Pulmonary Toxicity of Carbon Nanotubes: Ethical Implications and Human Risk Assessment

John T. James
NASA/Johnson Space Center
12 October 2006
Potential Energy Applications of Carbon Nanotubes

- Hydrogen storage in fuel cells
- Lithium storage in Li-ion batteries
- Supercapacitors
- Solar Cells
- Thermo-electric Devices
Ethical Framework

- Who benefits and who is placed at risk by the new technology and its application? Does who = any life?
- How much of the risk is real and how much is imagined?
- Is there synergy with other uncontrolled risk factors?
- If the risk is real, then how soon will we know its magnitude?
- Can we replace known risks with lesser risks, or are we just adding risk?
- Can risk be transferred to others, and is that ethical?
- What authority has responsibility and control over risks?
- Are those in control knowledgeable, ethical, and accountable?
- To whom are they accountable and when?
Framing the Nanotube Risk Assessment

Problem

• Potential for Human Exposures
  – Manufacturing facilities
  – Research Facilities
  – Shipping and use points
  – Military: Obscurants
  – Exposures by respiratory and dermal routes
  – Medical applications
  – Environmental (multi-walled nanotubes)
Framing the Risk Assessment Problem (continued)

- Inherent Toxicity of Single-walled nanotubes
  - Physical form
    - Shape
    - Surface area
    - Self adhesion
  - Chemistry
    - Impurities
    - Surface chemistry
  - Particle size distribution
  - Translocation within the organism
  - Persistency within the organism
  - Response of the organism to persistent exposure
Properties of SWNT

- Rolled up graphite sheets composed of “benzene” rings
- Diameter of the order of 1 nm
- Length in excess of 1 μm
- Tubes agglomerate into “tattered ropes” of >10nm diameter
- Metal Impurities present from manufacturing process

End cap is half a Buckyball
Preparation of SWNT

• Graphite Vaporization
  – Electric Arc Discharge onto metal particles
  – Laser Vaporization onto metal particles
• Chemical Vapor Deposition from CO under high pressure
• All products contain residual metal catalysts
• Purification can reduce metal content
SWNT PRODUCTS WE STUDIED

Raw HiPco NT  Purified HiPco NT  Carbolex Electric-arc NT
Experimental Protocol

• Determination of metal content of SWNT samples
• Preparation of dust suspensions
  – Suspended in heat inactivated mouse serum
  – 3 types of SWNTs, carbon black, quartz were tested
• Intratracheal instillation of suspended dust
  – Anesthetized male B6C3F1 mice (4-5 per group, 30 g/mouse)
  – 0.1 or 0.5 mg SWNT suspension delivered through small incision into trachea in 50 μl volume of heat-inactivated mouse serum
• Lung collection and histopathology
  – Lungs harvested after 7 and 90 days
  – Treatment group in 90-day study was unknown to the pathologist
### Metal content of SWNT and Carbon Black (% of total weight)

<table>
<thead>
<tr>
<th>Test Material</th>
<th>Raw SWNT</th>
<th>Purified SWNT</th>
<th>CarboLex SWNT</th>
<th>Carbon Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe</td>
<td>26.9</td>
<td>2.1</td>
<td>0.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ni</td>
<td>0.8</td>
<td>&lt;0.01</td>
<td>26.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Y</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>5.0</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Advantages of Intratracheal Instillation Compared to Inhalation

- Less test material required
- Less expensive than inhalation exposures
- Dose delivered is known more precisely
- No concomitant exposures via non-inhalation routes-oral & dermal
- Easier to control risks to those conducting the exposure if agent is highly toxic
- Bypass the filtering capabilities of rodent upper airways
- Can include comparison compounds of known toxicity
Disadvantages of Intratracheal Instillation Compared to Inhalation

- Unnatural delivery to site of effect
  - Slower clearance of instilled particles
  - Deeper penetration into lung
  - Increased bioavailability of soluble components
  - Effects on lung may be exaggerated
- Cannot discover effects on upper respiratory system
- Uneven distribution of material within lung—locally high
- Vehicle influence: delivery and properties of test material
- Animals must be anesthetized and mildly invasive procedure (transtracheal) often used
- Many of the disadvantages can be addressed by parallel testing using compounds of known inhalation toxicity
Granulomas from SWNTs, but not Carbon Black-Why?

Bundles: NTs pack tightly and in parallel to form ropes or clumps.

Structurally: Individual tubes or bundles are fibers, CB is amorphous
Histopathologic Micrographs of Lungs from Mice of the HD-90d Groups

Carbon Black

Quartz

Carbolex NT

Raw NT (low m.)

Raw NT (high m.)
Purified NT
Incidence of Lesions after 90 Days (n= 5)

<table>
<thead>
<tr>
<th>Dose of Material (mg)</th>
<th>Lesion</th>
<th>Carbon Black</th>
<th>Quartz NT</th>
<th>Raw NT</th>
<th>Purified NT</th>
<th>CarboLex NT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>Inflammation</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>0.1</td>
<td>Granuloma</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>0.5</td>
<td>Inflammation</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>0.5</td>
<td>Granuloma</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>
Relationship to Inhalation Exposures

- Assume: 40% of respirable dust deposits in pulmonary region of the lung
- Assume 30g mouse inhales 30 ml of air/minute
- Assume a concentration of 5 mg/m$^3$ for 8 hours/day (current PEL for respirable graphite dust)
- Accumulation would be 0.03 mg/day
- Total dose of 0.1 mg (our low dose) would be reached in <4 days and total dose of 0.5 mg (our high dose) would be reached in < 17 days
Conclusions

• On an equal weight basis, and if they reach the pulmonary regions of the lung, single-walled carbon nanotubes can be more toxic than quartz, which is a known occupational health hazard.

• Until more is known about the potential for nanotubes to reach deep into the lung, industrial hygiene practices should minimize any worker exposures.
Researching the Ethical Issues of Nanotube Use

• Discover the properties that make nanotubes toxic to reduce need to test every formulation created
• Monitor the workplace and use locations for respirable nanotubes in the air
• Monitor workers for health effects
• Determine environmental fate of nanotubes
Distribution of Nanotube Economic Value with Justice

- How much ($) and how long do the pioneers and risk takers benefit?
- Are military applications just?
- Whose livelihood will be destroyed?
- Whose environment will be altered?
- Are we passing difficult problems to subsequent generations?
- Who is denied the advantages of the technology because it is too expensive?