NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

NTRC | NANOTECHNOLOGY RESEARCH CENTER

TAPPI NANO DIVISION

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Progress in Understanding Worker Exposure and Risk for Cellulose Nanomaterials

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Nanotechnology Research Center
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

CDC Workplace Safety and Health

NIOSH

NIOSH Nanotechnology Research Center

Vision

Safe nanotechnology by delivering tools for safety and health at work through research and intervention.

Mission

Provide national and world leadership for research and guidance on the implications and applications of nanomaterials on occupational safety and health.

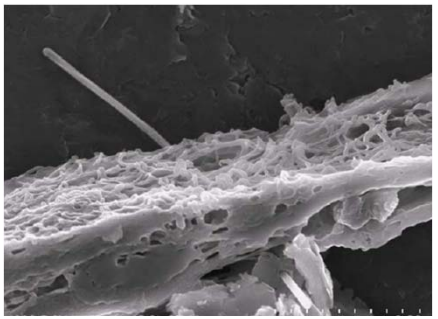
Why the Workplace?

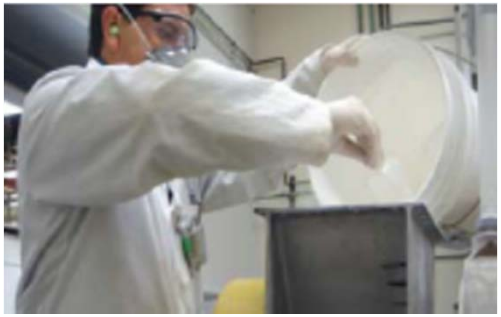
- Workers generally the first people in society exposed to any new technology and its materials
- Cellulosic Nanomaterial activity is no exception
- Workers make and use them; from R&D labs, to concept testing, to manufacturing
- First opportunity to understand any potential hazards or risks and develop good stewardship practices

Partnerships and Collaborations

FPL, TAPPI Nano, P3Nano, Private Companies







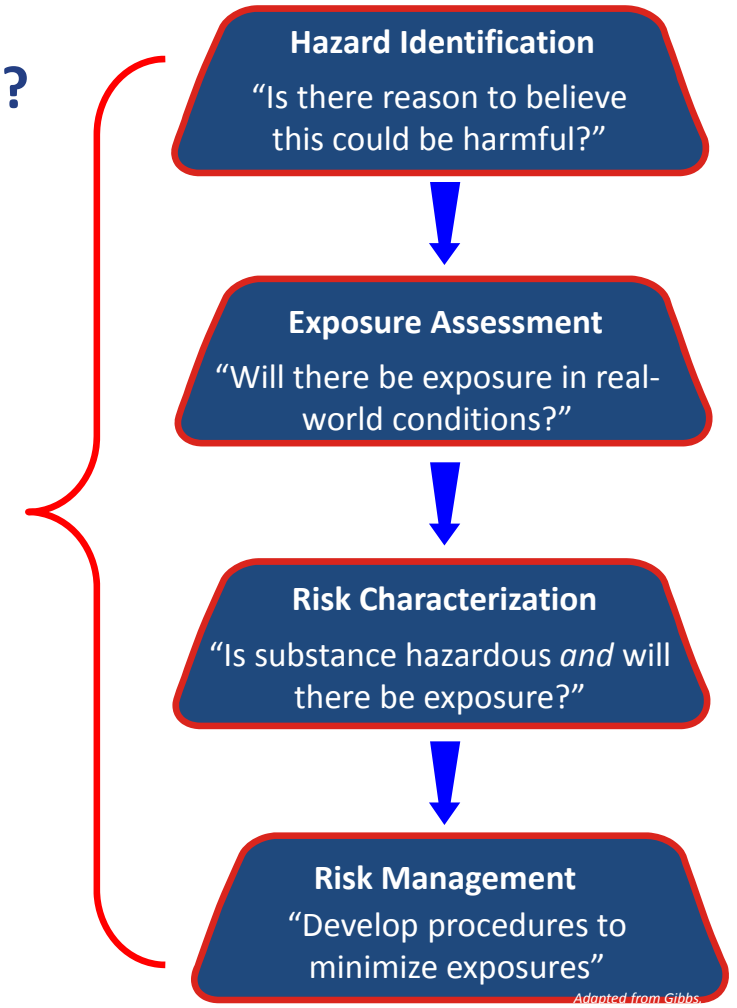

How to get started with CNC and CNF?

Use the Risk Model and focus on Three Basic Questions:

Are they hazardous?

Can they be measured?

Can they be controlled?



Adapted from Gibbs, 2006

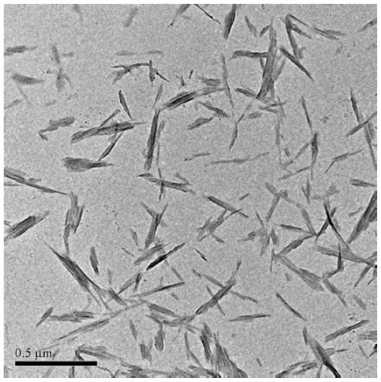
NIOSH Nanotechnology Critical Areas of Research

Areas of research in cellulosic nanomaterials to address the 'risk model questions'.

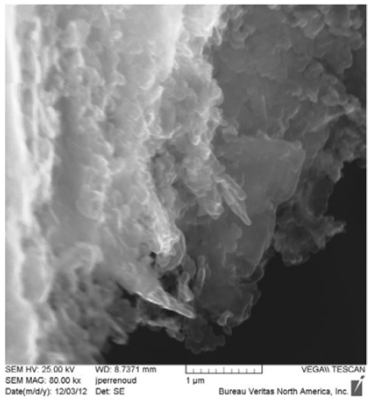
Nanocellulose – A unique challenge

- No validated analytical method for nanocellulose currently exists
- Electron microscopy allows for detection and visualization – but there are sample prep issues

Cellulose nanocrystals

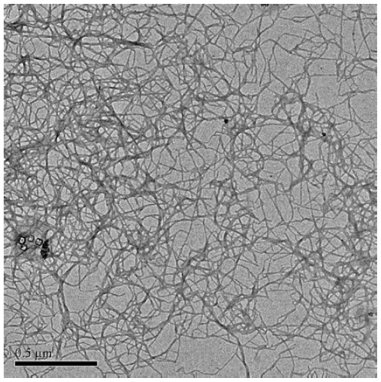


Ideal



Real world

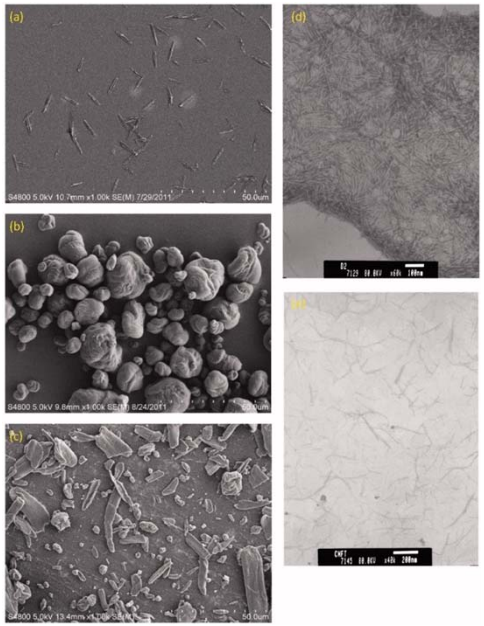
Cellulose nanofibrils



Ideal

Real world

NIOSH Pilot Toxicology Studies on CNC and CNF

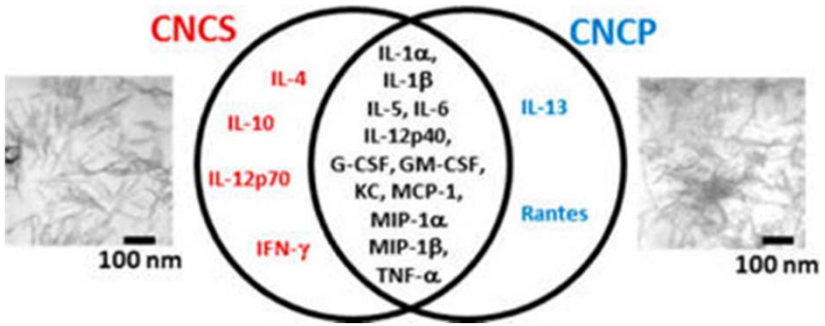


- Preliminary laboratory characterization studies have indicated:
  - CNCs and CNFs are biodurable in artificial lung airway lining fluid (up to 7 days) & alveolar macrophage phagolysosomal fluid (up to 9 months)
  - Increased hydroxyl radical production for CNCs
  - Based on biodurability, mechanical clearance would be the primary mechanism for lung clearance.

Stefaniak A, et. al. 2014. Lung durability and free radical production of cellulose nanomaterials. Inhalation Toxicology. 26(12): 733-749.

NIOSH Pilot Toxicology Studies on CNC

- Preliminary *in vivo CNC* studies have indicated the following:
  - Increased inflammatory response (PMNs) compared to asbestos control
  - Increased inflammatory mediators
  - Difference in respiratory response based on type of material exposure (suspension CNCS vs powder CNCP)



Yanamala N, et. al. 2014. In Vivo evaluation of the pulmonary toxicity of cellulose nanocrystals: a renewable and sustainable nonmaterial of the future. ACS Sustain Chem Eng. 2(7): 1691-1698.

Planned Pilot Toxicology Studies

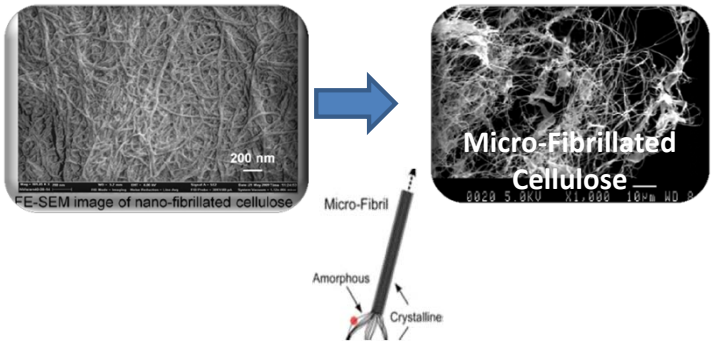
- Additional ongoing studies to include:
  - In vitro
    - Systematic evaluation of in vitro biological response indicating cell-type specific responses
    - Long term exposure to determine changes in human lung epithelial cells
  - In vivo pulmonary exposure
    - Gender differences in mouse pulmonary toxicity
    - Male reproductive system effects
- Compare multiple CNC and CNF within and between groups

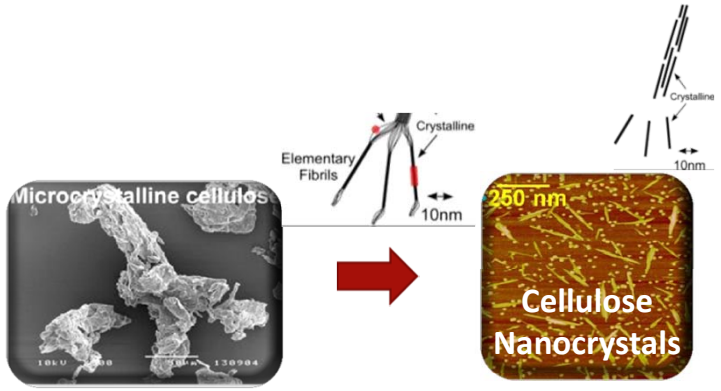
NIOSH Exposure Assessment Studies

- Four production facilities evaluated
  - All used wet processes for production
    - Mechanical shearing - fibrils
    - Chemical process - crystals
  - Two facilities produce dry material during ‘harvesting’
    - Freeze dryer
    - Spray dryer

Nanocellulose Pilot Production Facility Study

- Production process is based on one that was first published in 1949[1]
- Currently, facility produces:
  - Cellulose Nanocrystals - 5 nm diameter and 200 nm long
  - Cellulose Nanofibrils - 10-30 nm diameter and >100 nm long
- Based on the chemistry of the process, the products can be tagged by exchanging sodium ions with an alternative alkali metal





[1]Ranby BG. Aqueous colloidal solutions of cellulose micelles. Acta Chem. Scan.; 1949. p. 649-50.

NIOSH Pilot Exposure Assessment: NCC

- Filter-cassette based samples
  - Electron Microscopy (EM)
  - PBZ, Source/ Area, Background
  - Full shift and task specific
  - With and without cyclones
    - Cyclones used to collect respirable fraction
  - Polycarbonate filters
- Data logging with DRI's
  - Both Optical and Condensation Particle Counters used
  - Source/Area and Background

Eastlake A, Beaucham C, Martinez K, Dahm M, Sparks C, Hodson L, Geraci C. (In press) Refinement of the Nanoparticle Emission Assessment Technique into the Nanomaterial Exposure Assessment Technique (NEAT 2.0). Journal of Occupational & Environmental Hygiene. (In press)

NIOSH Exposure Assessment Studies: NCC

EM images of NC collected *in the field* onto Poly Carbonate filters

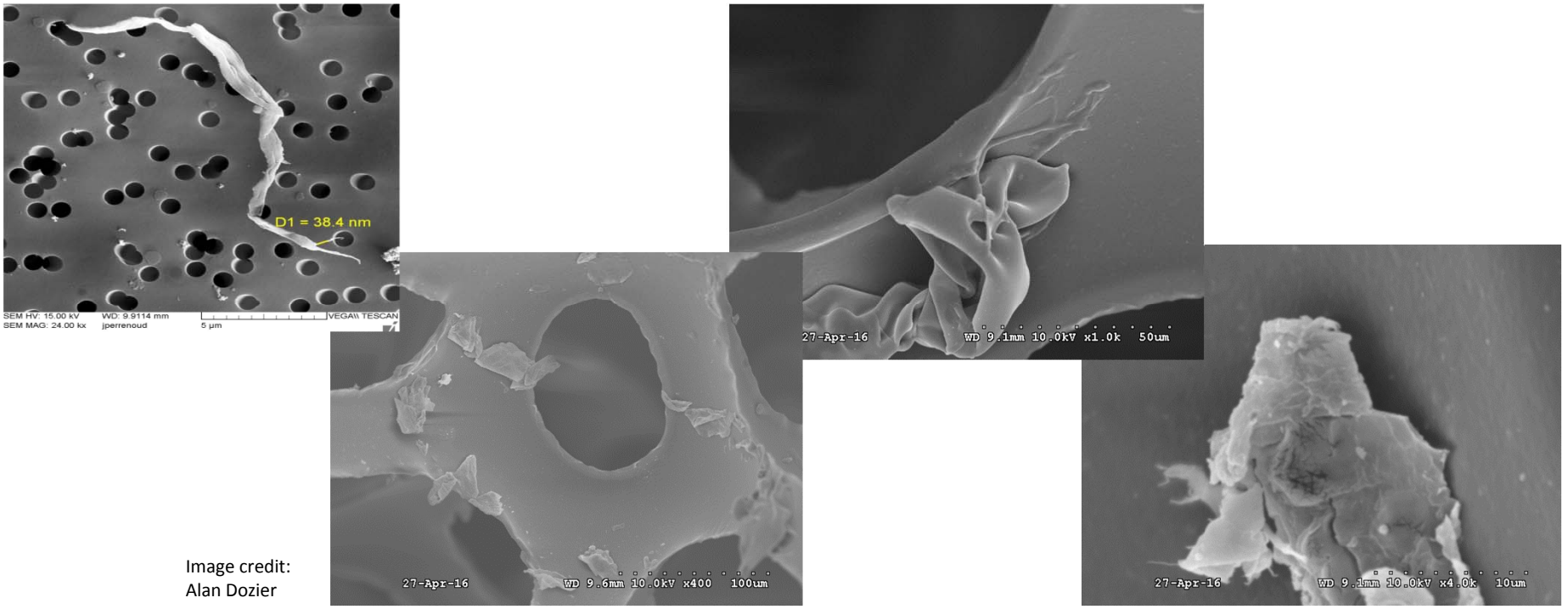


Image credit:
Alan Dozier

NIOSH Exposure Assessment Studies: NCF

STEM images of nanocellulose fibrils collected *in the field* directly onto an EM grid

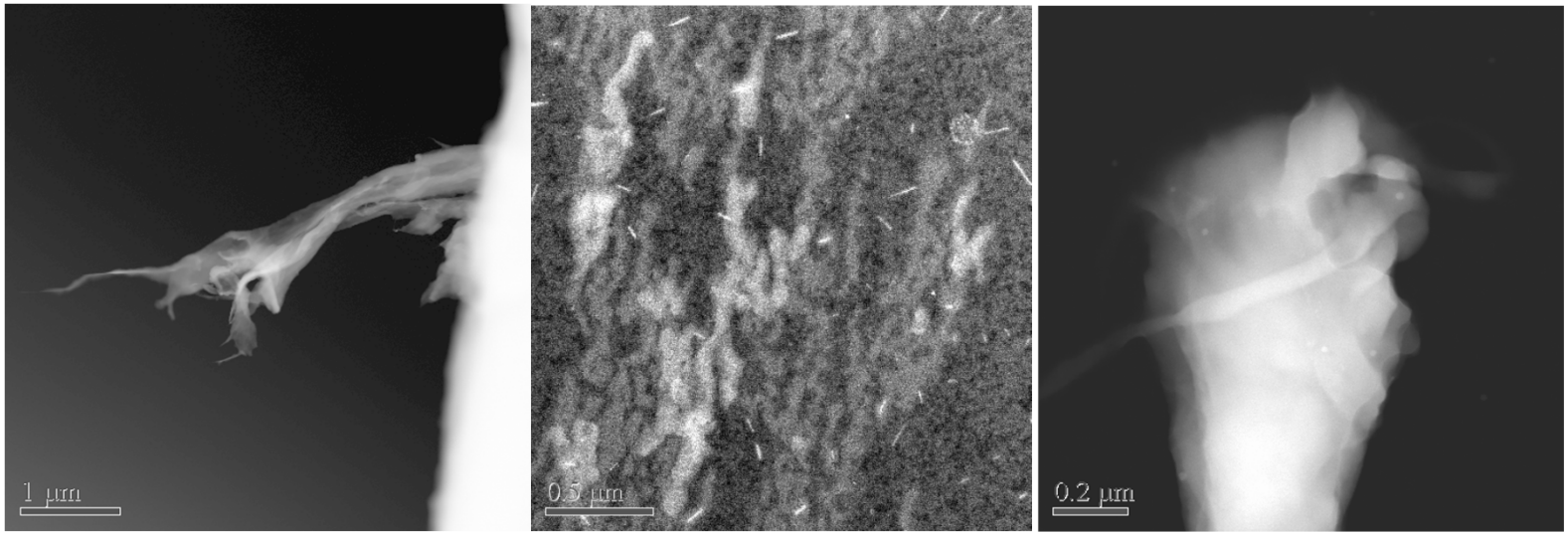


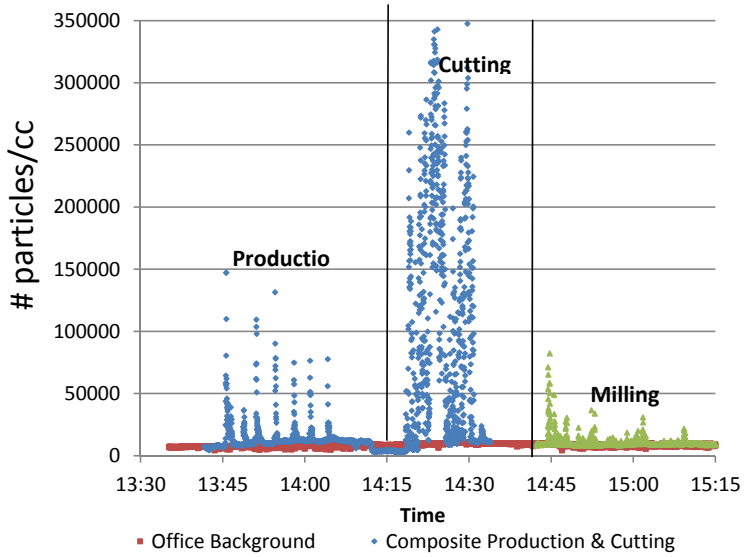
Image credit:
Alan Dozier

NIOSH Exposure Assessment: CNC

- Facility agreed to tag product with cesium to increase the ability for detection (a one-time opportunity)
- The following tasks involving the use of tagged product were evaluated:
  - Centrifugation of CNC product slurry
  - Removal of dried CNC product from a freeze dryer – general ventilation
  - Removal of dried CNF product from a freeze dryer - HEPA LEV
  - Production, cutting, and milling of CNC polymer composite




NIOSH Pilot Exposure Assessment: CNC



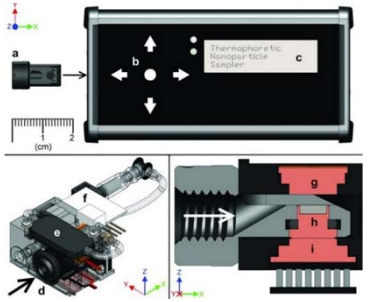
Condensation Particle Counter area and background during the production, cutting, and milling of cellulose nanocrystal composites

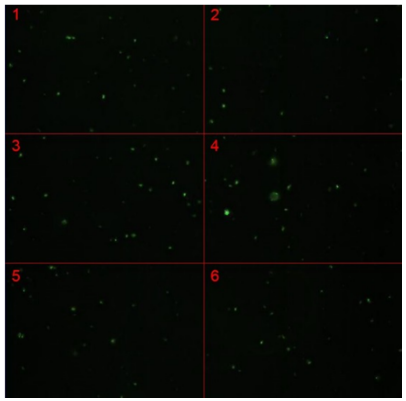
- Cesium-tagged CNC – a one-time trial:
  - Tagging proved to be informative for understanding potential occupational exposures in the absence of a cellulose-specific validated sampling and analytical method.
  - Elemental analysis for the Cs tag indicated that CNCs were being aerosolized during the following tasks:
    - Removal of dry product from freeze dryer/trays
      - LEV use decreased potential for exposure
    - Centrifugation of product slurry
    - Production, cutting, and milling of a CNC containing composite
  - No applicable occupational exposure limits for cesium were exceeded by any of the air samples.

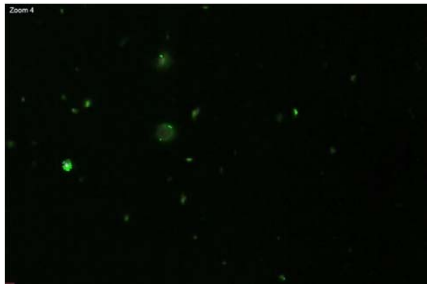
* Eastlake A, Rudie A, Geraci C. 2014. Nanocellulose – Evaluation of the full spectrum of workplace health and safety. TechConnect World Innovation Conference Technical Proceedings, Washington, D.C. Volume 3. Pp 105
* Martinez K, Eastlake A, Rudie A, Geraci C. Occupational Exposure Characterization during the Manufacture of Nanocellulose. In Production and Applications of Cellulose Nanomaterials, Eds. Postek M, Moon R, Rudie A, Bilodeau M, Technical Association for the Pulp and Paper Industry, Peachtree Corners, GA, June 2013.

NIOSH Exposure Assessment Studies: CNC

- Additional sampling devices in field use:
  - Collection directly onto a EM grid (thermophoretic or electrostatic sampling)
  - Analysis of filters by dark field hyperspectral imaging microscopy
  - Zefon Personal NRD (Nanoparticle Respiratory Deposition) sampler
    - 300 nm cut size, using for EM



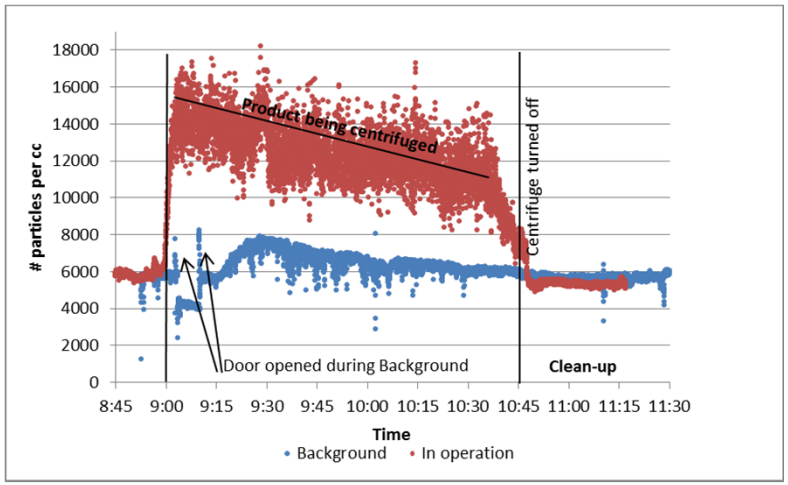




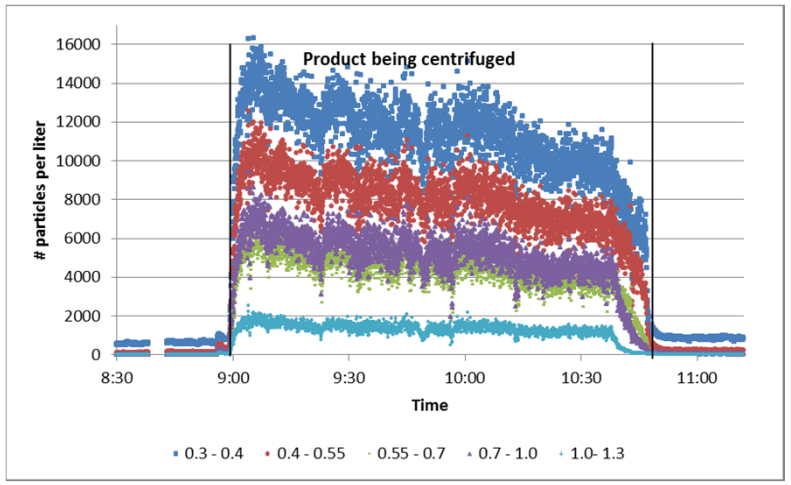
* Leith D, et. al. 2014. Development of a Transfer Function for a Personal Thermophoretic Nanoparticle Sampler. Aer Sci Tech 48(1):81-89
* Roth G, et. al. 2015. Hyperspectral microscopy as an analytical tool for nanomaterials. WIREs Nanomed Nanobiotechnol. 7:565-579.
* Cena L, et. al. 2011. A Personal Nanoparticle Respiratory Deposition (NRD) Sampler. Environ. Sci. Technol. 45: 6483-6490.

Centrifugation Exposure Characterization

CNC product



Condensation particle counter



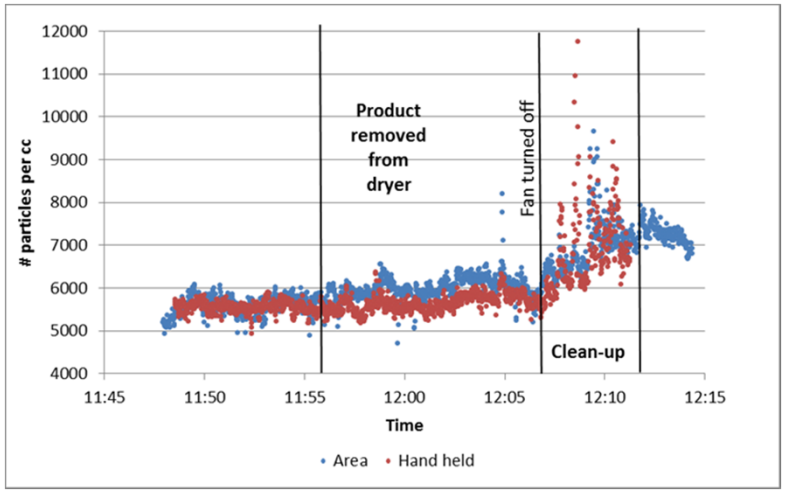
Optical particle sizer

- 3 open-face filter samples collected for cesium – all samples positive
- Highest level was inside centrifuge cabinet, second highest was just outside cabinet
- Both PBZ and Background (located away from process) showed cesium

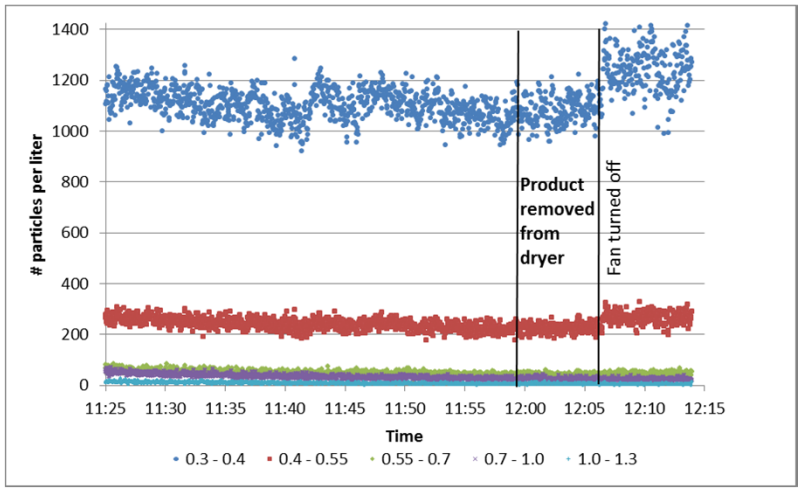
Facility no longer uses the centrifugation process

Freeze Dryer Exposure Characterization – Warehouse general ventilation

CNC product



Condensation Particle Counter

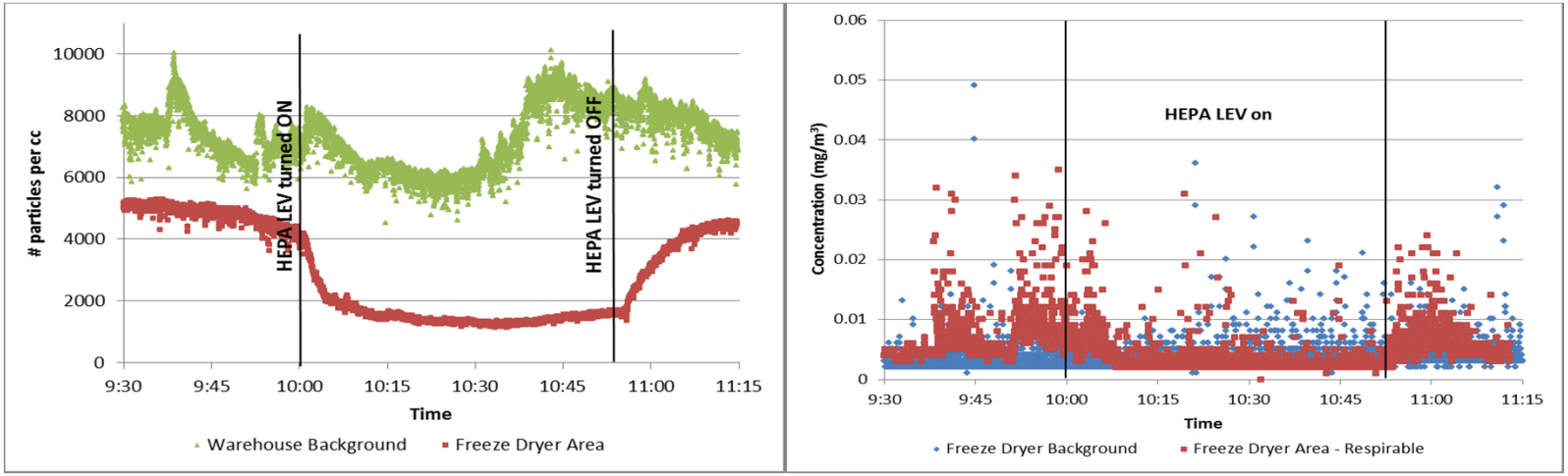


Optical Particle Sizer

- 3 samples collected for cesium – all samples positive
- Highest level was located on the freeze dryer, second was close to where dried product was being removed from the tray
- PBZ showed cesium

Freeze Dryer Exposure Characterization – Inside room using LEV

CNF product



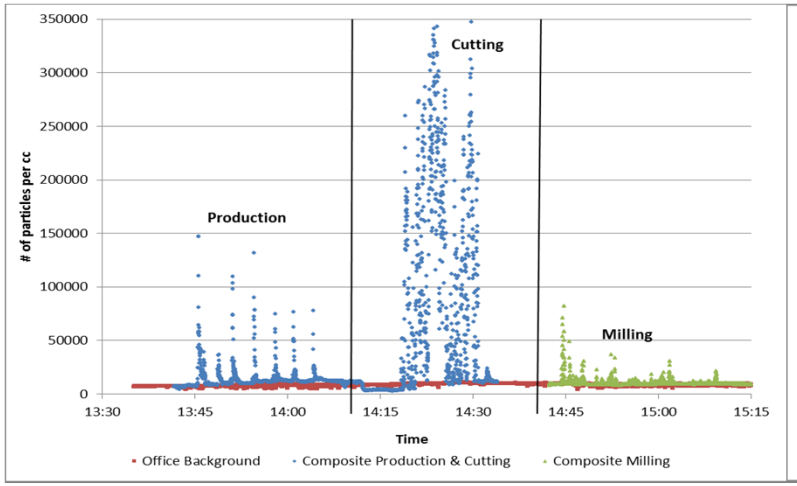
Condensation Particle Counter

Dust Trak

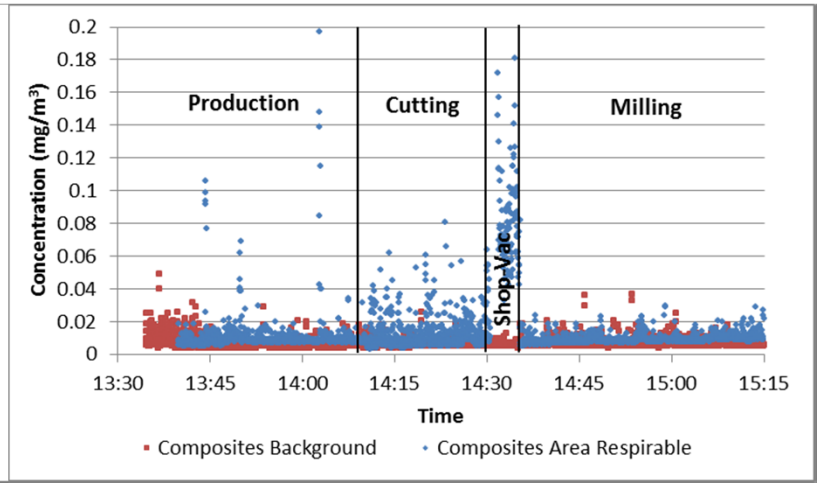
- Three area samples collected close to where dried product was being removed from the tray were analyzed for cesium –
  - One non-detectable
  - Two samples were between the LOD/LOQ (not reliably quantifiable)

Composite Production, Cutting, and Milling Exposure Characterization

CNC product



Condensation Particle Counter



Dust Trak

- 6 of 7 samples collected for cesium were positive
- Highest level was the PBZ sample, second was a source sample located close to the extruder mixer, and the third was located just between the extruder mixer and the composite press

Summary

- NIOSH continues toxicology testing of CNC and CNF materials
- NIOSH continues to evaluate CNC and CNF processes
- Dry processes do result in exposures
- Wet/slurry processes should be evaluated
- Conventional controls appear to be effective
- Markers and surrogates can be effective indicators of exposure
- Controls and guidance will be validated

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Nanotechnology Guidance Documents

http://www.cdc.gov/niosh/topics/nanotech/

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