Update on Carbon Nanotubes and Related Nanofibers

To: Science Advisory Board

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By: Michael Ellenbecker, ScD, CIH

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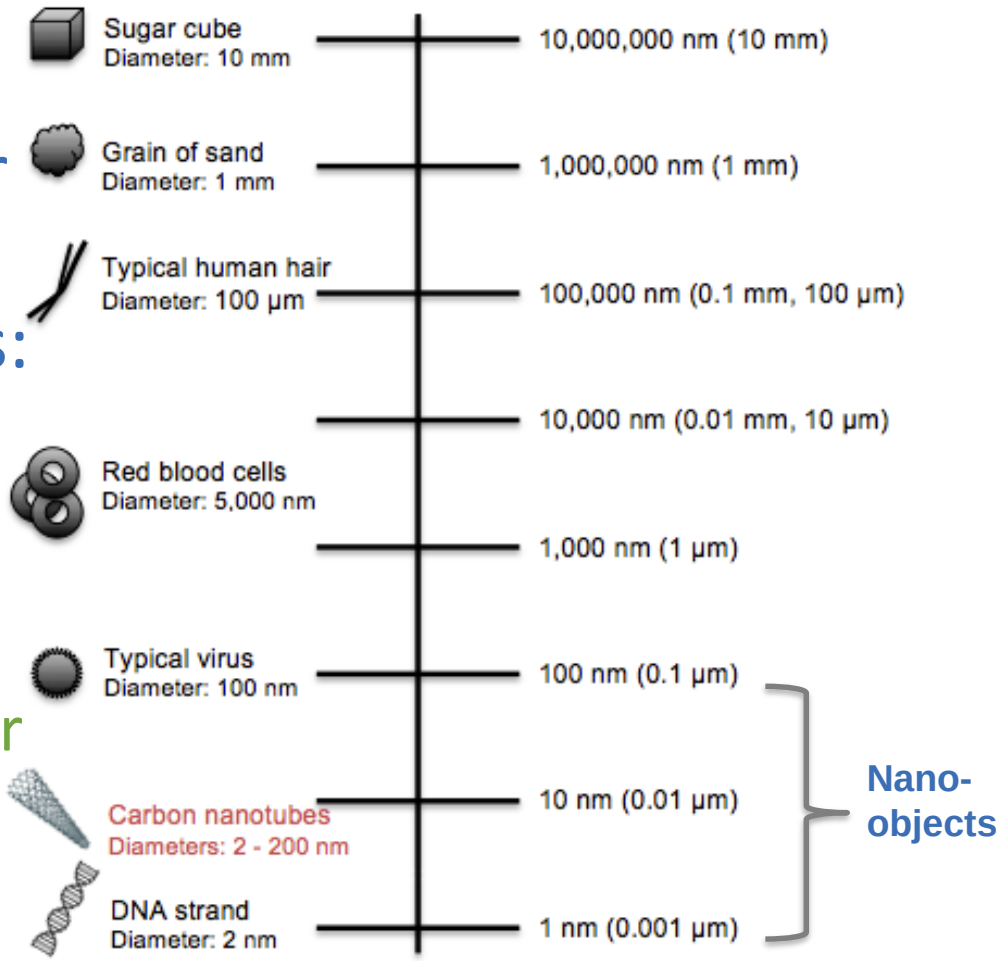
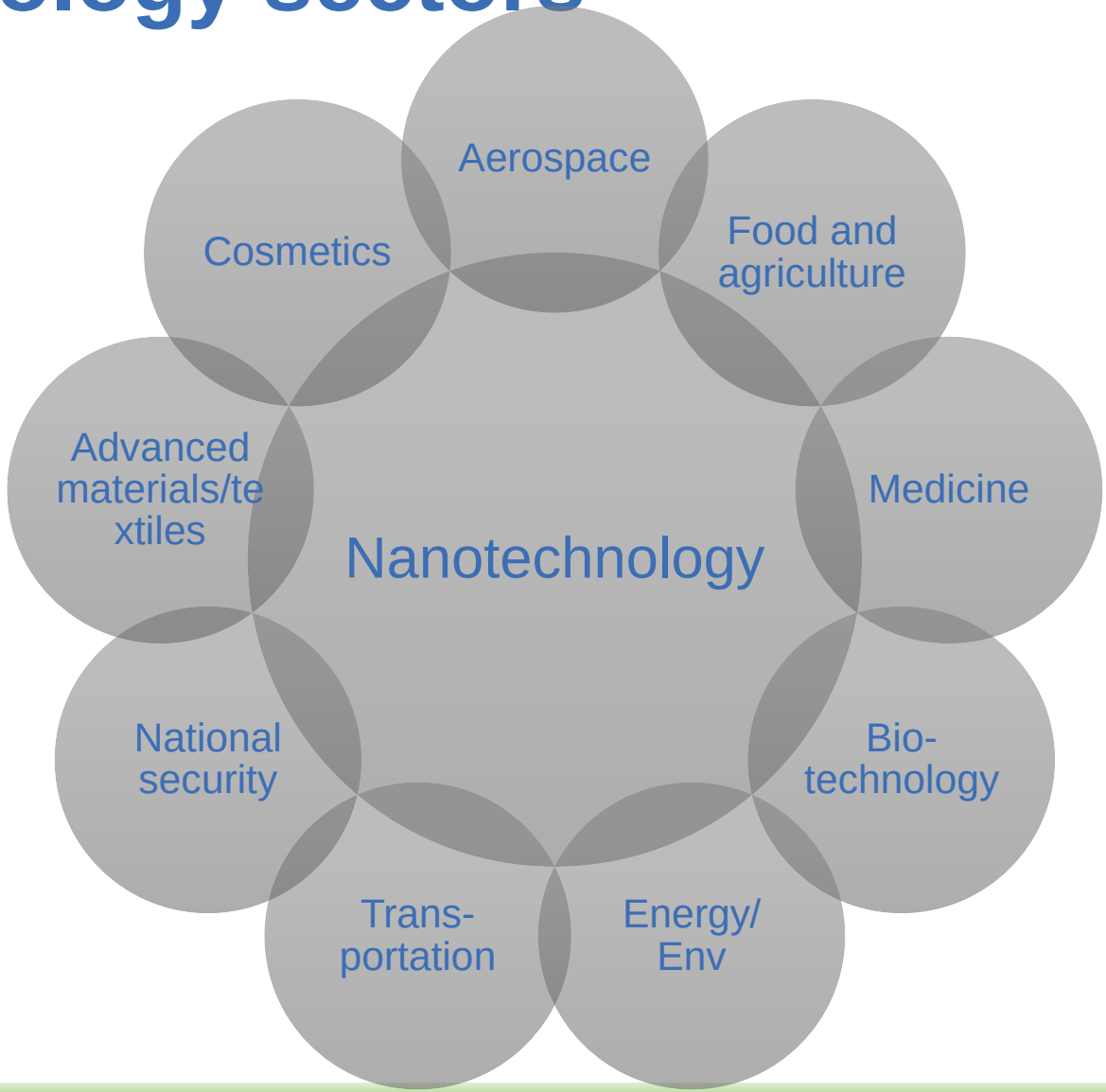
What is Nanotechnology

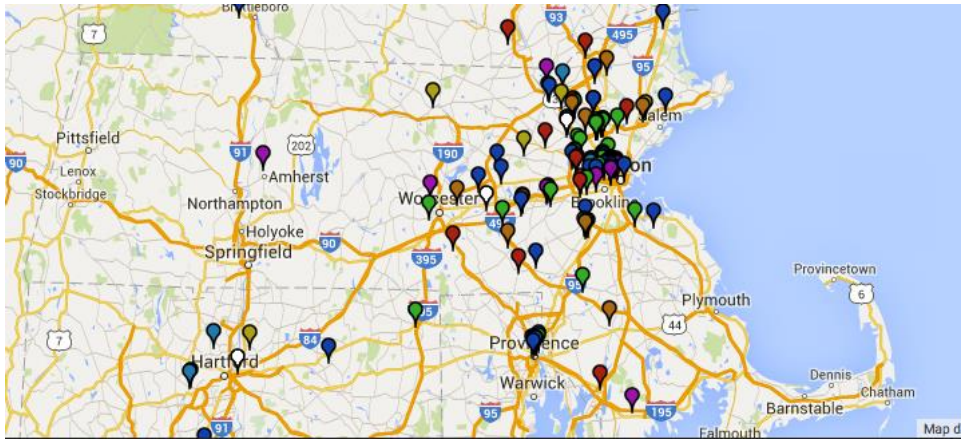
- The study of the controlling of matter on an atomic and molecular scale
- Engineered nano objects: at least one dimension between 1 to 100 nanometers (nm)
  - roughly 100,000 times smaller than the diameter of a human hair



R&D and Use – Spanning multiple technology sectors



Nanotechnology in the Commonwealth



According to Nanowerk, currently there are 68 companies in MA “with a nanotechnology focus”

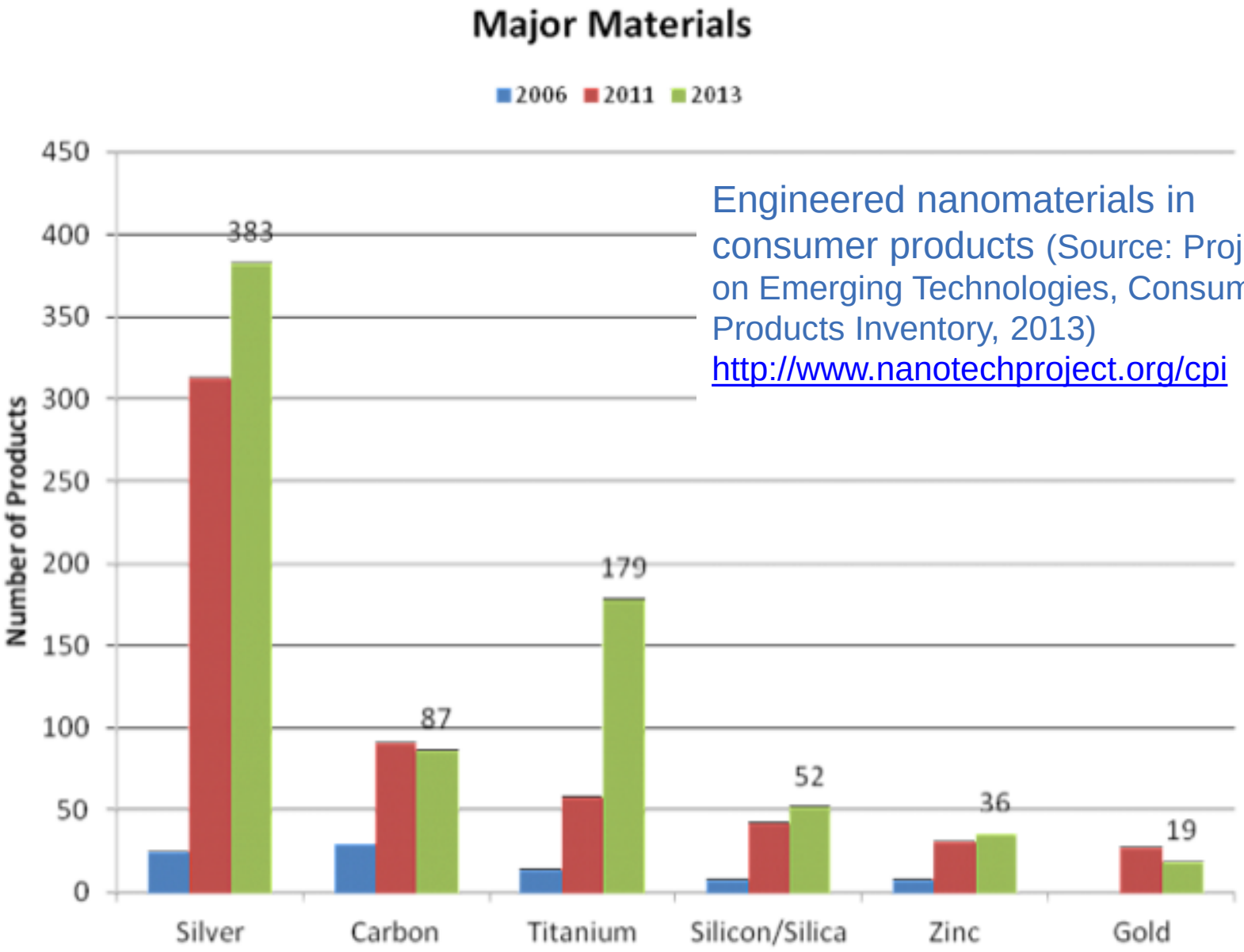
https://www.nanowerk.com/nanotechnology/Nanotechnology_Companies_Research_and_Degree_Programs_in_Massachusetts.php

MA is among the top 5 in the country for commercial and R&D activity on nanomaterials/nanotechnology

Types of Engineered Nanomaterials

Broad Categories: Engineered Nanomaterials

Carbon-based	Metal	Metal Oxides	Dendrimers	Composites
fullerenes, carbon nanotubes	Silver, gold, copper	Titanium dioxide, zinc oxide, iron oxide	Hyperbranched polymers, dendrigraft polymers, dendrons	Nano clays, polymer beads

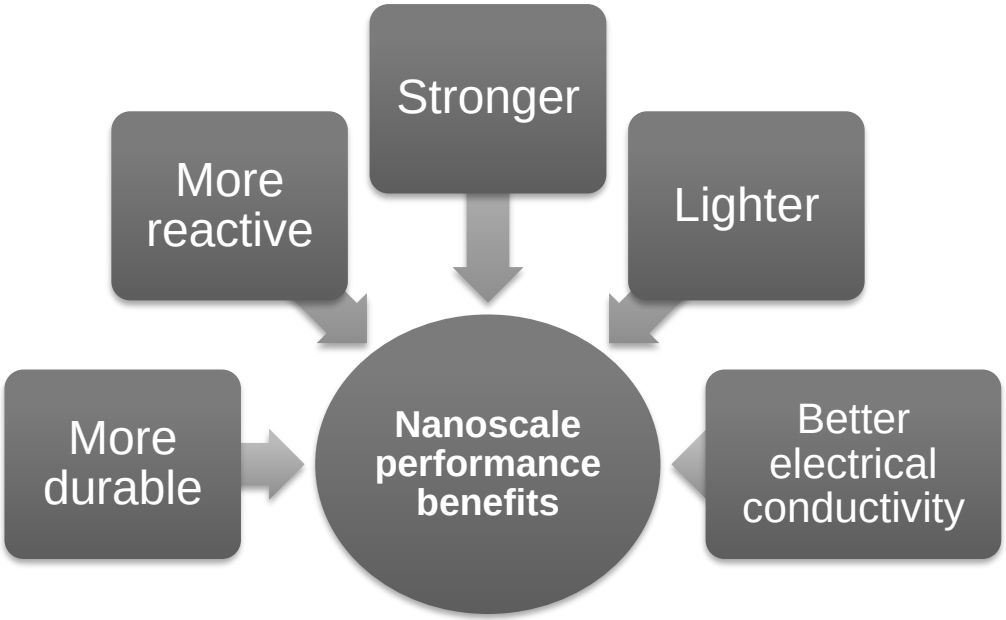


Engineered nanomaterials in consumer products (Source: Project on Emerging Technologies, Consumer Products Inventory, 2013) http://www.nanotechproject.org/cpi

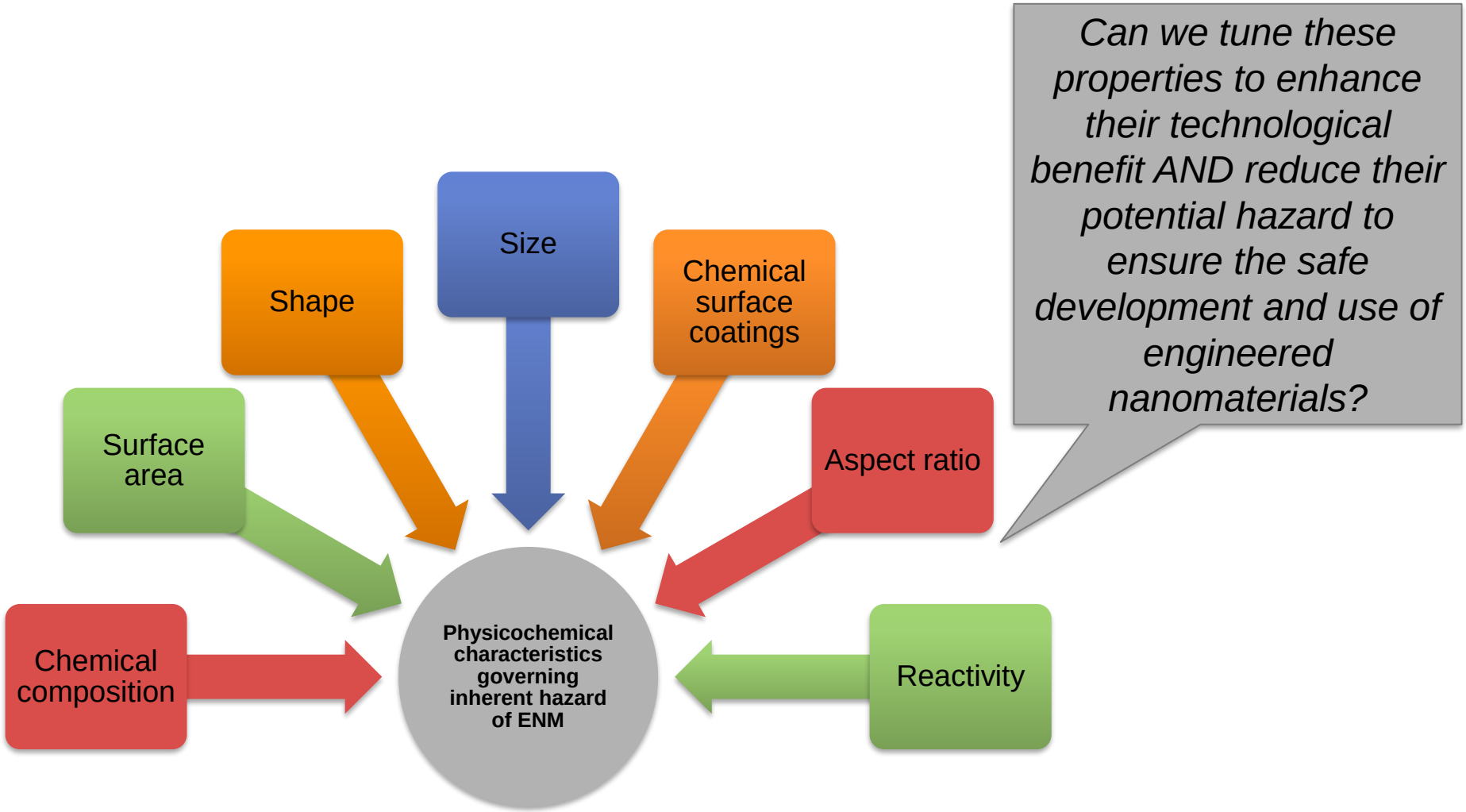
Figure 5. Numbers of products associated with specific materials.

Engineered nanomaterials: enhanced performance compared to their bulk counterparts

- At nano-scale:
  - material **properties change** - melting point, fluorescence, electrical conductivity, and chemical reactivity
  - **Surface size is larger** - more material comes into contact with surrounding materials and increases reactivity



Physical-chemical properties: key to performance AND inherent hazard



Overview: Carbon Nanotube Environmental and Occupational Health and Safety

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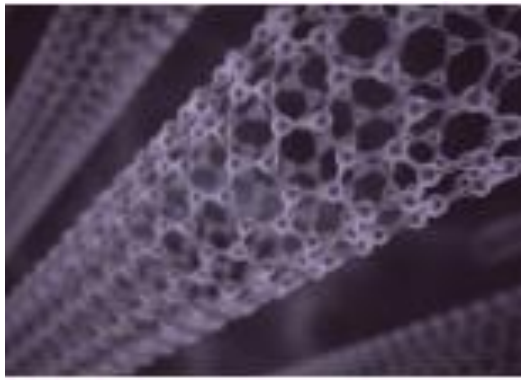
Engineered Carbon Nanotubes – What are They?

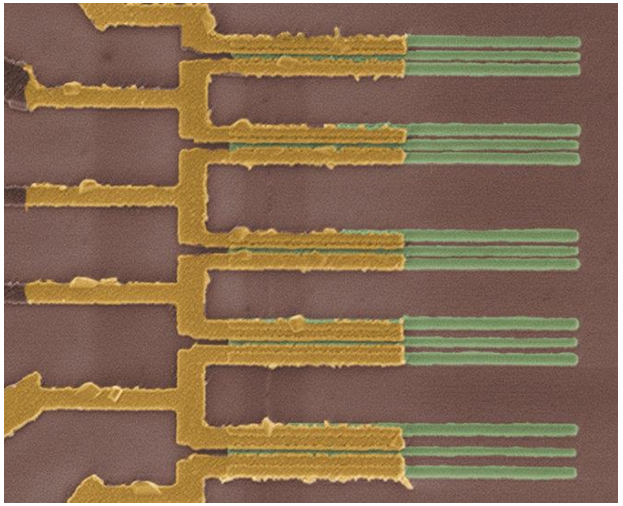


- Divided into 2 broad categories:
  - Single-walled CNTs (SWCNTs)
  - Multi-walled CNTs (MWCNTs)
- Carbon nanofibers (CNFs) – similar but cylinders are not perfectly formed
- Important: CNTs/CNFs are not a single material. ~50,000 SWCNTs and likely even more potential combinations of MWCNTs
  - Vary based on size, shape, chemical composition, reactivity, etc.

New York Times, 1 Oct 2015

"IBM Scientists Find New Way to Shrink Transistors"

- CNT field effect transistors
- Increase speed and/or reduce power use by a factor of 7



Emerging as substitutes for toxic chemicals

BIOCYL™ X1

Fouling release coatings

Anti-fouling marine paints [substitutes for tributyltin, copper boat paints, etc]

THERMOCYL™ X1

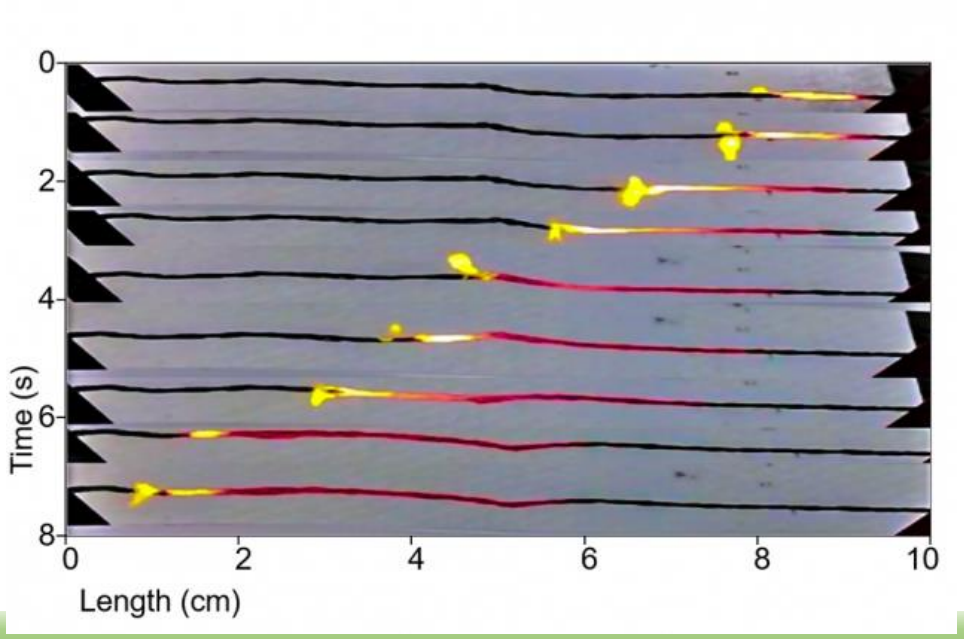
Flame retardant coatings for non-metallic substrates

Flame retardants for electronics, wire/cable, textiles, foams [substitutes for halogenated flame retardants]

Journal of Cleaner Production, 2017:
Carbon nanomaterials as potential substitutes for scarce metals. Rickard Arvidsson, A. Bjorn

Chemical Reviews, 2014:
Safe Clinical Use of Carbon Nanotubes as Innovative Biomaterials
Naoto Saito et al.

Introducing Sugar-Coated Carbon Nanotubes – A Nontoxic Alternative Source of Power



CNT Toxicity

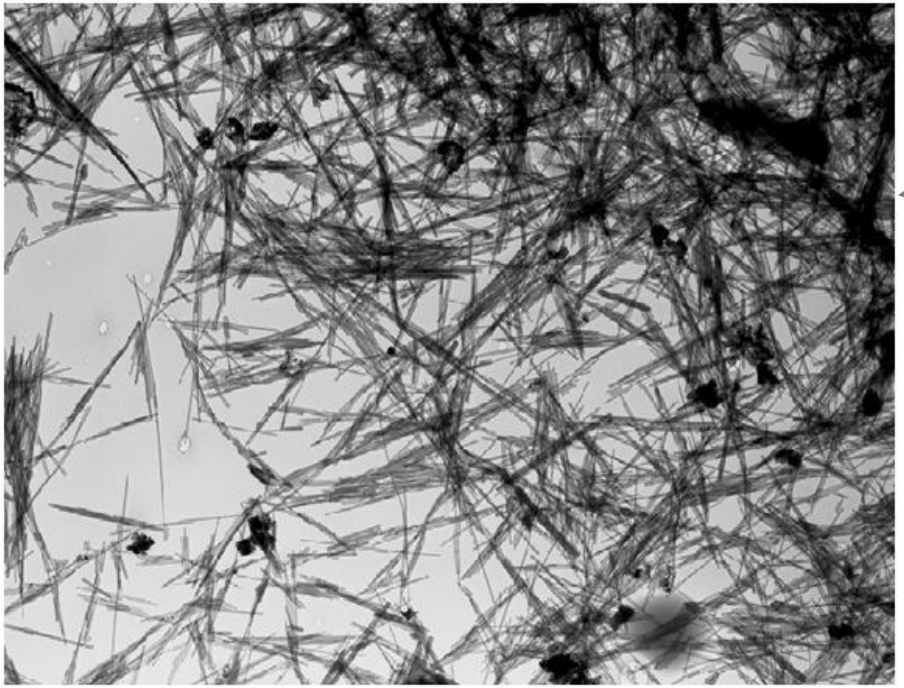
- Many studies published in the last 20 years
- Primary end points of concern:
  - Pulmonary fibrosis – SWCNT, MWCNT, CNF
  - Inflammation
    - Lung tissue - SWCNT, MWCNT, CNF
    - Cardiac tissue - SWCNT, MWCNT
- Cancer - MWCNT
  - Lung tumor promoter
  - Mesothelioma

Current Intelligence Bulletin 65, Occupational Exposure to Carbon Nanotubes and Nanofibers. Available at: http://www.cdc.gov/niosh/docs/2013-145/pdfs/2013-145.pdf.

Cancer & MWCNTs

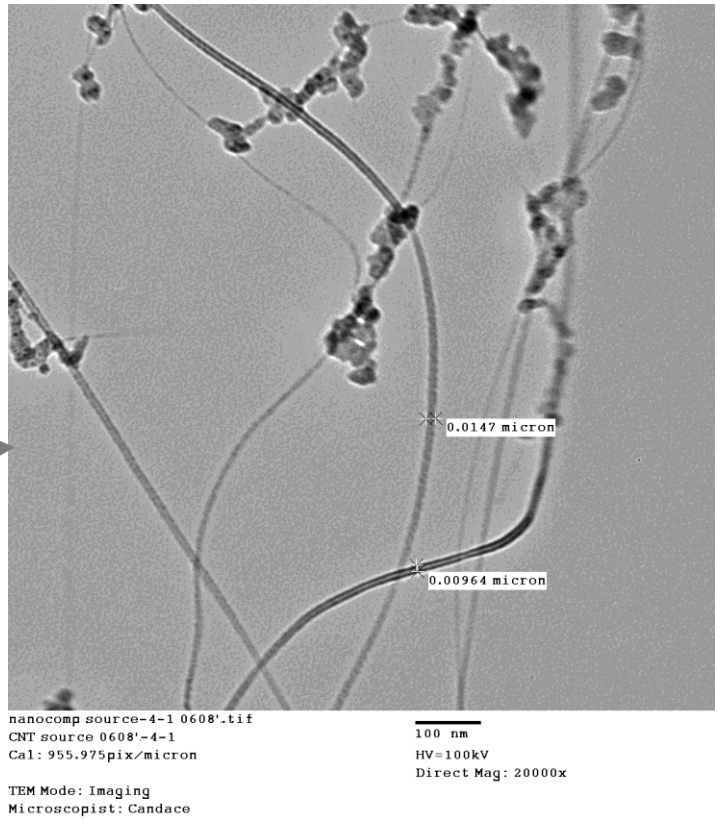
- Tumor promotion [high aspect ratio MWCNTs]:
  - mouse inhalation study, first exposed to methylcholanthrene (MCA) via intraperitoneal injection.
  - Strong promotion of lung tumors [pulmonary adenomas and adenocarcinomas]
  - Strong promotion of malignant serosal tumors consistent with sarcomatous mesothelioma

Sargent LM, et al. *Part Fibre Toxicol*. 2014 Jan 9;11:3. doi: 10.1186/1743-8977-11-3.



Asbestos

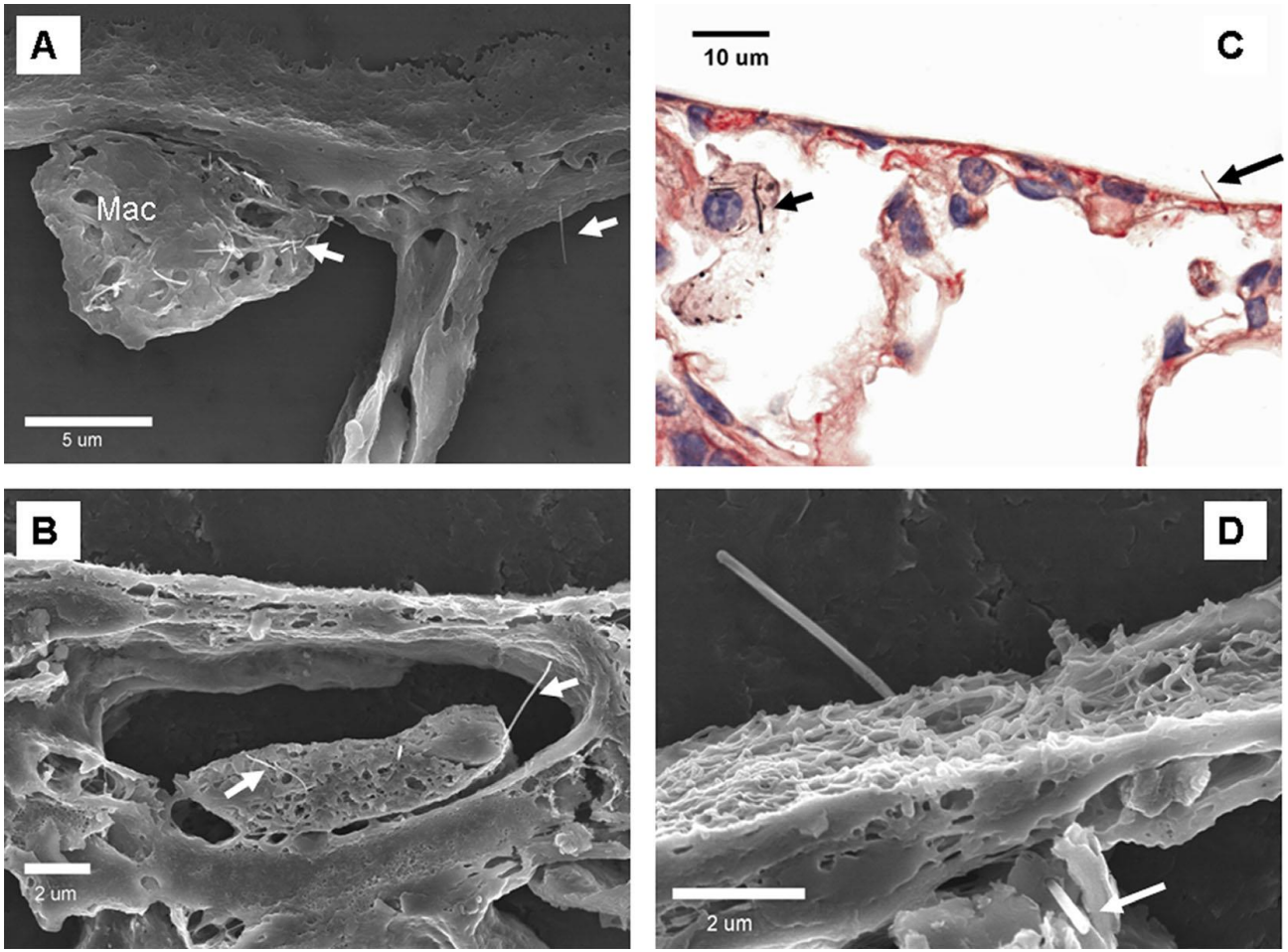
CNTs



CNTs cause Mesothelioma?

- Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study, Poland, et al., *Nature Nano*., 2008.
- Induction of mesothelioma in p53+/- mouse by intraperitoneal application of multi-wall carbon nanotube, Takagi, et al., *J. Toxicol. Sci*, 2008.

Mercer, et al., Distribution and persistence of pleural penetrations by multi-walled carbon nanotubes, *Part. Fibre Tox.*, 2010.



CNTs cause Mesothelioma?, *Cont.*

Poland: "Here we show that exposing the mesothelial lining of the body cavity of mice, as a surrogate for the mesothelial lining of the chest cavity, to long multiwalled carbon nanotubes results in asbestos-like, length-dependent, pathogenic behaviour… Our results suggest the need for further research and great caution before introducing such products into the market if long-term harm is to be avoided."

Dec 2014 – IARC designates "certain MWCNTs" as 2B, Possible Human Carcinogen

Grosse Y et al. *Lancet Oncol*. 2014;15(13): 1427-28.

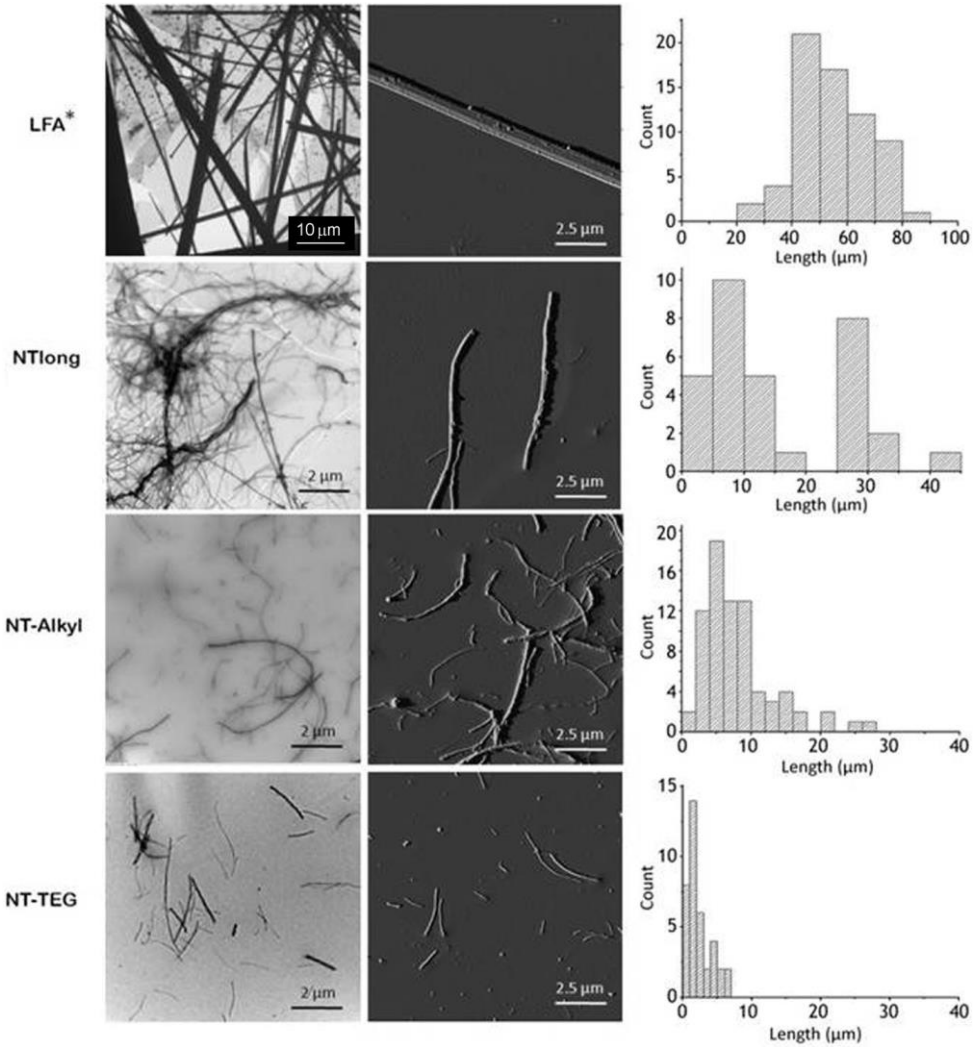
Fiber Morphology Important

- In animal studies thus far:
  - SWCNTs do not cause mesothelioma
  - Thin (d < 15 nm) MWCNTs – ditto
  - Thick (d > 150 nm) MWCNTs – ditto
- But – all commercially available MWCNTs :

  $15 \text{ nm} < d < 150 \text{ nm}$
- Short (L < 1-5 µm) MWCNTs – ditto

Can we make them all short?

Functionalization can affect Length



Ali-Boucetta, *et al*., *Angew. Chem. Int. Ed*. 2013, **52**, 2274 –2278, DOI: 10.1002/anie.201207664

Human Studies

- Few human studies to date
  - Case reports of CNTs found in the lungs of 911 first responders
  - Recent case-control study revealed MWCNT manufacturing workers (levels 3x above the NIOSH REL) found biomarkers of effect similar to conclusions from tox studies
    - increase in serum & sputum inflammatory & fibrotic biomarkers[IL-1**β**, IL6, TNF-**α**, inflammatory cytokines, KL-6, TGF-**β**1]

Wu, M. et al . *Environ. Health Perspect*. 2010. **118**: 499**–**504.
Fatkhutdinova LM et al. *Toxicol and App Pharmacol*. 2016; **299**: 125**–**131

- "Carbon nanotube and nanofiber exposure and sputum and blood biomarkers of early effect among U.S. workers," John D. Beard, et al. (NIOSH), Env. Int. 116:214-228 (2018).
  - We evaluated carbon nanotube/nanofiber (CNT/F) exposure in relation to biomarkers.
  - We assessed CNT/F exposure via personal breathing zone, filter-based air sampling.
  - We measured fibrosis, inflammation, oxidative stress, cardiovascular biomarkers.
  - Inhalable rather than respirable CNT/F was more often associated with biomarkers.
  - Sixteen biomarkers were associated with at least three CNT/F exposure metrics.

Emerging Ecotoxicity Concerns

- Daphnids *(Daphnia magna)*
  - Interferes with food uptake & movement at low concentrations [MWCNTs & SWCNTs]; More toxic with longer exposures; Impaired growth and reproduction at very low levels
- Juvenile rainbow trout *(Oncorhynchus mykiss)*
  - Systemic toxicity at very low levels (consistent with GHS classification of “extremely toxic to aquatic life)
- Powerful anti-microbial agent
  - Implications for sewage treatment plants

*variation in findings given differing physicochemical characteristics

Source: Petersen, et al. *Env Sci Technol* 2011; 45(23):9837-9856.

Setting Occupational Exposure Limits

- No consensus between different groups
- Basic difference: mass concentration vs. number concentration
- Mass concentration – easier, cheaper to measure
- Number concentration – more relevant biologically (e.g., asbestos), lower LOD

NIOSH REL for CNT/CNF

- NIOSH CIB 65
- REL = 1 µg/m^3 of respirable elemental carbon as an 8-h TWA
- Elemental carbon is readily measured using NIOSH Method 5040
- 1 µg/m^3 is the limit of quantification for Method 5040

NIOSH REL for CNT/CNF, Cont.

- “Recent observations indicate that exposure to CNF can cause respiratory effects similar to those observed in animals exposed to CNT”
- Because of residual risk at the REL, “NIOSH recommends that exposures to CNT and CNF be kept below the recommended exposure limit”

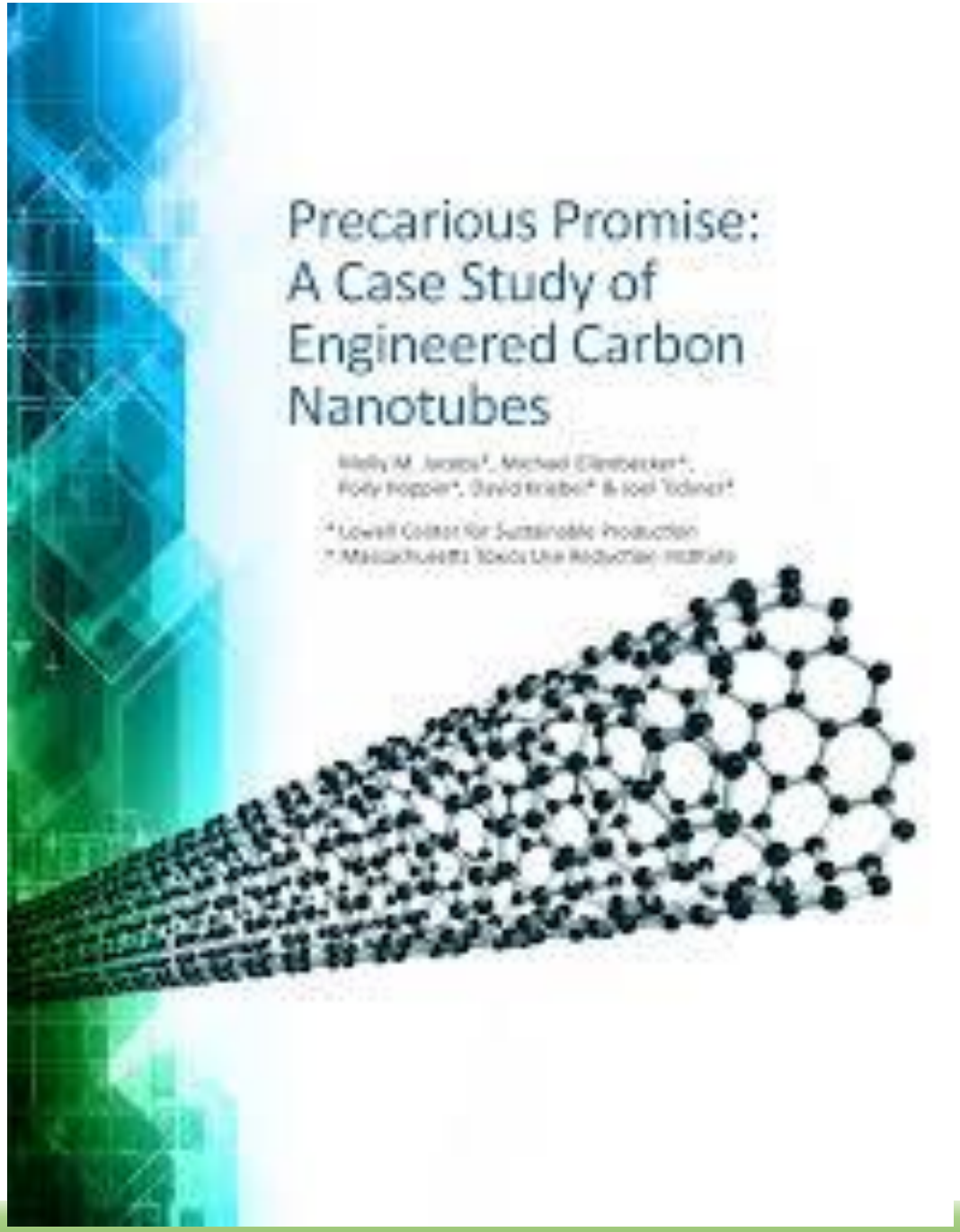
Agency or Company	Occupational Exposure Limit	
	Mass Concentration ($\mu g/m^3$)	Number Concentration (f/cm^3)
British Standards Institute		0.01
Bayer Schering Pharmaceuticals	50*	
Japanese National Institute of Advanced Industrial Science and Technology	30 (SWCNT)* 80 (MWCNT)*	
Swiss Accident Insurance Funds		0.01
German Institute for Occupational Safety and Health		0.01
National Institute for Occupational Safety and Health U.S.	1 (elemental carbon)*	

BUT……

- Depending on CNT fiber dimensions, 1 µg/m^3 can correspond to number concentrations ranging from 0.01 f/cm^3 (extremely large CNF) to 300,000 f/cm^3 (typical CNT)
- BSI – 0.01 f/cm^3

TURA Program Resources

- Nanomaterials Fact Sheet
- Nanomaterials EH&S Library Guide
- TURI Webpage on Nanomaterials
- TURI Library
  - Books
  - Reports
  - Databases


Precarious Promise:
A Case Study of
Engineered Carbon
Nanotubes