Working With Engineered Nanomaterials; Practical Experience from LLNL

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David Zalk, PhD, CIH; Wes Chase, CIH; Sam Paik, PhD, CIH

Lawrence Livermore National Laboratory

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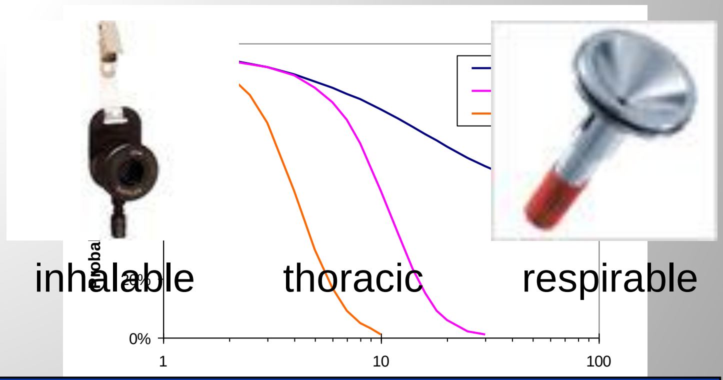
Overview

- Challenges in Traditional IH/OH Approach to ENM
- Advantages of Control Banding for ENM Risk Assessment
- Development, Application & Evaluation of CB Nanotool
- Quantitative Validation of CB Nanotool

Traditional IH Assumptions; Do these hold up when measuring nanoparticles?

- Sampled concentrations are representative of what the worker is breathing
- Exposure index pertaining to health effects is known
- Analytical methods are available to quantify exposure index
- Exposure levels at which particles produce adverse health effects are known



CONTROL BANDING IS AN ALTERNATIVE APPROACH TO TRADITIONAL IH

Overview

- Challenges in Traditional IH/OH Approach
- Advantages of Control Banding for ENM Risk Assessment
- Development, Application & Evaluation of CB Nanotool
- Quantitative Validation of CB Nanotool

Factors that Favor Control Banding (CB) for ENM

- Alternative to traditional IH/OH
- Efficacy of conventional controls
  - Fits well with a four band control outcome
- Product and Process Based – designed for use at the non-expert level
- Successful application internationally for over 20 years
- Works best in the absence of information

Overview

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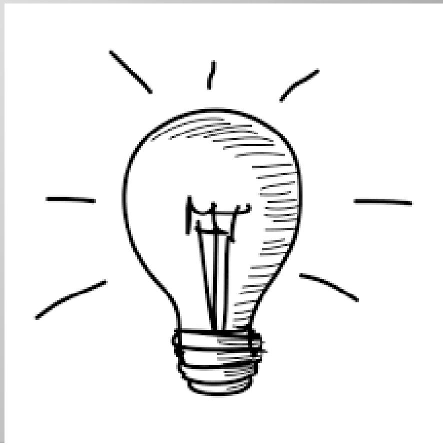
- Quantitative Validation of CB Nanotool

CB Nanotool Concept

- While there were theories of how CB could be applied to ENM, there were no comprehensive nano 'tools' available at the time (~2007*)

- Goal – Create a CB Nanotool
  - Feasibility of CB concept
  - Developing pilot tool
  - Use the latest and best research on ENM
  - Determine most important toxicological factors
  - Make it applicable to Research & Development
  - Pilot the CB Nanotool in practice



* Maynard, AD. (2007) Nanotechnology: the next big thing, or much ado about nothing? AnnOccHyg 51(1);1-12.

CB Nanotool: Severity Factors

- Nanomaterial: 70% of Severity Score
  - Surface Chemistry (10 pts)
  - Particle Shape (10 pts)
  - Particle Diameter (10 pts)
  - Solubility (10 pts)
  - Carcinogenicity (6 pts)
  - Reproductive Toxicity (6 pts)
  - Mutagenicity (6 pts)
  - Dermal Toxicity (6 pts)
  - Asthmagenicity (6 pts)

- Parent Material: 30% of Severity Score
  - Occupational Exposure Limit (10 pts)
  - Carcinogenicity (4 pts)
  - Reproductive Toxicity (4 pts)
  - Mutagenicity (4 pts)
  - Dermal Toxicity (4 pts)
  - Asthmagenicity (4 pts)
  - (Maximum points indicated in parentheses)

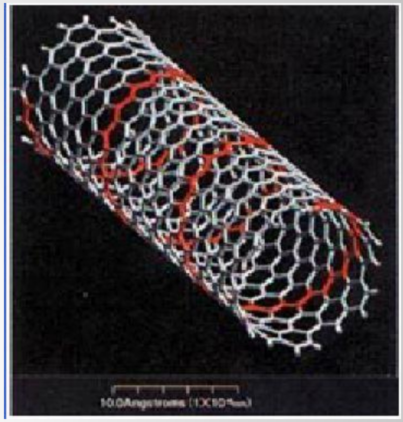
Probability

Severity		Extremely Unlikely (0-25)	Less Likely (26-50)	Likely (51-75)	Probable (76-100)
	Very High (76-100)	RL 3	RL 3	RL 4	RL 4
	High (51-75)	RL 2	RL 2	RL 3	RL 4
	Medium (26-50)	RL 1	RL 1	RL 2	RL 3
	Low (0-25)	RL 1	RL 1	RL 1	RL 2

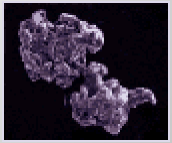
RL 1: General Ventilation
RL 2: Fume hoods or local exhaust ventilation
RL 3: Containment
RL 4: Seek specialist advice

Particle Shape (nanomaterial)

- Tubular/fibrous:
  high aspect ratio
  (e.g., carbon nanotubes)

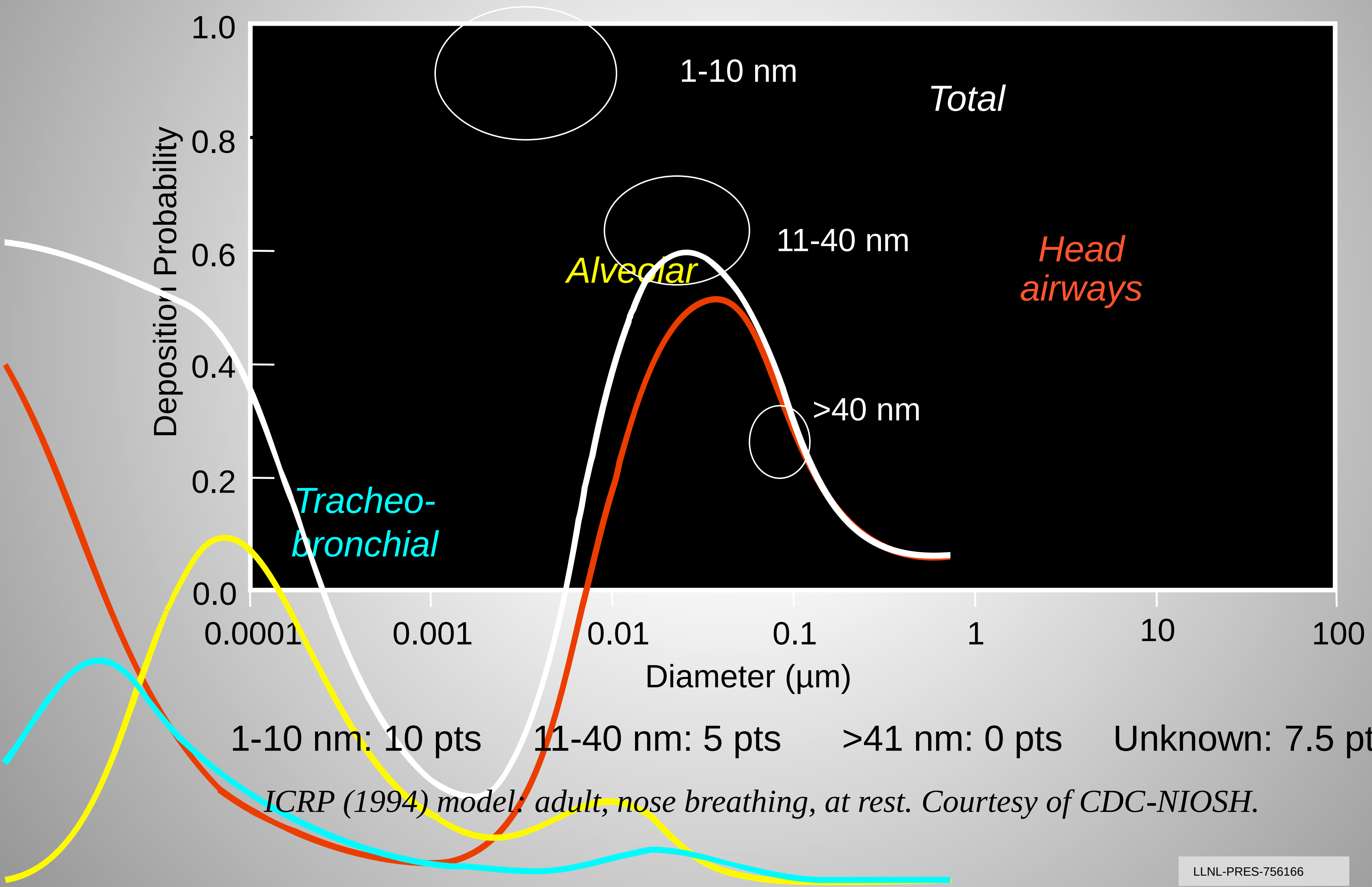


- Irregular shapes:
  generally more surface
  area than compact particles
  (e.g., iron powders)



- Tubular/fibrous: 10 pts Anisotropic: 5 pts Compact/spherical: 0 pts
- Unknown: 7.5 pts

Particle Diameter (nanomaterial)



1-10 nm: 10 pts   11-40 nm: 5 pts   >41 nm: 0 pts   Unknown: 7.5 pts

ICRP (1994) model: adult, nose breathing, at rest. Courtesy of CDC-NIOSH.

CB Nanotool: Probability Factors

- Estimated amount of material used (25 pts)
- Dustiness/mistiness (30 pts)
- Number of employees with similar exposure (15 pts)
- Frequency of operation (15 pts)
- Duration of operation (15 pts)

CB Nanotool: Control Outcomes

Probability

	Extremely Unlikely (0-25)	Less Likely (26-50)	Likely (51-75)	Probable (76-100)
Very High (76-100)	RL 3	RL 3	RL 4	RL 4
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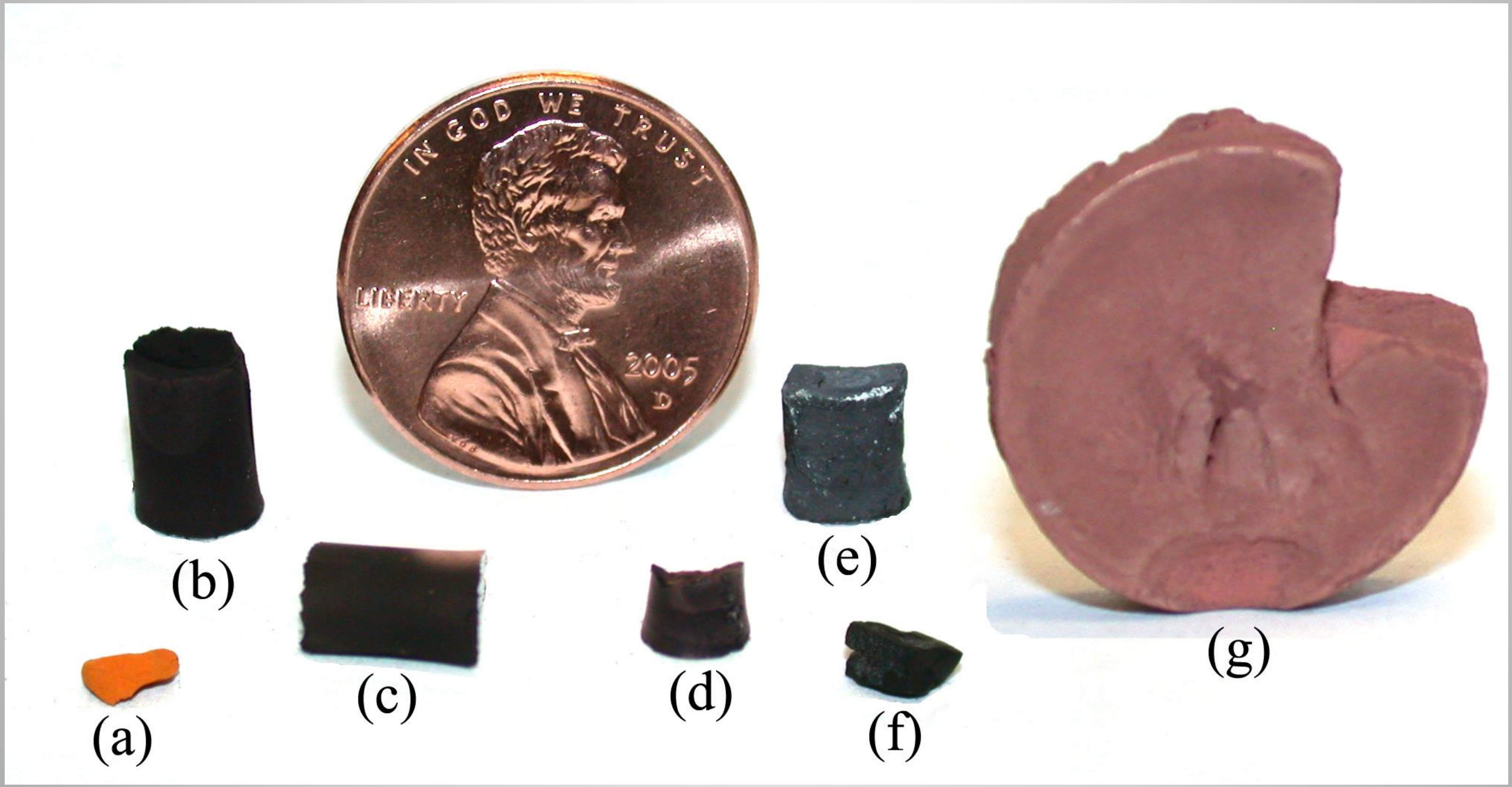
Severity

RL = Risk Level

RL 1: General Ventilation
RL 2: Fume hoods or local exhaust ventilation
RL 3: Containment
RL 4: Seek specialist advice

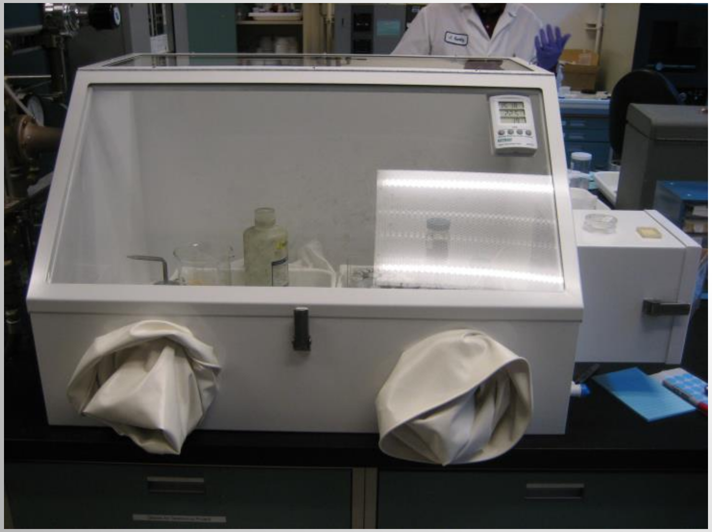
Synthesis of nanoporous metal foam

Application - Sensor applications, laser target fabrications



Synthesis of nanoporous metal foams

Step 1) Metal nanoparticles (Ni, Cu, Ag) are weighed and mixed with polystyrene spheres and water.



CB Nanotool

Activity Number	Scenario Description (free text)	Name or description of nanomaterial	CAS#	Activity classification	Current Engineering Control
1	Synthesis of metal foams by mixing metal nanoparticles with polystyrene latex nanoparticles in DI water. Dry powders are weighed inside glovebox and mixed with other nanoparticles inside plastic container.	Metal nanoparticles (Cu, Ni, Ag), polystyrene latex nanoparticles	Ni: 7440-02-0, Cu: 7440-50-8, Ag: 7440-22-4	Handling nanoparticles in powder form	Containment

CB Nanotool - continued

Parent material				
Lowest OEL (mcg/m3)	carcinogen?	reproductive hazard?	mutagen?	dermal hazard?
10	Yes	No	No	Yes

CB Nanotool - continued

Nanoscale material									
Surface reactivity	**Particle shape**	**Particle diameter (nm)**	**Solubility**	**carcinogen?**	**reproductive hazard?**	**mutagen?**	**dermal hazard?**	**Severity score**	**Severity band**
Unknown	Compact or spherical	1-10 nm	Insoluble	Unknown	Unknown	Unknown	Unknown	65	High

CB Nanotool - continued

Estimated maximum amount of chemical used in one day (mg)	Dustiness	Number of Employees with Similar Exposure	Frequency of Operation (annual)	Operation Duration (per shift)	Probability score	Probability band
400	High	1-5	Weekly	1-4 hr	75	Likely

Overall Risk Level Without Controls	Recommended Engineering Control Based on Risk Level	Upgrade Engineering Control?
RL3	Containment	No

Risk Level Matrix

Probability

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RL 1: General Ventilation
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Why a 4 x 4 risk matrix?

- Balances of ease-of-use with appropriate level of vigor.
  - 2 levels perfect
    - Impossible in workplace
  - 3 levels most accepted
    - "Stoplight" effect
    - Yellow abused
  - 5 levels is too prescriptive.
    - Given ENM uncertainties, 5 x 5 matrix is overly complex.
  - 4 x 4 matrix proven easiest to use
    - Fits classic 4 levels of CB controls

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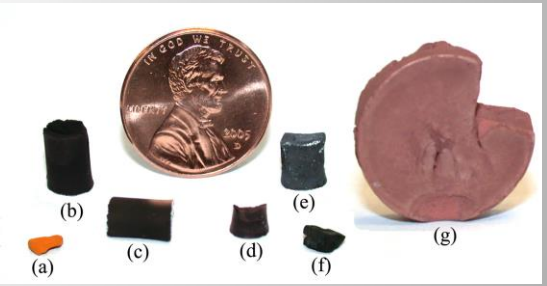
CB Nanotool: Treating Unknowns

- Fact in 2007: ENM Toxicology “unknown”
- Need to account for “unknown” in scoring
- Gave “unknown” 75% of highest point value
- Why 75%?
  - Everything unknown? RL3 = Containment
  - One “high” rating? RL4 = Seek Specialist
- Provides incentive to obtain “known”
- More information tends to lower scores
- Can re-do CB Nanotool assessment

Activities at LLNL (examples)

- Synthesis of nanoporous metal foams
- Flame synthesis of garnet ceramic nanoparticles by liquid injection
- Synthesis of carbon nanotubes and metal oxide nanowires onto substrates within tube furnace
- Deposition of liquid-suspended nanoparticles onto surface using low voltage electric fields
- Sample preparation of various nanomaterials by cutting, slicing, grinding, polishing, etching, etc.
- Use of gold nanoparticles for testing carbon nanotube filters
- Etching nanostructures onto semiconductors
- Addition of quantum dots onto porous glass
- Growth of palladium nanocatalysts
- Synthesis of aerogels
- Machining (e.g., turning, milling) of aerogels and nanofoams for laser target assembly
- Sample preparation and characterization of CdSe nanodots and carbon diamonoids



Qualitative Validation:
CB Nanotool vs Experts

- Application to current operations (Evaluation of outcomes vs IH/OH Experts)
  - 36 operations at LLNL evaluated by IHs
    - For 21 activities, CB Nanotool recommendation was equivalent to existing controls
    - For 9 activities, CB Nanotool recommended higher level of control than existing controls
    - For 6 activities, CB Nanotool recommended lower level of control than existing controls

CB Nanotool – As Policy

- LLNL decided to make CB Nanotool recommendation a requirement
- CB Nanotool is now policy within LLNL's Nanotechnology Safety Program

LLNL Nanomaterial Safety Program

- Key components of LLNL program
  - Risk assessment
    - CB Nanotool, Integration worksheet (work authorization document)
  - Controls
    - Eng. (Nanotool), Adm. (labels, signs, work practices, training), PPE
  - Verification of controls
    - Workplace monitoring, medical surveillance (identify UNP workers)
  - Transportation, waste management, emergency spills

7.0 Requirement Source Documents

Requirement	Title
DOE Order 456.1A	"The Safe Handling of Unbound Engineered Nanoparticles." (July 15, 2016).
DOE Policy 456.1	"Secretarial Policy Statement on Nanoscale Safety." (September 15, 2005).
10 CFR 851	Worker Safety and Health Program
29 CFR 1910.1020	Access to Employee Exposure and Medical Records

Activity classification

Clean-up of spills or waste material

A) Severity score

1- Surface reactivity	Medium	5
2- Particle Shape	Tubular or fibrous	10
3- Particle diameter	> 41-100 nm	0
4- Solubility	Soluble	5
5- Cancerogenicity	Unknown	4.5
6- Reproductive toxicity	Yes	6
7- Mutagenicity	Yes	6
8-Dermal toxicity	Yes	6
9- Asthmagen	Yes	6
10- Toxicity of parent material	< 10 µg/m³	10
11- Carcinogenicity of parent material	No	0
12- Reproductive toxicity of parent material	Yes	4
13- Mutagenicity of parent material	Yes	4
14- Dermal toxicity of parent material	No	0
15- Asthmagen of parent material	Yes	4

B) Probability score

1- Estimated amount of chemical used during task

2- Dustiness / mistiness

3-Number of employees with similar exposure

4- Frequency of operation

5- Operation duration

Result

Severity 70.5

Probability 60

RL 3

RL 3 : Containment

Upgrade ? **Yes**

Severity	Extremely unlikely (0-25)
Very High (>75-100)	
High (>50-75)	
Medium (>25-50)	
Low (0-25)	

Version 3,01

Overview

- Challenges in Traditional IH/OH Approach
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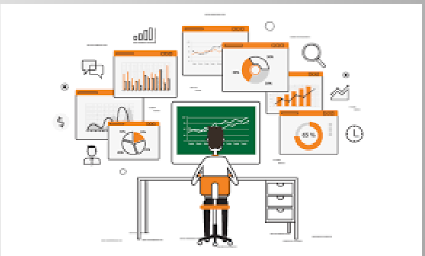
International Acceptance of CB CB Nanotool

- **Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST)**
  - IRSST (2009) Best practices guide to synthetic nanoparticle risk management. Report R-599, Institut de recherche Robert-Sauve en sante du travail (IRSST), Montreal, Quebec, Canada.
- **Nanomaterial Occupational Exposure Model (NOEM)**
- **ISO (ISO/TS 12901-2:2014)**
  - International Standard utilizing Control Banding
  - A good first approach to controlling workplace exposure
  - CB Nanotool is described as Proactive Approach
- **Multiple Journal Reviews of Nano CB Tools**
  - CB Nanotool's really good, but no quantitative validation

Quantitative Validation: Lawrence Berkeley National Laboratory – Independent Study

- 60 laboratories with various ENM are used for R&D activities
- Sampling performed by a 3rd party
- 21 activities assessed
- The quantitative data indicated that the control recommendations based on the CB Nanotool risk level outcomes were adequately protective of workers
- For 3 of the 21 activities, the quantitative data suggested a downgrade of controls from the CB Nanotool recommendation would be acceptable, if needed to conserve resources and maximize efficiency of operations
- Results of quantitative validation similar to qualitative validation
  - — In most cases, CB Nanotool control band determination was equivalent to qualitative or quantitative determination for a given activity, with a tendency to err on the safe side.



References:

- Department of Energy, Nanoscale Science Research Centers, *Approach to Nanomaterial ES&H*, Revision 3a, DOE Office of Science, May 12, 2008 (DOE 2008)
- Brouwer, D.H. (2012) Control Banding Approaches for Nanomaterials. Ann. Occup. Hyg. Vol. 56, No. 5, pp506-514, 2012.

Quantitative Validation: LLNL Methodology

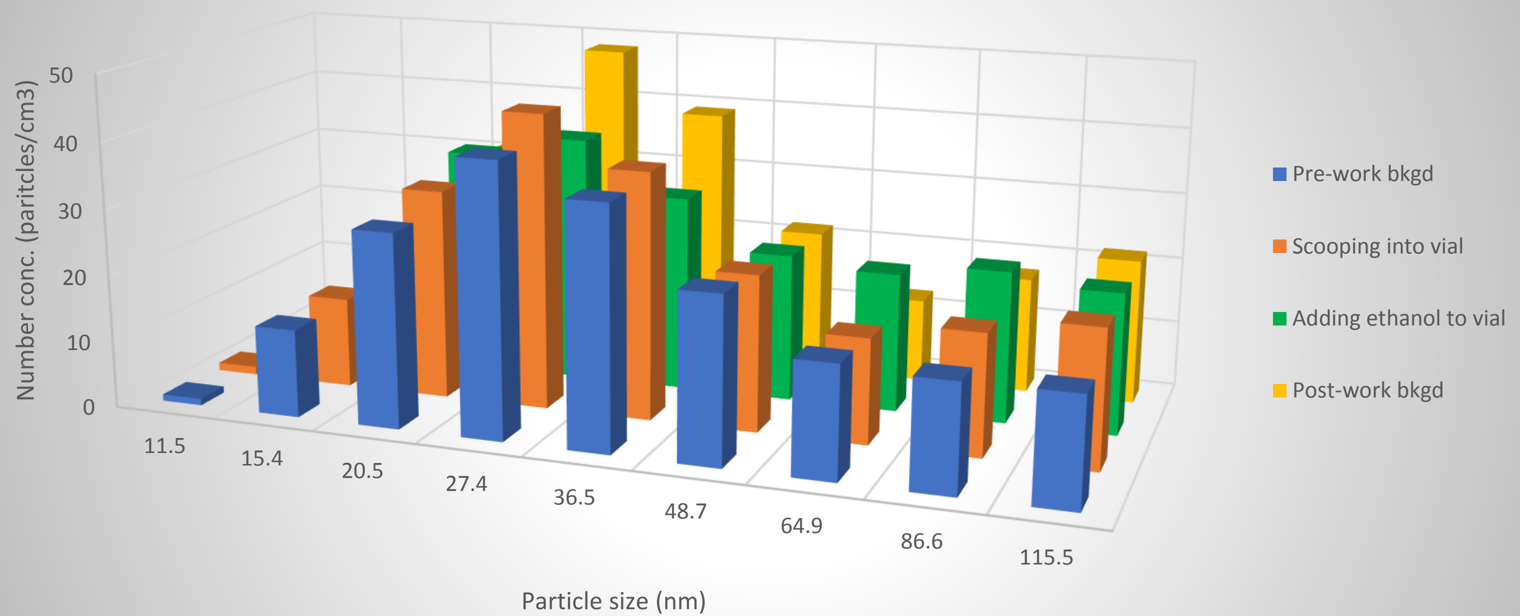
- Based on DOE sampling protocol in Nanoscale Science Research Centers (NSRC) “Approach to Nanomaterial ES&H”.
- Direct-reading particle counters & filtration-based sampling
  - Placed near nanoparticle source, at background, and in the workers breathing zone

Quantitative Validation: Various Nano Task Example Results

CB Nanotool and Air Monitoring Results at LLNL

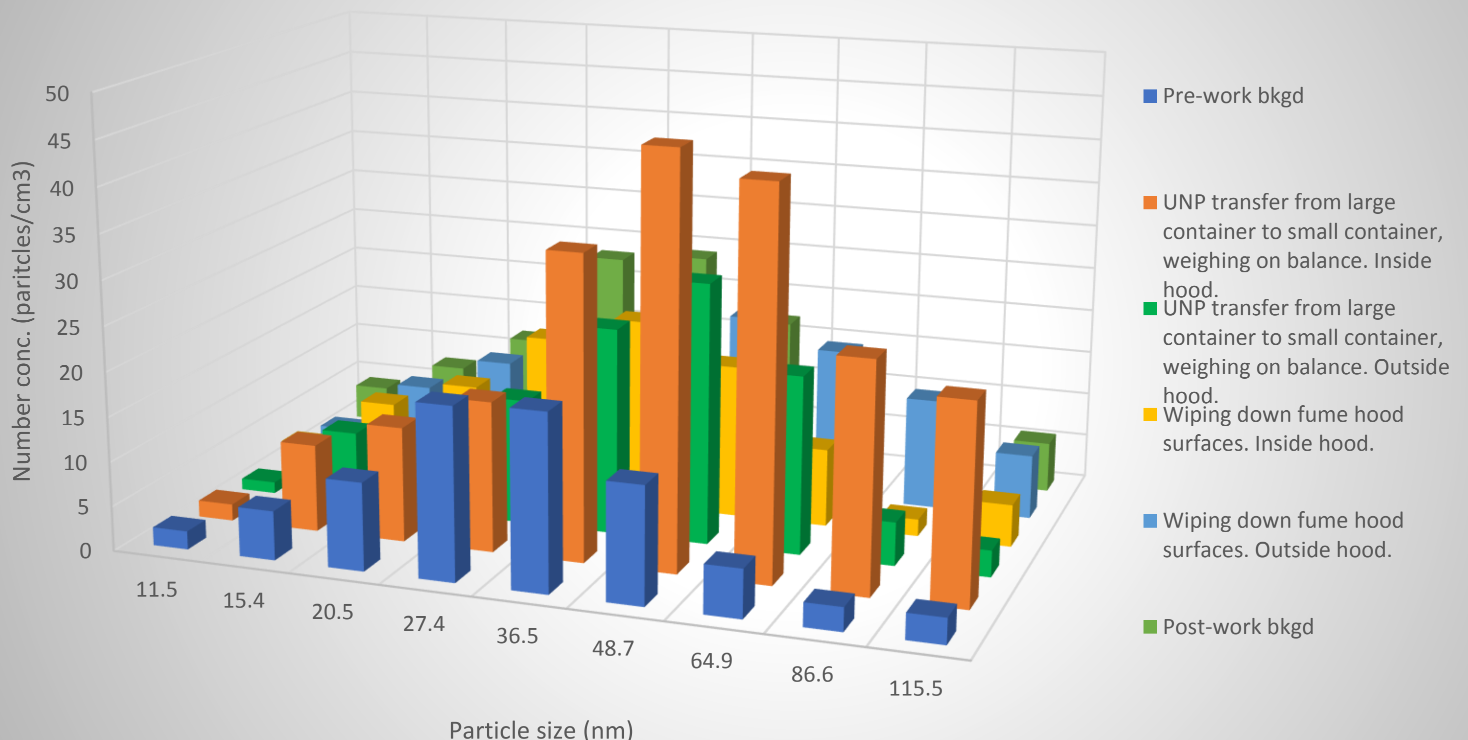
Activity Number	Scenario Description	Name or description of nanomaterial	Severity Band	Probability Band	CB Nanotool Risk Level	Air Monitoring Results	Do quantitative results support CB Nanotool risk level?
1	Stress testing, crash testing, harness testing, and explosive testing of carbon nanotubes. Test are carried out to the specimen's failure.	Carbon nanotubes	High	Less likely	2	NanoScan SMPS Model 3910 was used to measure particle distribution before, during, and after stress test. There was no discernable increase in number concentration during and after stress test.	Yes. While breaking the CNTs did not appear to increase the number concentration of CNTs, the mere introduction of CNTs into the enclosure increased the number concentration by around 3X. For this reason, RL2 controls are considered appropriate.
2	Sample preparation of carbon nanotubes, including weighing and mixing in liquid media	Carbon nanotubes	High	Likely	3	Air samples using 25-mm filter cassette and BGI cyclone were used to collect air samples from inside the fume hood, inside the lab away from the activity, and from the worker's breathing zone. Results were non-detect for elemental carbon for all samples.	Yes. Results suggest that RL1 controls would be adequate. However, given the uncertainties associated with CNT hazards and their measurement methodology, a fume hood (RL2 control) is recommended during this activity.
3	Machining, handling and processing of aerogels and foams can create dust that may contain UNP (specifically carbonized resorcinol formaldehyde).	Carbonized Resorcinol Formaldehyde	High	Less likely	2	A TSI P-track was used to compare background measurements to measurements during machining. Nothing beyond background was measured during machining.	Yes. Results suggest that RL1 controls would be adequate for the nanomaterial hazard. However, LEV is recommended due to the visible dust (likely larger than 100 nm) being generated during machining.

Quantitative Validation: Nano Task Example- Scooping/Weighing Samarium Cobalt Oxide Nanoparticles



Results show that RL1 controls would be adequate. Thus, a fume hood is considered a more than adequate control for this activity.

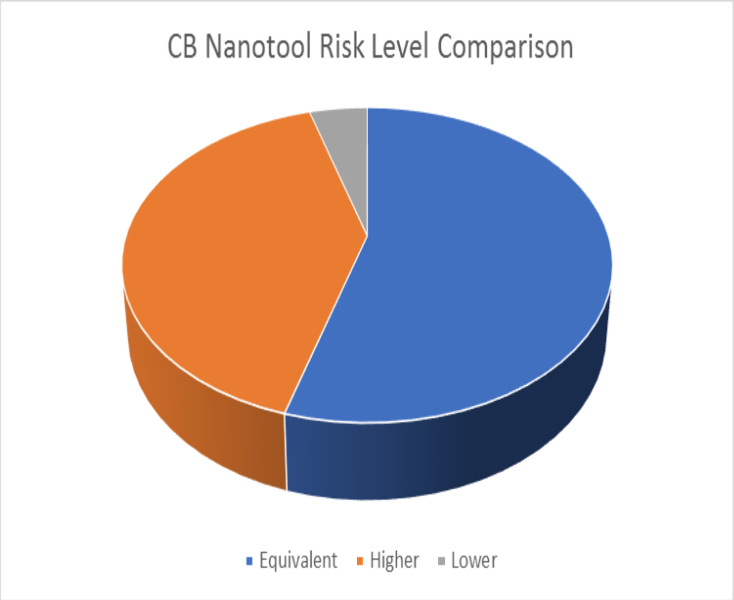
Quantitative Validation: Nano Task Example-Transferring Fused Silica Nanoparticles



Results suggest that RL2 controls are adequate for the UNP hazard. Measurements comparing number concentrations inside hood versus outside hood in worker's breathing zone indicate the necessity of performing this work in a fume hood.

Quantitative Validation: Summary of Results at LLNL

- 36 laboratory operations with various ENM are used for R&D activities
- Sampling performed by experienced IHs
- 22 activities assessed
  - For 12 activities, CB Nanotool recommendation was equivalent to existing controls
  - For 9 activities, CB Nanotool recommended higher level of control than existing controls
  - For 1 activity, CB Nanotool recommended lower level of control than existing controls
- The quantitative data indicated that the control recommendations based on the CB Nanotool risk level outcomes were adequately protective of workers.
- Results of quantitative validation similar to qualitative validation
  - In some cases, CB Nanotool control band determination was equivalent to qualitative or quantitative determination for a given activity, with a tendency to err on the safe side.



CB Nanotool – Quantitatively Validated

- Quantitative validation assessments conducted
- LBNL independent verification
- LLNL intensive quantitative confirmation
  - Quantitative sampling were in-line with RL outcomes
  - Controls from the CB Nanotool verified at LBNL & LLNL.
- CB Nanotool has addressed all remaining criteria
- CB Nanotool is a Gold standard for IH/OH ENM assessment in R&D

ICOH 2009 - Question asked; Can CB be better than traditional IH/OH?

IOHA 2018 – Question answered; Yes!

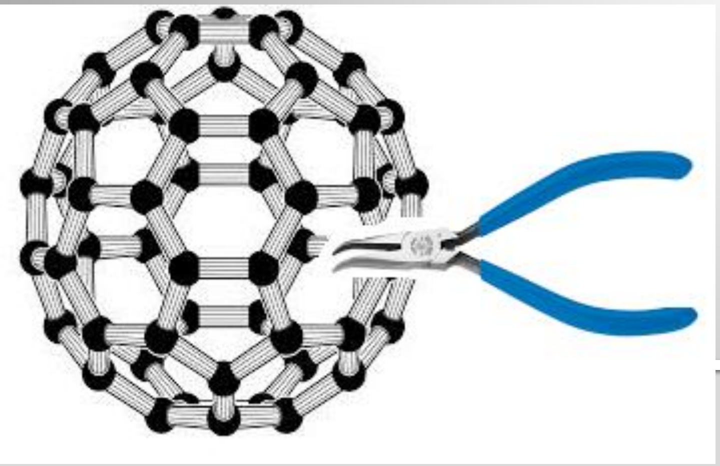
Publications

- Paik, S.Y., Zalk, D.M., and Swuste, P. (2008) Application of a pilot control banding tool for risk level assessment and control of nanoparticle exposures. *Annals of Occupational Hygiene,* 52(6):419–428.
- Zalk, D.M., Paik, S.Y., and Swuste, P. (2009) Evaluating the Control Banding Nanotool: a qualitative risk assessment method for controlling nanoparticle exposures. *Journal of Nanoparticle Research*, 11(7):1685-1704.
- Zalk, D.M. and Paik, S.Y. (2016) "Risk Assessment Using Control Banding". Assessing nanoparticle risks to human health. 2nd Edition. Ed. Gurumurthy Ramachandran. Elsevier, Inc., Waltham, Maryland. (1st Edition In 2011)
- Gasuccio, G, Ogle, R, Wahl, L, Pauer, R (2010) "Worker and Environmental Assessment of Potential Unbound Engineered Nanoparticle Releases, Phase III Final Report: Validation of Preliminary Control Band Assignments," RJ Lee Group, Inc., and Lawrence Berkeley National Laboratory.

CB Nanotool – Access

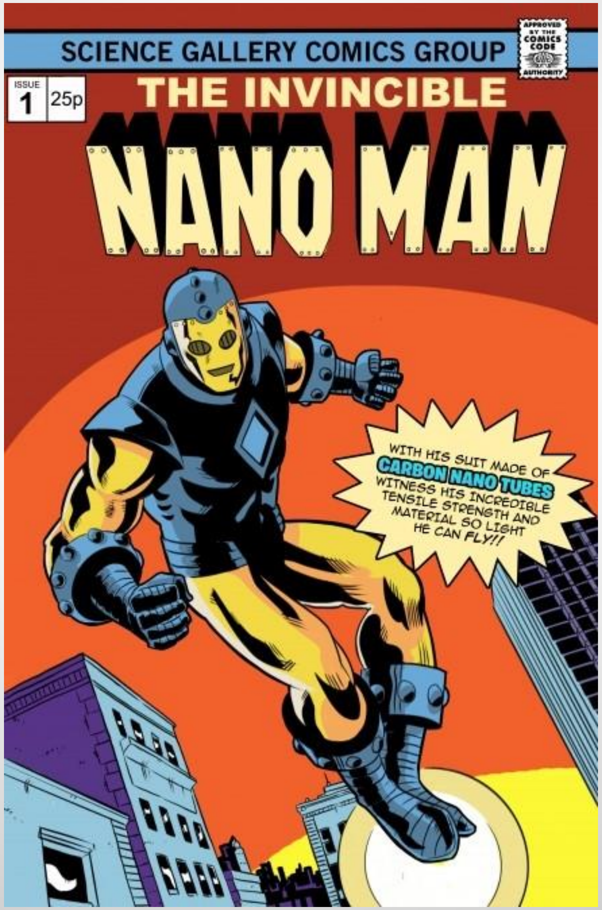
- The CB Nanotool can be accessed at:

https://www.llnl.gov/controlbanding



Your attention is appreciated!

Questions?



David M. Zalk, PhD, CIH
zalk1@llnl.gov
dzalk2@uic.edu