Assessing occupational health effects of engineered nanomaterials: developments across an international strategy

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Anticipating "new" and "emerging" risks

Any occupational risk that is both new and increasing

- **New**, i.e. the risk did not previously exist and is caused by new processes, new technologies, new types of workplace, or social or organisational change; or, a long-standing issue is newly considered as a risk due to a change in social or public perceptions; or, new scientific knowledge allows a long-standing issue to be identified as a risk.

- **Increasing** if the number of hazards leading to the risk is growing; or the exposure to the hazard leading to the risk is increasing (exposure level and/or the number of people exposed); or the effect of the hazard on workers’ health is getting worse (seriousness of health effects and/or the number of people affected).
Number of nanotechnology jobs in million and the share of nanotechnology jobs of all manufacturing jobs in percent

Source: Lux Research, 2004

Dilemmas in identifying workers exposed to engineered nanoparticles

Estimated number of workers actually exposed to engineered nanoparticles
Workplace tasks that may increase the risk of exposure to nanoparticles

- Source: NIOSH, 2007 -

- Working with NM in liquid media without adequate protection (e.g., gloves) will increase the risk of skin exposure.
- Working with NM in liquid during pouring or mixing operations, or where a high degree of agitation is involved, will lead to an increase likelihood of inhalable and respirable droplets being formed.
- Generating nanoparticles in the gas phase in non-enclosed systems will increase the chances of aerosol release to the workplace.
- Maintaining equipment and processes used to produce or fabricate NM or the clean-up of spills or waste material will pose a potential for exposure to workers performing these tasks.
- Cleaning of dust collection systems used to capture nanoparticles can pose a potential for both skin and inhalation exposure.
- Machining, sanding, drilling, or other mechanical disruptions of materials containing nanoparticles can potentially lead to aerosolization of NM.

Field Investigations carried out by US NIOSH

<table>
<thead>
<tr>
<th>Type of Facility</th>
<th>Type of Particle, Morphology</th>
<th>Size of Particle</th>
<th>Range of &quot;Potential&quot; Exposure Concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td>University Research lab</td>
<td>Carbon Nanotubes, 1-10 microns long</td>
<td>Approx. 100 nm diameter</td>
<td>60-600 μg/m³</td>
</tr>
<tr>
<td>Metal Oxide Manufacturer</td>
<td>TiO₂, Lithium Titanate, powder</td>
<td>100-200 nm</td>
<td>&lt;1.00 nm: 1.4 μg/m³ (TO)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total dust: 6-149 μg/m³ (TiO₂)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;1.00 nm: ND (L)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total dust: ND - 8 μg/m³ (L)</td>
</tr>
<tr>
<td>Research and Development lab</td>
<td>Quantum Dots, spheres</td>
<td>2-41 nm</td>
<td>ND</td>
</tr>
<tr>
<td>Research and Development lab (Pilot-Scale)</td>
<td>Manganese, Silver, Nickel, Cobalt, iron oxides, spheres</td>
<td>8-50 nm</td>
<td>67 - 3816 μg/m³</td>
</tr>
<tr>
<td>Research and Development lab</td>
<td>Aluminum, spheres</td>
<td>10 - 100 nm</td>
<td>40 - 278 μg/m³</td>
</tr>
<tr>
<td>Research and Development lab</td>
<td>Elemental Metals - Silver, Copper, TiO₂</td>
<td>15 - 40 nm</td>
<td>ND</td>
</tr>
<tr>
<td>Filter Media Manufacturer</td>
<td>Nylon 6 Nanofiber</td>
<td>70 - 920 nm diameter, continuous length</td>
<td>ND</td>
</tr>
</tbody>
</table>
If exposure cannot be prevented, it should be adequately controlled.
Strategies to assess occupational health effects

Chairs: Rosemary Gibson & Daniel Bloch

www.hsl.gov.uk
An Agency of the Health and Safety Executive

The European Network on the Health and Environmental Impact of Nanomaterials

Scientific approaches to assess occupational health

Michael Riediker, Institute for Work and Health, Switzerland
Thomas Kuhlbusch, Institute of Energy and Environmental Technology – IUTA, Germany
Markus Berges, Berufs-Genossenschaftliches Institut für Arbeitsschutz, Germany
Steve Hankin, Institute of Occupational Medicine, Edinbourgh, U.K.
Daniel Bloch, Commissariat à l’Énergie Atomique -Grenoble, France
Rosemary Gibson, Health and Safety Laboratory, United Kingdom
Steps to protect workers from hazards of ENM

Current challenges in Europe for Protecting Nanotech Workers from Health Risks

- Exposure assessment
  - No agreement on relevant metrics
  - No validated exposure determinants
  - No agreement on data format
  - **No standardized approach**

- Occupational health reporting schemes
  - Not standard to have a scheme
  - Some countries always assess health, some on demand
  - Each country with different measurements
  - Each country has different legal aspects
  - Many countries have varying economic descriptors
  - **No standardized approach**
OH reporting schemes in the UK
(How would we know about nano-health effects?)

- Self-reported Work-related Ill health (SWI) questions in the Labour Force Survey (LFS)
- The Health and Occupation Reporting Network (THOR) and THOR GP Survey
- Industrial Injuries Disablement Benefit (IIDB) Scheme
- The Reporting of Injuries, Diseases and Dangerous Occurrences Regulations (RIDDOR)
- Death certificates for asbestos-related and other occupational lung diseases
- Surveillance of work-related and occupational respiratory disease (SWORD)

According to EU Directives:

- **Occupational health surveillance is mandatory for every company**
  - It is the company’s responsibility to organize it and to finance it

- **Depending on the size of the company,**
  - An occupational health department must be implemented within the company (large company)
  - Small and middle enterprises usually rely on external occupational health departments

- **Medical surveillance is mandatory for every employee**
  - One initial medical examination
  - At least, periodic medical examinations every two years
  - Periodic medical examinations every year in case of potential exposure to hazardous chemicals or other occupational hazards.
  - A medical examination in the case of accidental exposure or incidental increase of exposure levels.
What occupational health surveillance should be recommended for workers potentially exposed to ENM?

Options for Occupational Health Surveillance of Workers Potentially Exposed to Engineered Nanoparticles: State of the Science

(Johns Hopkins University Press)

**Results:** Various options for occupational health surveillance were identified. The options ranged from no action targeted to nanotechnology workers to an approach that includes documentation of the presence of engineered nanoparticles, identification of potentially exposed workers, and general and targeted medical testing.

**Conclusions:** Although the first priority should be to implement appropriate primary preventive measures, additional efforts to monitor employee health may be warranted. Continued research is needed, and the collection of such information for exposure registries may be useful for future epidemiologic studies.

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**Occupational Health Surveillance for nanotechnology workers (NIOSH model)**

A] **Medical Surveillance**
- of individual workers, includes: - medical screening, tests on asymptomatic workers, leads to therapeutic actions [early effects; sentinel events]
- of groups of workers - assess group trends for early disease [are there biomarkers sensitive enough?]

B] **Hazard Surveillance**
- Identify processes and job tasks which pose hazards
- Periodically assess hazard in the workplace
Continuum of Occupational Health Surveillance

Multi-facility Epidemiologic Research

NO ACTION

Document the presence of ENP

Identify and record workers

General medical testing

Targeted medical testing

PROACTIVE RISK MANAGEMENT

Consideration for Exposure Registries

Group analysis for trend

Exposure characterization

Biological Monitoring

Proposed OELs for nanomaterials

<table>
<thead>
<tr>
<th>Nanomaterial</th>
<th>Parameter</th>
<th>OEL</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>0.004% risk level</td>
<td>Mass-based OEL: 15</td>
<td>OECD (2008)</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>0.1 risk level particles &lt; 100 nm</td>
<td>0.1 mg/m³</td>
<td>NIOSH (2005)</td>
</tr>
<tr>
<td>General dust</td>
<td>3 mg/m³</td>
<td></td>
<td>BAuA (2009)</td>
</tr>
<tr>
<td>Photocopier Toner</td>
<td>Tolerable risk 2009 acceptable risk</td>
<td>0.06 mg/m³</td>
<td>BAuA (2008a)</td>
</tr>
<tr>
<td></td>
<td>2018 acceptable risk</td>
<td>0.006 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Biopersistent granular materials (metal oxides, others)</td>
<td>Density &gt; 6,000 kg/m³</td>
<td>20,000 particles/cm³</td>
<td>IFA (2009)</td>
</tr>
<tr>
<td>Biopersistent granular materials</td>
<td>Density &lt; 6,000 kg/m³</td>
<td>40,000 particles/cm³</td>
<td>IFA 2009</td>
</tr>
<tr>
<td>CNTs</td>
<td>Exposure risk ratio for asbestos</td>
<td>0.01 1/cm²</td>
<td>IFA (2009)</td>
</tr>
<tr>
<td>Nanoscale liquid</td>
<td>Mass-based OEL</td>
<td>IFA (2009)</td>
<td></td>
</tr>
<tr>
<td>Fibers</td>
<td>3:1, length 75,000 nm</td>
<td>0.01 1/cm³</td>
<td>BSI (2007)</td>
</tr>
<tr>
<td>CMAR*</td>
<td>Mass-based OEL: 10</td>
<td>BSI (2007)</td>
<td></td>
</tr>
<tr>
<td>Soluble</td>
<td>Not fibrous</td>
<td>Mass-based OEL: 10</td>
<td>BSI (2007)</td>
</tr>
<tr>
<td>MWCNT</td>
<td>Böyer product only</td>
<td>0.05 mg/m³</td>
<td>Bayer (2010)</td>
</tr>
<tr>
<td>MWCNT</td>
<td>Nanocyl product only</td>
<td>0.0025 mg/m³</td>
<td>Nanocyl (2009)</td>
</tr>
</tbody>
</table>

* Carcinogenic, mutagenic, asthmogenic, and reproductive toxicants
Elements of a medical surveillance program:

1. An initial medical examination (pre-employment) and collection of medical and occupational histories.
2. Periodic medical examinations at regularly scheduled intervals, including specific medical screening tests when warranted.
3. More frequent and detailed medical examinations as indicated on the basis of findings from these examinations.
4. Post-incident examinations and medical screening following uncontrolled or non-routine increases in exposures such as spills.
5. Worker training to recognize symptoms of exposure to a given hazard (“sentinel events”).
6. A written report of medical findings.
7. Employer actions in response to identification of potential hazards and risks to health.

Stepwise approach to surveillance

- Needs Assessment
  - Is there a hazard?
  - Is there exposure?
  - What is the risk?
- Medical Screening (early signs/symptoms?)
- Systematic Data Collection (Epidemiological Surveillance)
- Exposure Registry
- Hazard Surveillance

- Make risk (Haz x Exp) determination
- Where data are incomplete, “qualitative”
- Periodic reassessment is important

The decision to carry out a targeted occupational medical surveillance at least requires:

1. knowledge about the existence - or at least possibility - of an exposure to a health hazard,
2. knowledge about specific health effect caused by such an exposure,
3. the availability of tests with a known sensitivity and specificity to detect such health effects in an early, preferably reversible or treatable, stage
4. establishment to a sufficient degree of the causal relation between exposure and effect.

Is there a rationale to propose specific medical screening for workers potentially exposed to NP?

Absence of consistent data about the possible disease endpoints of exposure to NP
- pulmonary, cardio-vascular diseases (increase morbidity and mortality among already affected people probably linked to pollution (ultrafine particles) but not clearly established.
- Main possible endpoints: pulmonary and cardio-vascular system, inflammation:
  - Non specific
  - High prevalence in the general population
  - Due to many non occupational risk factors
- No experimental data on long term possible effects of NP exposure

- NIOSH Current intelligence bulletin Nº 90: Interim guidance for medical screening and hazard surveillance for workers potentially exposed to engineered nanomaterials February 2009


**Summary**

- **Occupational health surveillance for nanotechnology workers**
  - Unique physical/chemical properties of nanomaterials
  - Information suggesting NMs pose safety and health risks

- **First step in surveillance program is needs assessment**
  - Hazard and exposure assessments
  - Data needed for assessment may be lacking
    - *periodic reassessment*
  - Qualitative risk determination

- **Evaluate need for medical (health effects) surveillance**

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**Critical issues in designing epidemiological studies of ENM workers**

1. **Heterogeneity** of nanoparticles;
2. Define the **disease endpoint**;
3. **Temporal factors** (likelihood to observe the outcome; short-term vs. long-term effects)
4. Identify the **target population**/study population;
5. Exposure **duration and intensity** (effectiveness)
Exposure registries

**DEFINITION:** An enrollment of persons exposed, or likely to have been exposed, to occupational or environmental hazards [that can serve as a means of identifying persons for primary or secondary preventive efforts]

**Purpose:**

- Delineate a population at risk
- Follow a cohort to ascertain exposure disease associations
- Follow a cohort to ensure appropriate primary and secondary preventions and medical surveillance
- Follow a cohort for appropriate social, legal, and economic support
- Demonstrate societal concern for a cohort
- Notify a cohort of important information not available when registry was initiated.

**Conclusion**

- Currently, no specific screening tests can be proposed for the medical surveillance of workers potentially exposed to engineered nanoparticles
- Periodic general medical examination is recommended *(if not mandatory)*
- Collection of health data should provide a body of information that might be useful for future epidemiological studies.
- The long term follow up of the exposed population *(epidemiological studies)* should be considered.
- Field studies and exposure characterization campaigns should be promoted
- There is a urgent need for biomarkers of exposure and early effects *(short term effects)*
- In the perspective of future epidemiological studies, all data relevant for assessing occupational exposure should be collected and recorded *(exposure registries)*