

## Session III: Air Quality and Pulmonary Pathways to Disease

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New Paths Conference

November 13, 2008



## New Understandings in Nose to Brain and Other Exotic Connections

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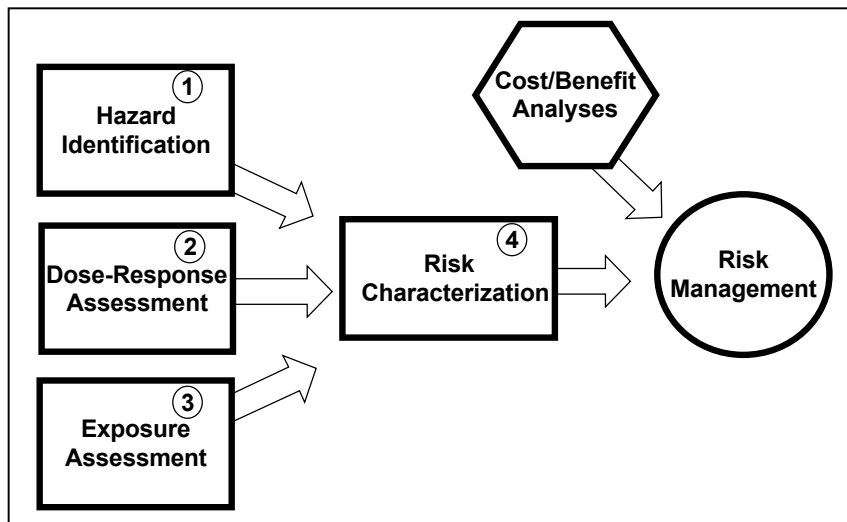
New Paths Conference

November 13, 2008



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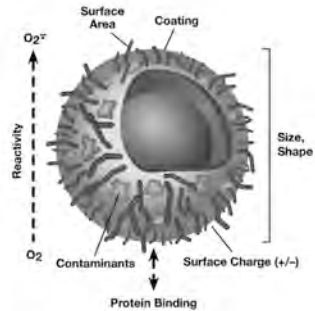
## Placing Particle Information in the Framework of Health Risk





## Particle Hazard Identification

- Chemical form
- Size
- Shape
- Surface area
- Number
- Density
- Mass
- Agglomeration
- Porosity
- Charge
- Reactivity
- Solubility
- Durability
- Crystalline structure
- Purity
- Antigenicity

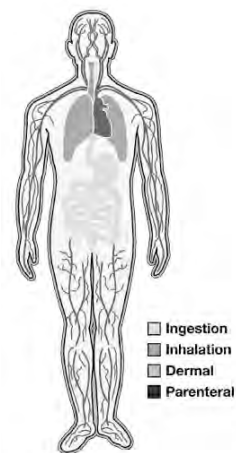


Stern and McNeil 2007



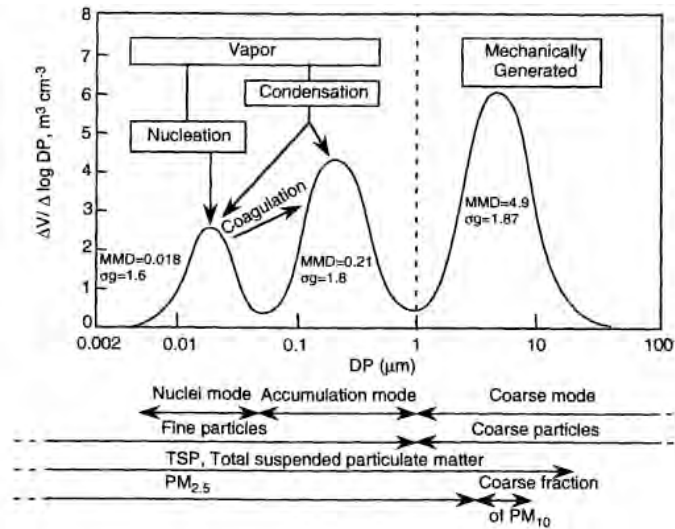
## Particle Toxicity Testing

- Mammalian
  - λ Pulmonary
  - λ Skin irritation and sensitization
  - λ Acute oral
  - λ Eye irritation
  - λ Systemic administration
- Genotoxicity
- In vitro screening



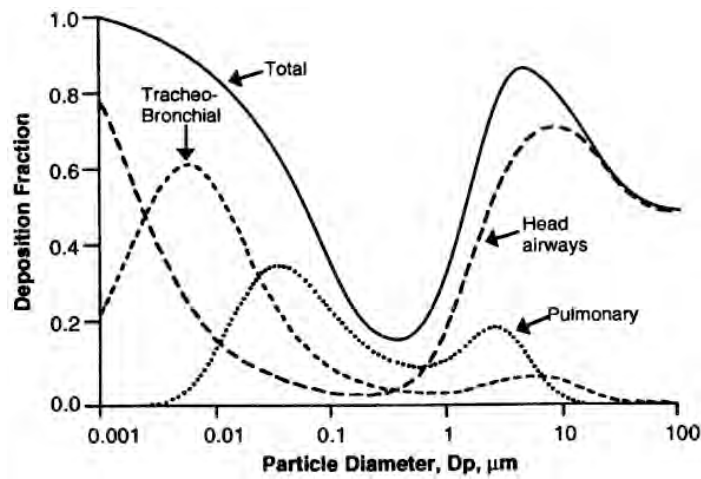
Oberdorster et al. 2005; Stern and McNeil 2007 (photo); Warheit et al. 2007

## Particle Behavior at Different Sizes



Wilson and Suh 3632

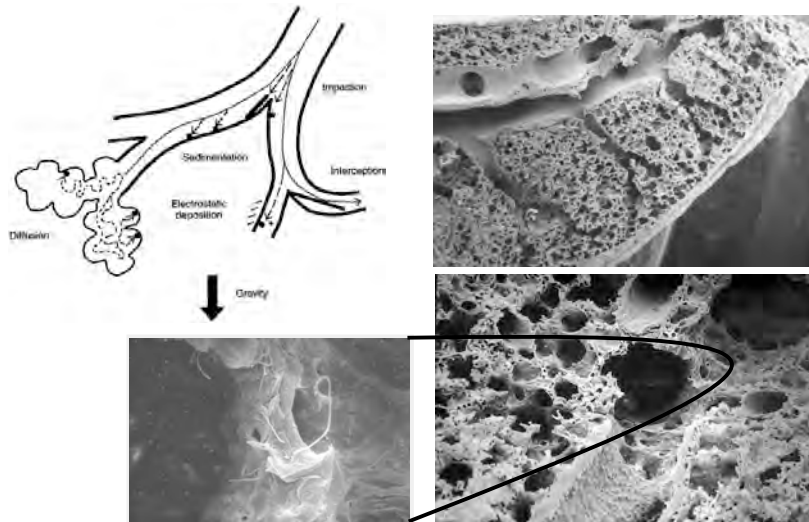
## Particle Deposition Patterns



International Commission on Radiological Protection

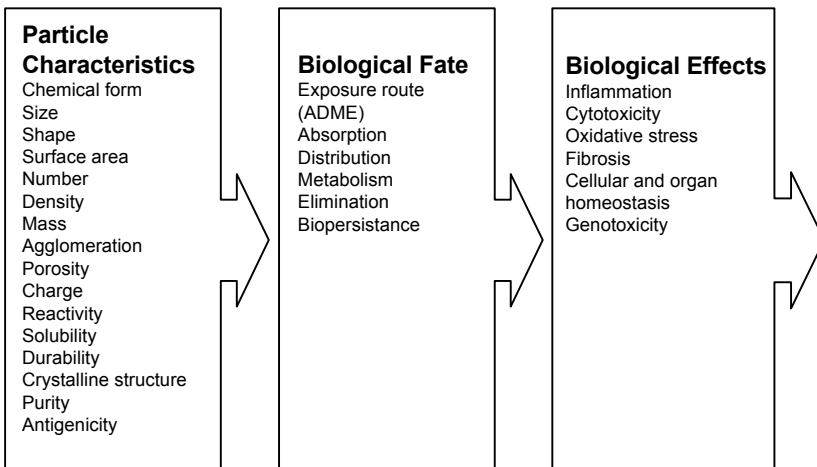
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## Particle “Hot Spots” in the Lung



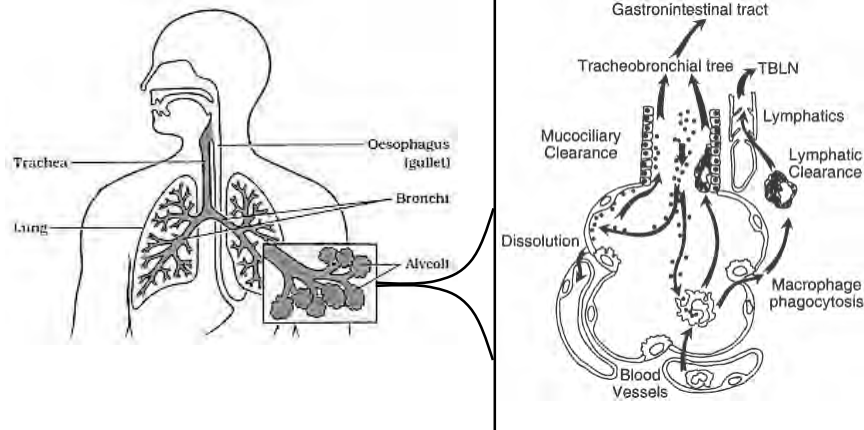
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## Dose-Response Assessment



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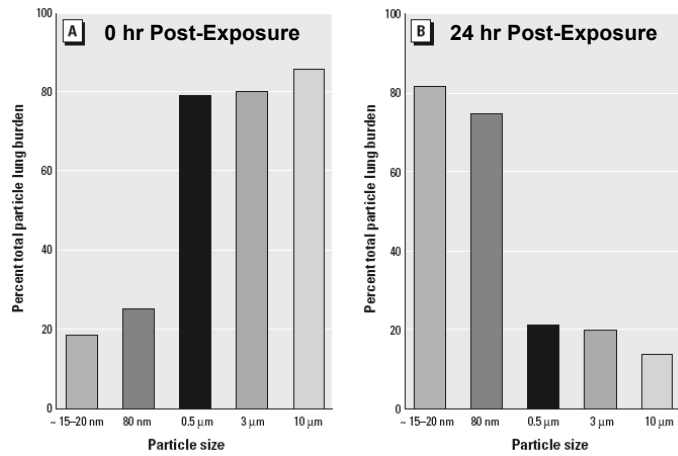
# Particle Fate and Transport



McClellan Comprehensive Toxicology

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# Retained Dose of Different Sized Particles



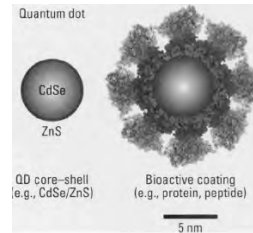
Oberdorster et al. 2005



# Quantum Dots



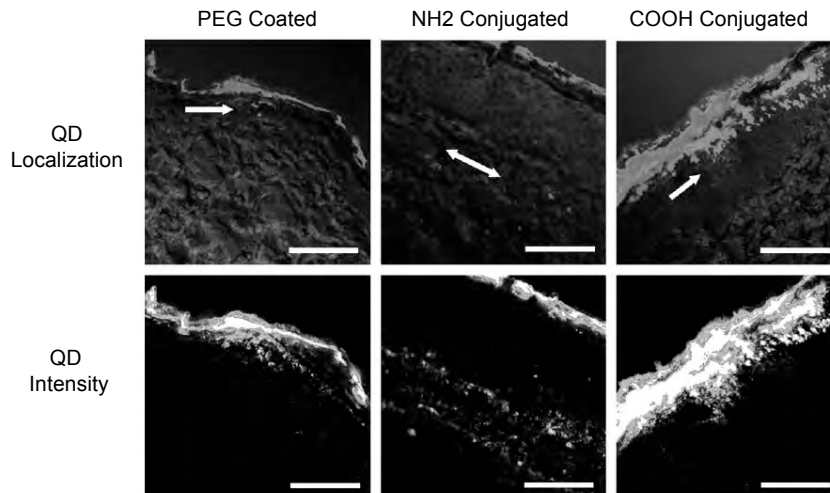
- Metalloid crystalline core with shell
- Available in various sizes and coatings
- Multiple applications
  - λ Surface coatings and charge
  - λ Particle fate and transport
  - λ Cellular imaging
- Inherent toxicity of metalloid core may influence effects



Hardman et al. 2006; [http://www.greenspine.ca/media/quantum\\_dots\\_c.jpg](http://www.greenspine.ca/media/quantum_dots_c.jpg) (photo)



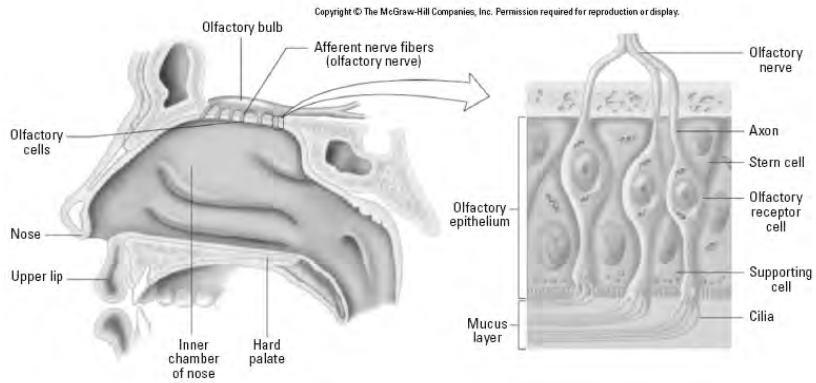
## Dermal Penetration of Quantum Dots (6nm): Effect of Surface Chemistry and Size (Ryman-Rasmussen et al. 2006)



Ryman-Rasmussen et al. 2006

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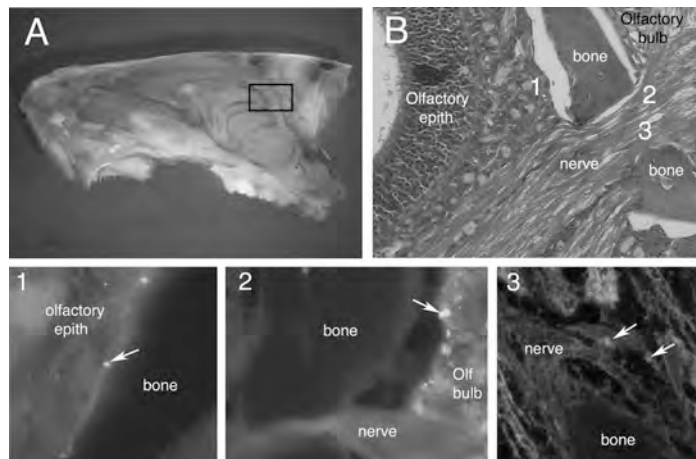
## Transport from the Nose



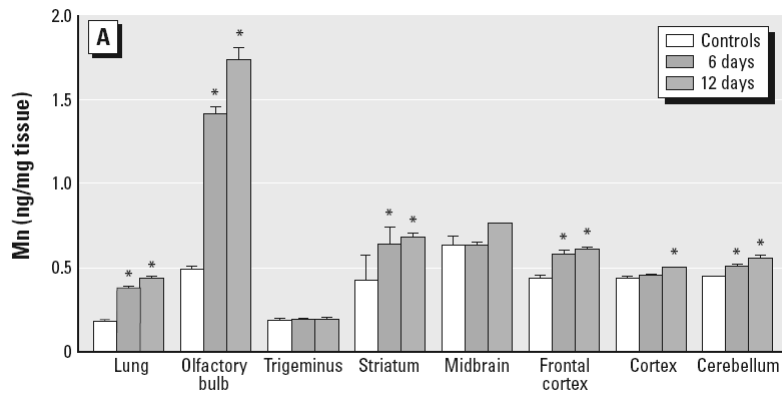
Widmaier EP, Raff H, Strang KT. 2004. Vander, Sherman & Luciano's Human Physiology: The Mechanisms of Body Functions. 9th ed. New York McGraw Hill. Also presented in Oberdorster et al. 2005 EHP 113:823.

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## Quantum Dots in the Olfactory Epithelium

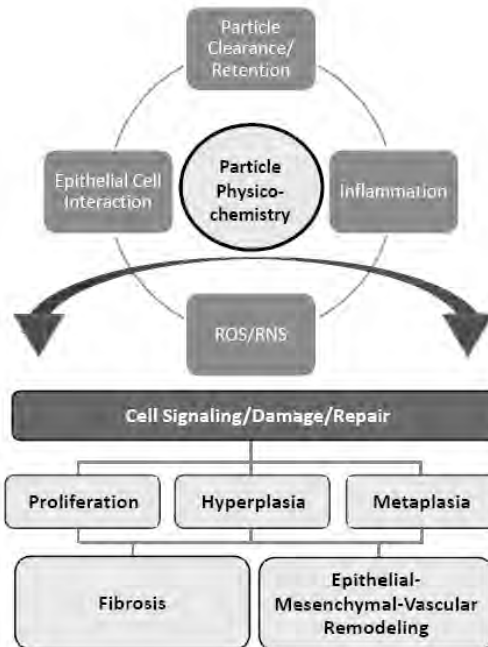


## Manganese in the Olfactory Bulb and Brain



Elder et al. 2006 EHP 114:1172

## Mechanisms of Toxicity





## Markers for Toxicity

- Inflammatory cell profile
- Cytokine patterns
- Oxidative stress
  - λ Reactive oxygen species
  - λ Lipid peroxidation
  - λ Antioxidant capacity
- Structural/cellular remodeling
- Collagen
- Cell proliferation
- Apoptosis
- Physiologic impairment
- Cell cytotoxicity
- Immune cell function
- Metabolic capacity
- Secretory defense

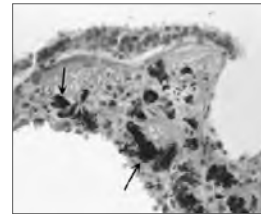
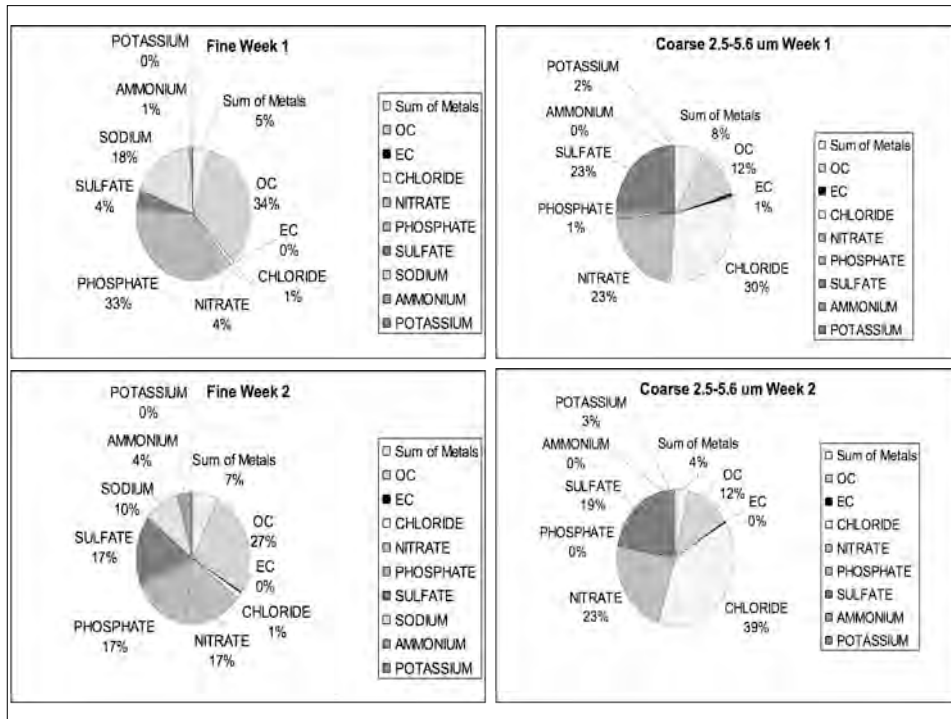
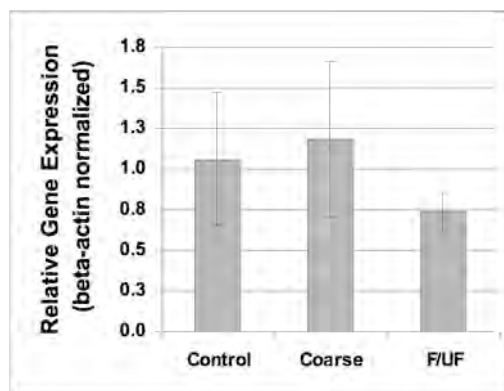


Image from Pinkerton et al. 2000 EHP 108:1063-1069





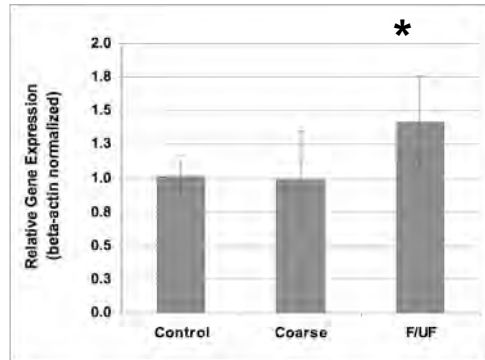
○ Tyrosine Hydroxylase Expression  
 ○ in Rat Brains  
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Real-time PCR was used to detect Tyrosine Hydroxylase expression levels in brains of rats exposed in Parlier, CA., June 2006

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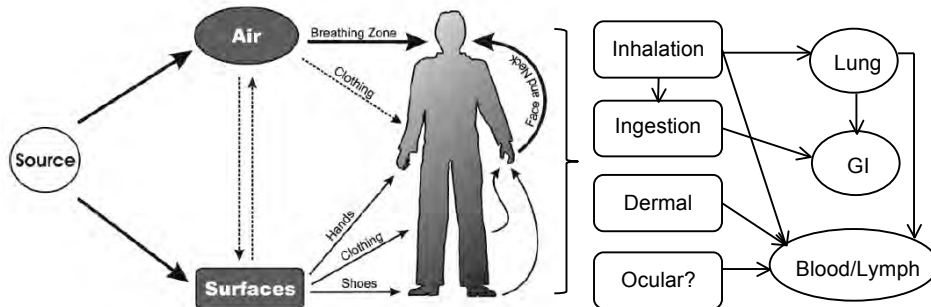
## Interleukin-6 Expression in Rat Brains



Real-time PCR was used to detect IL-6 expression levels in brains of rats exposed in Parlier, CA., June 2006. “\*” indicates  $p = 0.024$

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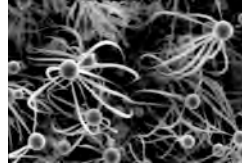
## Occupational Exposure Pathways



Beryllium Exposure Model (Day et al. 2007)



## Conclusions



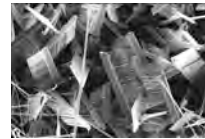
Nanoscience Images by Zhengwei Pan

- Nanoparticles have incredible potential for uptake, transport and retention throughout the respiratory system
- Nanoparticles found in agricultural settings may have respiratory, systemic and neurological consequences
- Evaluating the potential risks of nanoparticles will require assessment of the dynamics between particle size, chemical composition, exposure potential and biological fate

[http://www.cnms.ornl.gov/nanosci/lp5\\_shtm](http://www.cnms.ornl.gov/nanosci/lp5_shtm) (photo source)



## Acknowledgements



Nanoscience Images by Zhengwei Pan

- Amy Madl
- Laurie Hopkins
- Mai Ngo
- Stephen Teague
- Otto Raabe
- Ting Guo

NIOSH U07/CCU906162 (Western Center for Agricultural Health and Safety)  
USEPA 83171401 (San Joaquin Valley Health Effects Research Center)  
UC Toxic Substances Research & Teaching Program, Atmospheric Aerosols & Health

[http://www.cnms.ornl.gov/nanosci/lp5\\_shtm](http://www.cnms.ornl.gov/nanosci/lp5_shtm) (photo source)