RJ LeeGroup, Inc.
Analysis. Consulting. Development.

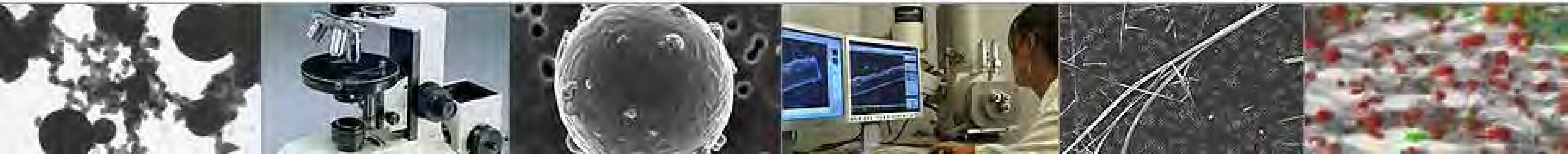
October 6-7, 2009
Arlington, VA

Measuring and Predicting Levels of Exposure of NM

Macro® Micro® Nano

Gary S. Casuccio
RJ Lee Group, Inc.

National Nanotechnology Initiative (NNI's) nanoEHS Workshop Series
Nanomaterials and the Environment & Instrumentation, Metrology, and Analytical Methods



Panel 3: Measuring and Predicting Levels of Exposure of NM

I3. Develop methods for standardizing assessment of particle size, size distribution, shape, structure, and surface area

I5. Develop methods to characterize a nanomaterial's spatio-chemical composition, purity and heterogeneity

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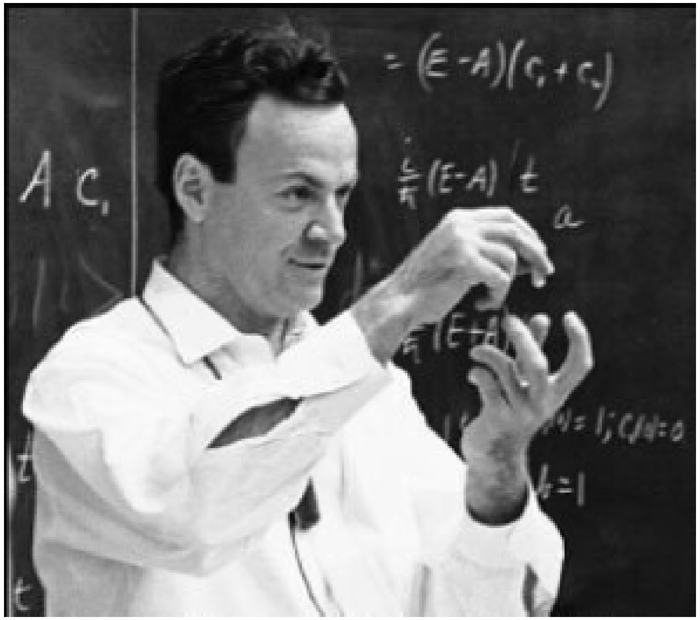
“What you should do in order for us to make more rapid progress is to make the electron microscope 100 times better.”

--- Richard P. Feynman, 1959
“There’s Plenty of Room at the Bottom”



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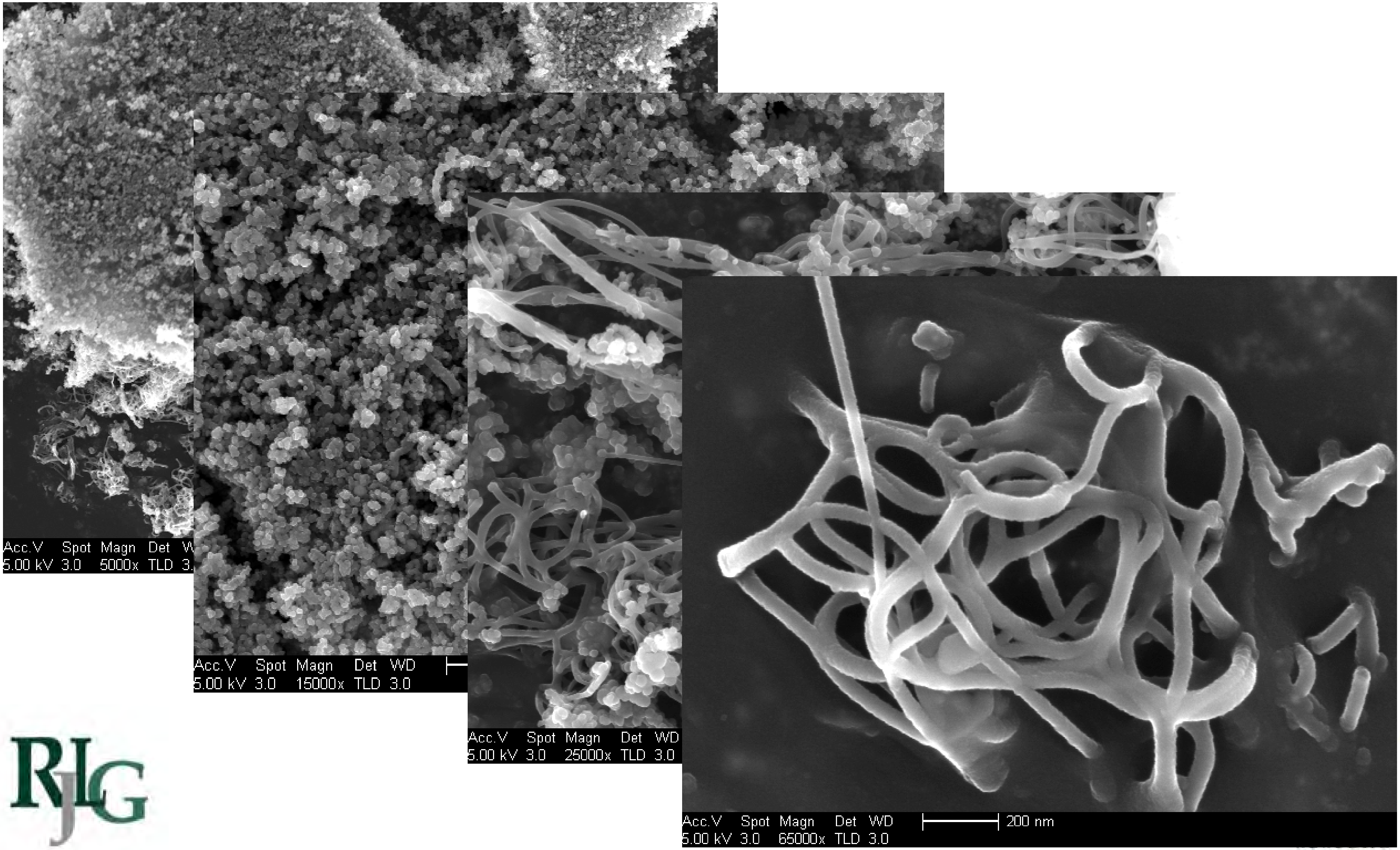
Nanometers
A Matter of Scale



Response to Case Study Questions

A Hypothetical Scenario For This Workshop

- Find the source of the problem (nanoparticles?) and control it.
- How would you go about identifying the one of potentially many nanomaterials in the air, soil or water that could have caused this ecological catastrophe?
- If nanoparticles were responsible, what were their associated critical physiochemical properties (size, shape, coating, composition) that lead to the observed biological effects?
- How could the transformations in the nanoparticle properties in the air, water or soil have been predicted?
- What biological and instrument methods could have been used to test all the nanomaterials produced by this company?

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Find the source of the problem

(Nano® Micro® Macro)

Proposed Approach (Air Quality)

- Identify suspect sources
- Collect samples of candidate sources
- Analyze source material and determine physical and chemical characteristics
  - Establish source signature
- Collect air, soil and water samples downstream of the manufacturing site
- Collect air, soil and water samples upstream of the manufacturing site (background)
- Analyze downstream and background samples and compare to source signature

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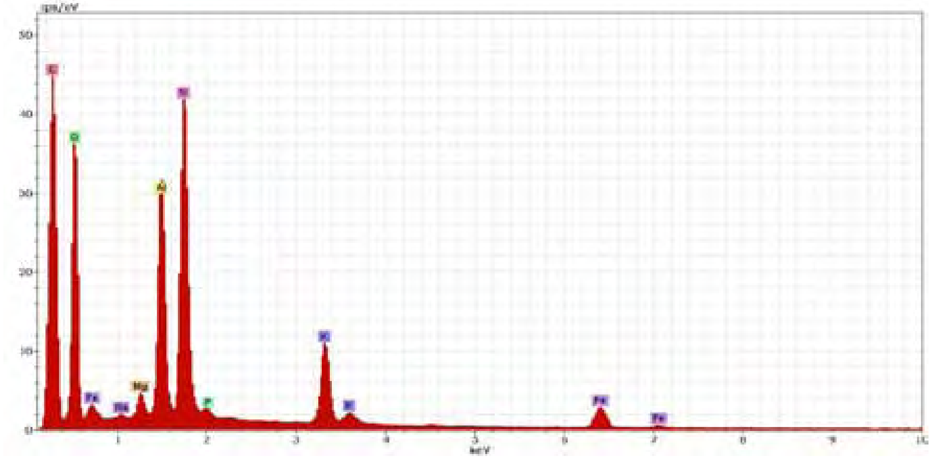
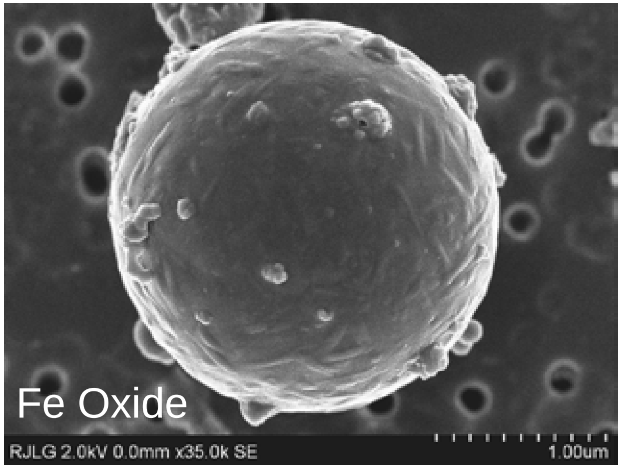
Source Apportionment of Ambient PM_{10}

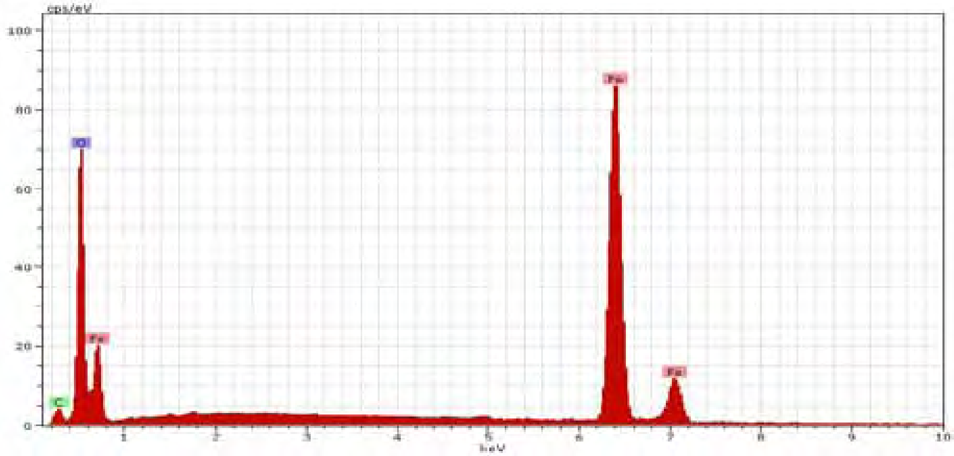
- Sample Collection
  - "Bulk" soil (source) samples collected near ambient monitors
  - Ambient PM_{10} collected at six monitoring sites onto PC filters over 24 hour period using "minivol" samplers operating at 5 l/min
- Develop profiles based on CCSEM analysis
  - Particles sorted into classes based on individual particle data
    - Elemental composition
  - Frequency/mass distributions determined for each class and for total sample
- Source and ambient CCSEM data used as input in EPA chemical mass balance (CMB) receptor model.

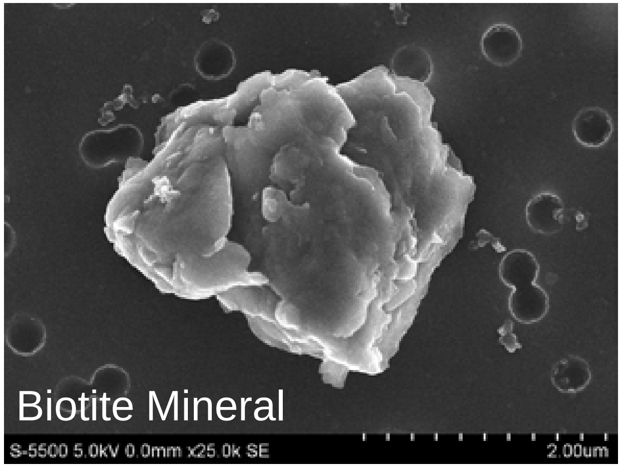
Minivol Sampler: 5 L/min

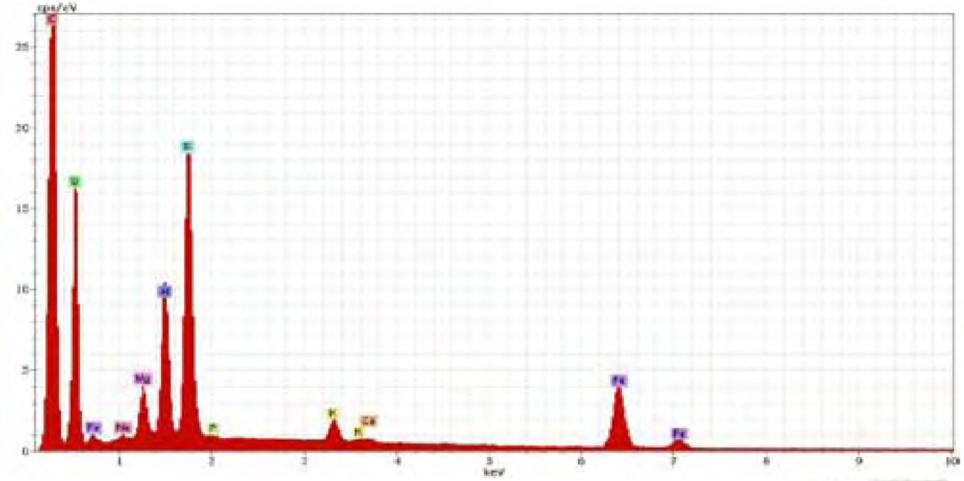

Fly Ash
S-5500 5.0kV 0.0mm x20.0k SE
2.00um



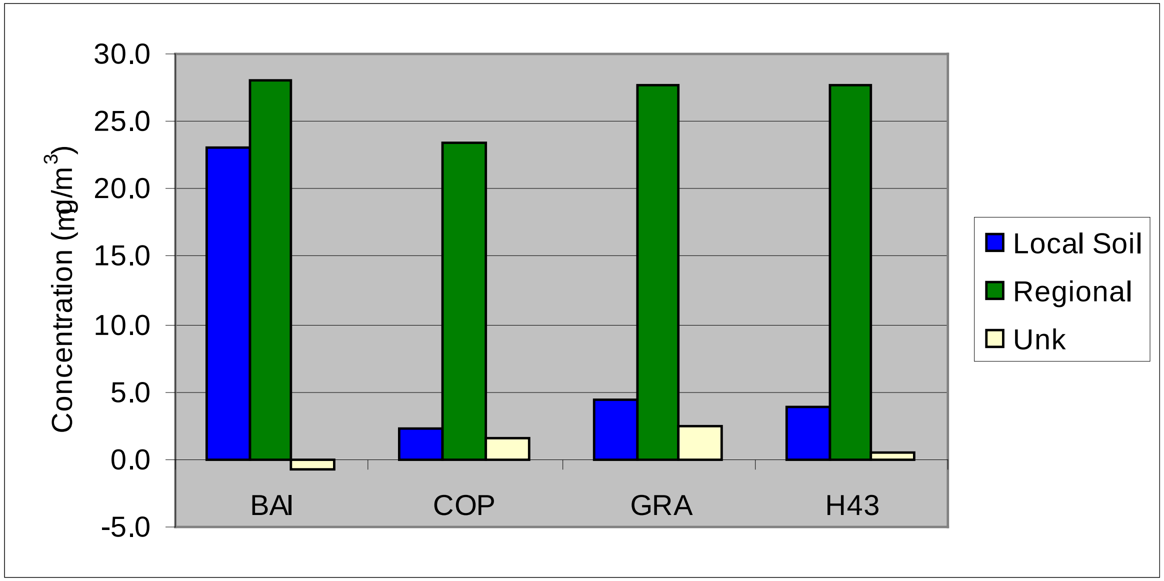

Fe Oxide
RJLG 2.0kV 0.0mm x35.0k SE
1.00um




Biotite Mineral
S-5500 5.0kV 0.0mm x25.0k SE
2.00um



Impact from Local and Regional Soils
CMB Results



Site	Concentration (µg/m³) Total	Concentration (µg/m³) Local Soil	Concentration (µg/m³) Regional	Concentration (µg/m³) Unk	Percent Local Soil	Percent Regional	Percent Unk	R^2	Chi^2
BAI	50.3	23.0	28.0	-0.7	45.7	55.6	-1.3	0.91	0.96
COP	27.4	2.2	23.5	1.6	8.2	85.8	6.0	0.90	0.80
GRA	34.5	4.5	27.6	2.4	13.0	80.1	6.9	0.92	0.63
H43	32.0	3.8	27.7	0.5	11.9	86.5	1.6	0.90	0.86

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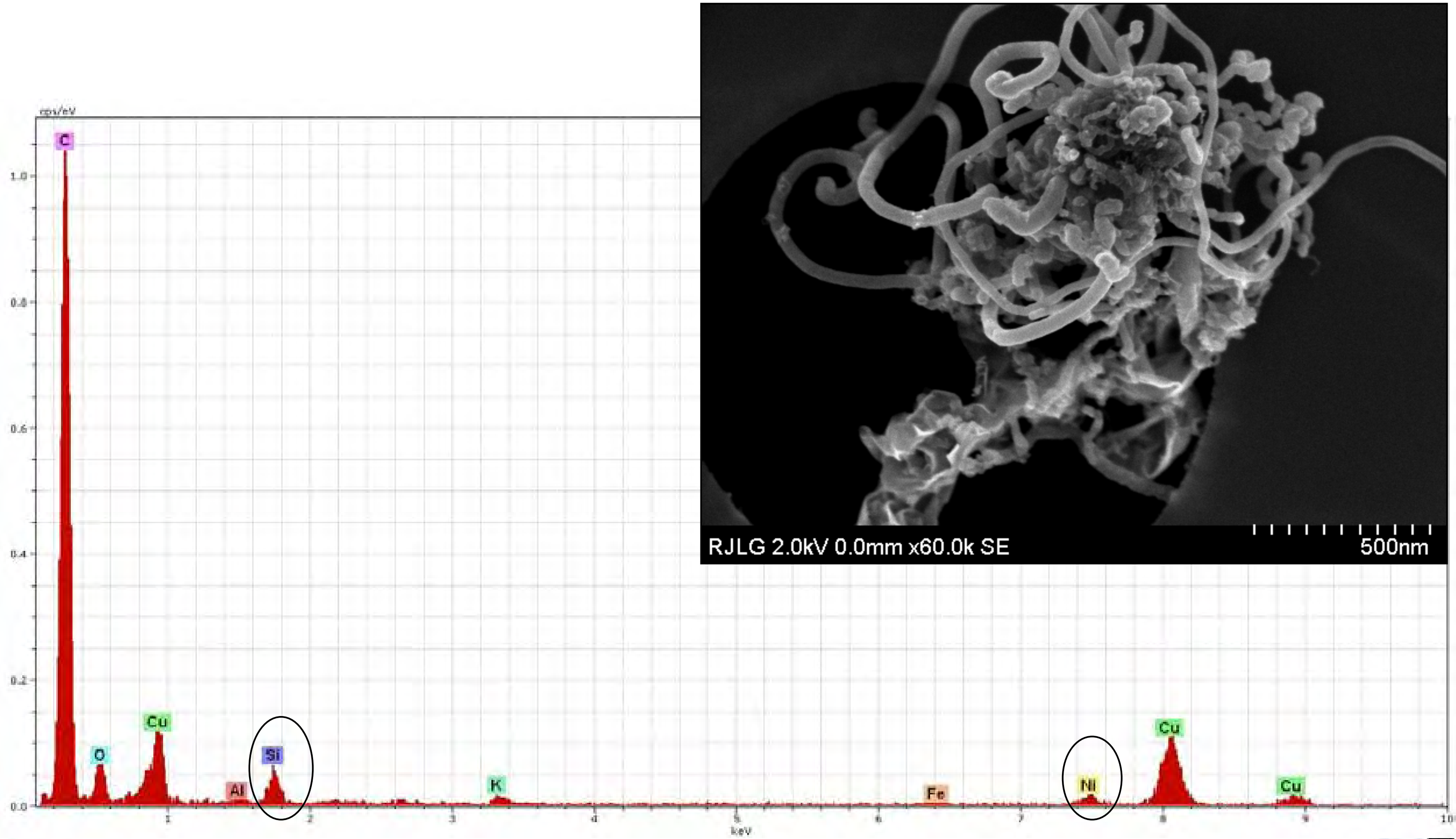
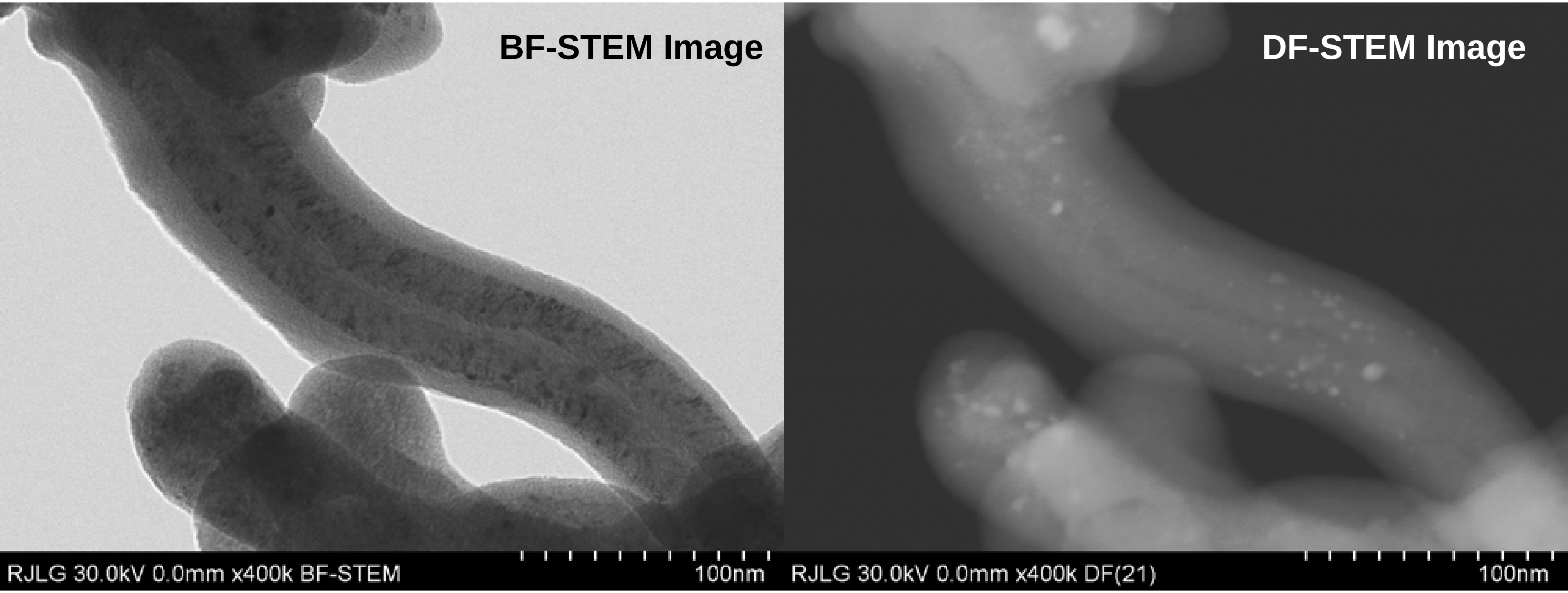
Nanomaterial Application: Characterize Source Material

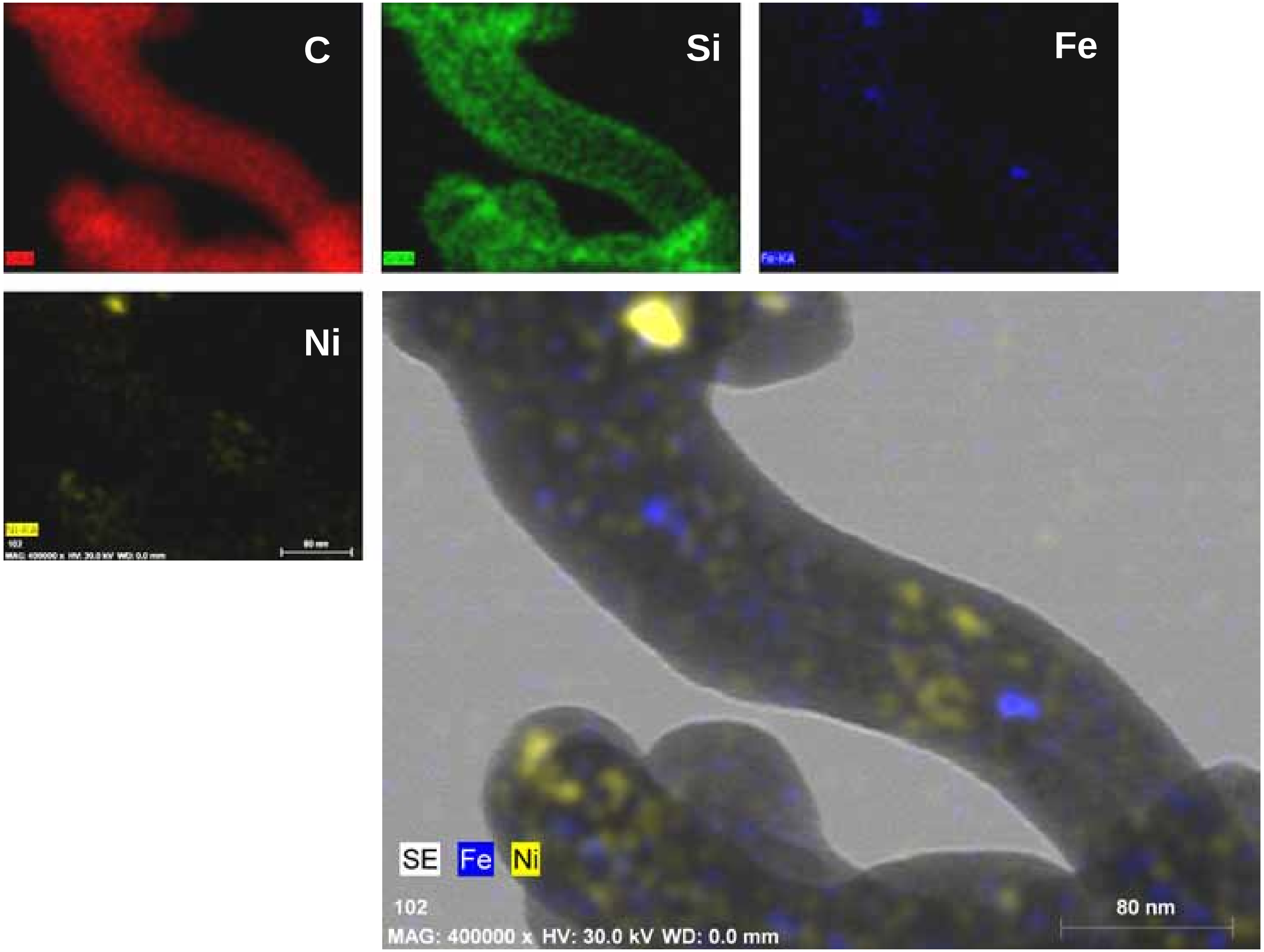


Nanomaterial Application: Characterize Source Material

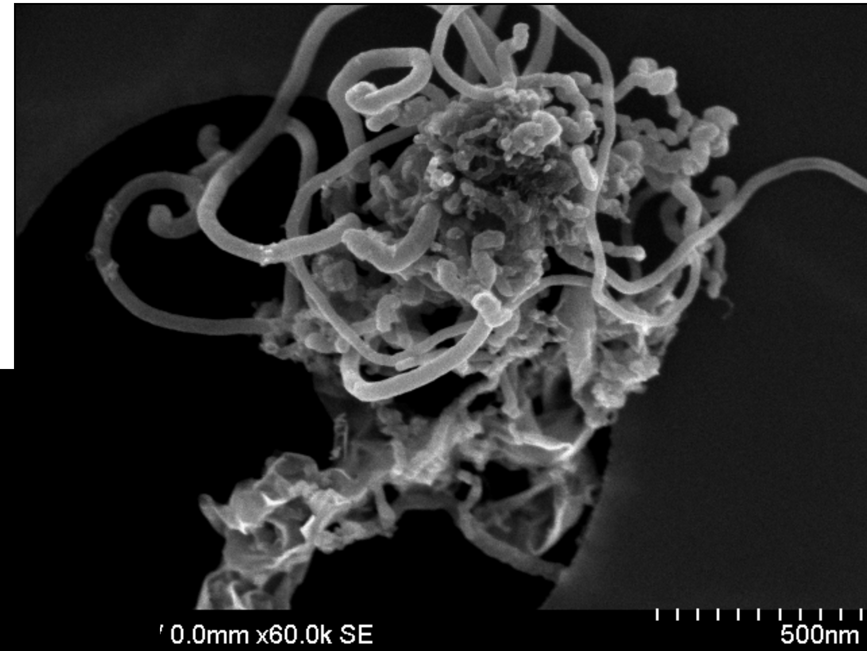


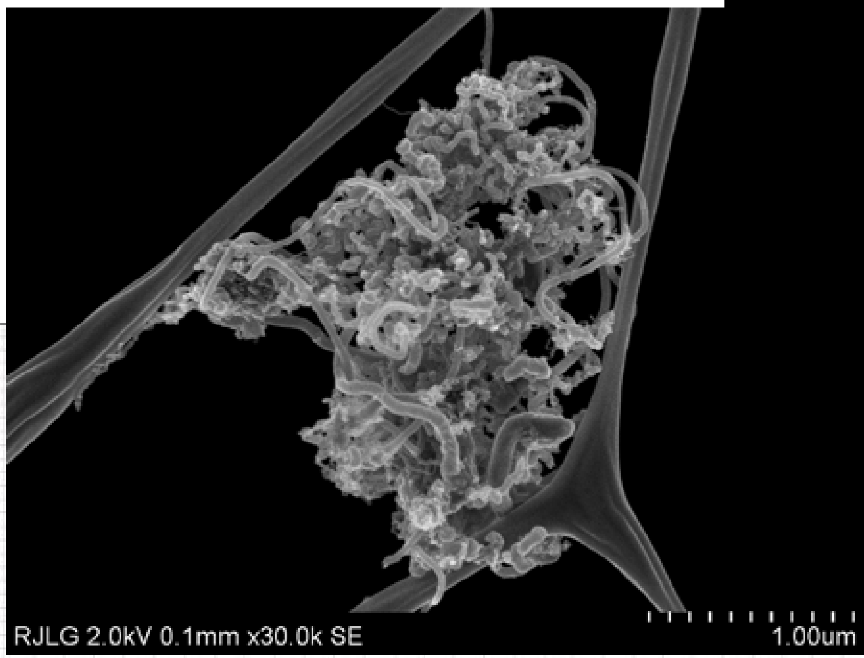
Example of Carbon Nanotubes with nickel and iron nanoparticles from the carbon particulate source material

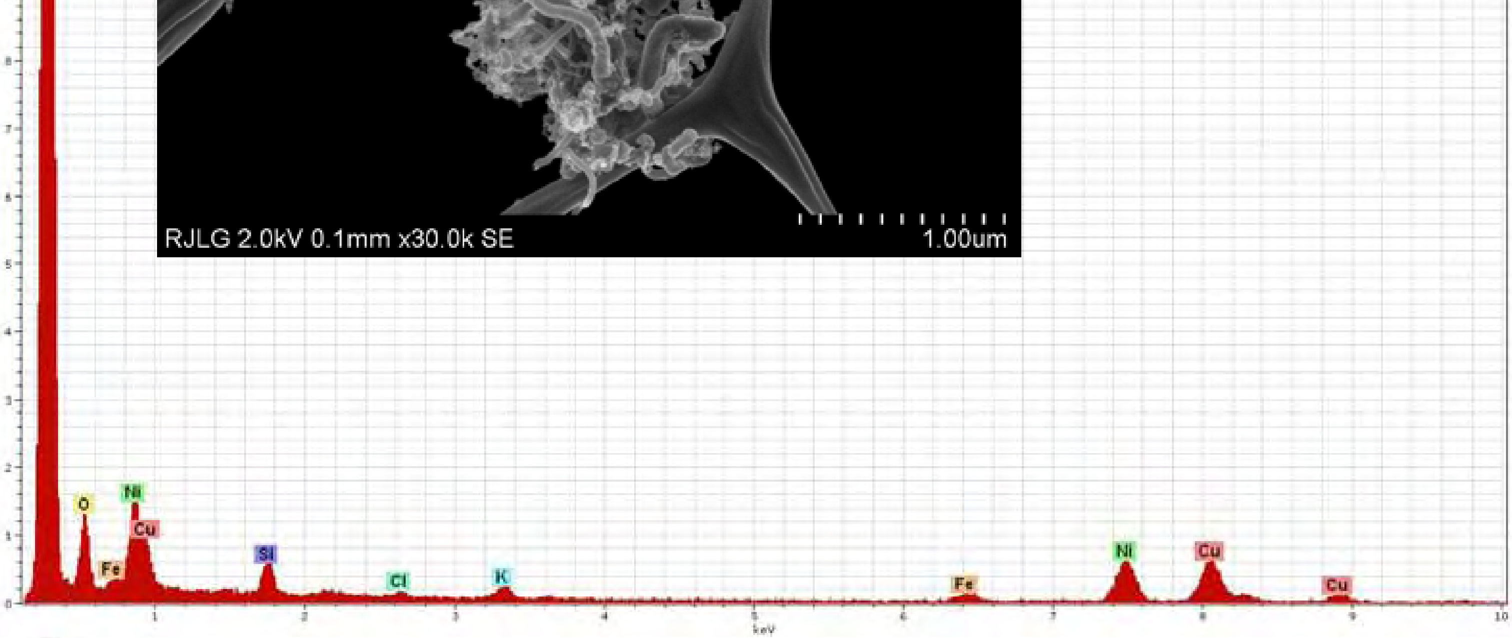
Nanomaterial Application: Characterize Source Material



Establish Source Signature







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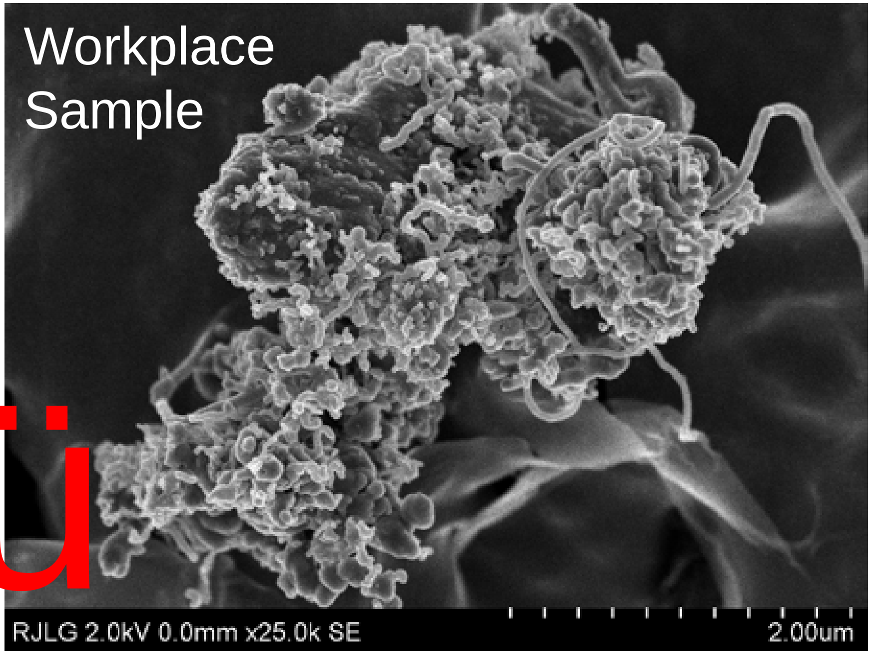
Workplace
Sample
RJLG 2.0kV 0.0mm x25.0k SE
2.00um

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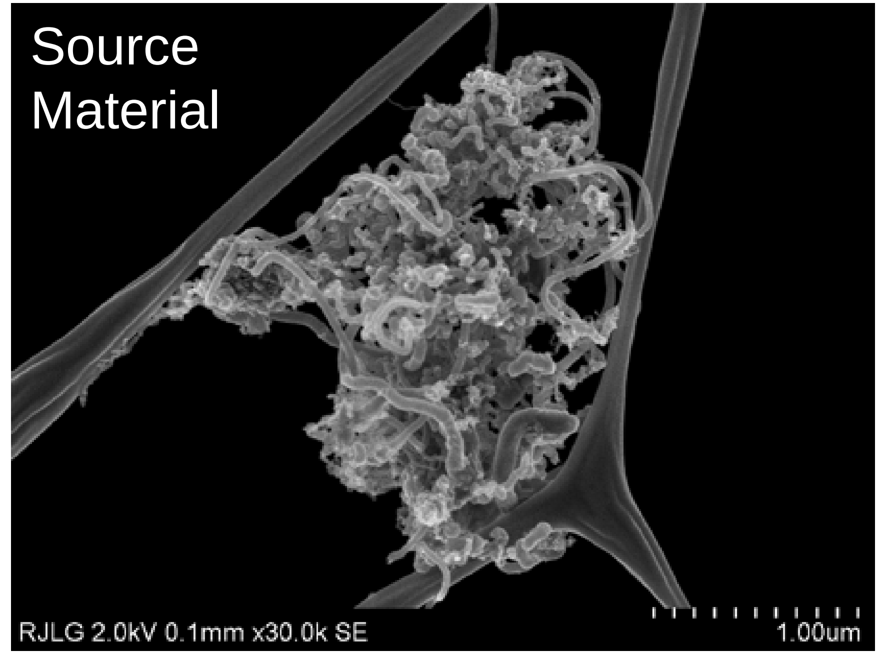
Source
Material
RJLG 2.0kV 0.1mm x30.0k SE
1.00um

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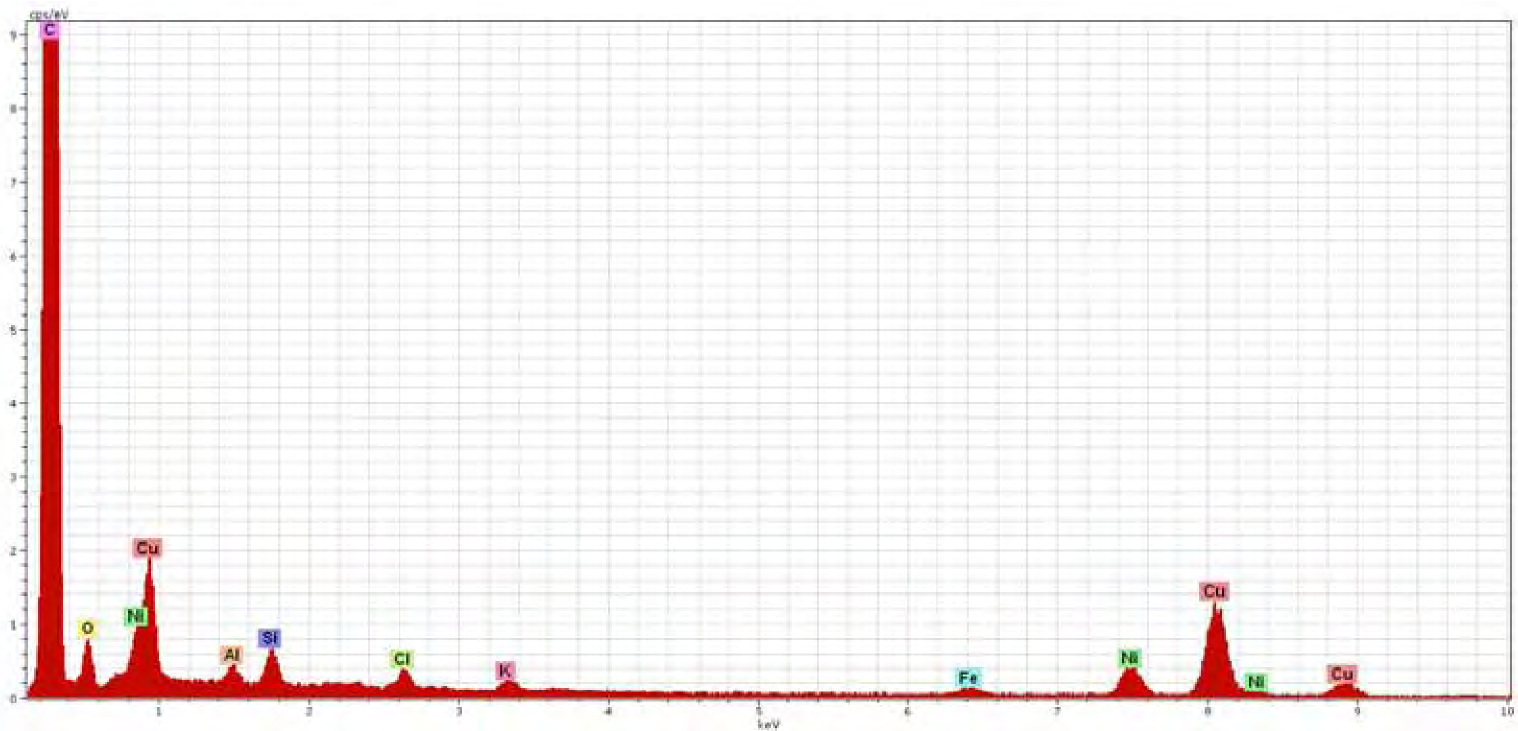
cps/eV
C
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Ni
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Ni
Cu
Ni
Cu
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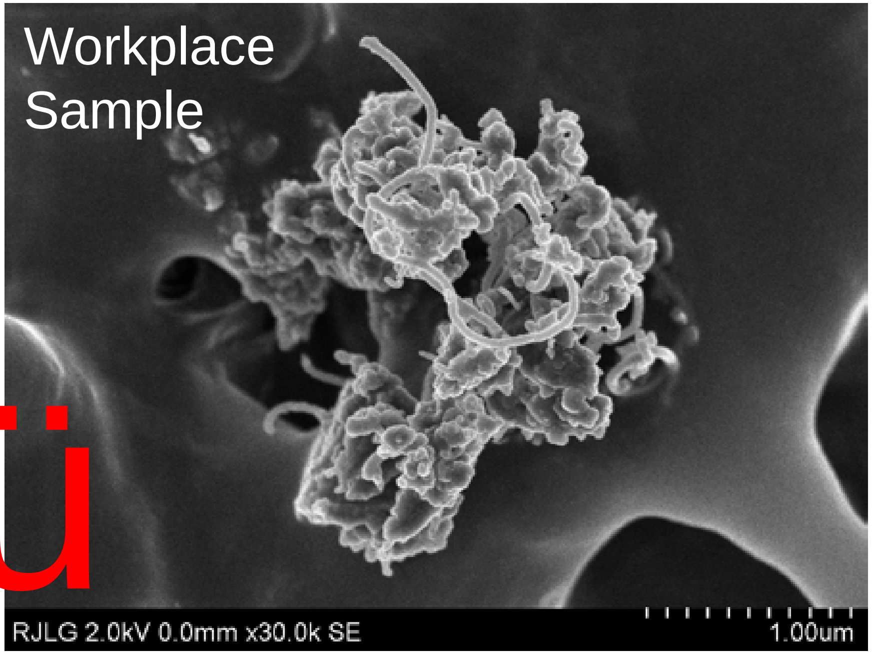
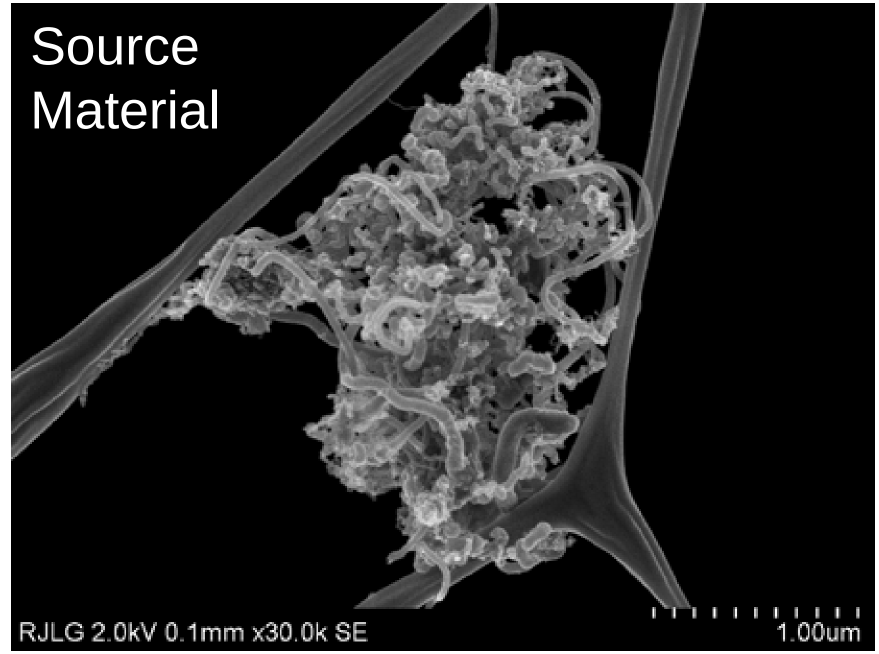

Workplace
Sample
RJLG 2.0kV 0.0mm x30.0k SE
1.00um


Source
Material
RJLG 2.0kV 0.1mm x30.0k SE
1.00um

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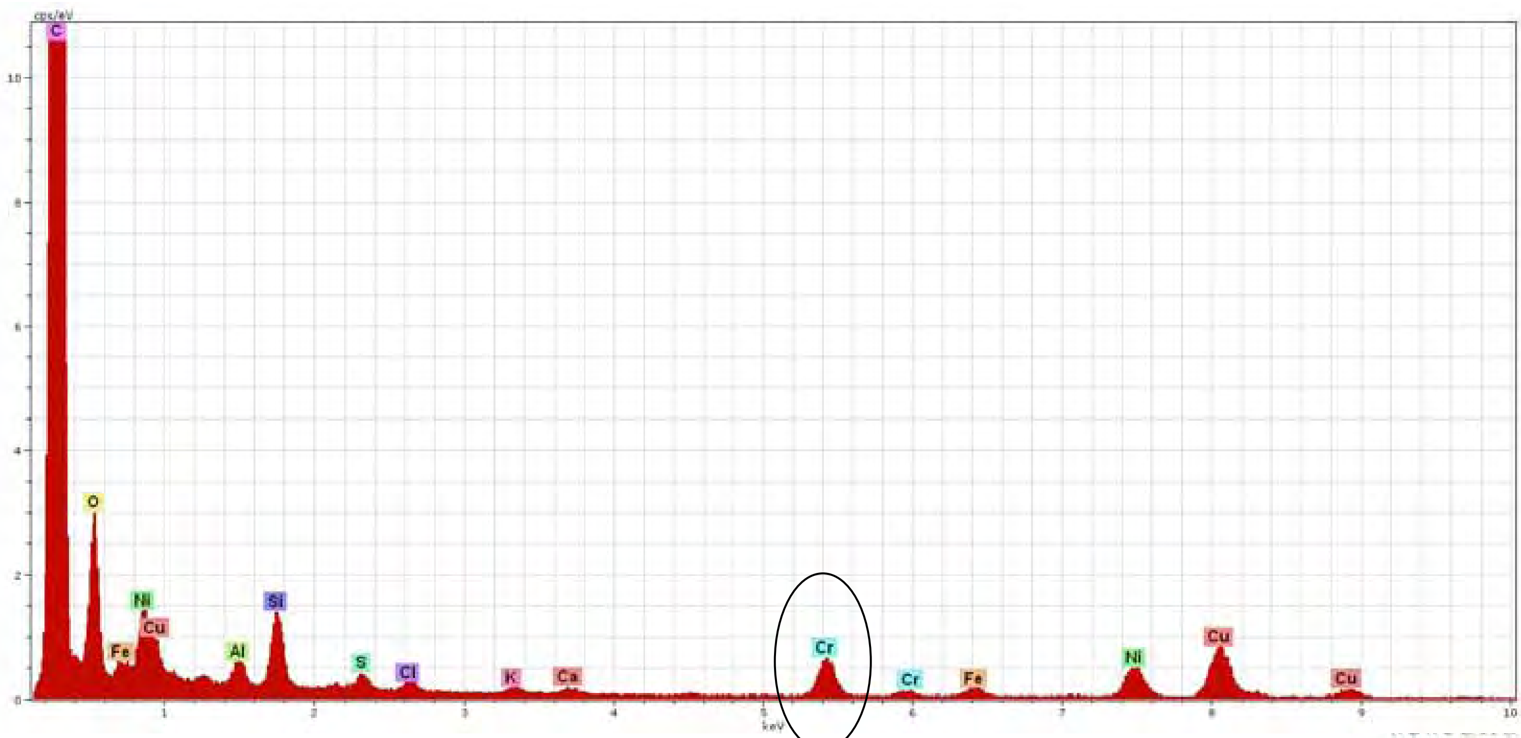
cps/eV
C
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Cr
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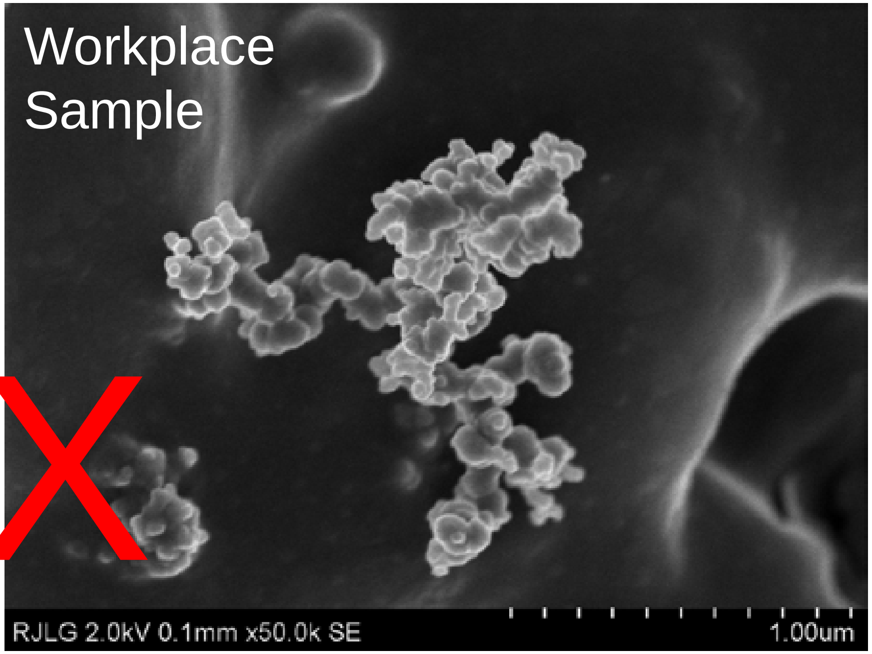
Workplace
Sample
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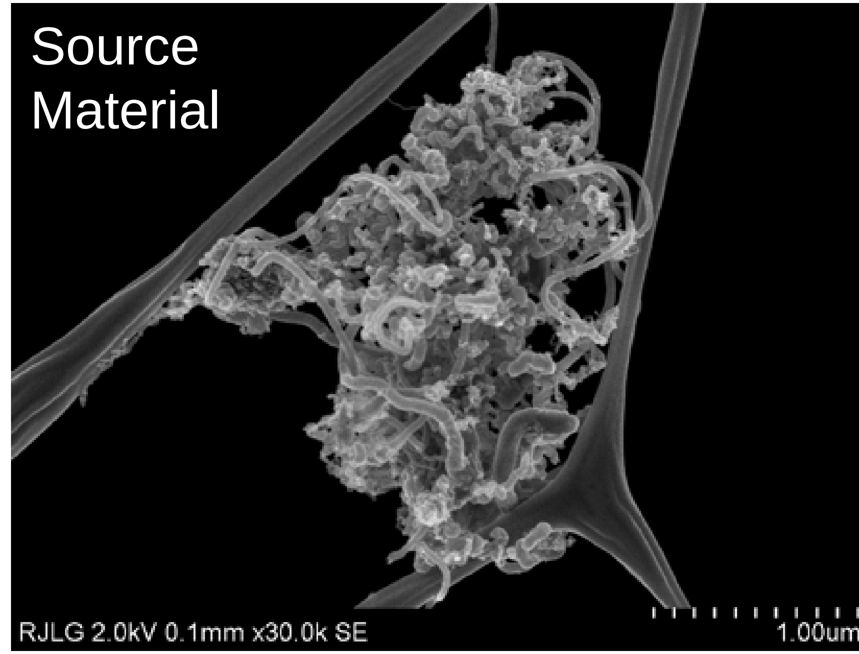
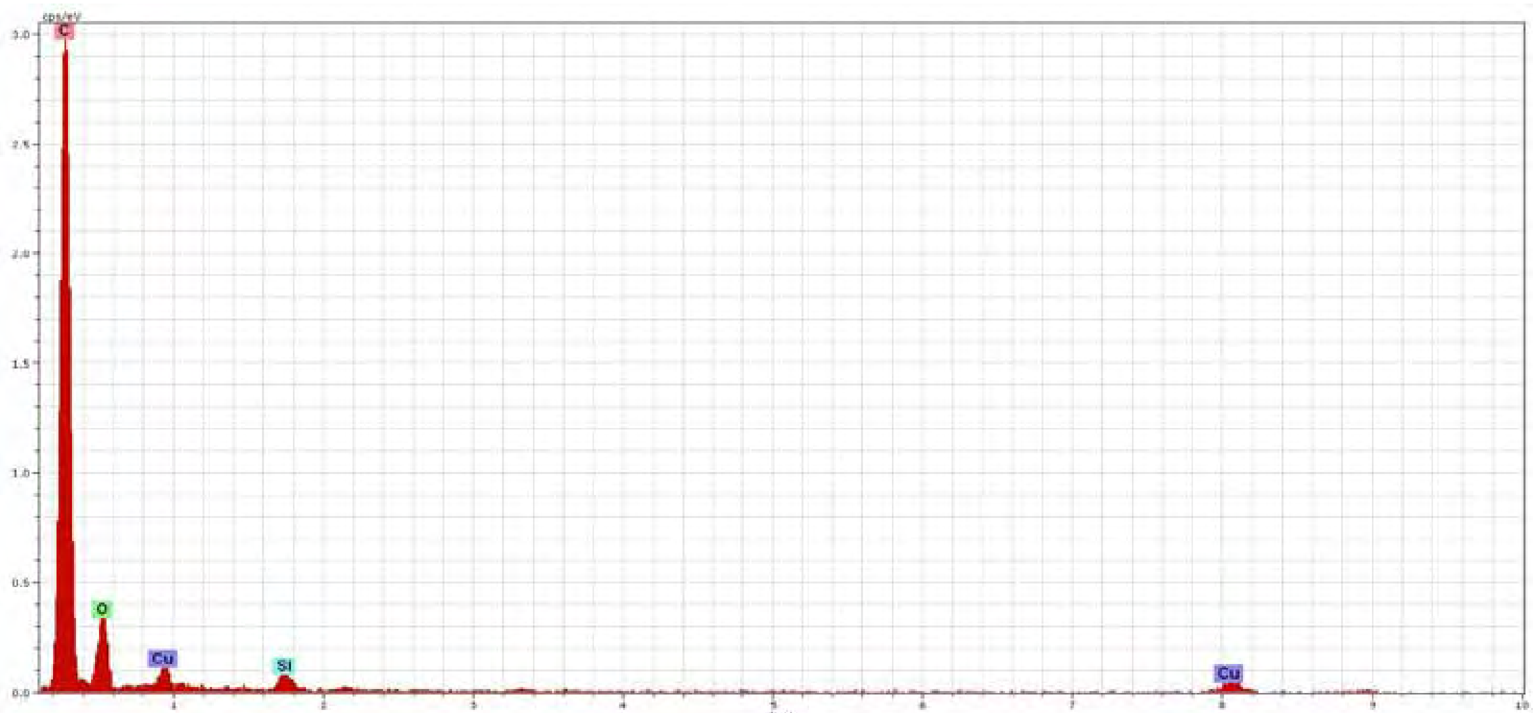
1.00um

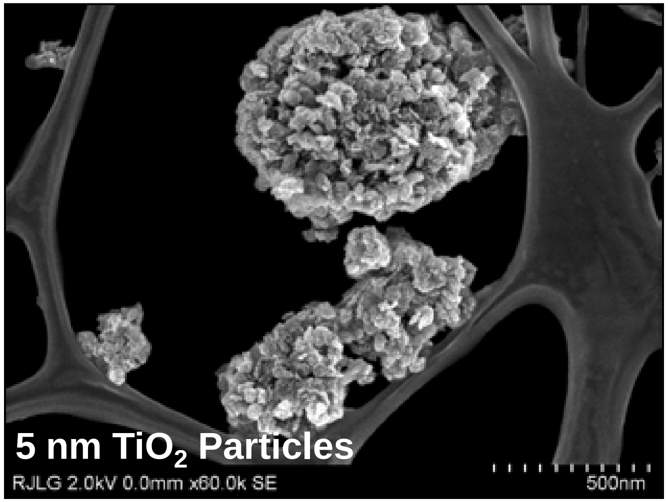

Source
Material
RJLG 2.0kV 0.1mm x30.0k SE
1.00um


cps/eV
C
O
Cu
Si
Cu
keV

If nanoparticles were responsible, what were their associated critical physiochemical properties (size, shape, coating, composition) that lead to the observed biological effects?

How do we determine critical physiochemical properties (size, shape, coating, composition) associated with nanoparticles?

- Information can be provided through microscopic characterization of source and receptor samples
  - Instrumentation is expensive
  - Automation is needed



- Once source(s) has been identified, *in vitro* and *in vivo* tests can be performed to determine biological effects
  - Conducted in concert with health effects experts

- Surface coating information provided through special studies

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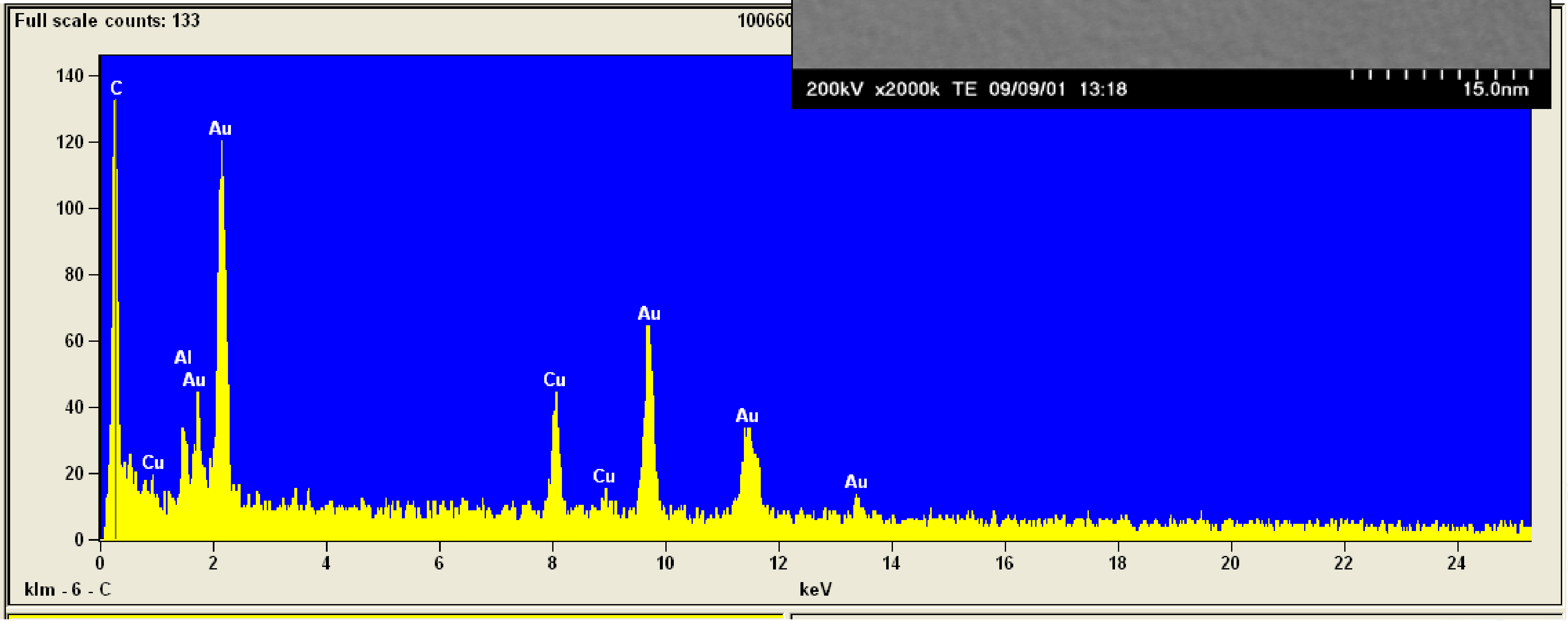
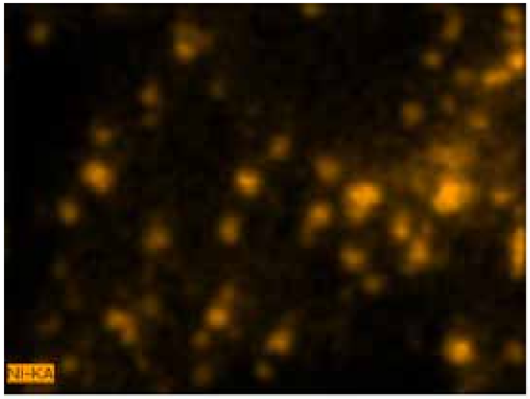
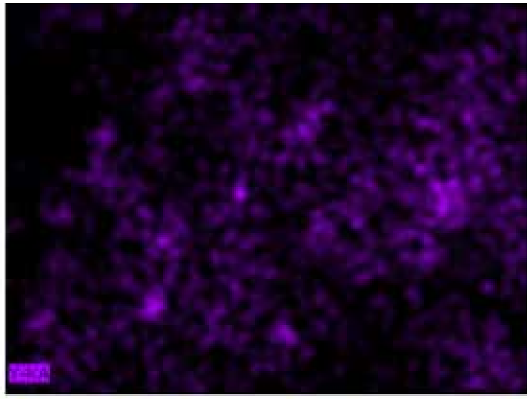
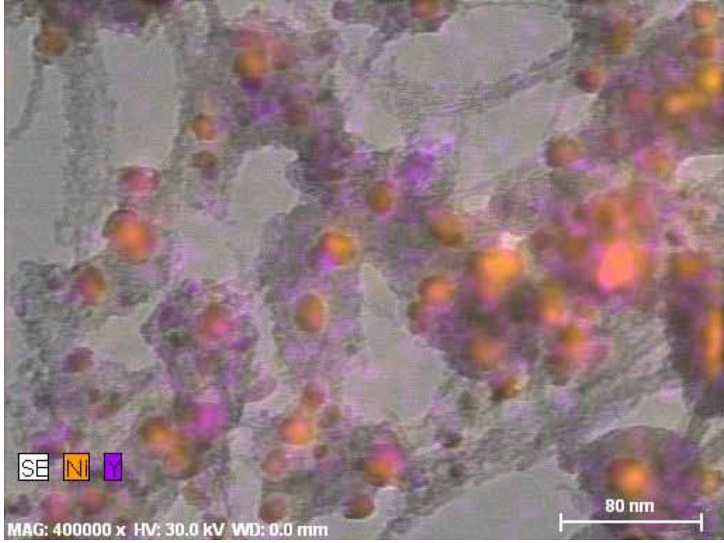
3 nm Gold Nanoparticles

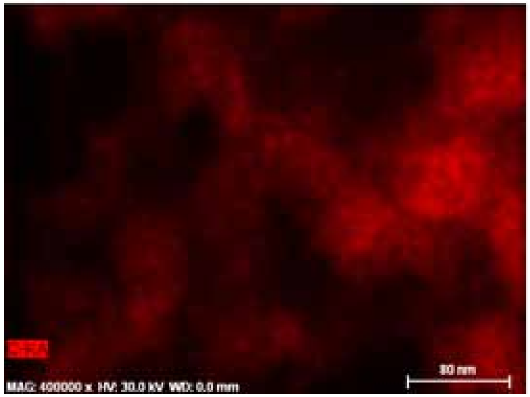


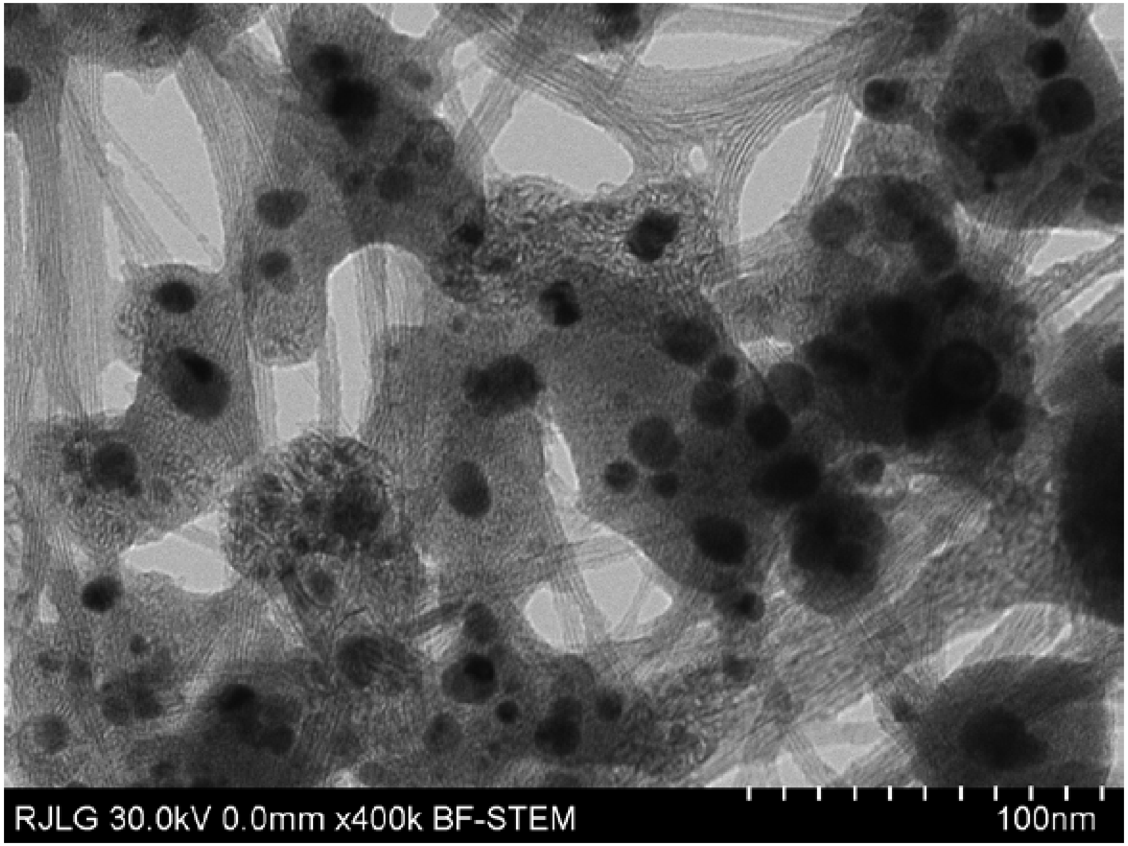
CNT with catalyst coating







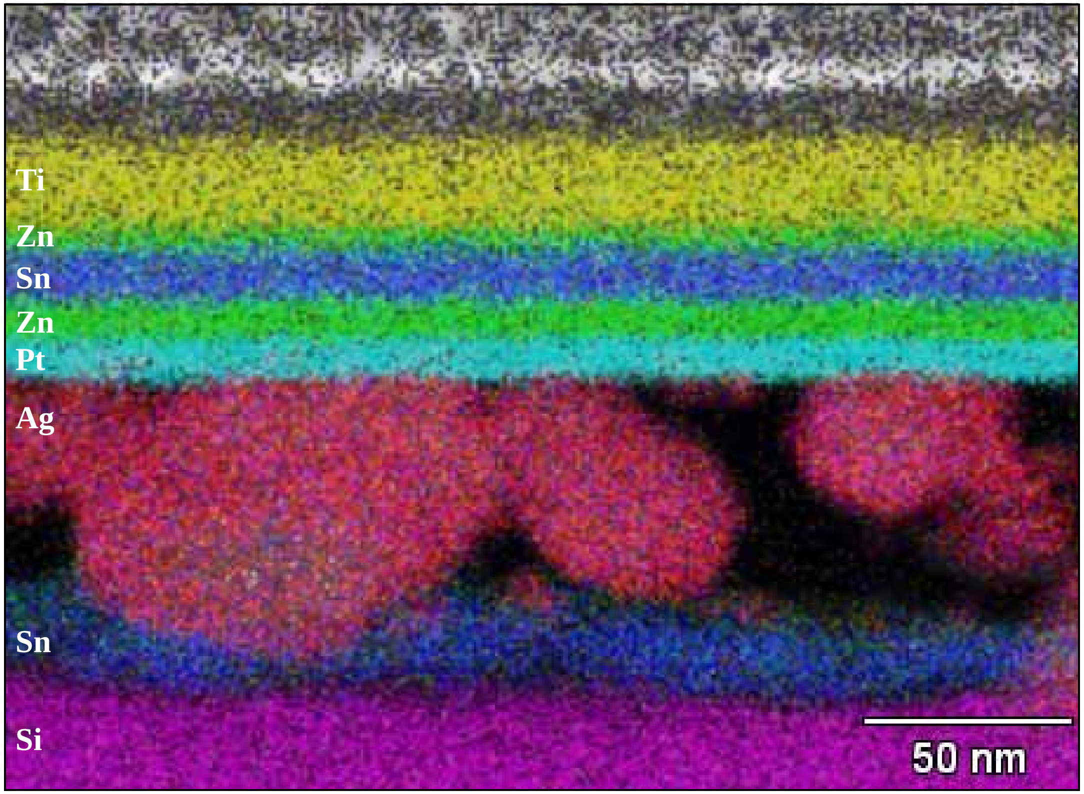




Spectral map showing distribution of Ni, Y and C 400,000x

High Resolution Compositional Information

- Coatings, Dispersions, etc.



Low emissivity ("Low-E") glass coatings for solar heat control showing 8 layers of the sample (10 nm to 60 nm)

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Factors affecting toxicity

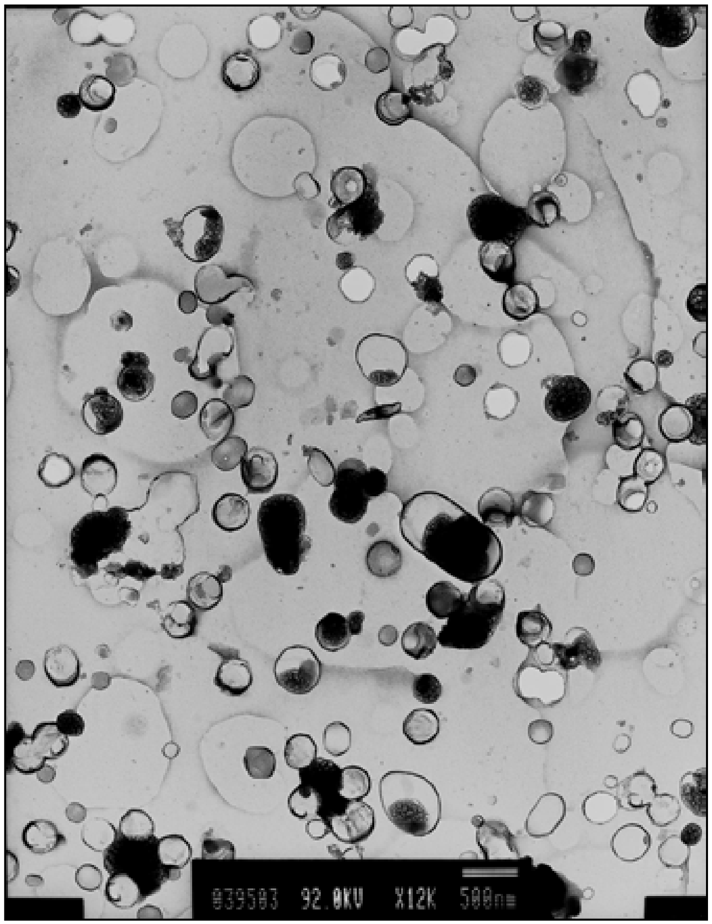
- Size
- Shape
- Concentration
  - Mass
  - Number
- Surface Area
- Surface reactivity
- Complexity (purity and heterogeneity; aerodynamic behavior)
- Durability
- ***Size, shape, concentration, surface area, complexity can be evaluated with microscopy***
- ***Need real time measurements that can be correlated with microscopy and reactivity (in-vitro, in-vivo)***

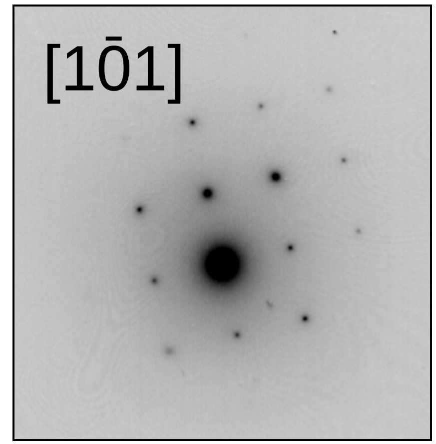
How could the transformations in the nanoparticle properties in the air, water or soil have been predicted?

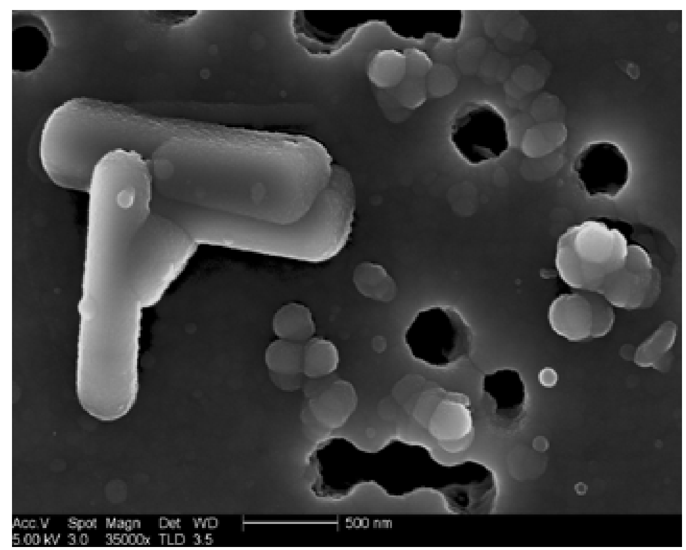
Evaluating nanoparticle transformations in air, water or soil

- Information can be provided through microscopy studies utilizing cryo-stages/environmental chambers
- Micro® Nano
- Air quality example of particle transformation

TEM image and selected area electron diffraction (SAED)pattern of an ammonium sulfate particle







What biological and instrument methods could have been used to test all the nanomaterials produced by this company?

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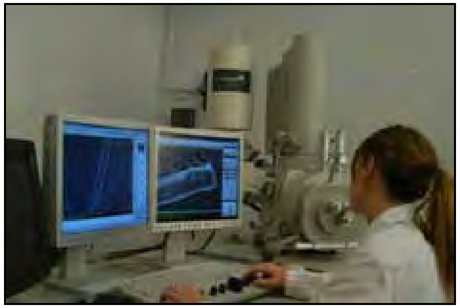
What biological and instrument methods could be used to test nanomaterials?

- The goal is to minimize potential release of nanoparticles through air, water or solid waste
  - Use combination of real-time particle counters with microscopy
  - Biological testing (*in vitro*; *in vivo*)
  - Risk assessment
    - Control banding
      - Lawrence Berkeley National Laboratory (LBNL) pilot study



LBNL Pilot Study
Step 1: Survey

- Assess potential for exposure of nanoparticles to the worker and the environment

- Four phase study
  - Survey labs
  - Interviewed researchers
  - Evaluate existing controls/programs
  - Analyzed nanomaterials used in process
  - Develop preliminary control band for each process
  - Perform monitoring of the process and finalize control band
  - Establish periodic sampling program

Worker and Environmental Assessment of Potential Unbound Engineered Nanoparticle Releases, Phase I Final Report, G. Casuccio and R. Ogle, RJ Lee Group, Inc., L. Wahl and R. Pauer, Lawrence Berkeley National Laboratory, September 2009.

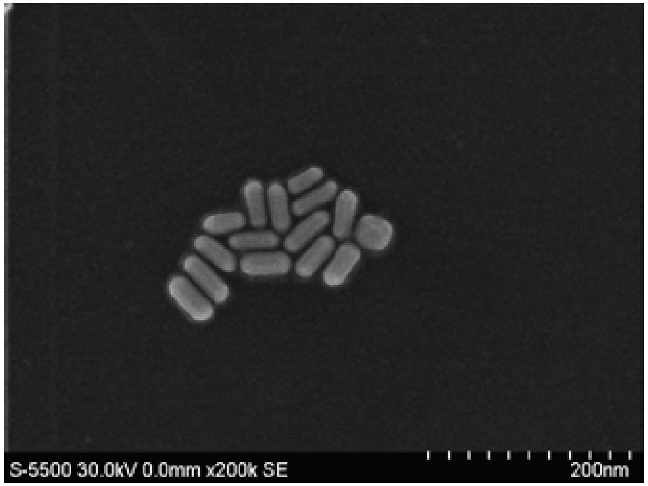
Step 2: Characterize

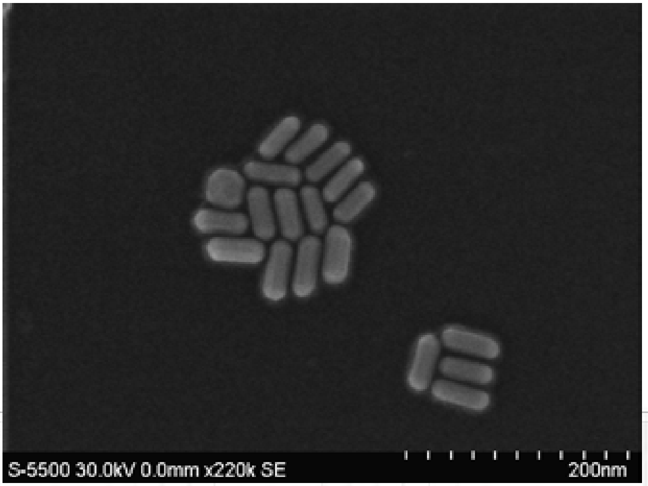
Table 19 Specific Risk Attributes Associated with Detection of Toxic Species

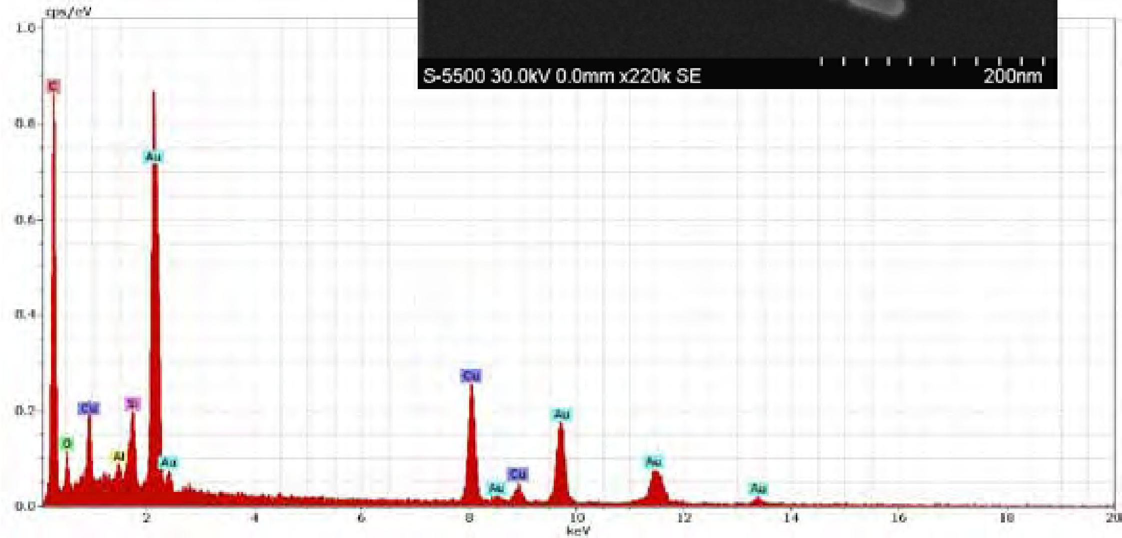
Risk Attribute	Building 70 Labs 291/293 Gold Nanorods
Particle size	Rod-shaped particles ~20 nanometers (nm) in diameter and ~50 nm in length; rounded and spherical particles were ~40–50 nm in diameter
Particle morphology	Primarily rod-shaped particles; rounded and spherical particles; observed in clusters
Elemental chemistry	SEM/EDS: Au; Si residue
Solubility (water)	Insoluble
Toxicity of nanomaterial	High
Amount of material used	< 10 mg
Dustiness/airborne potential	Low
Number of people doing the work	1–3
Duration of the operation	< 10 min
Frequency of the operation	1–5 x/week

Table 20 Preliminary Control Band Termination for Detection of Toxic Species

	Building 70 Labs 291/293 Gold Nanorods
Release/Exposure Probability	2
Worker/Environmental Hazard	C
Preliminary Control Band	II







Step 3: Risk Assessment

Worker/Environmental Hazard + Release/Exposure Probability = Risk (Degree of Hazard) Level

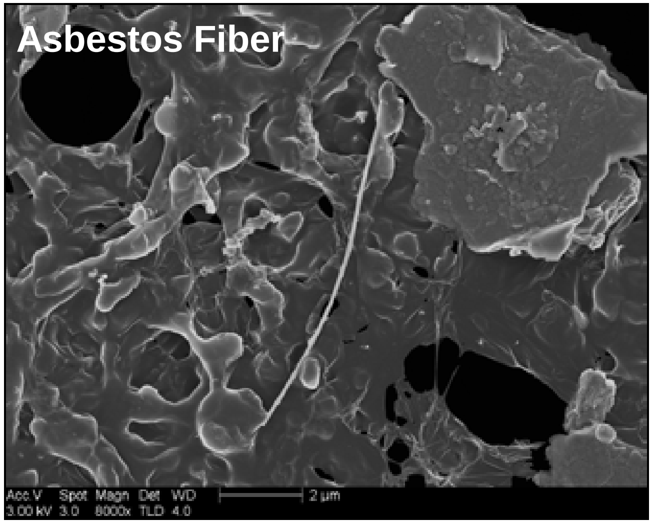
Worker/Environmental Hazard	Release/Exposure Probability: Unlikely (1)	Low (2)	Likely(3)	Probable (4)
Very High or Unknown (D)	Control Level III	Control Level III	Control Level IV	Control Level IV
High (C)	Control Level II	Control Level II	Control Level III	Control Level IV
Medium (B)	Control Level I	Control Level I	Control Level II	Control Level III
Low (A)	Control Level I	Control Level I	Control Level I	Control Level II

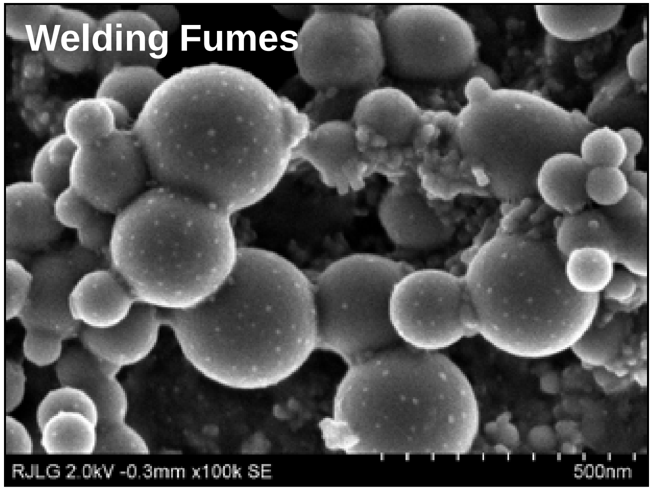
Worker and Environmental Assessment of Potential Unbound Engineered Nanoparticle Releases, Phase I Final Report, G. Casuccio and R. Ogle, RJ Lee Group, Inc., L. Wahl and R. Pauer, Lawrence Berkeley National Laboratory, September 2009.

Research Needs/Science & Technology Barriers

Where do we stand today?

- Powerful analytical tools
  - Expensive and labor intensive
- Real-time particle counters
  - No information on chemistry or morphology
- Well established IH approaches
  - Appropriate for nano?
- Knowledge of similar materials
  - Asbestos
  - Welding Fumes
  - Lead
- Risk assessment methods





What do we need to do?

- Extrapolate knowledge from known materials to unknown materials
  - Particle size & chemistry
  - Surface area
  - Health effects of known materials
- Evaluate extent to which the methods transfer to nanoparticles
  - Sampling and analysis methods
  - Nano presents a far more complex distribution of size, shape, morphology
- Address issues that were never solved in asbestos and other particle world
- Develop screening tests to relate known toxicity to materials we think are similar for which we have no exposure data
  - Control bands
- Make groups aware of guidance documents that are available

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What do we need to do next…..

Communicate

Recommendations

- Automation of EM (Nano® Micro® Macro)
- Bring different disciplines together (scientists-health effects experts-instrument developers)
  - Exchange of knowledge
  - Develop guidance documents; state of the art of the knowledge
  - Develop sampling instrumentation designed for the analysis
- We know a lot about control strategies today; identify the ones that are optimum and review their weaknesses and implement programs to address the knowledge gaps
  - This should lead to a monitoring program at every facility that is using nanomaterials
  - What is the effect of size, shape, and composition on ability to penetrate lungs or other organs
    - Ability to translocate?
  - Need to take methods that exist for exposure assessment and correlate real time measurements with microscopic techniques and develop counting techniques

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Recommendations

- The real answer is start with what we know today, make best estimates of likely behavior of these nanoparticles in the environment……
  - Use state-of-the-art analytical tools
  - Develop control strategies based on risk analysis (control banding)
  - Perform exposure assessment studies
  - Identify weaknesses in current methods and instrumentation
  - Develop automated procedures that do no exist today (Macro® Micro® Nano)
  - Develop counting strategies that recognize the differences in particle size, shape and complexity

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Gary Casuccio

- 30+ years experience in particle characterization
  - Particulate sampling and analysis; specialize in particle identification and apportionment using EM and automation EM techniques; consultant to industry and government agencies
- Pioneer of automated EM particle analysis systems
- Method Development
  - Automated EM (CCSEM)
  - Measurement of ceramic whiskers using optical and EM
    - DOE-ORNL method Þ ASTM methods
- Nanoparticle sampling and characterization
  - EPA, NIOSH, NIST, DOE, National Laboratories, Universities, Industry
  - Invited speaker at the NSRC Symposium on Safe Handling of Engineered Nanoscale Materials

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- Analytical-based materials science consulting organization
  - Spin-off of U.S. Steel Research
  - Environmental/Industrial Hygiene; Metallurgical; Forensics; Bio-Medical; Pharmaceutical; Nanotechnology; Educational Outreach
  - 200+ employees
- Particle analysis and identification
  - Air quality studies incorporating electron microscopy (1975 - today)
- Development of asbestos electron microscopy (EM) standards
  - EPA AHERA (air)
  - ISO (air)
  - Water
- Experts in automation of EM

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