Operational Exposure Guides for the Assessment and Control of Nano Materials at CNMS

NSRC Symposium

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Exposure Control of Nano Sized Aerosols Starts with the Development of Limits

Department of Energy (DOE) Nanoscale Science Research Centers (NSRC) developing *Approach to Nanomaterial ES&H*

- *The CNMS Approach*
  - *Establish Exposure Control Guide (ECG)*
  - *Characterize Aerosol*
    - *Collect and interpret data*
  - *Assign Process to a Control Band*

Exposure Limits and Control Guidelines

- Currently there are no standards specifically targeted at employee exposure to "nanomaterials"
- Guidelines are becoming available

Precautionary Principle

- Presume that nanoparticles may exhibit enhanced or different toxicological characteristics than larger size materials with same chemical composition,
- and that chemicals added to nanoparticles may exhibit enhanced or different toxicological characteristics from the parent chemical.

More specifically, Prudent Practice applied to nanoparticles in the absence of information to the contrary:

- Assumes material previously designated as "inert" is toxic,
- assumes material designated as "toxic" has increased toxicity,
- assumes nanomaterial is not agglomerating,
- assumes flocculated nanomaterial easily separates into discrete particles, and
- assumes that agglomerated material separates in water/pulmonary surfactant into discrete particles.

"Gotta" Have The Numbers

- Can't wait for complete understanding of the nature and extent of effects in the form of standards. Exposure control guidelines are needed for
  - Hazard assessment
  - Respirator selection
  - Control requirements
- Corporations have a history of developing internal exposure guidelines
- ACGIH TLV's are operational exposure guidelines
  - Fully developed toxicological basis often not available at establishment
  - Open to change
  - Most changes are towards lower exposure limits

Formulation of working guidelines are essential to "good stewardship" and "prudent practice"

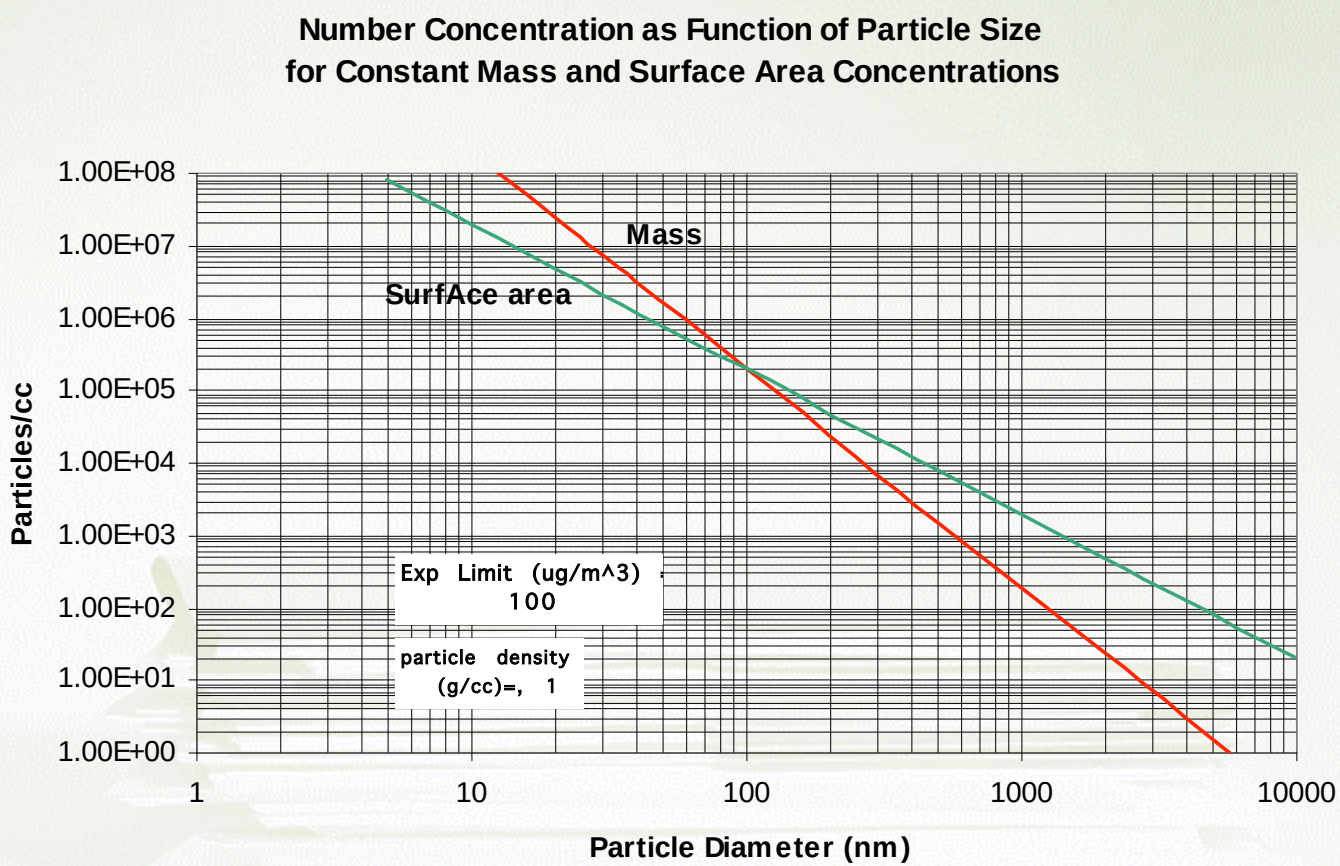
Safety Factor approach for adjustments to Existing Occupational Exposure Limits or TLV's for same Materials in nano size.

- Known carcinogens – EL/1 to 10
- Acutely toxic – EL/1 to 100 (no bioaccumulation)
- Chronic toxicity – EL/1 to 1000 (bioaccumulation)
- Low solubility/low toxicity/inert – 100 $\mu g/m^3$ /1 to 10

Some Examples

- Asbestos (carcinogen) – 0.1 f/cc (UNCHANGED)
- Zinc oxide (metal fume fever) – 2 mg/m^3 (unchanged as fume is assumed to be nano-size)
- Lead (chronic high toxicity) – 0.05 $mg/m^3/2$ = 0.025 the inorganic mercury vapor limit or more stringently 0.05/25 = 0.002 mg/m^3 to = beryllium limit
- Graphite (inert or low tox/low sol) – NIOSH draft Guide for TiO_2 ultrafine particulate or OSHA 530 p/cc (unchanged)

Number Concentration In the OEG



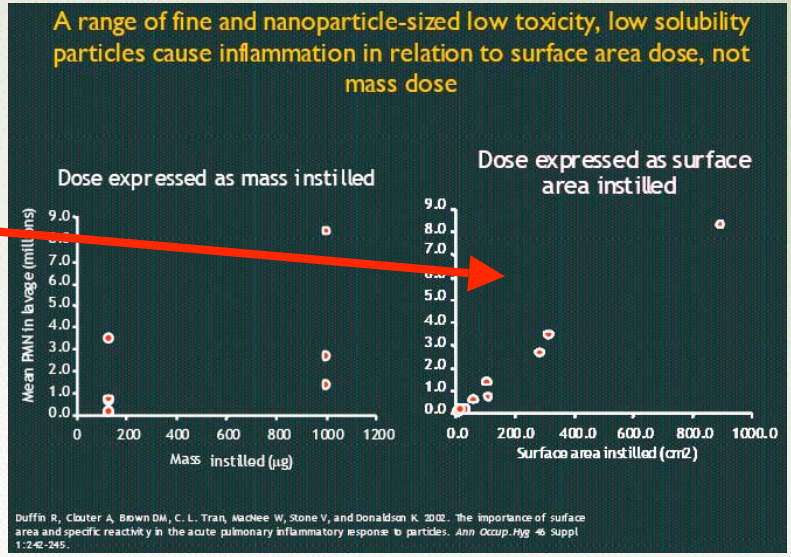
Does the Application of the OSHA PEL (530 p/cc) for Natural Graphite Satisfy the Precautionary Principle and Prudent Practice?

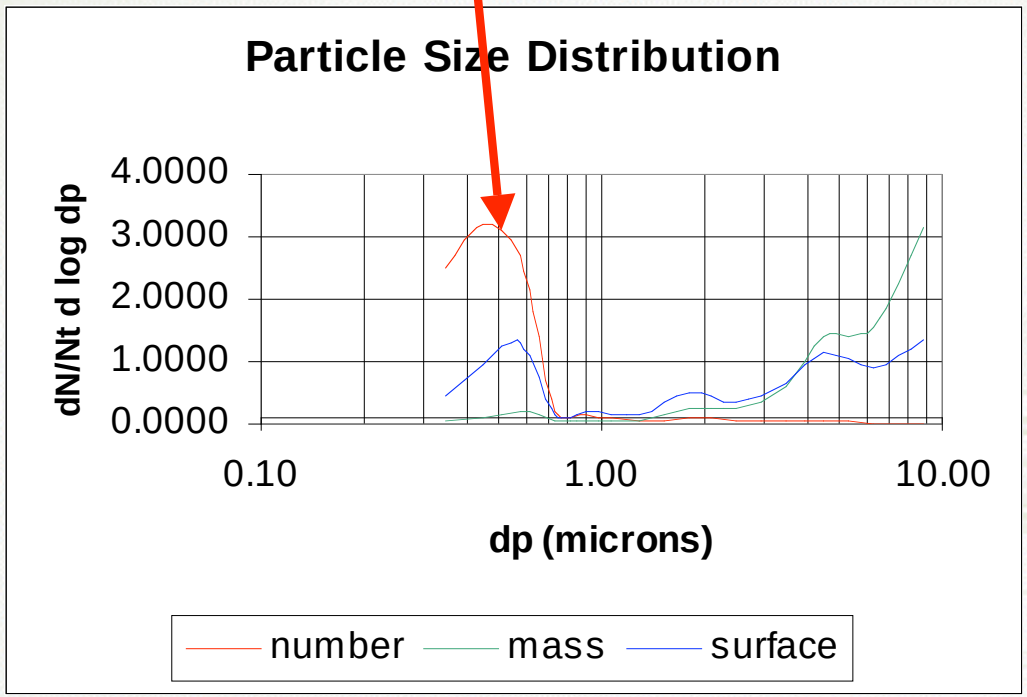
Desirable characteristics of an Operational Exposure Guide

- Physical and biological plausibility
- Based on existing limit
- Safety conservative
- Consistent with other standard(s)
- Capable of being measured
- Realistically achievable

Physical and biological plausibility

Surface area as dominant characteristic contributing to toxicity is plausible





Physical and biological plausibility

Demonstrated effects on lung defense mechanisms for smaller sized particles.

•**Particle clearance** – macrophage function **impaired** when inhaled particles occupy more than 6% of cell volume (1ul/g of lung) (Morrow, 1988 and Oberdorster et al., 1992).

•**FEV_1 reduced** 17% by each increase of 1um^2 in macrophage carbon content (Eulkarni, et al, 2006).

•A coating of nanoparticles may affect many cellular functions. In inhalation toxicology, **particle overload** is a significant determinant of adverse pulmonary response following exposure to certain, formerly considered "inert", particles (Moss, 2006).

•Carbon black and TiO2 can produce chronic **pulmonary inflammation**, pulmonary fibrosis, and lung tumors through mechanisms that are independent of any unique physiochemical property of the particles (Morrow 1988, Oberdorster et al., 1992, 1995).

•Gold and carbon UFP (ultra fine particles, < 100 nm) **migrate via the olfactory neuronal** pathway to CNS and result in inflammation (Elder et al., 2005).

Based on existing limit

There is an existing standard for a similar material.

(note that decreasing particle size while holding mass concentration constant increases total surface area, but holding the number concentration constant for a smaller particle size decreases both mass and surface area concentrations)

TABLE Z-3—MINERAL DUSTS

Substance	mppcf[a]	mg/m³
Silica:		
Crystalline		
Quartz (Respirable)	250[b] / %SiO_2+5	10 mg/m³[c] / % SiO_2 + 2
Quartz (Total Dust)		30 mg/m³ / % SiO_2 + 2
Cristobalite: Use ½ the value calculated from the count or mass formulae for quartz		
Tridymite: Use ½ the value calculated from the formulae for quartz		
Amorphous, including natural diatomaceous earth	20	80 mg/m³ / %SiO_2
Silicates (less than 1% crystalline silica):		
Mica	20	
Soapstone	20	
Talc (not containing asbestos)	20[c]	
Talc (containing asbestos) Use asbestos limit.		
Tremolite, asbestiform (see 29 CFR 1910.1001).		
Portland cement	50	
Graphite (Natural)	15	
Coal Dust:		

530 p/cc

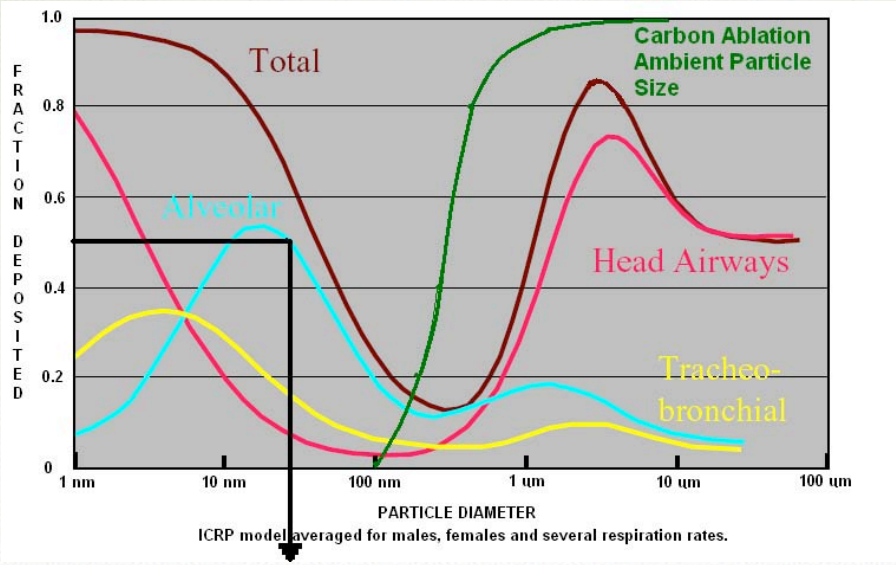
Note—Conversion factors - mppcf × 35.3 = million particles per cubic meter = particles per c.c.

[a] Millions of particles per cubic foot of air, based on impinger samples counted by light-field techniques.

Consistent with changes in other standards for decreasing particle size

- Last Change in the Ambient air quality regulation for fine particulate mater (PM-2.5)
- NIOSH draft proposal for TiO2 ultra fine particles (PM 0.1)
- CNMS OEG for carbon ultra fine particles (PM-0.1)

530 p/cc is safety conservative



~ 50% D_{p50} ~50nm, unit density spheres penetrate to alveolar spaces

daily volumetric alveolar loading at 215 p/cc ~ 1.75 E -8 µl/g·day

Overload Phenomena

Macrophage clearance function is impaired when particles occupy ~1 **µl/g of lung (Morrow, 1988; Oberdörster et al., 1992)**

The amount of this aerosol reaching the alveolar spaces is << than that predicted as a threshold for "Overload"

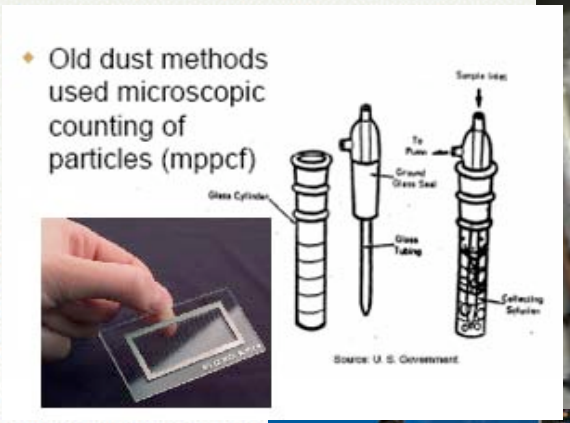
530 p/cc is safety conservative

Comparison of various exposure limits that could be applied to graphite/carbon						
Source	d_{ae} (μm)	Num Conc (p/cc)	Mass Conc (μg/m^3)	Source mass conc/CNMS mass conc	SA Conc (μm^2/cc)	Source SA conc/CNMS SA conc
OSHA OEL	3.5	530	1.2 E +4*	4 E+4	2 E+4	1176
NIOSH REL	0.1	1.9 E+5	100	357	6 E+3	353
EPA AAQS	2.5	4.3 (12.9)	35**	125 (375)	8.4 E+1	5 (15)
CNMS OEG	0.1	530	0.28	--	1.7 E+1	--

*calculated value based on number concentration
**24 hour TWA

Capable of being measured

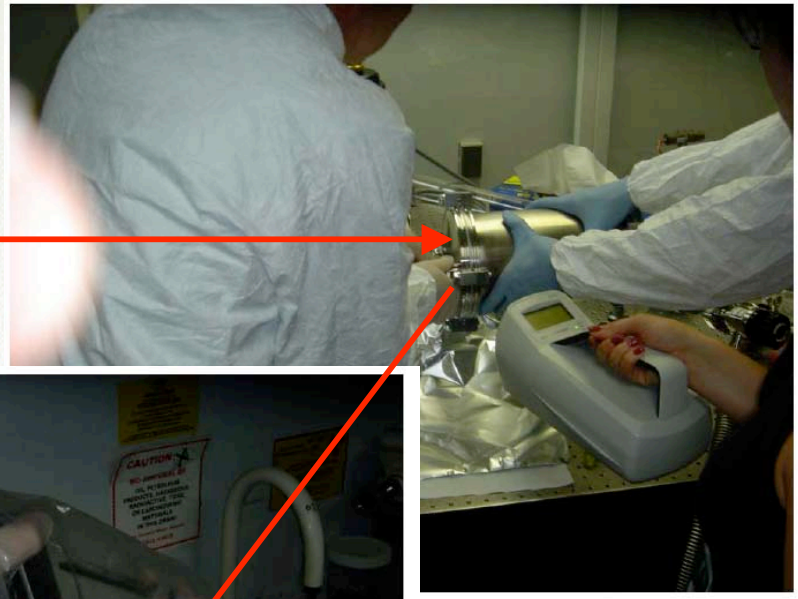
both old and new methods exist



Realistically achievable

Can the limit, 530 p/cc be reasonably met?

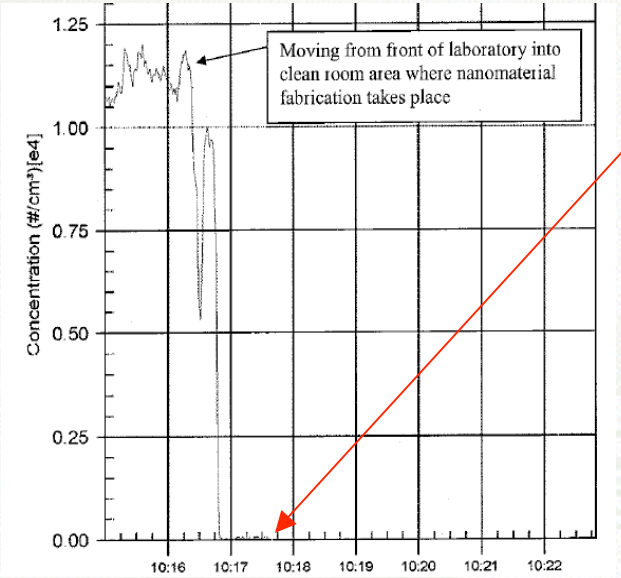
Laser ablation set up. Quartz tube holds laser t
nanomaterials.

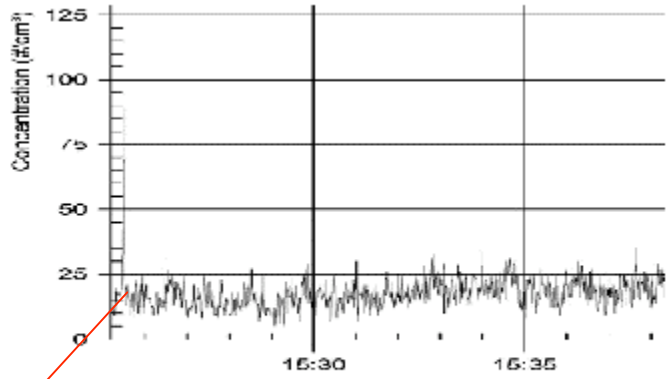


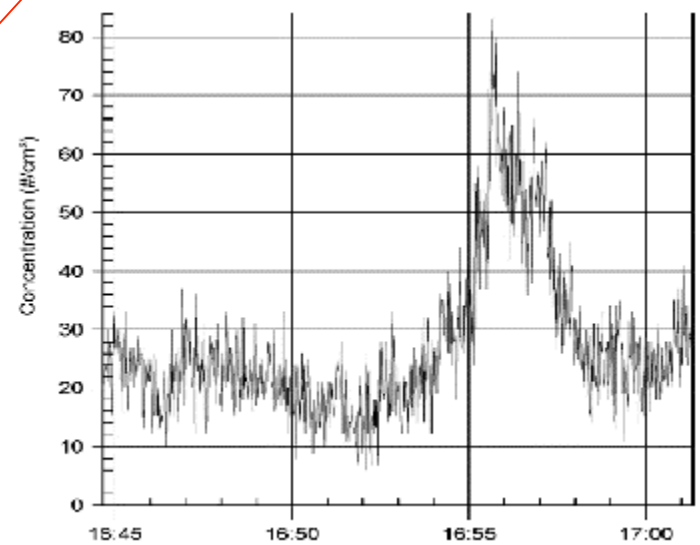
Harvesting nanomaterials inside glove bag, inside down draft hood.

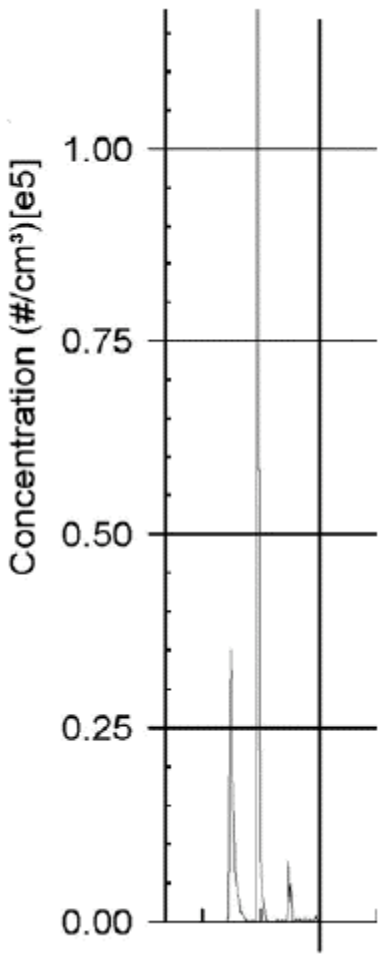
Realistically achievable

Both Measurable and Achievable (310 particles/cc during harvesting of carbon nanoparticles with controls in place)







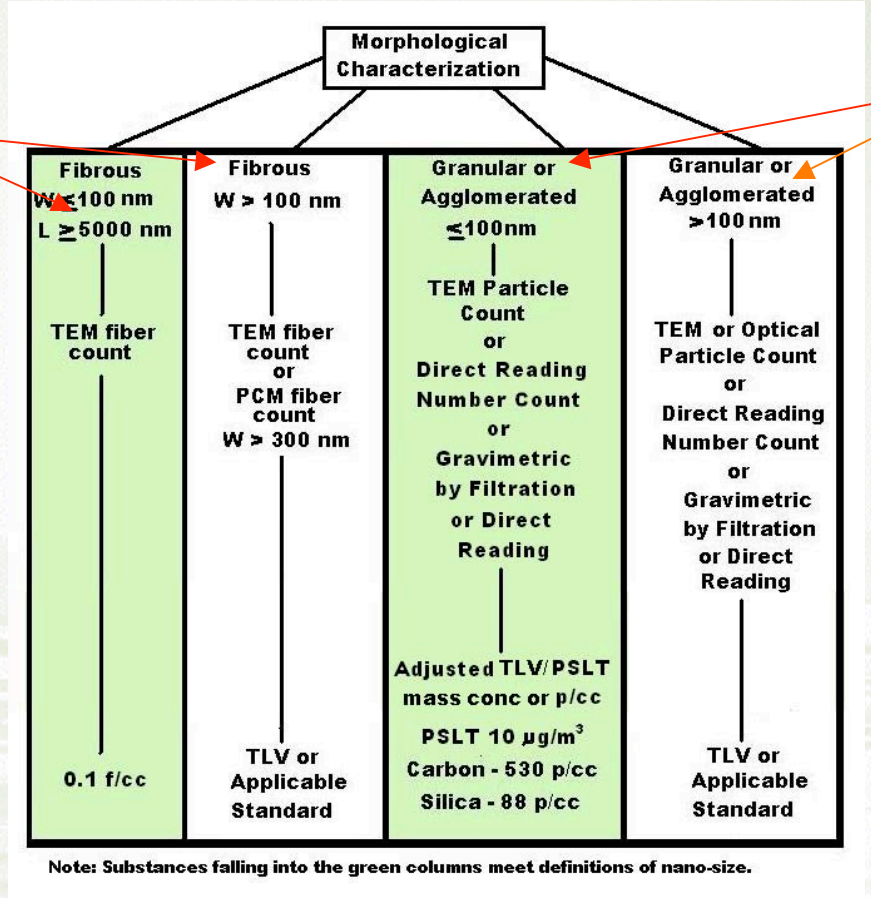
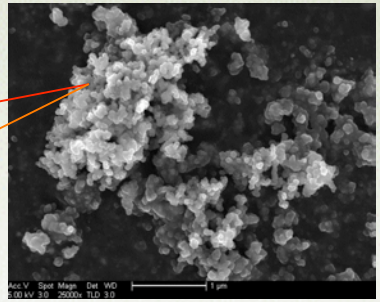


530 p/cc carbon OEG Conclusions

- Using the OSHA 15 mppcf limit represents a reduction in surface area by a factor of 15 to 1200
- Proposed limit consistent with reasonable risk

  in range of typical EPA uncertainty (safety) factors (1 to 10,000 for sub-chronic and chronic effects, most at 100 and 1000).

  EPA Health Effects Assessment Summary Tables, 1991
- Consistent with reduced EPA air pollution standard and NIOSH draft recommendation for TiO_2 – below levels believed to impair particle clearance, induce inflammation, or reduce FEV1
- Exposure Measurable and Control Achievable

A Closing Note

(Particle Characteristics Determine Sampling, Analysis, and Exposure Control Guidelines)