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)
Nanotechnology & OEHS Good Practices
“A Global Approach to Harmonization”
Nanotechnology & OEHS Good Practices
“A Global Approach to Harmonization”
“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.

"I'm looking for a loophole!"
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 Good Practices
“A Global Approach to Harmonization”

Nanotechnology OEHS Schemes:

- REACH
- IG DHS MARK
- NANOMARK
- NANOSURE
- NANOSAFE
- CENARIOS
- DP NANORISK
- RESP NANOCODE
- ASSUREDNANO

**SHE Scheme**
**Toxicology**
**Product Qualification Scheme**

**Flow:**
- RESEARCH ➔ DEVELOPMENT ➔ MANUFACTURING ➔ DISTRIBUTION ➔ DISPOSAL
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
ISO/NP 45001

Occupational health and safety management systems -- Requirements
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.
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

Advisory Panel

Harmonized Nanotechnology OEHS Standards

Academy Training Programs

Certification Community  Auditor Certification

Nanotechnology OEHS Management Program Certification
nOMS Certification Program

Advisory Panel

Program Administrator

AP Member

AP Member

EU Co-Chair

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 established.
   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

Tom van Teunenbroek; Ministry of Infrastructure and Environment

Lawrence Gibbs; Stanford University

Henriette Selck; Roskilde University

Dr. Hubert Rauscher; European Commission

Nathan A. Baker; Pacific Northwest National Laboratory

Steve Klaine, Clemson University

Dr Derk Brouwer; TNO, The Netherlands

Mark R. Wiesner; Duke University

Richard Canady, ILSI Research Foundation

Martie van Tongeren, Institute of Occupational Medicine

Bengt Fadeel; Karolinska Institutet

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

<table>
<thead>
<tr>
<th>Fundamental OEHS Program Elements</th>
<th>Hazard Identification &amp; Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure Containment &amp; Control</td>
<td>Communication Education &amp; Training</td>
</tr>
</tbody>
</table>
Nanomaterial OEHS Lifecycle

- Medical Management
- Nanoparticle Characterization
- Exposure Assessment
- Nanotoxicology
- Product Stewardship
- Health Banding
- Corporate Sustainability
- Nanotechnology & OEHS Good Practices
- Control Banding
- Crisis Management
- Corporate Sustainability
- Process FMEA
- Engineering Controls
- Containment Validation
- OEHS Program Assessment
- Method Validation

“A Global Approach to Harmonization”
Leadership Perspective

Confirming Our IH Decision-Making Framework

By MARC A. KASKER, TOX SPECIALIST, MTH BIOLOGIST, ALAN Z. FURSTENBERG, COP/C, LEADER, HELIX, AND J. MELVIN M. WILSON

For most of the last century, our nation’s workplaces have relied on OSHA’s’s Occupational Safety and Health Program to ensure worker safety and health. The program, however, has faced significant challenges, including a lack of resources, inconsistent enforcement, and a fragmented approach to regulatory oversight. As a result, workers continue to face risks from exposure to hazardous substances and conditions.

A Community Partnership is key to reducing these risks. By collaborating with industry, government, and other stakeholders, we can develop innovative solutions and best practices to protect worker health and safety. A Community Partnership approach emphasizes collaboration, transparency, and shared responsibility.

缺陷管理

确认我们的工作决策制定框架

由 MARC A. KASKER, TOX 特别专员，MTH 生物学家，ALAN Z. FURSTENBERG，COP/C，领导，HELIX，和 J. MELVIN M. WILSON

在过去的世纪中，我们的国家工作场所依赖 OSHA 的职业安全与健康计划来确保工人的安全和健康。然而，计划面临了重大挑战，包括资源的缺乏，一致的实施，和对监管监督的分割。因此，工人们继续面临来自接触危险物质和条件的风险。

一个社区伙伴关系是减少这些风险的关键。通过与行业，政府，和其他利益相关者合作，我们可以开发创新的解决方案和最佳做法来保护工人的健康和安全。一个社区伙伴关系的方法强调合作，透明度，和共同的责任。
Nanomaterial OEHS Lifecycle

- Medical Management
- Exposure Assessment
- Method Validation
- Control Banding
- Engineering Controls
- Containment Validation
- Nanoparticle Characterization
- Nanotoxicology
- Health Banding
- Corporate Sustainability
- Crisis Management
- OEHS Program Assessment
- Process FMEA

ANTICIPATE

CONTROL

EVALUATE

CONFIRM

ANTICIPATE

CONTROL

EVALUATE

CONFIRM

Nanotechnology & OEHS Good Practices
“A Global Approach to Harmonization”
An Audit & Accreditation Model
(nOMS Certification)

“Setting the Standard in Risk Management”

Measuring & Reporting OEHS Performance
Nanotechnology & OEHS Good Practices
“A Global Approach to Harmonization”

[Image of a Nanoparticle Manufacture Process Review Table]

<table>
<thead>
<tr>
<th>Material</th>
<th>Process</th>
<th>Properties</th>
<th>Testing</th>
<th>Compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nanoparticle</td>
<td>Synthesis</td>
<td>Physical</td>
<td>Quality</td>
<td>Reg.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chemical</td>
<td>Assurance</td>
<td>Check</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Toxicity</td>
<td>Analysis</td>
<td>Protocol</td>
</tr>
</tbody>
</table>

[Diagram of a Global Approach to Harmonization]
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?
- **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)
Possible Benchmark Particles for Comparative Potency Analyses

- <1 µg/m³
- 1 – 10 µg/m³
- 10 – 100 µg/m³
- 0.1 – 1 mg/m³
- >1 mg/m³

Nanomaterial examples:
- CNTs
- TiO₂-UF

Established materials:
- “Bulk” materials with quantitative risk-based exposure limits

*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 (TiO₂-UF). Adverse lung effects in animals include pulmonary inflammation & fibrosis (CNT), and lung tumors (TiO₂-UF).
Nanotechnology & OEHS Good Practices
“A Global Approach to Harmonization”

NIOSH - Current Intelligence Bulletin (Nov 30th Draft)

Categorization for: Carbon Nanotubes & Fibers

Current Applications and Environments: Carbon nanotubes and fibers are used in numerous industrial and biomedical applications, including electronics, biofuel batteries, solar cells, super capacitors, reinforced plastics, microfabrication composites, and polymers microstructural components. They also enhance electron scanning microscopy imaging techniques, and are in plans for medical devices for bone grafting, tissue repair, drug delivery, and medical diagnostics.

CNT and CNF can be encountered in facilities ranging from research laboratories to 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 CNTs and CNFs indicate the range of environments in which engineered nanomaterials occur.

Environmental Pharmacology, Mechanism of Action: The results of subchronic animal inhalation studies involving CNTs and fibers showed no systemic toxicity. If exposure caused hyperalgesic responses in the nasal cavity and upper airways (nose and mouth) along with granulomatus inflammation in the lung and in lung-associated lymph nodes at all exposure concentrations. The incidence and severity of the effects were concentration-related. No long-term effects were observed, but pronounced alveolar hypoproteinsin may 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. Nanopharmacologic studies—being quite different from clinical approaches for drug and chemicals—are mainly focused on the physiological functions represented by cellular recognition, opsonization, adhesion, and uptake processes. Some points might be kept in consideration. The first is that for inorganic fibers, decay in blood concentrations might be related to the compound movement into the from which further clearance does not occur. Instead, when inorganic fibers are used to accommodate in the lung and to be incorporated or retained, a substantial system bound to turn proteins. In these cases, blood into may reach pathologically short. The second is that nanomaterials may also be transported through lymphatic ways and their fate may complicate pharmacokinetic analysis based on blood tests. Another important implication is that all such transported nanomaterials have the potential to interact with the immunologic system resident in regional lymph nodes.

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

Histological: 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. [2009] reported that the immunosuppression mechanism of MWCNT
### nanoTox Categorization – GHS Compliant Grouping

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Nanomaterial Categorization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E (5)</td>
</tr>
<tr>
<td>REL</td>
<td>&lt; 1 mg/m³</td>
</tr>
<tr>
<td>Acute Toxicity - Oral</td>
<td>Super Toxic</td>
</tr>
<tr>
<td>Acute Toxicity - Dermal</td>
<td>Super Toxic</td>
</tr>
<tr>
<td>Acute Toxicity - Inhalation</td>
<td>Super Toxic</td>
</tr>
<tr>
<td>Aspiration Hazard</td>
<td>5</td>
</tr>
<tr>
<td>Corrosion/Irritation - Skin</td>
<td>Extreme</td>
</tr>
<tr>
<td>Corrosion/Irritation - Eye</td>
<td>Severe to Extreme</td>
</tr>
<tr>
<td>Respiratory Sensitization</td>
<td>Severe to Extreme</td>
</tr>
<tr>
<td>Skin Sensitization</td>
<td>Severe to Extreme</td>
</tr>
<tr>
<td>Germ Cell Mutagenicity</td>
<td>Yes</td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>Defined Medical Case Studies</td>
</tr>
<tr>
<td>Reproductive Toxicity - Fertility</td>
<td>Moderate to Known (Lactation)</td>
</tr>
<tr>
<td>Reproductive Toxicity - Development</td>
<td>Moderate to Known</td>
</tr>
<tr>
<td>Specific Target Organ Toxicity - Single Dose</td>
<td>Severe to Extreme</td>
</tr>
<tr>
<td>Specific Target Organ Toxicity - Repeated Dose</td>
<td>Moderate to Severe</td>
</tr>
</tbody>
</table>

“A Global Approach to Harmonization”
**Categorization x nOMS Assessment Values = RPN**

<table>
<thead>
<tr>
<th>Categorization</th>
<th>E</th>
<th>D</th>
<th>C</th>
<th>B</th>
<th>A</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
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</table>

<table>
<thead>
<tr>
<th>Site Assessment</th>
<th>Not Available for Assessment</th>
<th>Doesn’t Exist</th>
<th>Partially Meets / Needs Improving</th>
<th>Meets Standards</th>
<th>Exceeds Standards</th>
</tr>
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<tbody>
<tr>
<td>Fundamentals</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Toxicity Analysis</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Exposure Controls</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Training &amp; Education</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

**Total Score (RPN)**

- **3125**
- **1024**
- **243**
- **32**
- **1**
<table>
<thead>
<tr>
<th>Health Band x OEHS Program Maturity = RPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>3125</td>
</tr>
</tbody>
</table>

- **Cannot Certify**
- **Meets Standards**
- **Fully Certifiable**
- **Exceeds Standards**
Nanotechnology & OEHS Good Practices
“A Global Approach to Harmonization”

nanoTox Academy

The Nanotechnology OEHS Campus

nanoTox Academy, together with Fulbright & Jaworski, is pleased to offer our Winter Nanotechnology OEHS Boot Camp

“Training Tomorrows OEHS Professionals Today”

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
Assessing the Risks of Emerging Nanomaterials

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