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Summary of Toxicological Data

Nanotubes and Nanofibers

Occupational Exposure to Carbon

NIOH CIB
Inhalation (1 – 90 days) aspiration, intertracheal instillation, aspirated (dispersed), smaller structures (more dispersed), poorly structured sizes: agglomerates (poorly CNF treated to remove metals).

B. Purity: raw CNT (metal catalysts), purified

A. CNT types: SWCNT and MWNT

The CIB Pulmonary Toxicology Studies Reviewed for
structures into the alveolar septa.
associated with the migration of more dispersed
C. Rapid and persistent interstitial fibrosis
agglomerates.

Granulomatous lesions at deposition sites of
B. Rapid and persistent formation of inflammatory
control levels over 3 months post-exposure.
1-7 days post-exposure then return toward
peak at

A. Rapid but transient elevation of BAL markers of
Pulmonary responses commonly
Reported after CNT exposure
MWCNT-Induced Granuloma
Particle Fibre Toxicol 7:28, 2010
post aspiration of 80 µg/mouse (Mercer et al.

1. 12'000 MWCNT in the Interpleural space 2-6 days

2. 4'747-751, 2009
Ryman-Rasmussen et al. Nature Nanotech

weeks after inhalation (30 mg/m³ for 6 hr)
MWCNT can reach the Subpleural tissue 2-6

1. MWCNT exposed to the Subpleural Lung

A. MWCNT migration to the Subpleural Lung

after CNT Exposure

Other Pulmonary Responses Reported
MWCNT Penetration of Pleura
(Shvedova et al. Am J Respir Cell Mol Biol. 38:
3. 5-fold increase in bacterial CFU from lung tissue
2. 10 days after aspiration of Listeria
1. Pretreatment of mice with 40 μg SWCNT for 3
pulmonary infection
B. SWCNT: enhanced susceptibility to
after CNT Exposure
Other Pulmonary Responses Reported

579-590, 2008)
The Toxicologist, 2011)

3. SWCNT more potent than MWNT (Stueckle et al.

Growth in soft agar

2. Increased – cell proliferation, invasive potential,

0.024 μg/cm²; long term (25 weeks) in vitro exposure

1. Bronchial epithelial cells exposed to CNT (low dose

B. Cell Transformation


b. MWNT – monopolar

a. SWCNT – multipolar

1. Bronchial epithelial cells in vitro

A. Disruption of mitosis

with CNT

Other Issues of Pulmonary Concern
Red = spindle tubulin, blue = DNA, black = SWCNT

E. SWCNT alter the number of spindle poles

II. Effect of SWCNT on BEAS-2B cells.

In Vitro Cytotoxicity

3. Intrascrotal injection of MWNT caused abdominal mesothelioma (Sakamoto et al., J.


Granulomatous lesions on the diaphragm (Poland

2. Long MWNT more potent in causing


induced mesothelioma (Takagi et al., J. Toxicol Sc.

1. Abdominal injection of a high dose of MWNT

C. Mesothelioma

With CNT

Other Issues of Pulmonary Concern
exposure (Stapleton et al., The Toxicologist, 2011)
arterioles in response to acetylcholine 24 hr post-
burden) MWCNT in rats. Blocked dilation of coronary
Inhalation (5 hr at 26 mg/m³ to give a 22 kg

2. Environment Health Perspective 115: 77-82, 2007).
Apo E-/ mice increased aortic plaques (Li et al.
Multiple aspirations (20 μg/mouse, 4x) to SWCNT in

1. Cardiovascular effects of pulmonary exposure

A. Systemic issues with CNT
(Sriram et al. The Toxicologist 108: A2197, 2009)
bull, frontal cortex, midbrain and hippocampus.

blood/brain barrier damage in the olfactory

and cytokines as well as selections (markers of

increased mRNA for inflammatory cytokines

exposure

Aspiration of MWCNT (80 μg) in mice; 24 hr post-

B. CNS effects of pulmonary exposure

Systemic issues with CNT
A. Calculate lung burden in rodent models
B. Normalize lung burden/alveolar epithelial surface area

Toxicology Data

Risk Analyses using Available Pulmonary

(Stone et al. Am J Respir Cell Mol Biol 6: 235-243,

3. Mouse = 0.05 m²
2. Rat = 0.4 m²
1. Human = 102 m²)
Lifet ime (5 d/w, 50 w/yr, 45 yrs) would result in this lung burden in a working workplace airborne concentration which from the benchmark dose calculate the dose.

Lung burden giving 10% risk (benchmark interstitial fibrosis calculate the animal model granulomatous inflammation or).

Toxicology Data
Risk Analysis using Available Pulmonary
<table>
<thead>
<tr>
<th>benchmark (µg/m³)</th>
<th>exposure</th>
<th>species</th>
<th>study</th>
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</thead>
<tbody>
<tr>
<td>0.5</td>
<td>inhalation</td>
<td>rat</td>
<td>ma-hock et al (2009)</td>
</tr>
<tr>
<td>0.8</td>
<td>inhalation</td>
<td>rat</td>
<td>paullinh (2010)</td>
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<tr>
<td>3.8</td>
<td>inhalation</td>
<td>rat</td>
<td>ellinger - ziegler &amp;</td>
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<tr>
<td>0.6</td>
<td>aspiration</td>
<td>mouse</td>
<td>porter et al (2010)</td>
</tr>
<tr>
<td>18</td>
<td>it</td>
<td>rat</td>
<td>muller et al (2005)</td>
</tr>
</tbody>
</table>

Human exposure calculation of benchmark workplace level for rodent endpoints (10% risk).

- Granulomatous inflammation or fibrosis,
Summary

A. Studies with SWCNT or MWCNT
   1. Mice or rats
   2. Raw or pure
   3. Agglomerated or more disperse
   4. Bolus or inhalation exposure

Give qualitatively similar responses: rapid and persistent inflammatory granulomas and/or interstitial fibrosis
4. CNS changes
3. Cardiac dysfunction
2. Mesothelioma
1. Lung cancer

B. Other responses requiring further research:

Summary