A Exposure Assessment Strategy for Nanoparticles

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Key Elements of Risk Management

Hazard Identification

"Is there reason to believe this could be harmful"

Exposure Assessment

"Will there be exposure in real-world conditions?"

Focus for today

Risk Characterization

"Is substance hazardous and will there be exposure?"

Risk Management

"Develop procedures to minimize exposures."

NTRC Field Studies Team Background

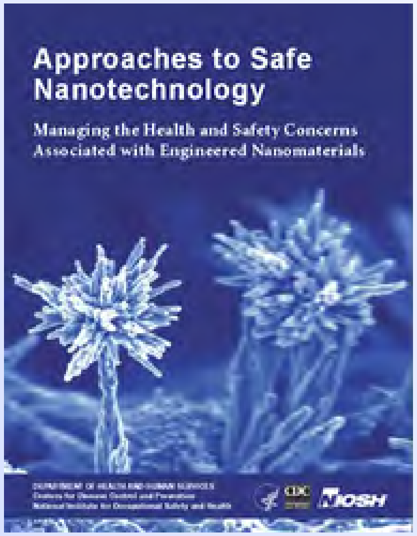
- Formally organized in 2006 as a component of the NIOSH Nanotechnology Research Center
- Conducted 50 site visits in a variety of work places
- Tasked with "learning nanomaterial processes"…
- Attempting to fill an important knowledge gap regarding nanomaterial creation and use:
  - ***Is there a release?***
  - ***To what extent?***
  - ***Is there potential worker exposure?***

NFST Goals

- Evaluates the entire material flow of a process and identifies points of potential material emission that can result in worker exposure
- Uses an array of instruments and conventional air sampling methods to characterize exposures
- Evaluates engineering controls and their effectiveness in reducing emissions and exposures
- Evaluates work practices used during the production or use of nanomaterials
- Evaluates the use of Personal Protective Equipment in use, if any, including respiratory protection

Nanotechnology Emissions Assessment Technique (NEAT)

- NEAT was developed as an initial step to semi-quantitatively evaluate emissions in nanomaterial workplaces and consists of a combination of field portable, ***direct reading instrumentation (DRI)*** and ***filter-based air sampling*** with subsequent laboratory analysis
- Assessment steps
  - Develop list of target areas, processes, or tasks for DRI
  - Identify potential emission sources
    - Review process and process flow
    - Examine material inputs and discharges
    - Evaluate worker practices and tasks
    - Review literature



NEAT

- Potential emission sources
  - Observational walk-through
  - Determine frequency and duration of operations
  - Determine types of process equipment
  - Characterize use of engineering controls
  - Identify intentional breach points
    - Product retrieval
    - Maintenance activities
  - Determine if ENMs are being released

NEAT – 2005 to 2010

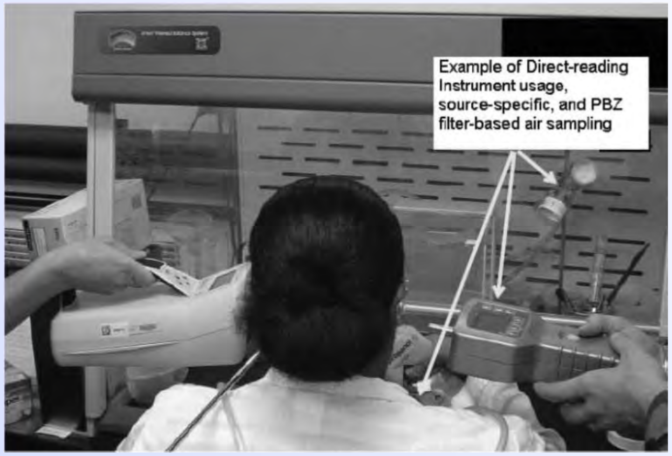
Methods

- DRI (CPC and OPC)
  - Characterize background concentrations
    - At process and in adjacent work areas
    - Average pre task and post task concentrations
    - Short sample times (approximately 1 minute)
    - Document background contributing activities
  - At emission source
  - Compare emission source versus background (differential evaluation)
    - ↑ CPC ↑ OPC (300nm – 500nm) ◊ Presence of nanomaterials
    - ↓ CPC ↑ OPC (>1000nm) ◊ Presence of large particles and/or agglomerates

NEAT – 2005 to 2010

Methods

- Integrated Sampling (filter cassette based)
  - 37-mm open faced
    - Mass concentration (elemental analysis)
    - Electron microscopy
      - TEM with energy dispersive X-ray spectrometry
  - Collected at emission source locations
    - PBZ
    - Area
  - Not full-shift
  - High flow rate to compensate for short sampling times
  - Respirable fraction
    - Cyclone or cascade impactor



NEAT – 2005 to 2010

20 Field Studies

Types of facilities	Number of sites
Primary producer of nanomaterials	7
Secondary user of nanomaterials (manufacturer)	6
Secondary user of nanomaterials (research and development)	6
Tertiary user of product containing nanomaterials	1

NEAT – 2005 to 2010

20 Field Studies

Type of nanomaterial	Number of sites
Carbon Nanotubes (Single wall and Multi-wall)	11
Carbon Nanofibers	4
Nano-Metals	3
Nano-Metal Oxides	3
Nano-Graphene Platelets	2
Others (Carbon Nanopearls, Nano-silica/Iron, Fullerenes, Boron Carbide)	4

** Some facilities used multiple types of nanomaterials.*

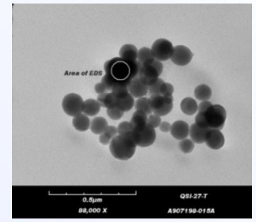
NEAT – 2005 to 2010

Methods (filter-based)

Type of sample taken	Type of filter used	Number of samples taken
Mass concentration (Elemental Carbon)	37-mm open-faced QFF	167
Mass concentration (Metal or Metal Oxide)	37-mm open-faced MCE	48
Mass concentration (Boron Carbide)	37-mm PVC with cyclone	57
TEM with energy dispersive spectroscopy	37-mm open-faced MCE	222

NEAT – 2005 to 2010

Case Studies



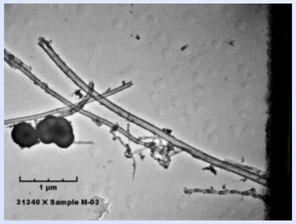
- **Process Description:** Gas phase condensation synthesis of manganese oxide and iron oxide nanoparticles
- **Nanomaterial size**: approximately 20 nm diameter (Roughly spherical)
- **Production Scale**: 1kg per day
- **Number of workers**: 2
- **Task Description**: Elemental manganese or iron powder is loaded into the reactor and heated with argon and oxygen until the metal becomes gaseous creating nanoparticles, which are deposited on the sides of the reactor. A mechanical scraper removes deposited particles, and are collected via gravity in a jar at the bottom of the reactor.
- **Possible Interferences**: Facility also synthesizes nanosized nickel and cobalt, however not on the sampling day

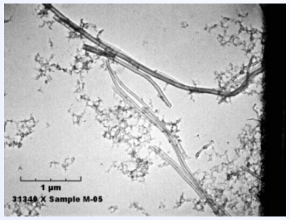
Results of Case Study 1

- **Surface Sampling Results**: Manganese was detected on every wipe sample collected. The highest amounts were found in the production area and the lowest amounts were found in the office.
- **Air sampling Results**: Specific process tasks such as pouring powdered manganese into the hopper feed mechanism, changing the collection jar (107 µg/m^3), cleaning and brushing the open manganese reactor (67 µg/m^3) and separating the reactor halves (3619 µg/m^3) generated the highest concentrations. The general area sample collected prior to synthesis contained 4.0 µg/m^3), manganese.

Location and Activity	Size range 1-1000 nm (CPC)	Size range 1000-10,000 nm
Pouring powdered manganese into reactor hopper	75,832	158
Clean out manganese reactor	29,063	170
During manganese reactor separation	>100,000	6
Manganese reactor during collection jar change	33,498	13
Office conference room (background)	10,121	2

Case Study 2





- **Process Description:** Preparation of Carbon Nanofibers (CNF) by chemical vapor deposition.
- **Nanomaterial size**: 70-100 nm diameter, 50-100 μm length
- **Production Scale**: approximately 250 pounds per day
- **Number of workers**: 6
- **Task Description:** Reactor(s) create batches of plugs of CNF. The CNF are then brought to a mixer and mixed with alcohol and water. The CNF slurry is collected in gravity feed buckets and then transferred for heat treatment. Material is then transferred to a pyrolytic stripper and a mechanical screw feeder deposits the final product into plastic-lined cardboard boxes.
- **Possible interferences**: Potentially toxic gases in use, heaters/dryers used to dry product

Results of Case Study 2

- **Air Sampling Results**: Based on the analysis of the filter-based air samples for total carbon (TC), there are specific processes releasing CNFs to the plant atmosphere. Airborne concentrations in six of the eight processing areas were 3 to 155 times higher than that found in an office area or in the plant away from specific processes. In addition to the air samples collected and analyzed for TC, all of the process-specific air samples collected an submitted for TEM analysis showed microscopic evidence of CNFs, validating the value of the TC method as an effective surrogate.

Sample location/operation	0-.3	.3-.5	.5-1	1-3	3-5	5-10
Plant Control Room (Background)	33,807	3270	984	117	18	1
Loading pyrolytic stripper hopper	147,510	115,909	10,170	958	609	530
Manual scooping of final product and dumping it into shipping container	140,008	140,456	132,814	13,382	12,429	82,244
Oven room while trays of heat-treated product cool	121,883	12,441	2.786	287	43	11

Case Study 3

- **Process Description:** Dispensing, weighing, and making aqueous suspensions of various types of titanium dioxide, copper, and silver engineered nanoparticles for toxicological studies
- **Nanomaterial size**: TiO2: 6 nm and 40 nm, Cu: 40 and 60 nm, Ag: 15 nm
- **Production Scale**: Laboratory scale, unpredictable duration and frequency
- **Number of workers**: 3 full time, 3 part-time, 3 graduate (other duties outside of the production of the nanoparticles for all)
- **Task Description:** Weighing 1mg of ENM onto a transfer paper inside unventilated microbalance and transfer to a glass vial. Take the vial to single pass fume hood and use contents to make a stock suspension of the material in sterile water.
- **Possible interferences**: None

Results of Case Study 3

- No mass based air samples were collected. This study relies strictly on the results of the real-time instruments.
- No substantial increase in NP concentrations compared to ambient background levels were visualized based on ten real-time measurements taken with a CPC and OPC.
- Two background samples were collected during the sampling period, which was subtracted from the measured number concentration to yield the adjusted number concentration.

Process	Particle size (nm)	Measured Number Concentration	Average Background Number Concentration	Adjusted Number Concentration *
Transferring elemental Silver paste (25nm diameter)	300	19,417	23,298	0
	500	1,450	1,862	0
	1,000	69	85	0
	3,000	8	3	5
	5,000	0	0	0
	10,000	0	0	0
	(10 - 1000)	3,850	3,790	60
Pipetting slurry of Aluminum Oxide (30 nm diameter)	300	21,925	23,298	0
	500	1,792	1,862	0
	1,000	80	85	0
	3,000	11	3	8
	5,000	0	0	0
	10,000	1	0	1
	(10 - 1000)	3,800	3,790	10

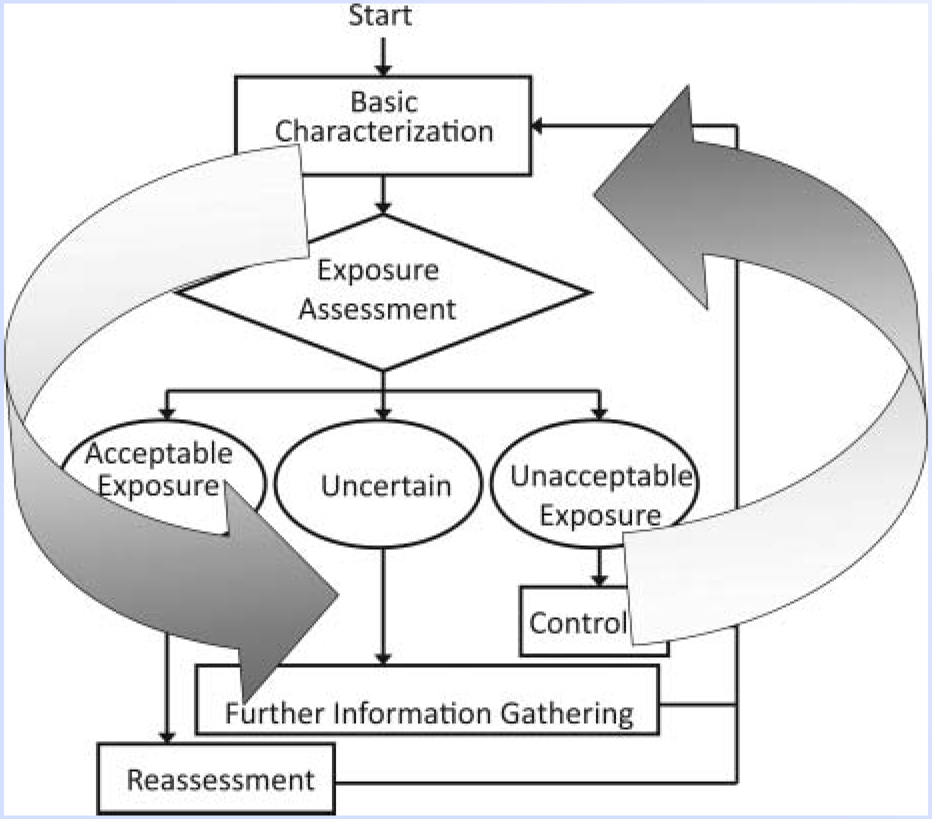
NEAT – Lessons Learned

- Real-Time Instrumentation
  - Background concentrations fluctuate significantly
    - In excess of 10^6 particles/cm^3
    - Variations by
      - Season
      - Day
      - Within day
    - Averaging pre and post task does not adequately address background influences
    - Data logging would better capture and account for background variations
    - Documentation of critical events essential
    - Careful attention to selection of background location
    - Real-Time Instruments alone are insufficient to adequately evaluate a worksite

JOEH – November 2011

A Strategy for Assessing Workplace Exposures to Nanomaterials

- Based on AIHA exposure assessment strategy



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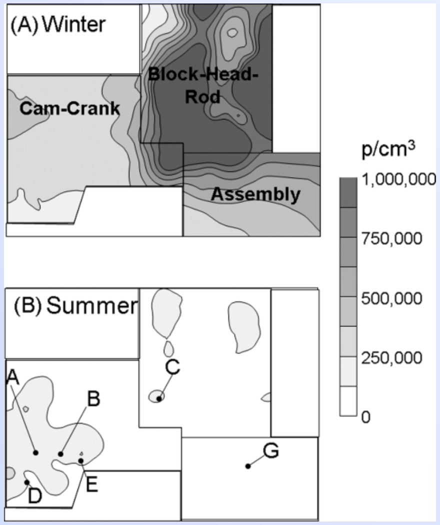
A Strategy for Assessing Workplace Exposures to Nanomaterials

- Basic Characterization
  - Workplace, work force, and environmental agents documentation
    - Nanomaterial of concern; sources of exposures (ENM and natural); processes, equipment, tasks, work practices and controls
  - Understanding exposure potential from processes
    - Research laboratory versus production scale
    - IH training and experience may not address subtle differences in nanomaterial characteristics
  - Characterizing nanomaterials
    - Singlets at the source
    - Agglomerates distal
  - Background particles and incidental materials
    - Pre and post process monitoring

JOEH – November 2011

A Strategy for Assessing Workplace Exposures to Nanomaterials

- Exposure Assessment
  - Construction of similarly exposed groups (SEG)
    - Classification of workers is subjective and based on professional judgment of IHs
      - Calibrated to visual cues
      - Not reliable for nano metrics; number and surface area
  - Concentration mapping
    - Assist in determining SEGs
    - Portable cart
      - 60 grid points
      - 1-2 minute samples
    - Too labor-intensive for IH
    - Not a substitute for personal sampling



Heitbrink, 2007

JOEH – November 2011

A Strategy for Assessing Workplace Exposures to Nanomaterials

- Exposure Assessment
  - Job-related task measurements
  - Prioritization of SEGs
    - Use of a screening tool to rank risk
  - Exposure metrics
    - *Count* versus *surface area* versus *mass concentration*
    - SEG could be misclassified with selection of inappropriate metric
    - Recommend using all metrics for area or job task-related measurements
    - Time averaging (acute versus chronic exposures)
  - Direct-reading instruments
    - *OPC/CPC* versus *DC* versus *aerosol photometer*
  - Time-integrated measurements
    - TEM/SEM

JOEH – November 2011

A Strategy for Assessing Workplace Exposures to Nanomaterials

- Exposure Assessment
  - Occupational Exposure Limits (OEL)
    - OELs do not exist for nanomaterials
    - IHs should assume a conservative approach
    - Option: ad hoc OELs
      - If uncertainty is high, use large safety factor
  - Defining the exposure profile
    - SEG exposure characterization compared to applicable OEL
    - Monitoring data should be the priority
      - 95th percentile of exposure distribution relative to OEL
      - One of four categories of exposure profiles
  - Follow-up and control

NFST – 2011 to Present

Goals

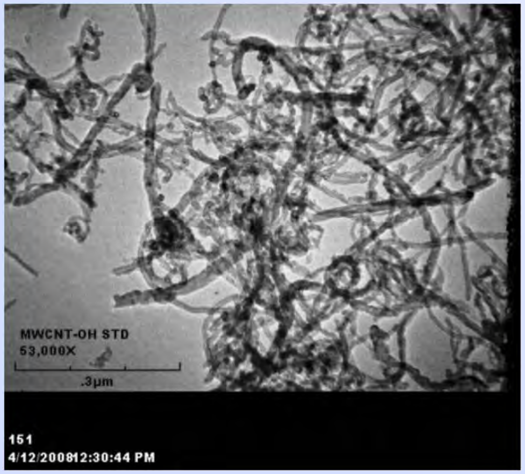
- Evaluates the entire material flow of a process and identifies points of potential material emission that can result in worker ***exposure***
- Uses an array of instruments and conventional air sampling methods to characterize exposures
  - Available to the practicing industrial hygienist
- Evaluates ***engineering controls*** and their effectiveness in reducing emissions and exposures
- Evaluates ***work practices*** used during the production or use of nanomaterials
- Evaluates the use of Personal Protective Equipment in use, if any, including respiratory protection

NFST – 2011 to Present

Methods

- Preassessment
  - Collect basic workplace characterization data

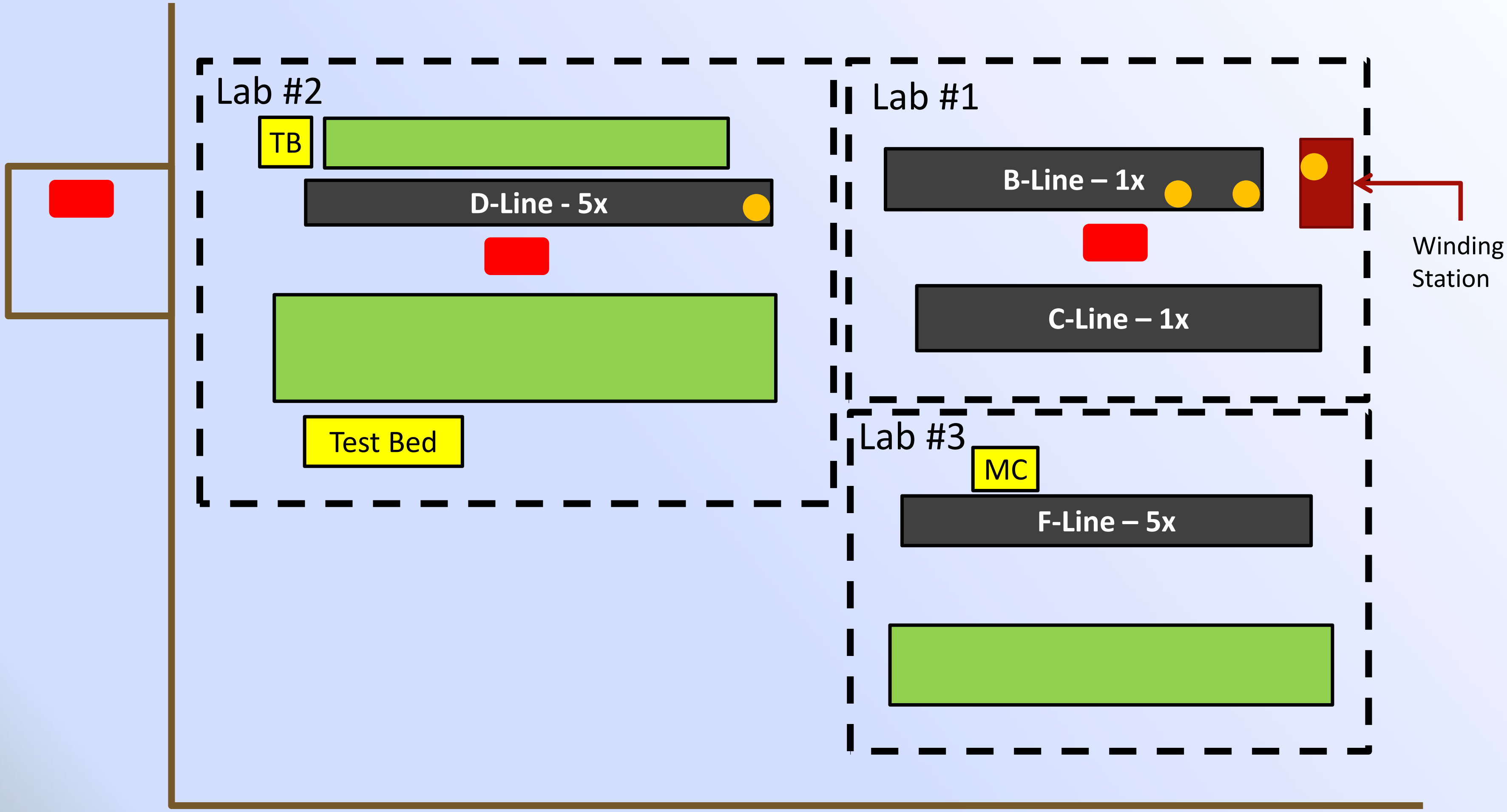
    Contact company representative for
    - Process description (including floor plan) and flow
    - Number of employees and job descriptions
    - MSDS
  - Determine analytical method for mass concentration
    - NIOSH, OSHA, etc.
    - Determine filters
    - Respirable sampling?
    - Examine interferences
    - Determine flow rates
  - Microscopic analysis
    - TEM versus SEM
    - Determine filters
    - Bulk sample



NFST – 2011 to Present

Methods

- Preassessment
  - Occupational exposure limits and health effects
    - Review pertinent literature
      - Toxicology
      - Epidemiology
    - Provides context of interpretation of data
  - Develop sampling strategy
    - Integrated samples
    - Direct Reading Instruments (DRI)
    - Wipe sampling



Area Sample Location (real-time equipment plus filter cassettes)

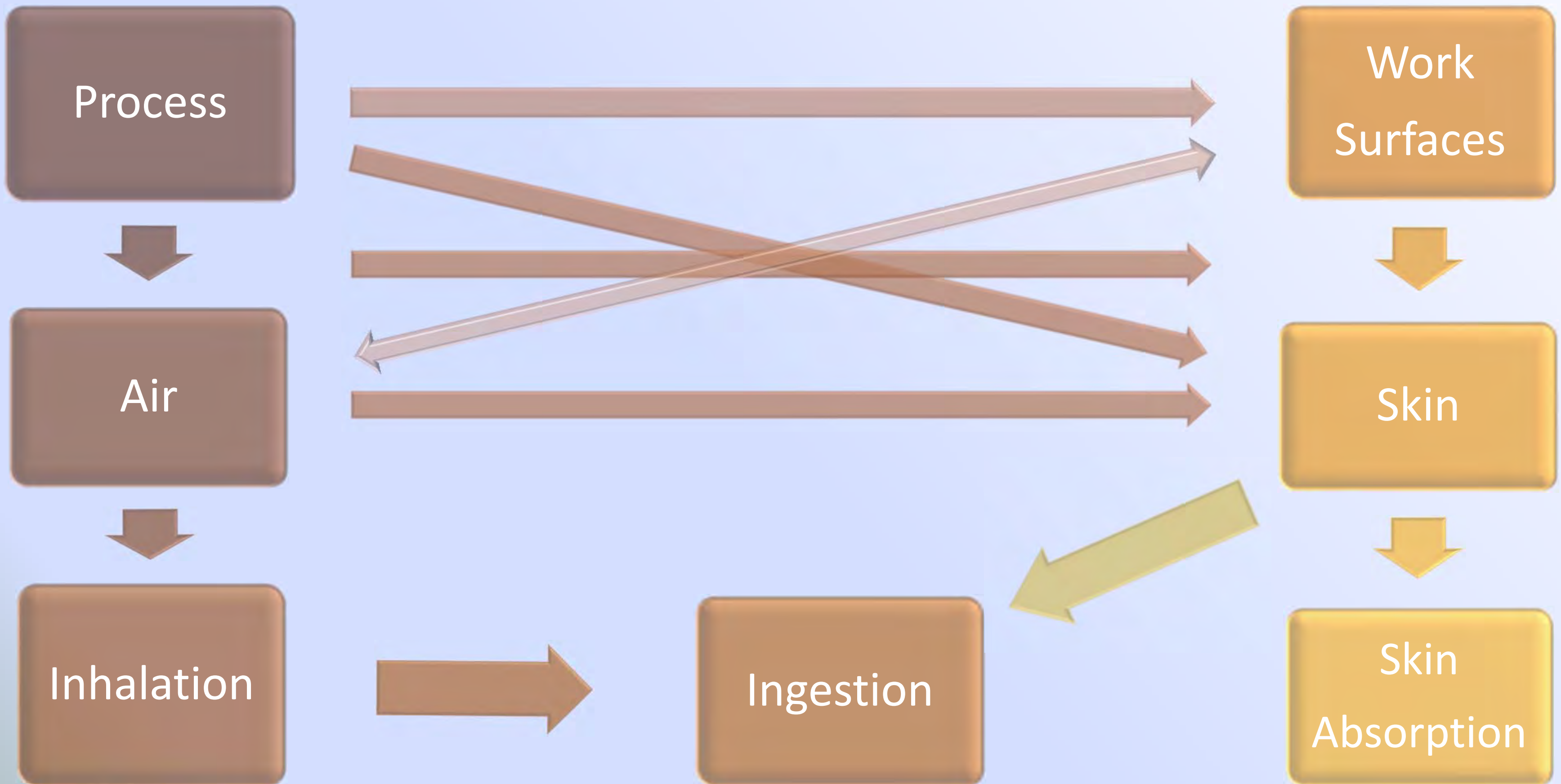
Area Sample Location (filter cassettes only)

What metric to use?

Metric	Qualification
Mass	Standard (NIOSH CNT and TiO_2 CIB)
Surface Area	Advantage for low solubility particles
Surface Chemistry	Toxicological studies
Particle Number	Relevance
Particle Size	Translocation
Particle Shape	HAR versus spheres

Exposure Pathway Model

Mulhausen and Damiano



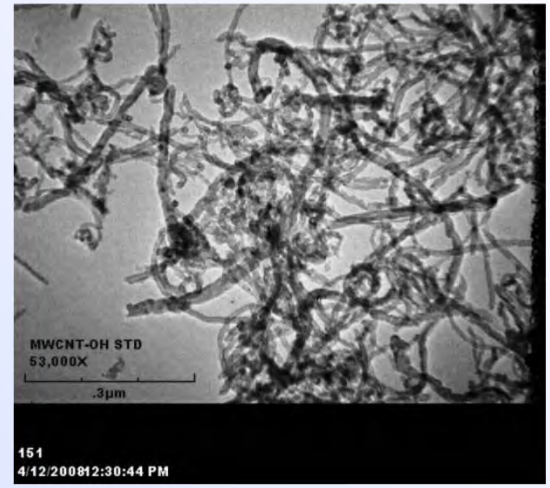
NFST – 2011 to Present

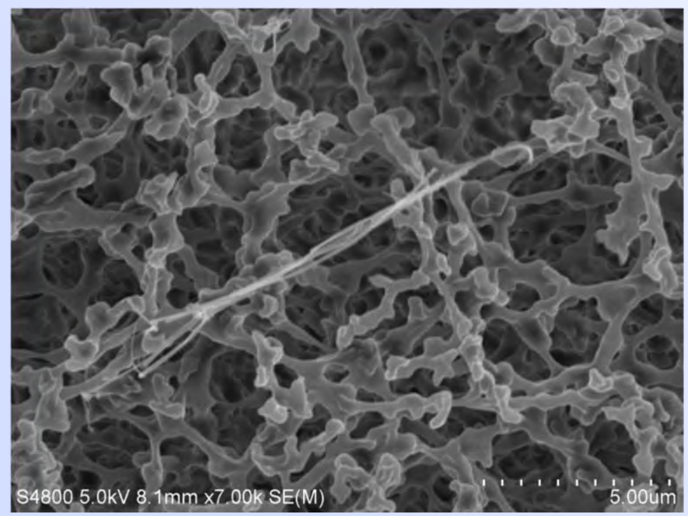
Methods

- Sampling Strategy
  - Integrated samples
    - *Core component of exposure assessment*
    - Filter-cassette based
      - Elements
      - Electron Microscopy
    - Area and personal breathing zone
    - Full-shift and task-based

Integrated Sampling

- Elemental mass
  - Sampling and analytical methods not designed for nanomaterials
    - Specificity
      NMAM 5040 (elemental carbon) versus NMAM 7300 (cadmium)
    - Sensitivity
      10 µm particle weighs the same as 10^9 (1 billion) 10 nm particles
- Electron microscopy
  - TEM versus SEM
  - Morphology
  - EDS for chemical composition
  - Particle count
  - No counting convention exists
- Respirable fraction

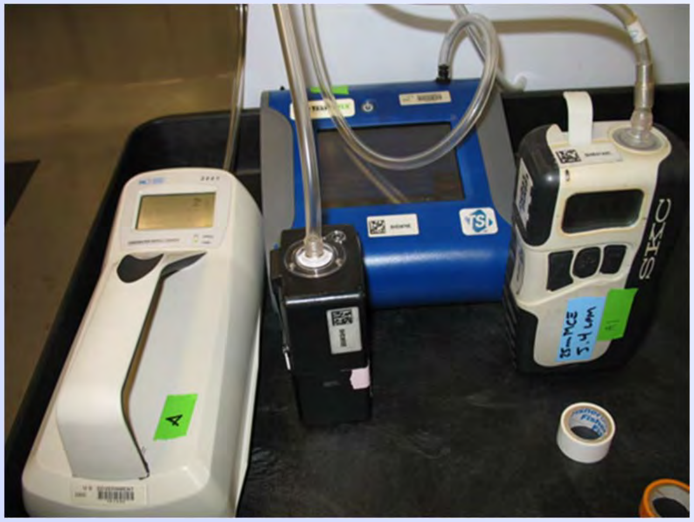




Inhalable	• 100 µm diameter	Thoracic	• 10 µm diameter	Respirable	• 4 µm diameter

Integrated Sampling

- Pumps
  - Same for PBZ and area
  - High flow
  - Tolerance for back pressure



Integrated Sampling

- Personal breathing zone
  - "True" indicator of worker's exposure
  - Determines levels of exposure throughout workday
  - Can be compared to OELs
- Area
  - Survey sources of contaminant
  - Evaluate engineering controls
- Background
  - Other contributions not related to the process

Integrated Sampling

- Full-Shift versus Task-Based
  - Most OELs are based on TWA
    - \+ Full-shift
    - \- No OELs exist for nanoparticles
      - Except NIOSH (CNT and TiO_2)
  - Identify level of source contribution
    - \+ Task-based
    - \- Activities may be of short duration
      - Analytical sensitivity ↓

Direct Reading Instruments

- TSI CPC 3007 (TSI Inc., Shoreview, MN)
- TSI OPS 3330 (TSI Inc., Shoreview, MN)
- TSI DustTrak DRX (TSI Inc., Shoreview, MN)

Condensation Particle Counter

- Evaporates and condenses liquid onto particle
- Concentration range on the order of 10^5 particles/cm^3
- Measures particles between 10 nm and ~ 1 µm
- Slight variability between instruments
  - Size range
  - Concentration range

http://www.tsi.com/Condensation-Particle-Counter-3007/

Optical Particle Sizer (OPS)

- Capable of sizing particles into 16 user-definable bins
  - Wide size range
    - 300 nm – 10 µm
  - Not applicable for high aspect ratio particles
- High concentration range
  - Up to 3000 pt/cc
- Filter based sample

http://www.tsi.com/Optical-Particle-Sizer-3330/

Optical Particle Counter (DustTrak)

- Measures particle mass concentrations
- Capable of sizing particles into 4 bins
  - PM1
  - PM2.5
  - Respirable
  - PM10
- Concentrations up to 150 mg/m^3
- Filter based sample

http://www.tsi.com/DUSTTRAK-DRX-Aerosol-Monitor-8533/

Appropriate Use of DRIs

- Assess efficacy of engineering controls
- Assess potential for emission of specific processes/tasks
- Identify general increases or decreases in total particle concentration
- Provide supporting evidence for integrated samples

Operation of DRIs

- Must determine appropriate mode of operation
  - Log mode
- All settings must be verified
  - Date
  - Time
  - Sampling interval

Operation of DRIs

- Sampling should be performed simultaneously with integrated samples
- Background measurements should be taken simultaneously but in separate area
  - Same general environment, but far enough away so as not to be directly affected by process/task emissions
- All activities and times should be recorded for use in data analysis
  - Video recording can be very useful if permitted

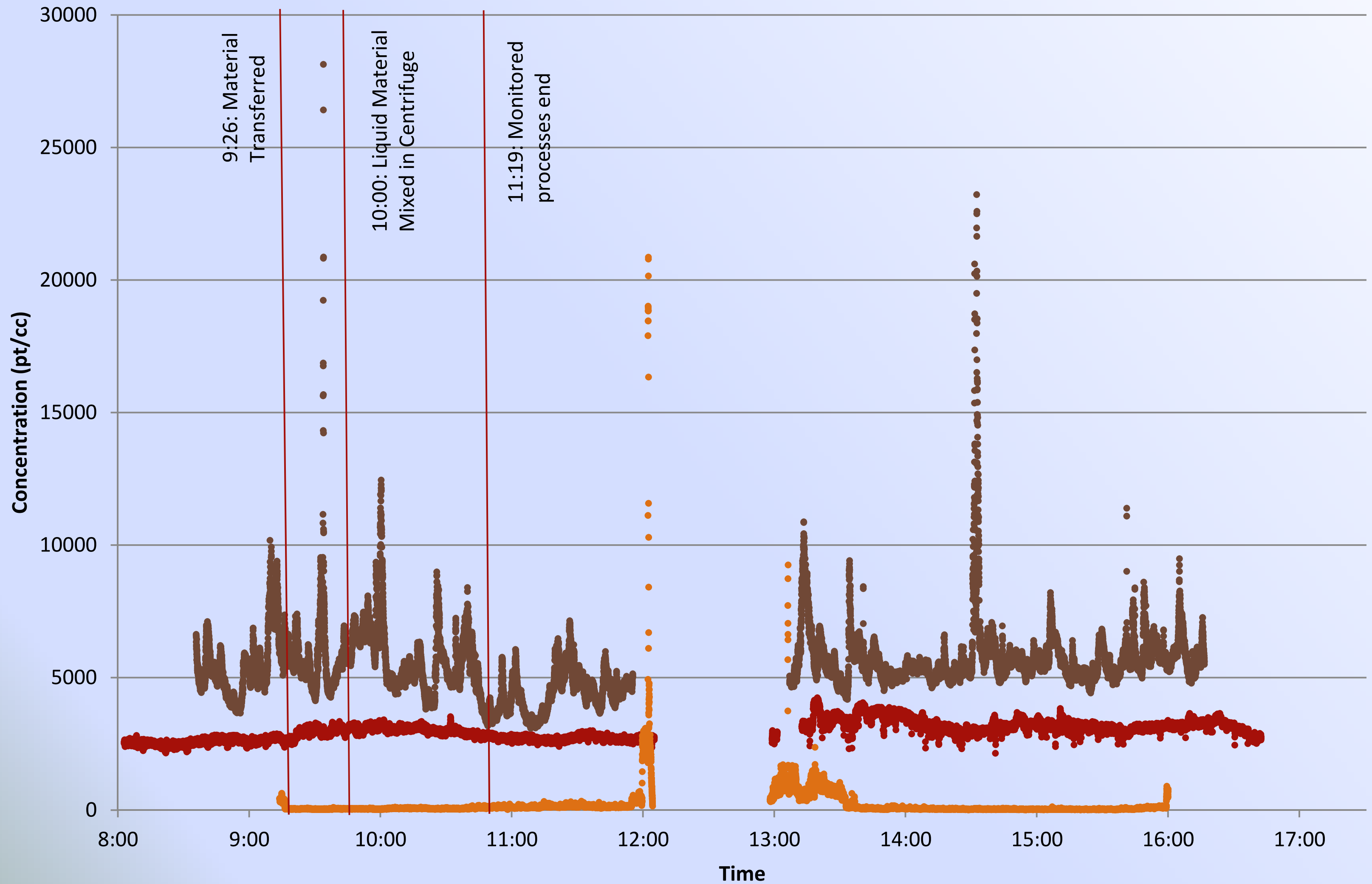
Data Transfer

- Most DRIs come with software compatible with the instrument
  - TSI TrakPro™ Data Analysis Software
  - TSI Aerosol Instrument Manager
- Many different data transfer cables
  - USB-USB
  - Data-Serial-USB
- All data must be downloaded as .txt or .xls file
  - Delimitation

Data Analysis

- Once data is transferred, it should be categorized
  - Size distributions
    - Focusing on the contribution of smaller particles to the overall particle number concentration
- All data should be organized into spreadsheet form
- Data from each DRI should be checked for accuracy
  - Within the effective concentration range of the DRI

Interpretation of Data



Limitations of DRIs

- ***No*** material identification
- Condensation Particle Counter
  - Engineered to measure ‘particle’ concentrations – not fibers
  - Upper dynamic range in the order of 10^5 pt/cc
- Small inlet can become clogged with larger particles

- Optical Particle Counters
  - DustTrak
  - OPS 3330
- Unable to accurately assign ‘size bin’ to fibrous materials
  - Total count

Overview

- Wide size range of particles measured
  - 0.01 – 10 µm
- Data, in conjunction with integrated data, can be used to show deficiencies in worker practices or engineering controls
- Autocorrelation must be addressed if predictive modeling is being performed
- Must not attempt to over-analyze data

Wipe Sampling

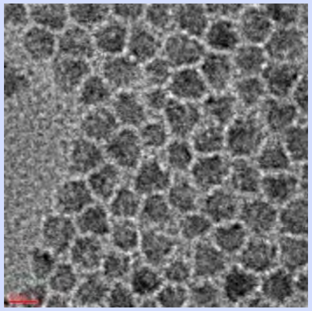
- Surface contamination
- No correlation with worker inhalation exposures
- Assess worker hygiene practice
- NMAM 9102
  - Elements
  - Wash ‘n Dry or ASTM equivalent
    - Pre-packaged moist disposable towelette
  - Analysis by inductively coupled argon plasma atomic emission spectroscopy

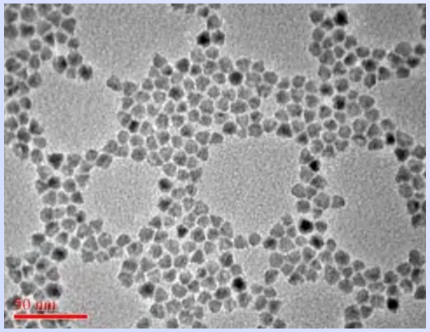
Vacuum Sampling

- Surface contamination
  - Filter sock
    - More mass
    - Less time
    - Use of a template
    - Analysis requires resuspension
  - 37-mm filter cassette
    - Good for hard to reach areas
    - Less mass
    - Labor intensive
    - Amenable to standard sample analysis and EM

Case Study 1

- **Process Description:** Synthesis of quantum dots and fabrication of QD products
- **Nanomaterial size**: 3 nm core and 6-8 nm shell
- **Production Scale**: Pilot production scale
- **Task Description:** Wet chemistry inside of a fume hood to produce quantum dots, purification of QD solution, fabrication of ink containing QDs, printing on glass film, and experimental processes



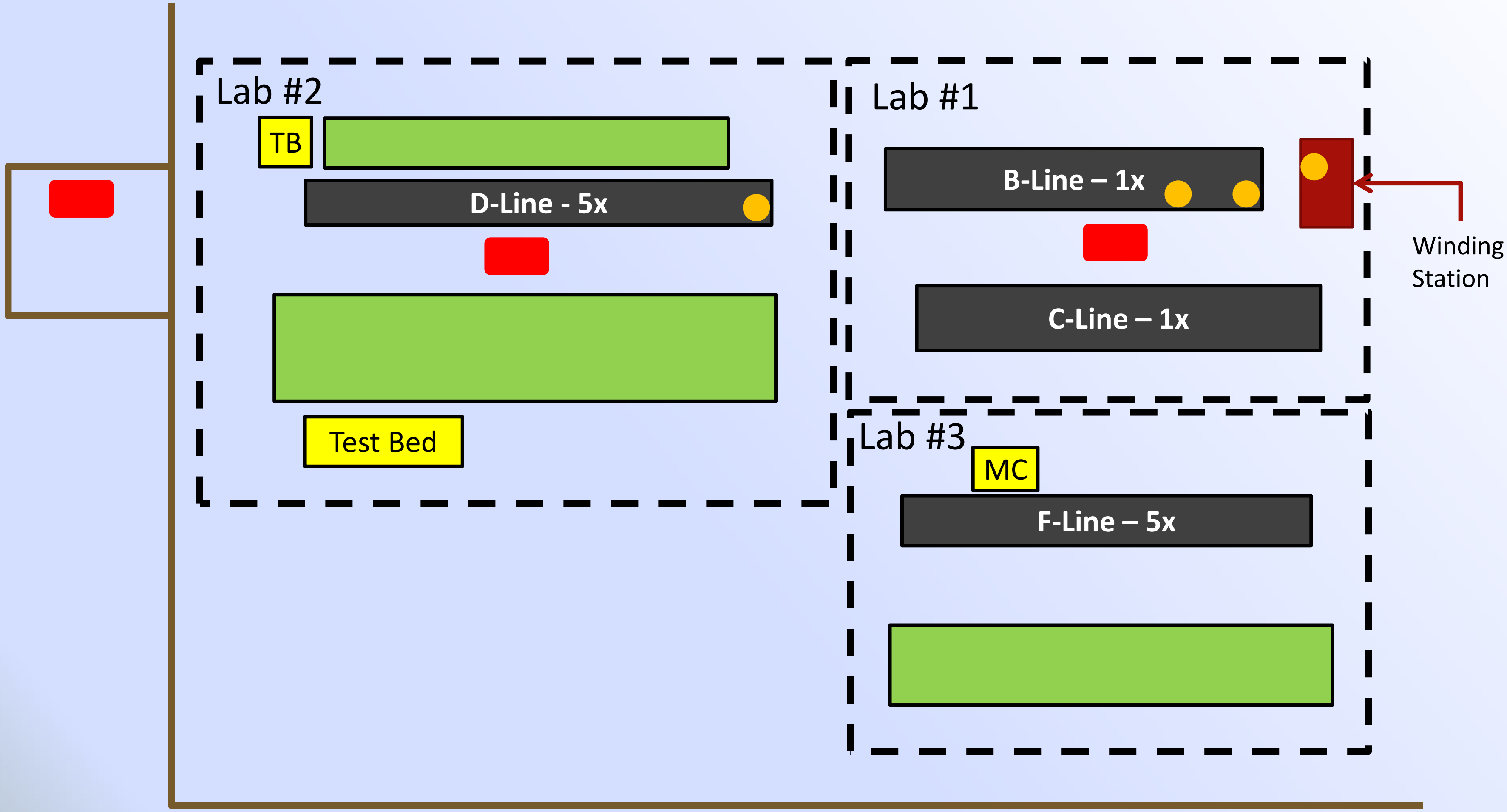


Results of the Case Study 1

- Ventilation Assessment performed
  - Pressure differential measurements indicate potential for contamination to migrate to the office areas
  - All fume hoods had been certified within the last year
- Wipe samples
  - Samples taken to determine potential dermal exposures and migration pathways
  - 16 of 25 wipe samples detected cadmium above the LOQ
  - Production areas resulted in “above housekeeping” levels of contamination
  - Non-production areas did indicate the presence of cadmium
- Air Samples
  - Low levels of cadmium may be emitted from the synthesis and processing of QDs
  - The absence of QDs on the TEM samples suggest that Cadmium may be from the precursor material

Case study 2

- **Process Description:** Synthesis of carbon nanotube structures on fiberglass threads
- **Nanomaterial size**: 10s nm width by 10s µm length
- **Production Scale**: Pilot production scale
- **Task Description:** Production operator, growth chamber clean-out, winding of carbon nanotube structure threads, machining of carbon nanostructure thread containing composites



Area Sample Location (real-time equipment plus filter cassettes)

Area Sample Location (filter cassettes only)

Results of the Case Study 2

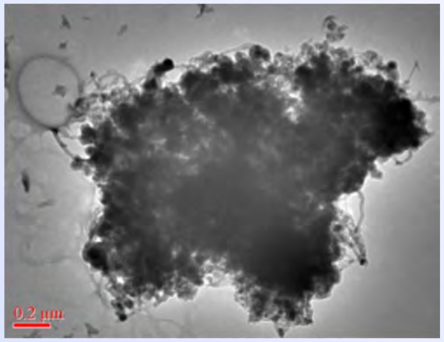
- Ventilation Assessment performed
  - Pressure differential measurements indicate varying degrees of negative pressure
  - Leakage (as subsequently pressure) was based on the “tightness” of enclosures
- Integrated Air Samples
  - 17 of 20 for EC above the LOD

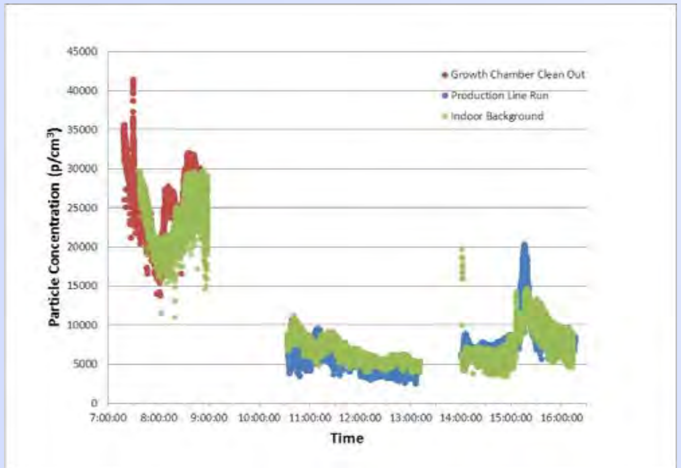
    Ranged up to 2400 µ/m^3

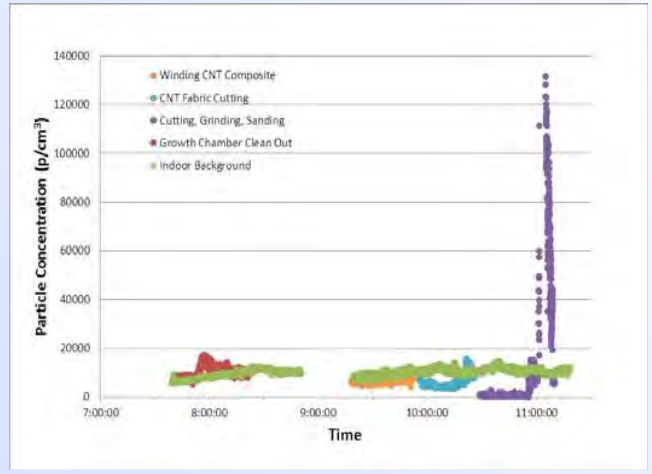
    - Highest value in machining (16% EC)

    - Growth chamber clean-out at 130 µ/m^3
  - 7 of 15 positive for CNS

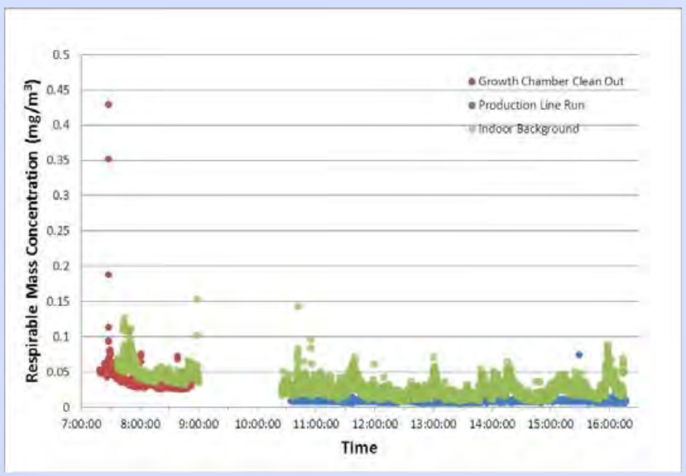
    Highest structure count observed during growth chamber clean-out
- RTI
  - All instruments detected significant events during growth chamber clean-out and machining

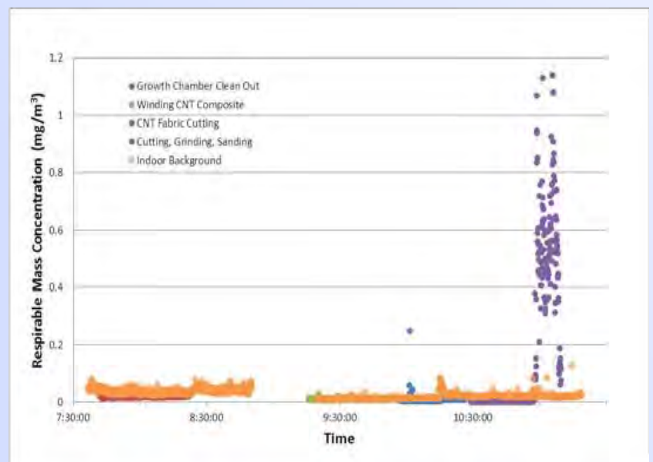






Condensation Particle Counter





Photometer

Summary

- Toxicology
  - New toxicological data helps to guide future field team efforts
- Market research
  - Assessment of the market trends also guides field studies
- The field team sampling strategy continues to evolve
  - Additional direct reading instruments will be evaluated
  - Investigate additional possibilities for TEM and structure counts
  - Research method interference from incidental nanomaterials or macro scale material with the same chemical composition
    - CNT and 5040

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Thank you!

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The findings and conclusions in this presentation have not been formally reviewed by the National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.

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