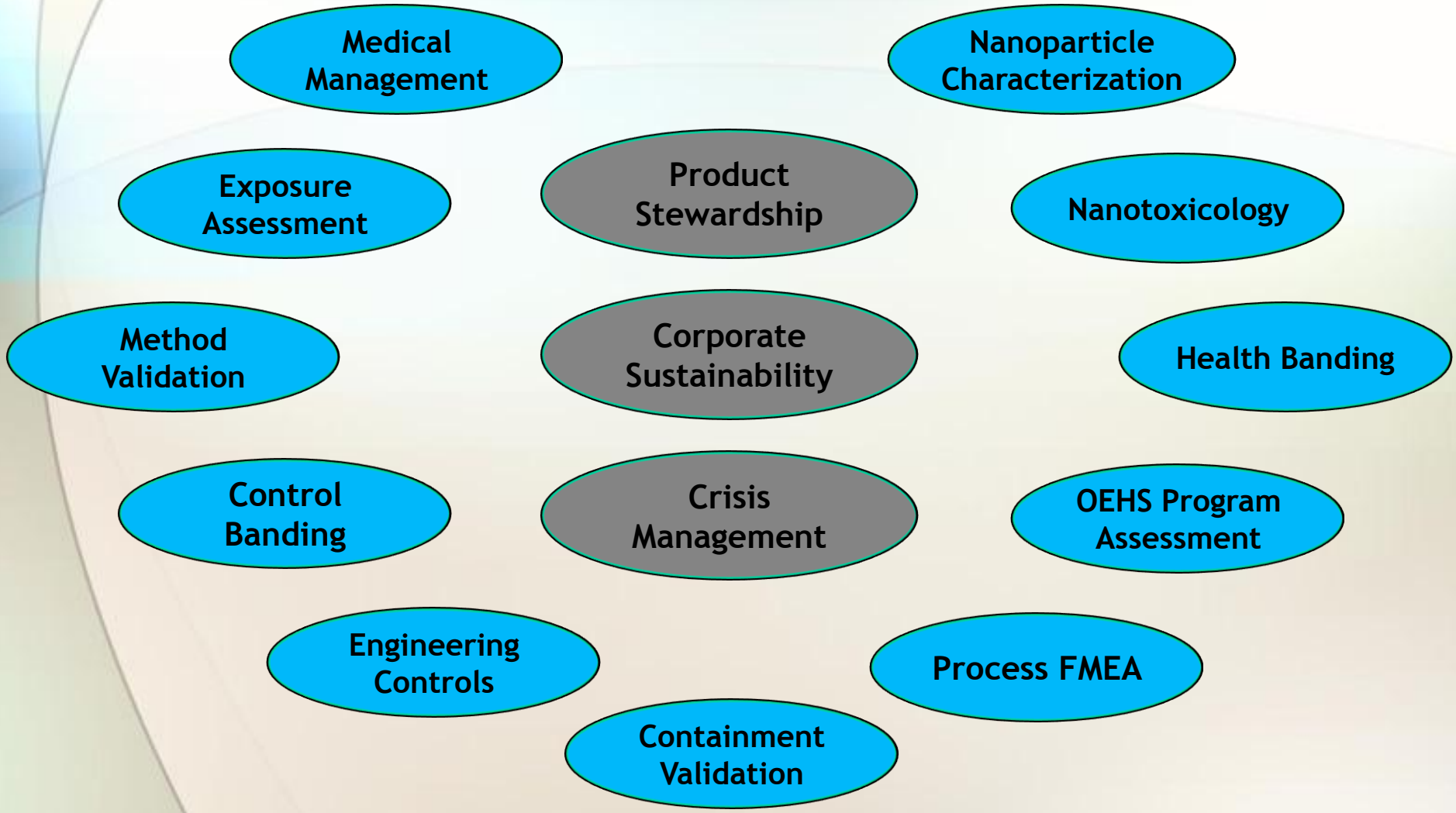
"Setting the Standard in Risk Management"

Measuring & Reporting OEHS Performance

A Comprehensive OEHS Assessment Process

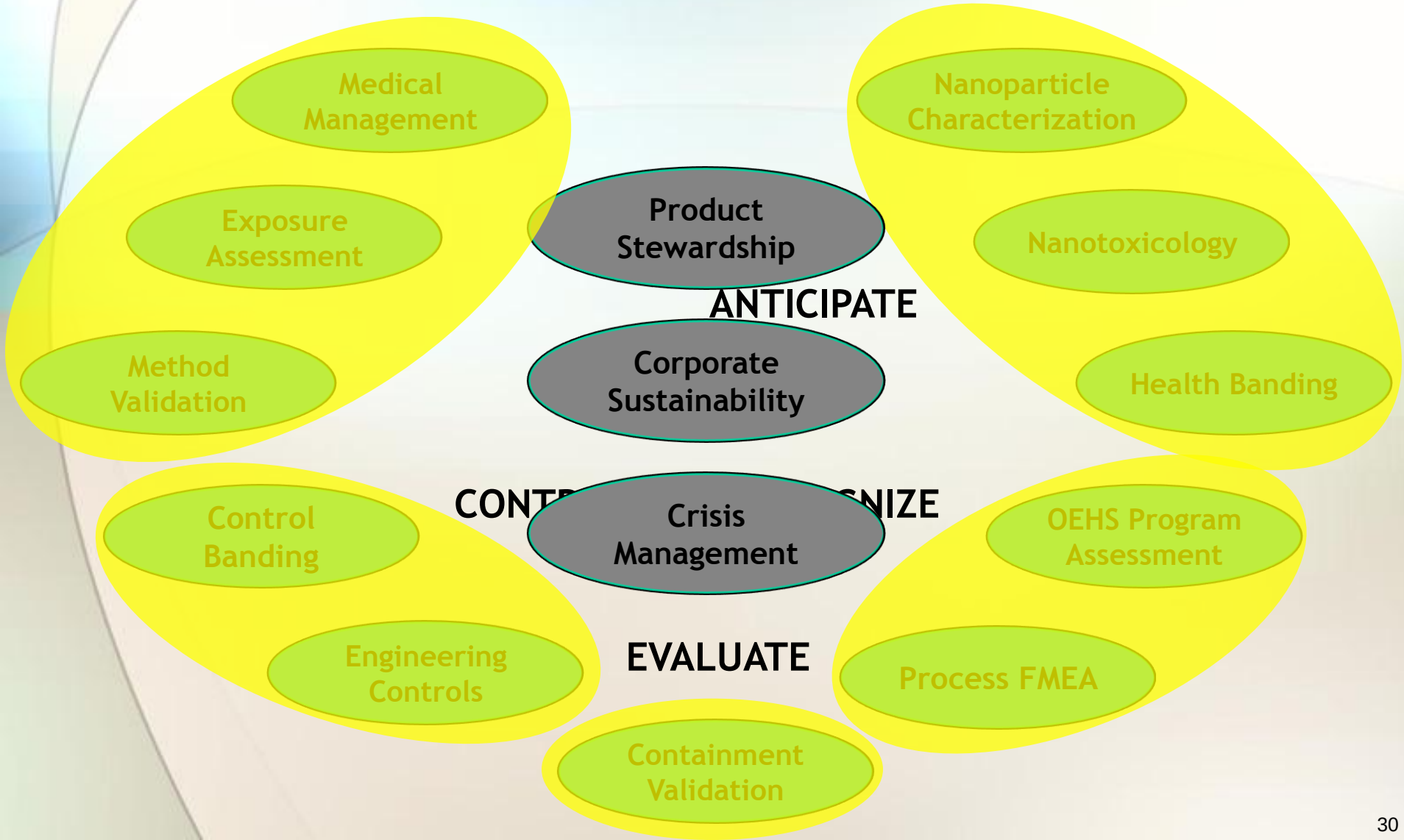


Nanomaterial OEHS Lifecycle




THE Synergist
1/11
www.aiha.org
Sound the Alarm
SHOULD WE BE WORRIED ABOUT WOOD DUST EXPOSURES?
10 Confirming Our IH Decision-Making Framework
22 Frank Mirer on the Precautionary Principle
27 Secure Your Smart Phone
29 The State of the OEHS Profession
COLUMN | LEADERSHIP PERSPECTIVE
Leadership Perspective
Confirming Our IH Decision-Making Framework
BY MARK D. HOOVER, TOM ARMSTRONG, TIM BLODGETT, ALLAN K. FLEEGER, PERRY W. LOGAN, BILL MCARTHUR, AND PAUL J. MIDDENDORF
Confirm
Anticipate
Control
Risk Management Decision-Making Framework
Documentation and Improvement
Recognize
Evaluate
Rationale for "Confirm"
A Community Opportunity
10
The Synergist ■ January 2011

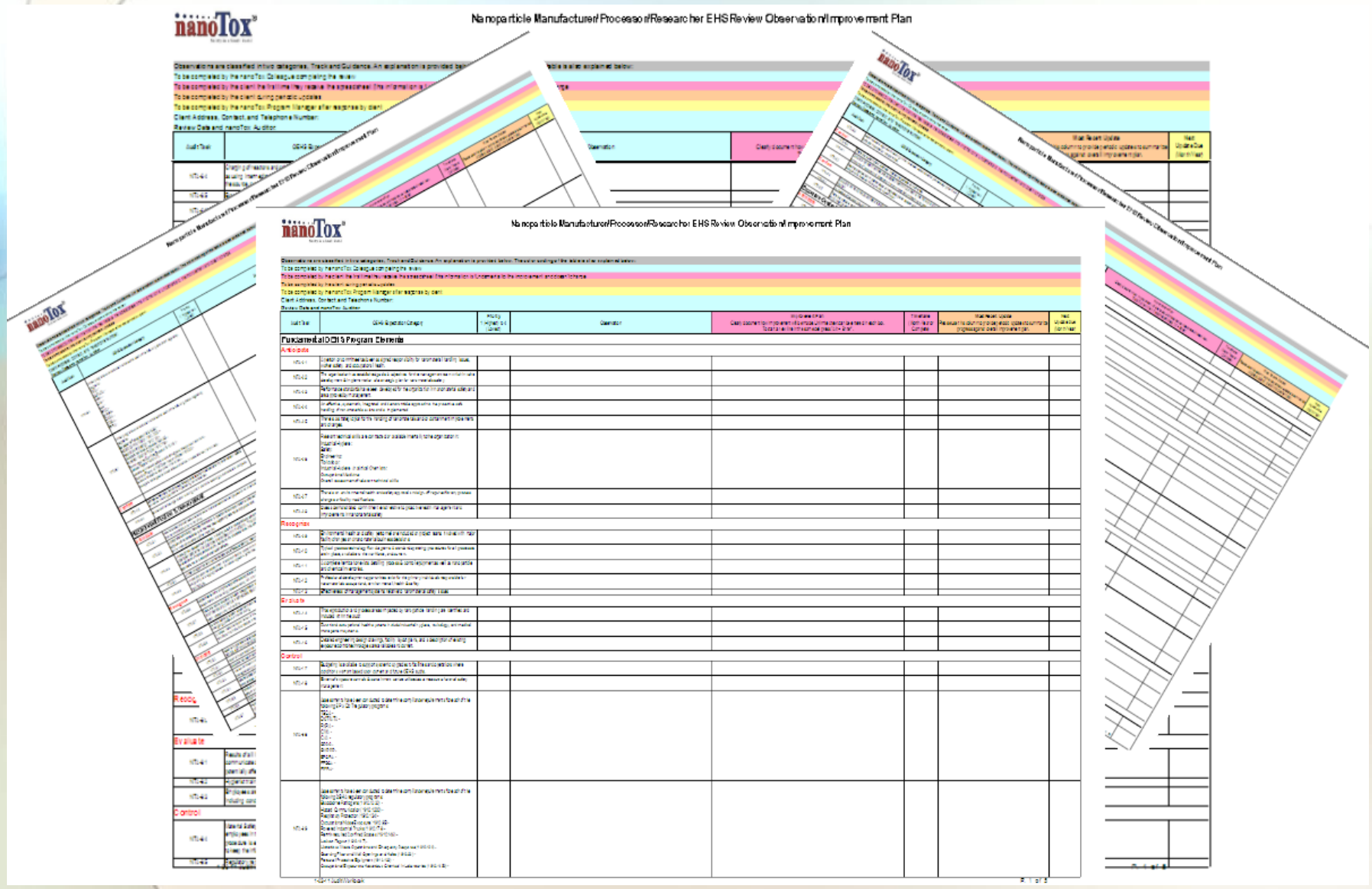
Nanomaterial OEHS Lifecycle



An Audit & Accreditation Model
(nOMS Certification)

"Setting the Standard in Risk Management"

Measuring & Reporting OEHS Performance


nanoTox
Nanoparticle Manufacturer/Processor/Researcher EHS Review Observation/Improvement Plan
Fundamental OEHS Program Elements
Anticipate
Recognize
Evaluate
Control

nanoTox OEHS Assessment Services

- Fundamental OEHS Program Elements
  - *Is there a demonstrated commitment to OEHS?*
  - *Does a viable and robust OEHS program exist?*
  - *Is regulatory compliance more than a day-to-day requirement?*
  - *Do OEHS initiatives have senior management participation?*
- Hazard Identification and Evaluation
  - *Does information exists relative to environmental fate & effect?*
  - *Is appropriate technology implemented to minimize exposure?*
  - *Do health surveillance programs exist and are they sufficient?*
  - Are all processes defined by TWA's exposure levels?

nanoTox OEHS Assessment Services

- Exposure Containment & Control
  - *Do exposure controls consistently rely on engineering practices?*
  - *Are facilities in place to contain and control exposures?*
  - *Do preventative maintenance & change control programs exist?*
  - *Are worker exposures continuously monitored and controlled?*
- Communication, Education & Training
  - *Is training at the appropriate levels available and provided?*
  - *Do changes in process controls occur based on exposure?*
  - *Is there employee engagement in OEHS at all levels?*
  - *Are exposure and medical monitoring results communicated?*

OEHS Assessment and Evaluation Criteria (EC)

(5 Points) NA - Not available for assessment

When the entity claims that the program element but, is unable to provide any substantiation or evidence of activity.

(4 Points) D - Do not have

When the entity has not established the program element.

(3 Points) N - Needs improvement/Partially meets industry standards

When the program element exists but, isn't robust or capable of meeting the expectation.

(2 Points) M - Meets industry standards

When the program element exists and satisfies the expectation in accordance with industry standards.

(1 Points) E - Exceeds industry standards

When the program element not only exists and satisfies the expectation but also, exceeds industry standards and establishes a new threshold for performance.

The Risk Product Number (RPN)
(nOMS Certification)

"Setting the Standard in Risk Management"

Measuring & Reporting OEHS Performance

OSHA and Nanotechnology: Current Activities and Regulatory Considerations
TAPPI Conference – 2006 *(L. D. Schuman, PhD, DABT, Senior Toxicologist)*

MATERIAL SAFETY DATA SHEET

Manufacturer: Phone: Fax: E-mail:

Product: Single Wall Carbon Nanotubes

Section 1 Product Identification

Chemical Name:	Carbon Fullerene
Formula:	Carbon
Chemical Family:	Synthetic Graphite
Synonyms:	Single Wall Carbon Nanotubes, SWNT
CAS Number:	7782-42-5 (Graphite)

Section 2 Composition and Information on Ingredients

Component	%	OSHA/PEL	ACGIH/TLV
Synthetic graphite	Up to 100%	15 mg/m^3 (total dust) 5 mg/m^3 (respirable fraction)	2 mg/m^3 TWA
Metallic impurity	Balance		

Section 3 Hazards Identification

Potential Health Effects

Eye Contact:	May cause eye irritation
Skin Contact:	No known hazards, but may be mildly irritating
Inhalation:	May cause irritation to respiratory tract
Ingestion:	No known hazards, but may irritate gastrointestinal tract
Acute and Chronic Health Effects:	High concentration of dusts may be irritating to eyes, skin, mucus membranes and respiratory tract.

Section 11 Toxicological Information

Effects: No known toxicological effects

MATERIAL SAFETY DATA SHEET

SECTION 1. ---------- CHEMICAL IDENTIFICATION----------

NAME: CARBON NANOTUBES, MULTI-WALL

SECTION 2. ----- COMPOSITION/INFORMATION ON INGREDIENTS ------
CAS #:NONE
EC NO: 231-153-3

SECTION 3. ---------- HAZARDS IDENTIFICATION ---------
LABEL PRECAUTIONARY STATEMENTS IRRITANT IRRITATING TO EYES AND RESPIRATORY SYSTEM. IN CASE OF CONTACT WITH EYES, RINSE IMMEDIATELY WITH PLENTY OF WATER AND SEEK MEDICAL ADVICE. WEAR SUITABLE PROTECTIVE CLOTHING.

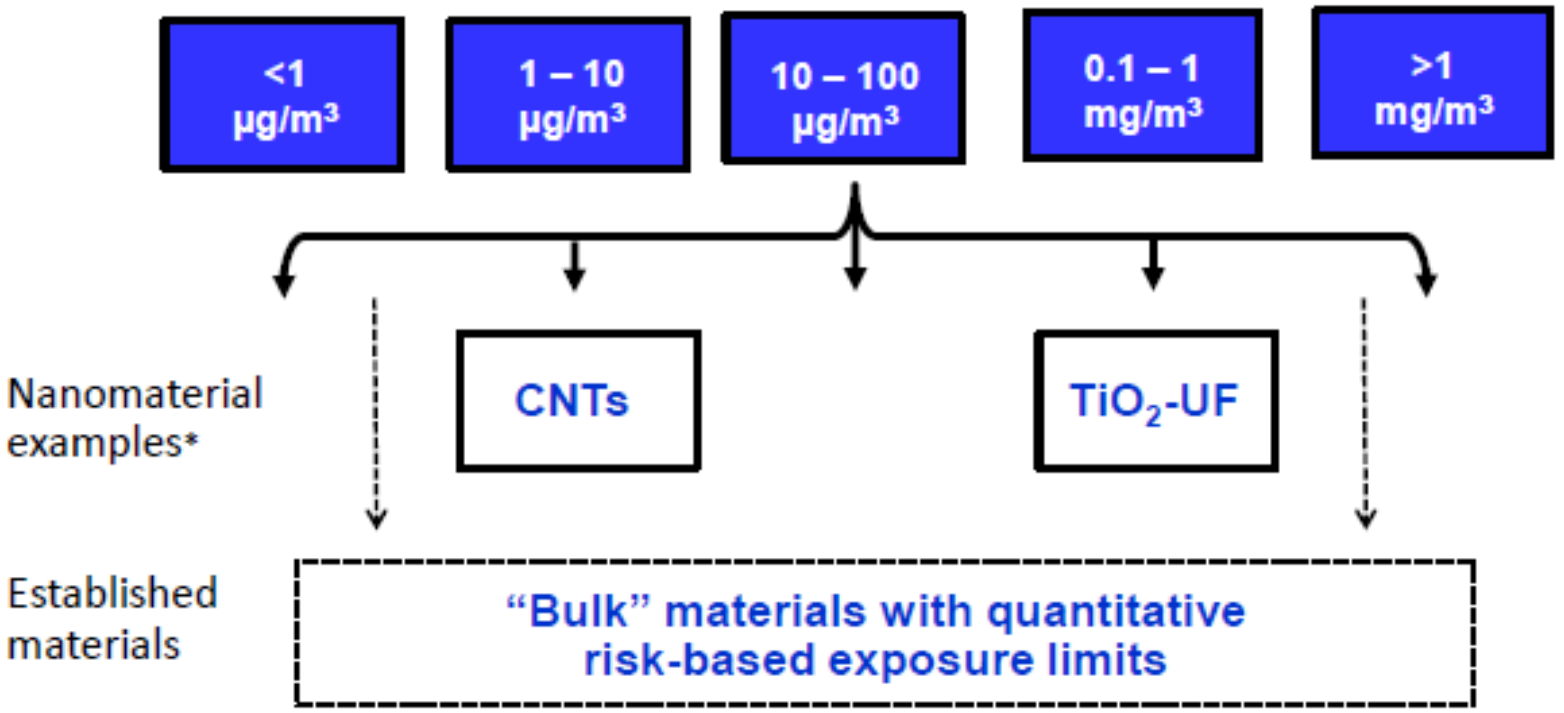
SECTION 11. ---------- TOXICOLOGICAL INFORMATION --------
ACUTE EFFECTS MAY BE HARMFUL IF ABSORBED THROUGH THE SKIN. MAY BE HARMFUL IF SWALLOWED. TO THE BEST OF OUR KNOWLEDGE, THE CHEMICAL, PHYSICAL, AND TOXICOLOGICAL PROPERTIES HAVE NOT BEEN THOROUGHLY INVESTIGATED. MAY CAUSE SKIN IRRITATION. CAUSES EYE IRRITATION. MATERIAL IS IRRITATING TO MUCOUS MEMBRANES AND UPPER RESPIRATORY TRACT. MAY BE HARMFUL BY INHALATION, INGESTION, OR SKIN ABSORPTION.

SECTION 15. ---------- REGULATORY INFORMATION ----------
EUROPEAN INFORMATION IRRITANT R 36/37 IRRITATING TO EYES AND RESPIRATORY SYSTEM. S 26 IN CASE OF CONTACT WITH EYES, RINSE IMMEDIATELY WITH PLENTY OF WATER AND SEEK MEDICAL ADVICE. S 36 WEAR SUITABLE PROTECTIVE CLOTHING.

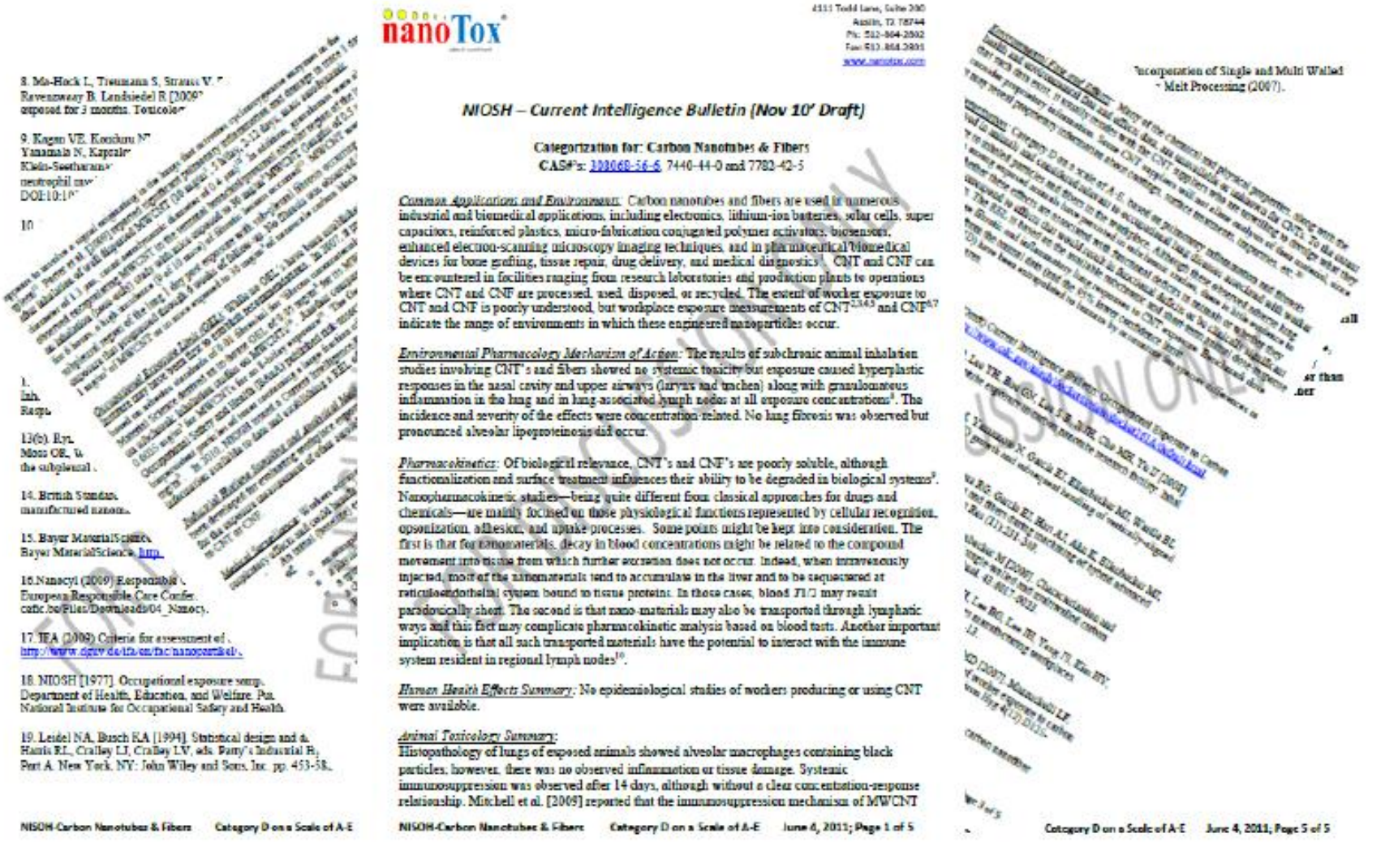
Note lack of CAS and PEL/TLV

National Institute for Occupational Safety and Health
NIOSH

Possible Benchmark Particles for Comparative Potency Analyses



*Categories assigned based on NIOSH recommended exposure limit (REL) of 1 µg/m³ for carbon nanotubes (CNTs) and 0.3 mg/m³ for ultrafine titanium dioxide (TiO_2-UF). Adverse lung effects in animals include pulmonary inflammation & fibrosis (CNT), and lung tumors (TiO_2-UF).



nanoTox

4111 Todd Lane, Suite 200
Austin, TX 78744
Ph: 512-864-2502
Fax: 512-864-2501
www.nanotox.com

NIOSH – Current Intelligence Bulletin (Nov 10' Draft)

Categorization for: Carbon Nanotubes & Fibers
CAS#'s: 308068-56-6, 7440-44-0 and 7782-42-5

Common Applications and Environment: Carbon nanotubes and fibers are used in numerous industrial and biomedical applications, including electronics, lithium-ion batteries, solar cells, super capacitors, reinforced plastics, micro-fabrication conjugated polymer actuators, biosensors, enhanced electron-scanning microscopy imaging techniques, and in pharmaceutical/biomedical devices for bone grafting, tissue repair, drug delivery, and medical diagnostics[1]. CNT and CNF can be encountered in facilities ranging from research laboratories and production plants to operations where CNT and CNF are processed, used, disposed, or recycled. The extent of worker exposure to CNT and CNF is poorly understood, but workplace exposure measurements of CNT[2,3,4,5] and CNF[6,7] indicate the range of environments in which these engineered nanoparticles occur.

Environmental Pharmacology Mechanism of Action: The results of subchronic animal inhalation studies involving CNT's and fibers showed no systemic toxicity but exposure caused hyperplastic responses in the nasal cavity and upper airways (larynx and trachea) along with granulomatous inflammation in the lung and in lung-associated lymph nodes at all exposure concentrations[8]. The incidence and severity of the effects were concentration-related. No lung fibrosis was observed but pronounced alveolar lipoproteinosis did occur.

Pharmacokinetics: Of biological relevance, CNT's and CNF's are poorly soluble, although functionalization and surface treatment influences their ability to be degraded in biological systems[9]. Nanopharmacokinetic studies—being quite different from classical approaches for drugs and chemicals—are mainly focused on those physiological functions represented by cellular recognition, opsonization, adhesion, and uptake processes. Some points might be kept into consideration. The first is that for nanomaterials, decay in blood concentrations might be related to the compound movement into tissue from which further excretion does not occur. Indeed, when intravenously injected, most of the nanomaterials tend to accumulate in the liver and to be sequestered at reticuloendothelial system bound to tissue proteins. In these cases, blood $T1/2$ may result paradoxically short. The second is that nano-materials may also be transported through lymphatic ways and this fact may complicate pharmacokinetic analysis based on blood tests. Another important implication is that all such transported materials have the potential to interact with the immune system resident in regional lymph nodes[10].

Human Health Effects Summary: No epidemiological studies of workers producing or using CNT were available.

Animal Toxicology Summary:
Histopathology of lungs of exposed animals showed alveolar macrophages containing black particles; however, there was no observed inflammation or tissue damage. Systemic immunosuppression was observed after 14 days, although without a clear concentration-response relationship. Mitchell et al. [2008] reported that the immunosuppression mechanism of MWCNT

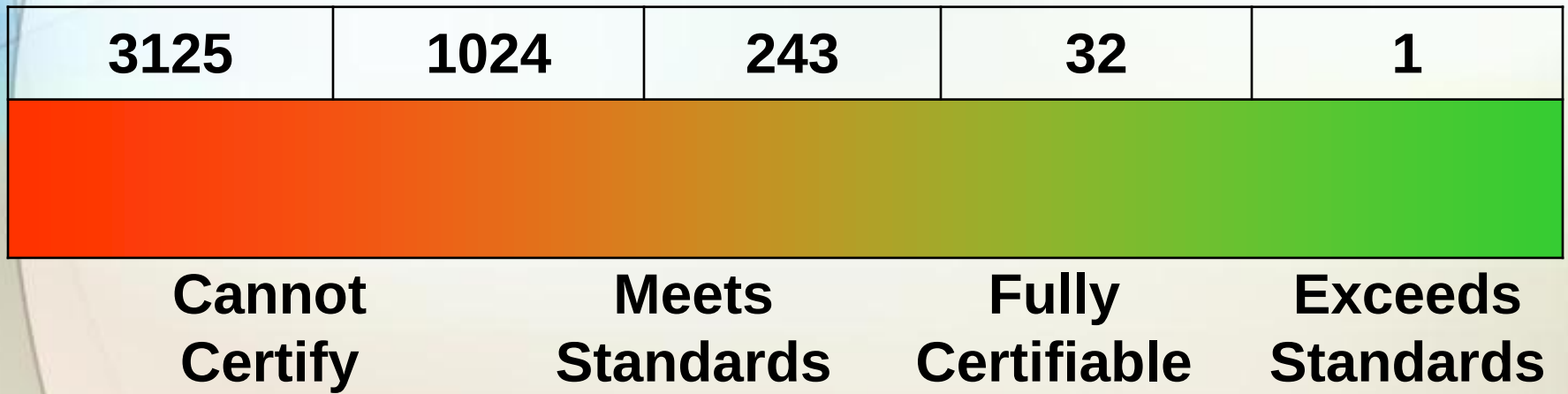
nanoTox Categorization – GHS Compliant Grouping

Criteria	Nanomaterial Categorization				
	E (5)	D (4)	C (3)	B (2)	A (1)
REL	< 1 µg/m³	1 to < 10 µg/m³	10 to <100 µg/m³	0.10 to <1 mg/m³	>1 mg/m³
Acute Toxicity - Oral	Super Toxic	Extremely Toxic	Highly Toxic	Moderately Toxic	Slightly Toxic
Acute Toxicity - Dermal	Super Toxic	Extremely Toxic	Highly Toxic	Moderately Toxic	Slightly Toxic
Acute Toxicity - Inhalation	Super Toxic	Extremely Toxic	Highly Toxic	Moderately Toxic	Slightly Toxic
Aspiration Hazard	5	4	3	2	1
Corrosion/Irritation - Skin	Extreme	Severe to Extreme	Moderate to Severe	None to Moderate	None
Corrosion/Irritation - Eye	Severe to Extreme		Moderate		None to Moderate
Respiratory Sensitization	Severe to Extreme		Moderate		None to Moderate
Skin Sensitization	Severe to Extreme		Moderate		None to Moderate
Germ Cell Mutagenicity	Severe		Yes		None
Carcinogenicity	Defined Medical Case Studies		Suspected-Confirmed Animal		Negative
Reproductive Toxicity - Fertility	Moderate to Known (Lactation)		Slight to Moderate		None to Slight
Reproductive Toxicity - Development	Moderate to Known		Slight to Moderate		None to Slight
Specific Target Organ Toxicity - Single Dose:	Severe to Extreme		Mild to Severe		None to Mild
Specific Target Organ Toxicity - Repeated Dose:	Moderate to Severe			None to Moderate	

Categorization x nOMS Assessment Values = RPN

Categorization	E	D	C	B	A
	5	4	3	2	1
Site Assessment	**Not Available for Assessment**	**Doesn't Exist**	**Partially Meets / Needs Improving**	**Meets Standards**	**Exceeds Standards**
Fundamentals	5	4	3	2	1
Toxicity Analysis	5	4	3	2	1
Exposure Controls	5	4	3	2	1
Training & Education	5	4	3	2	1
Total Score (RPN)	**3125**	**1024**	**243**	**32**	**1**

Health Band x OEHS Program Maturity = RPN



www.nanotoxacademy.com

nOMS Certification - Training & Licensing Curriculum

2-Hour, Introductory Seminar Program; General Attendance

1-Day, Intermediate nOMS Training; General Attendance

2- Day, Advanced nOMS Training; General Attendance

+ 1-Day, Hands On Field Practicum (General Attendance)

+ 1-Day, Auditor Certification (Auditor Attendance)

The Challenges Ahead
(nOMS Certification)

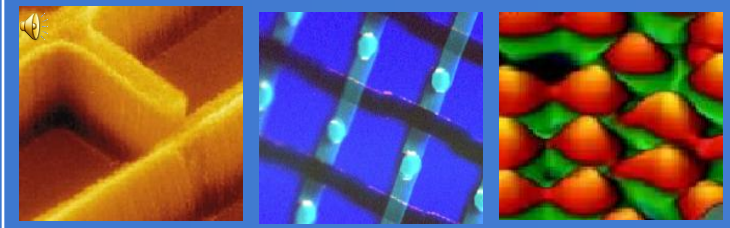
"Setting the Standard in Risk Management"

Measuring & Reporting OEHS Performance

nanOEHS Certification Program

Where Do We Go From Here?

- ✓ How Do Interested Advisory Panel Members Join In
- ✓ Who Will Co-Chair Inauguration of the Program
- ✓ How Long Will it Take to Develop a Model
- ✓ What Happens if We Can't Agree on a Model
- ✓ Who is Going to Manage This Program
- ✓ Doesn't This Program Compete With Existing ISO
- ✓ How do We Assure Program Sustainability
- ✓ How Much of My Time is This all Going to Take
- ✓ What if I Become Disinterested Once the Program Begins
- ✓ Who's Paying to Implement and Support all of This



Thank You For Participating

nanoTox Field Services Capabilities

- Global Provider of Nanotechnology OEHS Program Services
- Originator of the nanoTox Categorization System
- Regulatory Compliance Specialists (US and EU)
- Fast-Track OEHS Program Evaluations and Assessments
  - Fundamental OEHS Program Elements
  - Hazard Identification & Development
  - Exposure Containment & Control
  - Communication, Education & Training
- Health And Safety Plan – HASP Development Specialists
- Medical Management, Surveillance and Registry Experts