

TLVs for Nanoparticles

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Chair, TLV Committee

OELs for Nanoparticles?

- No EU OELs
- National initiatives
 - Germany – OEL for silica dioxide
 - UK – benchmark levels – pragmatic guidance
 - 0.066 x OEL – insoluble
 - 0.5 x OEL – soluble
 - 0.1 x OEL – CMAR
 - 0.01 fibre/ml – fibrous
 - NIOSH REL for ultrafine/nanoscale TiO_2
 - NIOSH REL for CNT
 - TLV for respirable ZnO (UF particles) and TiO_2 is currently Understudy

TLV[©] Development Process

TLV-CS Committee

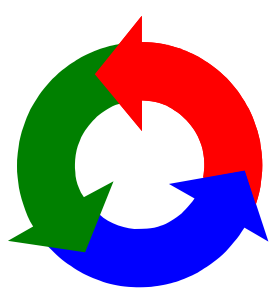
- Committee consists of volunteers, who develop scientific guidelines and publications
 - ✓ Primary goal is to develop scientifically-based guidelines that OHS professionals can rely upon to make decisions regarding employee health
 - ✓ Committee expenses (travel and literature searches) are supported by ACGIH
 - ✓ Time is donated by the members

TLV Subcommittees

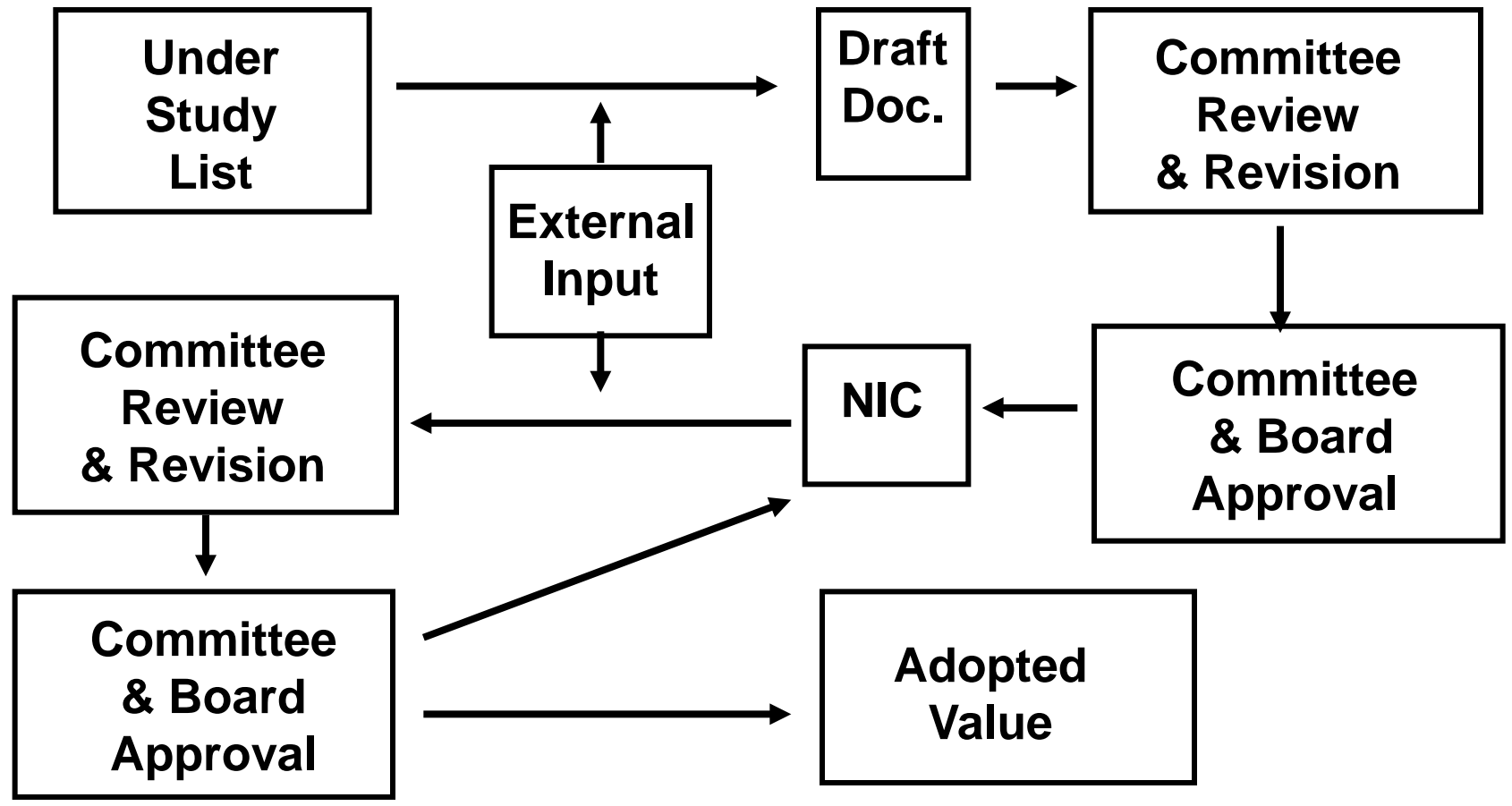
- D&I, MISCO, and HOC
- Up to 10 members on each
- Membership from academia, government, labor, industry within 4 key disciplines:
 - ✓ Industrial hygiene
 - ✓ Toxicology
 - ✓ Occupational Medicine
 - ✓ Occupational Epidemiology

How Are TLVs[©] Made?

- Scientific judgment
 - Review published literature
 - Identify NOAELs and LOAELS (or BMD)
 - Apply uncertainty factor – no hard numbers
 - NOAEL or LOAEL?
 - Animal or human data?
 - Adverse effect – eye irritation or lung cancer?



TLV[©] Development Process



2 Common Misconceptions Regarding TLV Setting

- *Scientific literature*
- *Uncertainty factors*
- *Technical, economic, and analytic feasibility*

Scientific Literature

- *Principal Sources*
 - Published and Peer Reviewed
- *Secondary Sources*
 - Review Articles
 - Unpublished (e.g., contract lab; robust summaries; NTP cancer bioassays)
 - ✓ Before Use: Owner must give ACGIH permission to use and cite the report, and release the report to a third party
 - ✓ Consideration of TLVs is not deferred pending completion of on-going or planned research
- Not a review of all available literature
 - ✓ Emphasis on peer-reviewed literature
 - ✓ Emphasis on literature pertinent to the issue

Uncertainty Factors

- TLV committee does not use a fixed set of uncertainty factors (e.g., 10X for extrapolation from animal data)
- TLV committee uses 'common sense' based upon:
 - severity of the critical effect
 - extrapolation issues

- Core TLV Principles

- ✓ Focus on airborne exposures in occupational settings
- ✓ Utilize the “threshold” concept
- ✓ Primary users are industrial hygienists
- ✓ Goal is toward protection of “nearly all” workers
- ✓ Technical, economic, and analytic feasibility are NOT considered

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What role do technical, economic, and analytic feasibility play in a nanoparticle TLV?

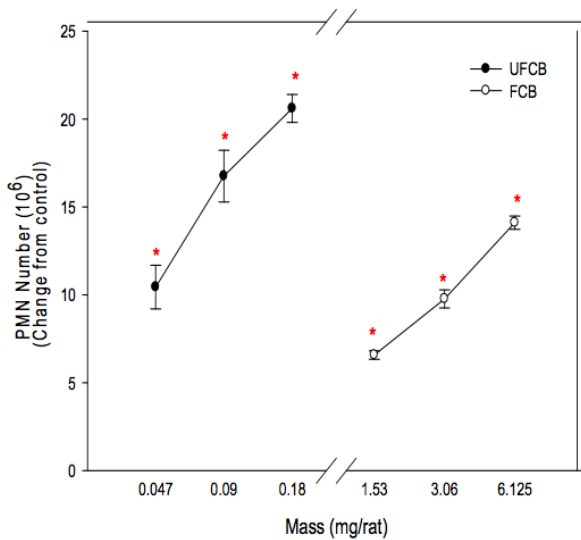
- Technical
 - Instrument may not be portable for personal/breathing zone measurements
 - Size cut samplers work by inertial forces; not suitable for nanoparticles
- Economic
 - Instrument could be very costly compared to a gravimetric filter
 - Impede small business development of new nanoparticles
- Analytic
 - Surface area measurements in real time?
 - What drives toxicity?
 - agglomerate size or primary particles?
 - Measurement of a complex nanoparticle
 - e.g., CNT or metal used in 'growing' CNT

Issues in Setting an TLV[©] for a Nanoparticle

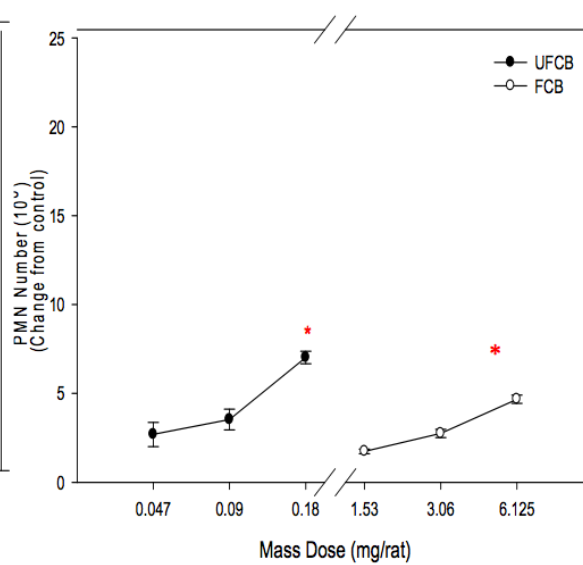
- Little toxicology data (particularly human epi)
 1. Do more research?
 2. Apply common safety factor to respirable TLV?
 3. Mass or surface area?
 4. Hazard banding?
 5. Algorithms?
 - a. Solubility
 - b. Carcinogen
 - c. Fiber
 - d. Particle size
- Measurement of nanoparticle in the work place

Can a Constant Safety Factor Be Used to Convert a Respirable OEL to a Nano OEL?

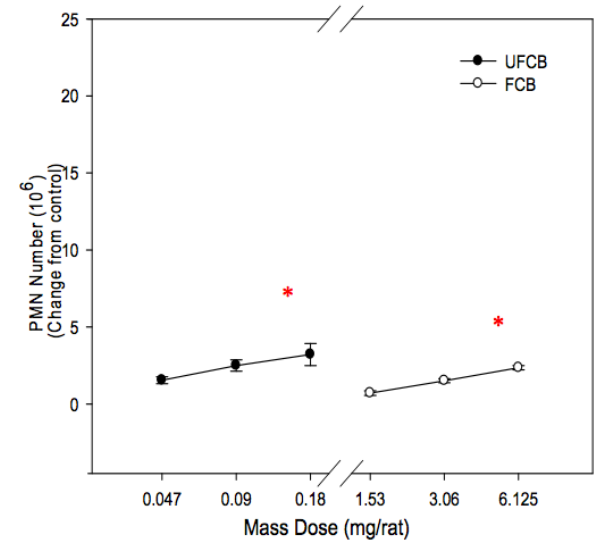
A. 1 Day



B. 7 Days

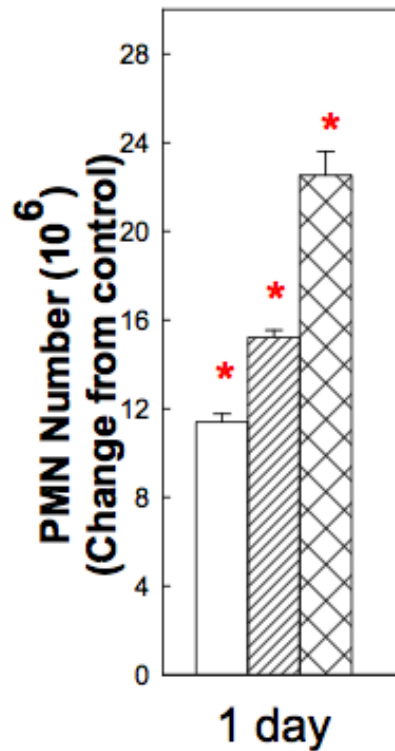


C. 42 Days

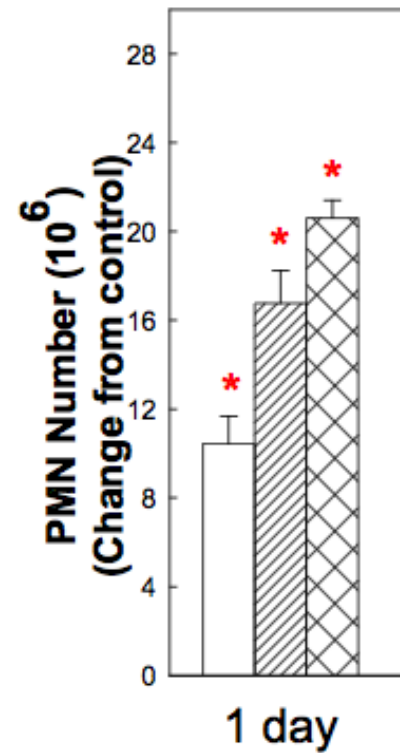


Can the Same Safety Factor Be Used to Convert All Nanoparticles?

A. UFTiO₂

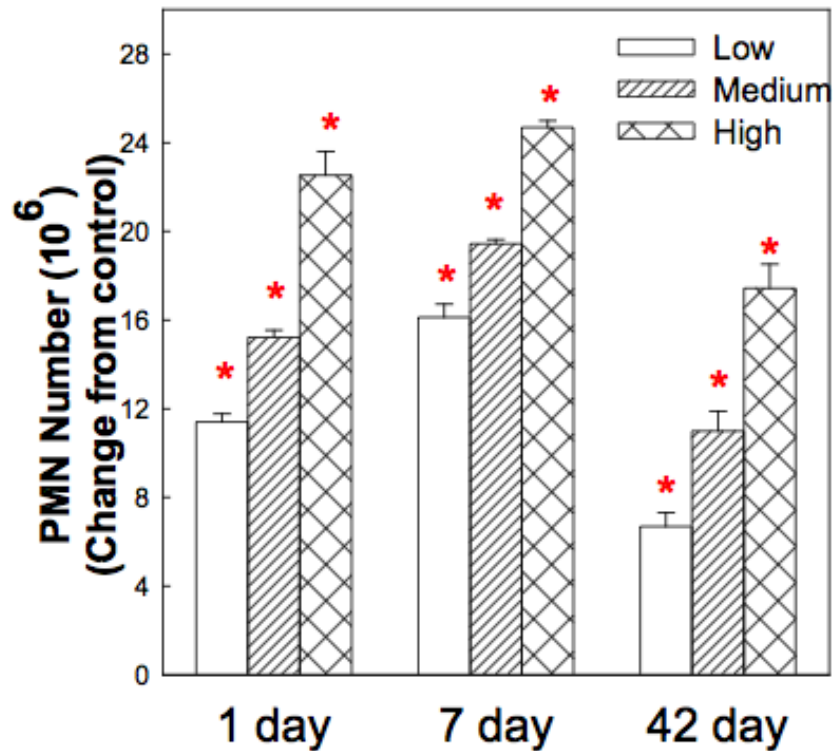


B. UFCB

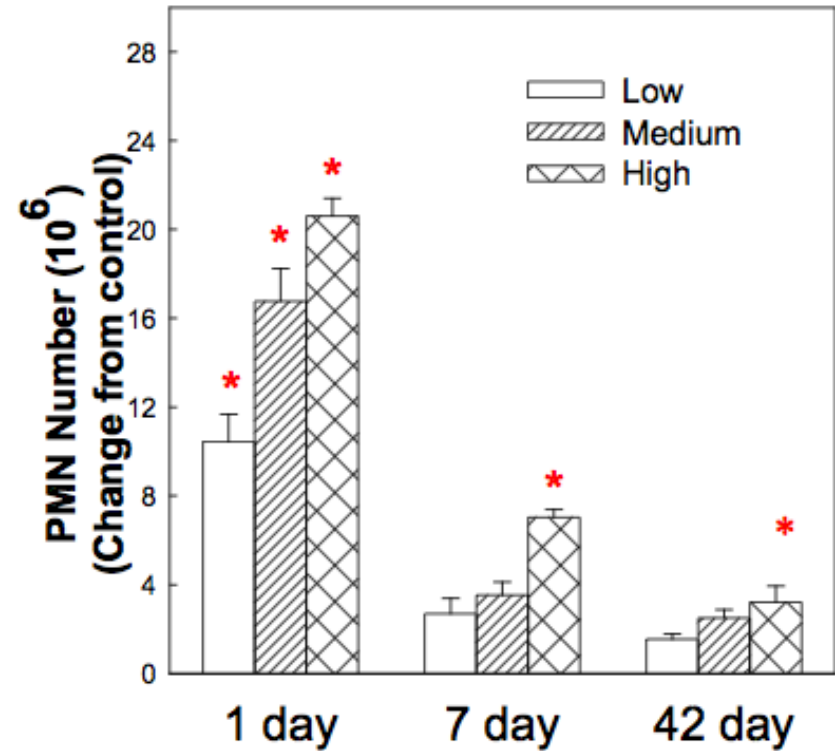


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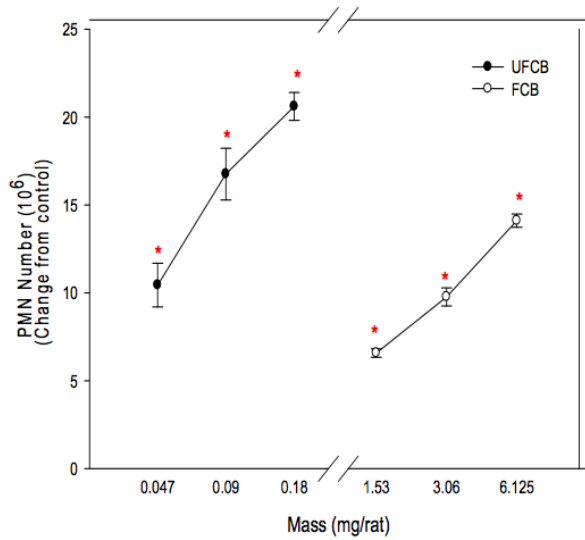


B. UFCB

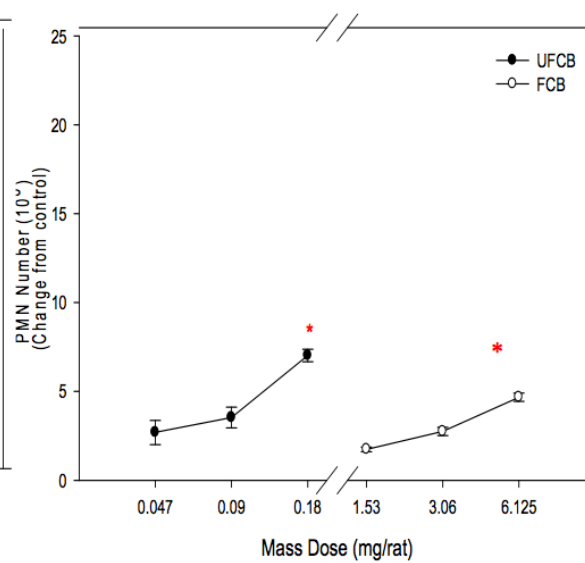


Should Nanoparticles OELs Be Based Upon Mass Concentration?

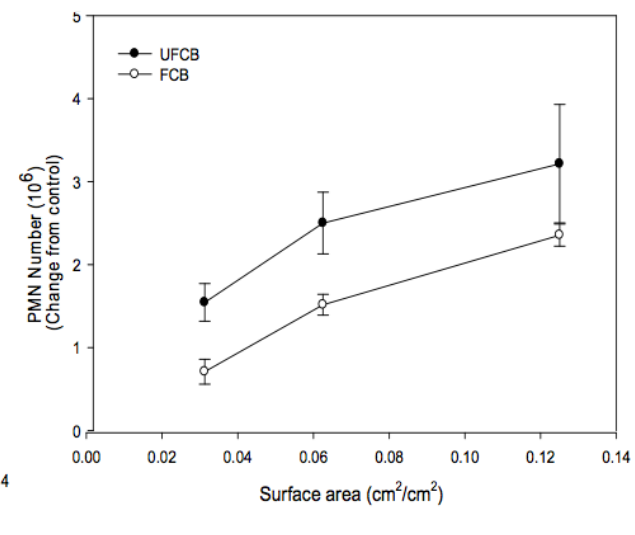
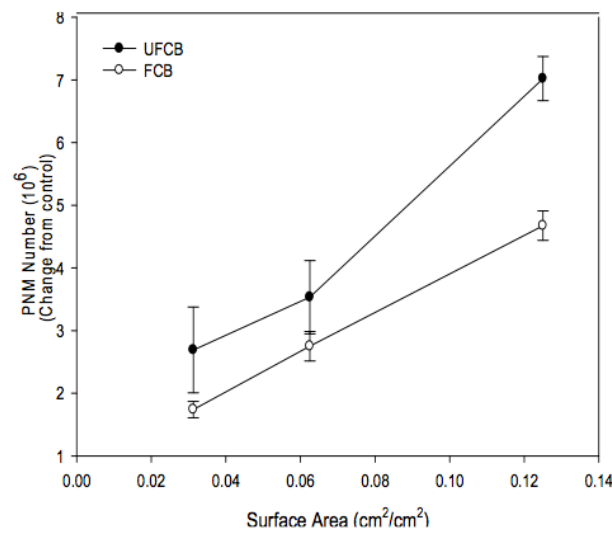
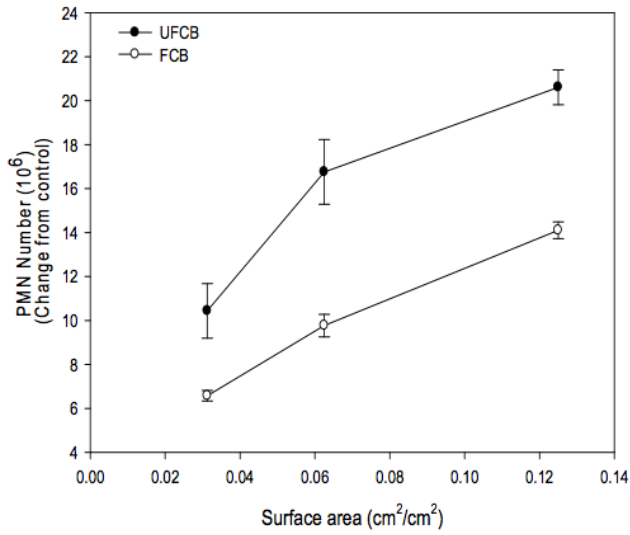
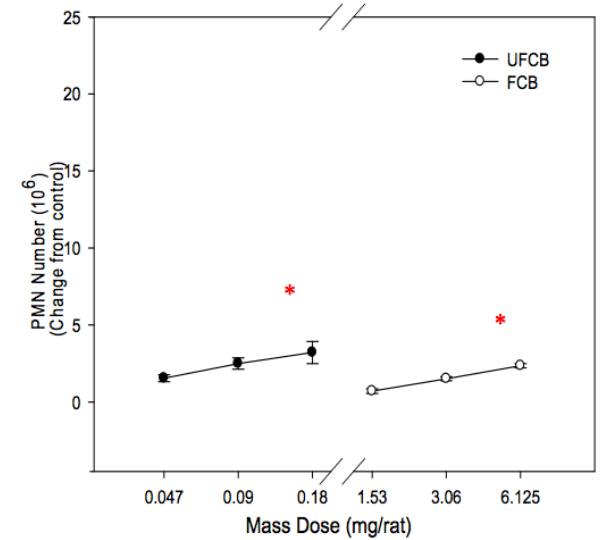
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C. 42 Days



Another Problem to Consider for Setting a TLV for a Nanoparticle

- **Size selective TLVs** (inhalable, thoracic, respirable)
 1. Size selective TLVs aren't set just because of deposition patterns and we can measure different sizes
 2. In general, we're concerned about location of respiratory effects
 - a. Deposition pattern of nanoparticles is 'different'
 - Primary vs. agglomerates
 3. Animal studies – compared to larger inhaled particles, less uncertainty in extrapolation because nanos probably act/deposit the same in rodent and human airways

So, How Could a Nanoparticle TLV[©] Be Set in the Future?

- Good, old-fashioned way
 - if plenty of data
- Common uncertainty factor to convert current TLV to Nano TLV
 - only if validated for several to many nanoparticles or a ‘class of nanoparticles’
- ‘Fancy’ risk assessment algorithm
 - If validated for several to many nanoparticles
- Hazard banding

Rapidly Growing Database to Help Set a TLV

Main Effects of Inhalation Exposure to Nanos

- No clear evidence of toxic effects on organs other than lungs

Main Effects of Inhalation Exposure to Nanos

- No clear evidence of toxic effects on organs other than lungs
 - Now there is evidence for extrapulmonary effects
 - liver
 - in utero
 - brain
 - cardiovascular

If Plenty of Data, Can a Nanoparticle TLV[©] Be Set in the Near Future?

- Good, old-fashioned way
- Validated uncertainty factors to convert current TLV to Nano TLV
- Hazard banding