

# **Critical Gaps and Needed Industrial Hygiene Actions to Understand and Prevent Beryllium Sensitization and CBD**

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Centers for Disease Control and Prevention**



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# What is our starting place?

There is a model for

## Beryllium Management Planning (BMP):

- Technical interventions for the effective control of beryllium focus on achieving 8 operational goals:

- **Keep Beryllium:**

- work areas & processes clean
- out of the lungs
- off of the skin
- off of the clothing
- at the source
- in the work area
- on the plant site
- workers prepared

This is a proactive, preventive approach...

What else do we need?

# Hypotheses

- Beryllium sensitization may occur by the dermal route as well as by the inhalation route.
- CBD requires the persistent availability of Be in lung
  - From repeated exposures to a soluble material or
  - From discrete exposure(s) to less soluble materials.
- Understanding bioavailability is key to understanding both sensitization and CBD
- Bioavailability depends on the timing, concentration, and physico-chemical properties of particles:
  - Aerodynamic size (dispersion and deposition in the respiratory tract),
  - Physical size (composition, particle number, and number of affected cells),
  - Intrinsic solubility (response to surfactant and phagocytic solvents)
  - Surface area (contact of the beryllium material with the solvents)

# AREAS OF RESEARCH



# Critical Questions for Bioavailability

- How do the intensity and duration of bioavailable beryllium contribute to beryllium sensitization and CBD?
- Is the activation threshold for sensitization higher than the threshold for granuloma formation?
- What combinations of chemical dissolution rate constant, specific surface area, and deposited mass of respirable particles result in release of beryllium ions at rates sufficient to activate T-lymphocytes and *initiate* a granulomatous response?

# Critical Questions for Bioavailability

- What combinations of chemical dissolution rate constant, specific surface area, and deposited mass of respirable particles result in release of beryllium ions at rates sufficient to *maintain* a granulomatous response?
- How does intracellular particle dissolution affect the viability and function of antigen-presenting cells?
- To what extent do beryllium particles penetrate into the pulmonary alveolar interstitium?
  - Do the particles remain free or are they sequestered in macrophages or some other cell type?

# Critical Questions for Bioavailability

- What is the role of skin exposure?
- How do beryllium ions or particles that penetrate the epidermis interact with immunologically active cells?
- Should there be similar concerns for the deposition and bioavailability of particles in the nasal and conducting airways?

# Critical Questions for Bioavailability

- In which biological compartments (e.g., macrophages, pulmonary alveolar interstitium, or other cell locations or types) does beryllium dissolution most contribute to the disease process?
- What is an appropriate exposure-response metric or dose-response metric for sensitization and CBD?
  - Several metrics of lung deposition and bioavailability may need to be investigated, including peak, average, or cumulative beryllium ions/g-lung/day.

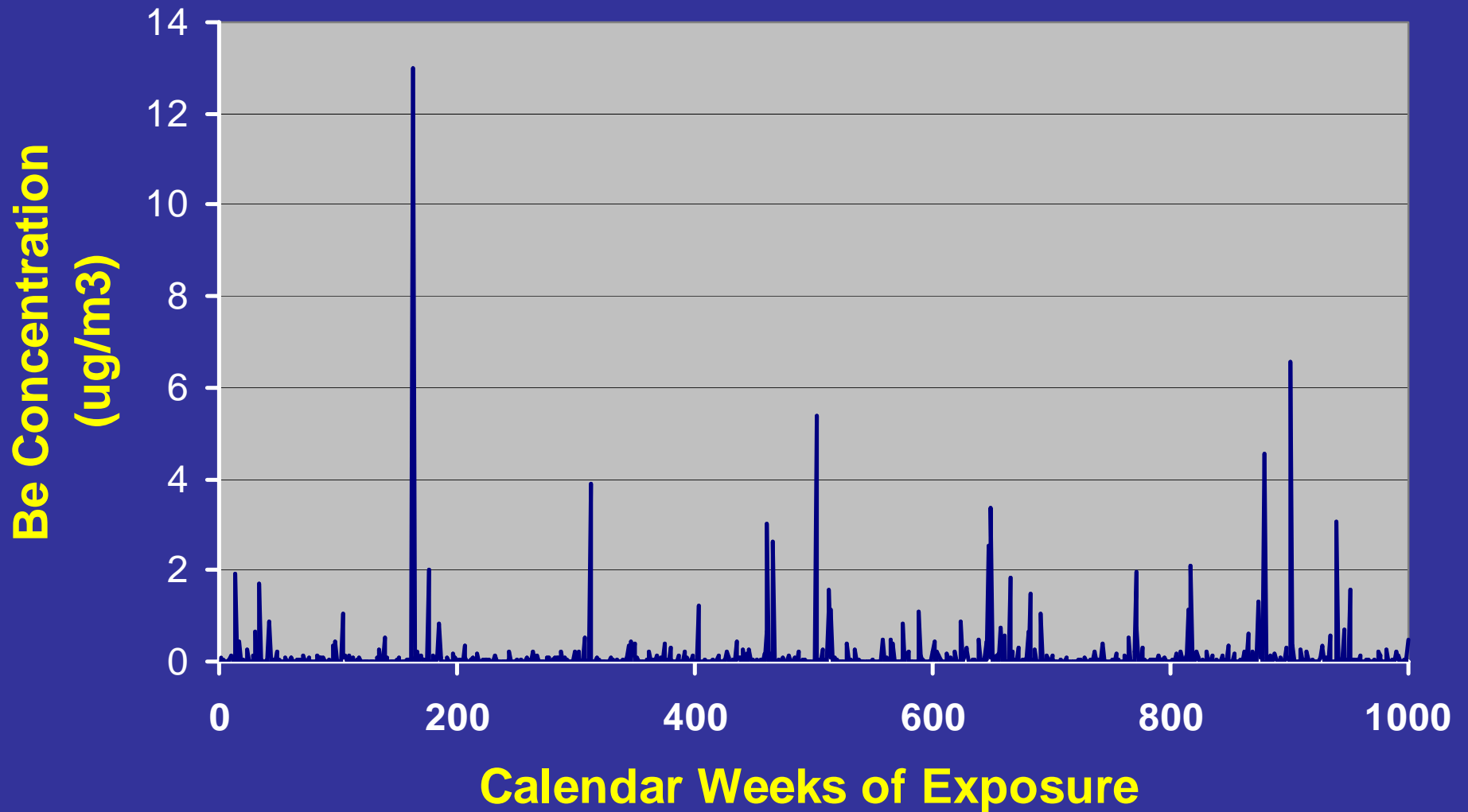
# Progression for Exposure Assessment

- **Airborne beryllium mass concentration**
  - Average ( $\mu\text{g}/\text{m}^3$ )
  - Peak ( $\mu\text{g}/\text{m}^3$ )
  - Cumulative ( $\mu\text{g}/\text{m}^3\cdot\text{days}$ )
- **Alveolar-deposited beryllium**
  - Inhalable, thoracic, or respirable
  - Mass, number, surface area
- **Biologically available beryllium**
  - Dissolved Be (ions / gram lung / day)
  - Peak, average, cumulative, instantaneous

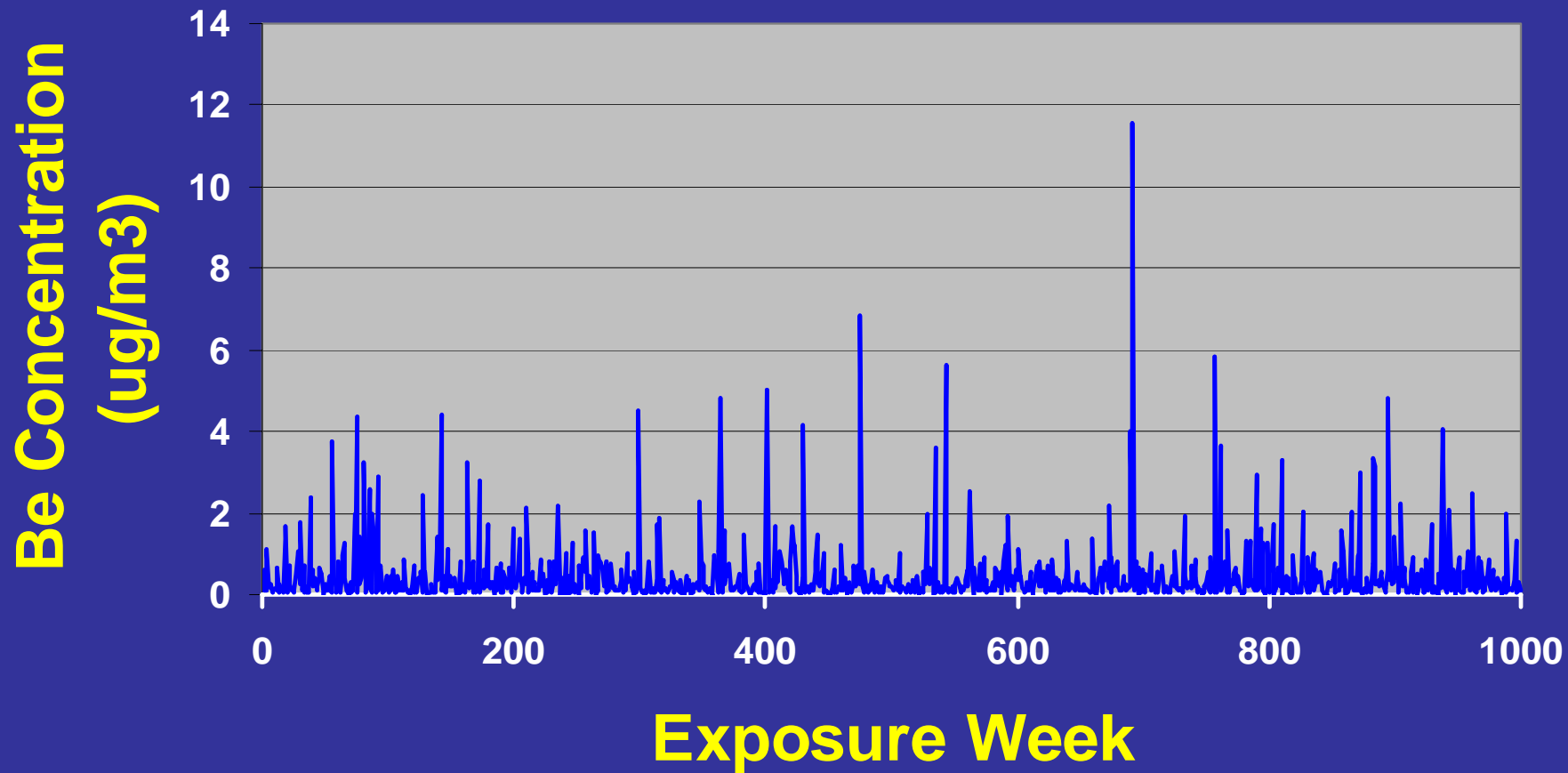
# An Example of the Strategy

- Monte Carlo (probability) simulation of worker exposures over 20 years of work experience
- Weekly personal sampling results for average airborne concentration of beryllium ( $\mu\text{g}/\text{m}^3$ )
- “Typical” lognormal concentration distribution
  - Median concentration:  $0.2 \mu\text{g}/\text{m}^3$
  - Geometric standard deviation: 3.5
- Data from Monte Carlo Simulation
  - Crystal Ball (Decisioneering, Inc.)

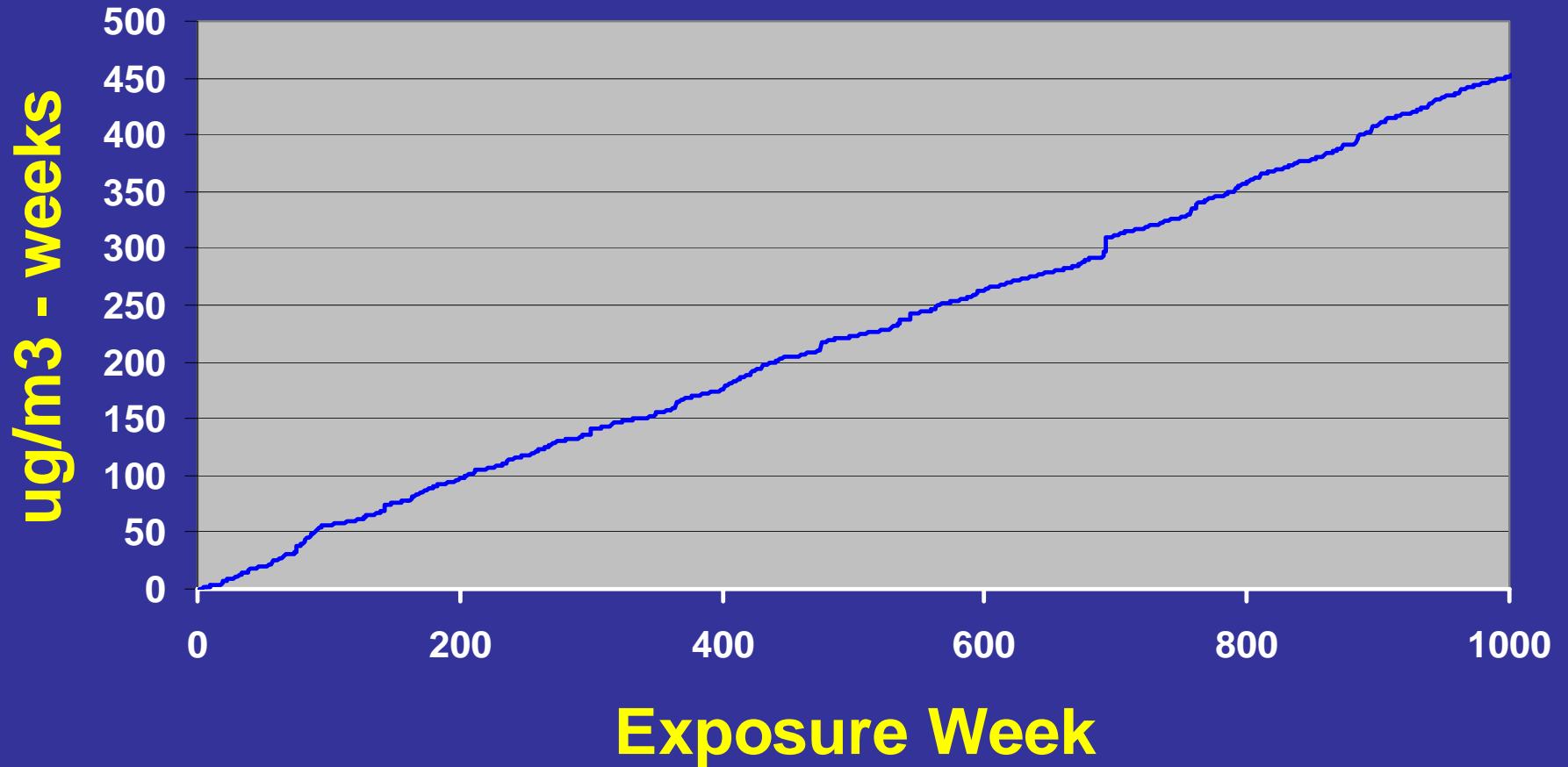
# Be Aerosol Concentration



# Exposure History - Worker 1

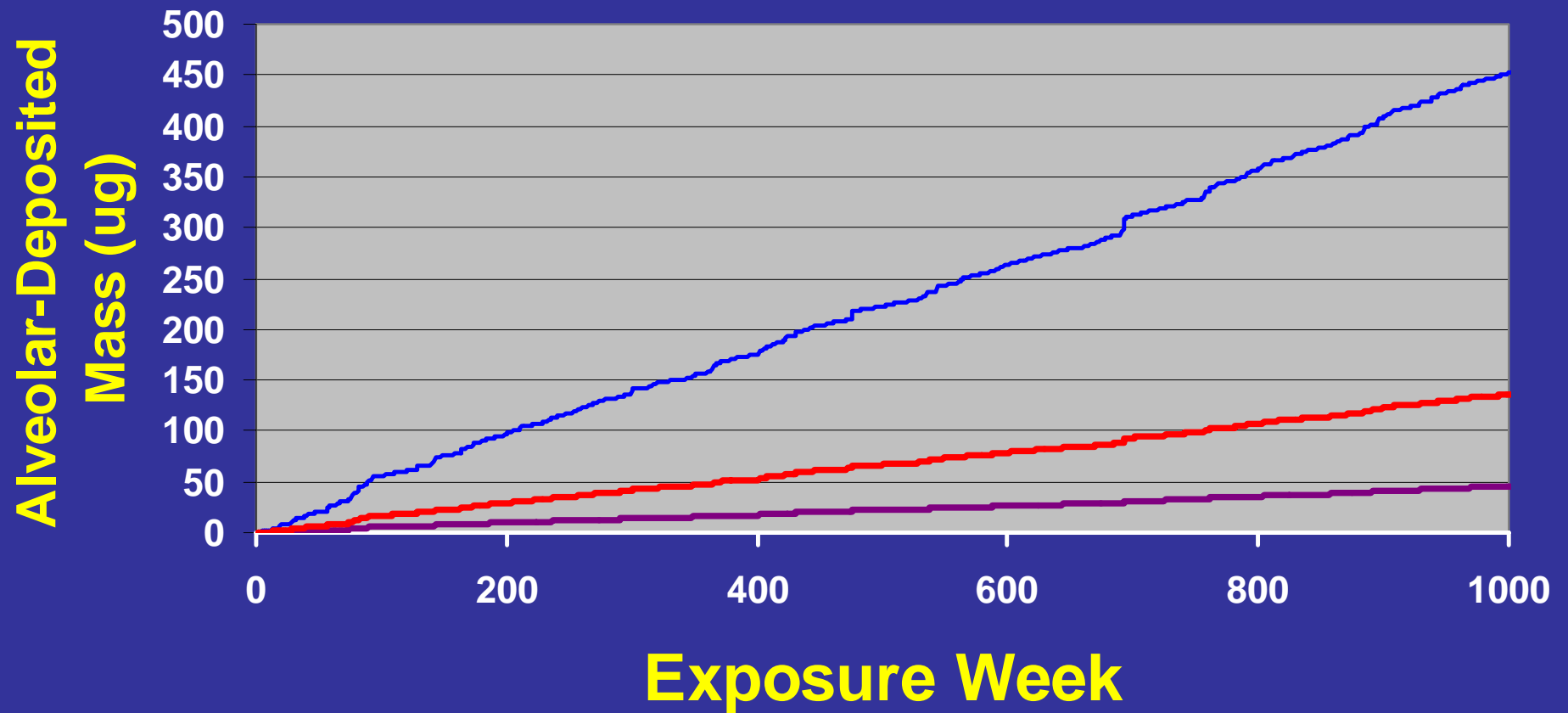


# Cumulative Exposure - Worker 1

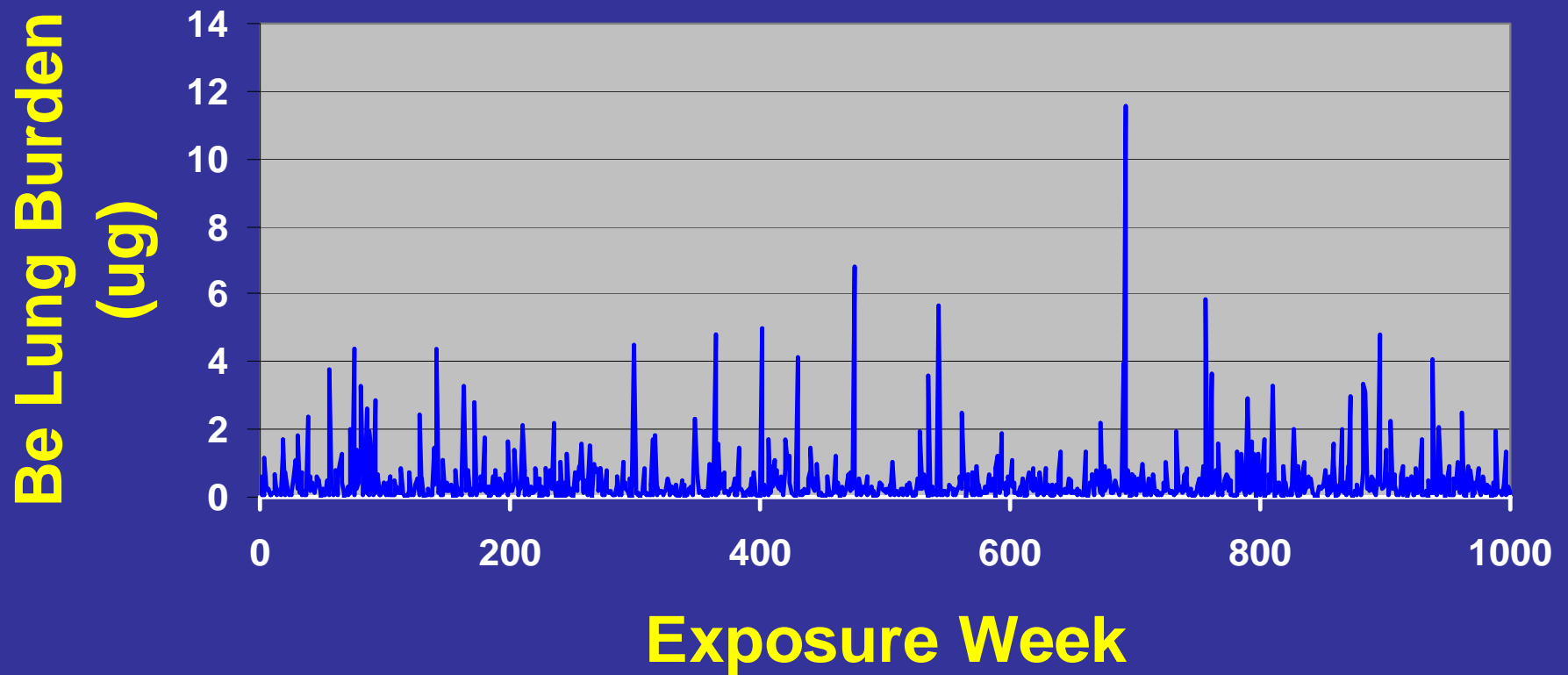


# Cumulative Exposure - Worker 1

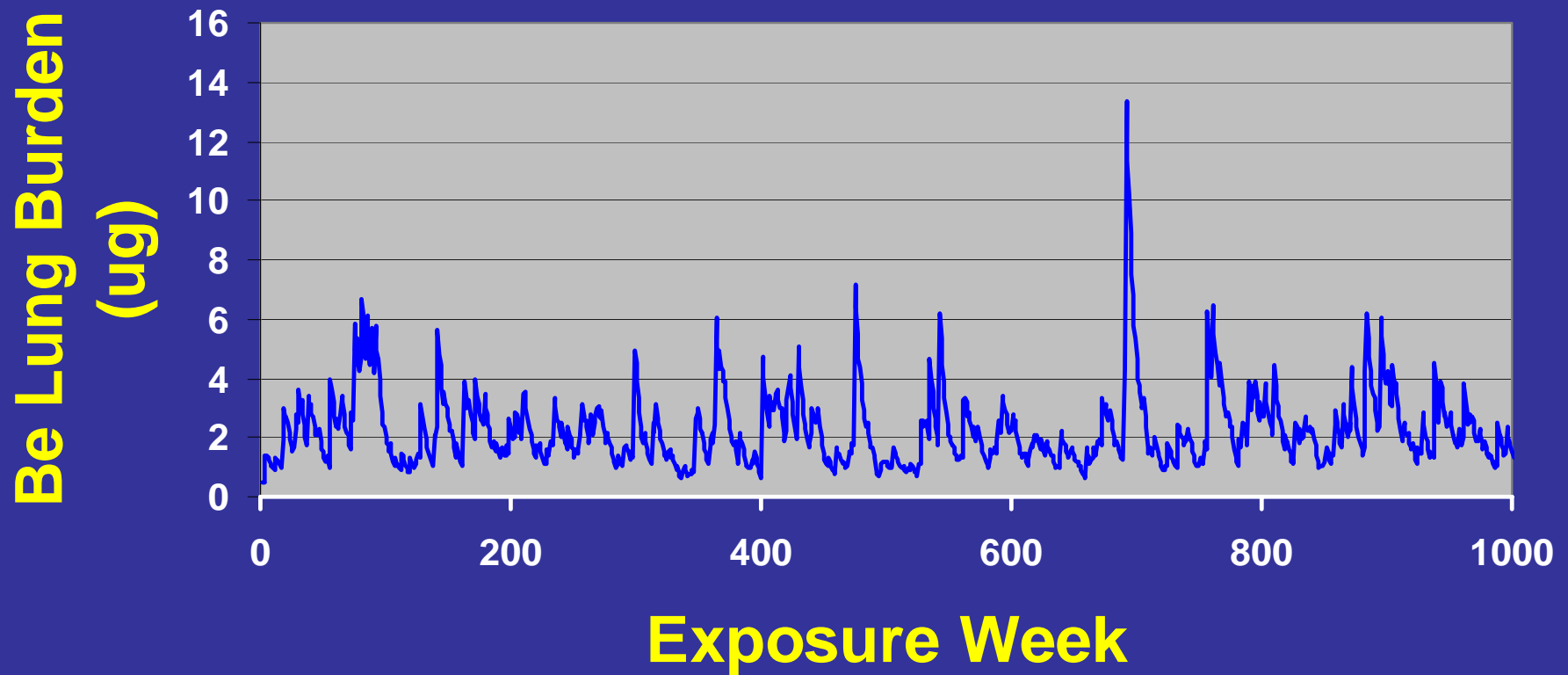
(blue-inhaled, red-0.005 um, purple 1 um)



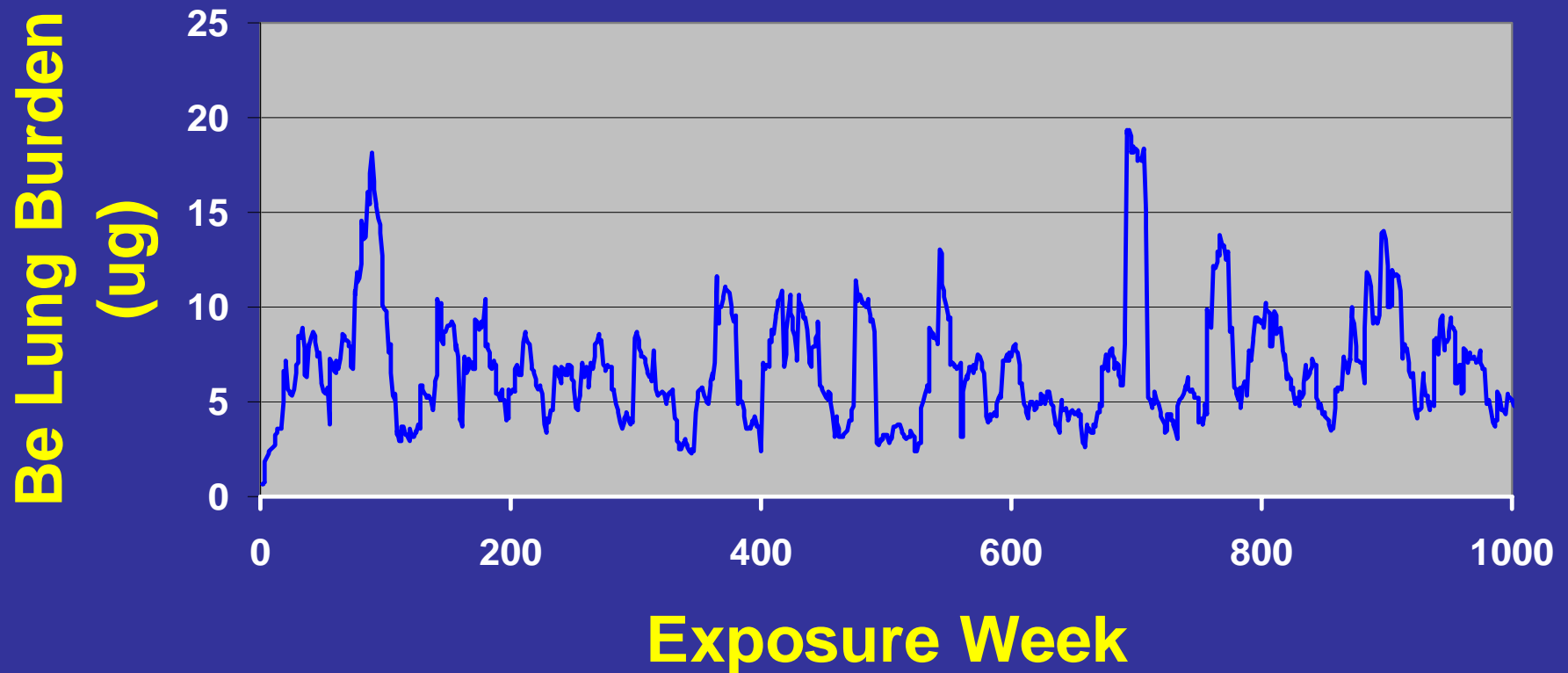
# Lung Burden History - Worker 1 (1 d clearance halftime)



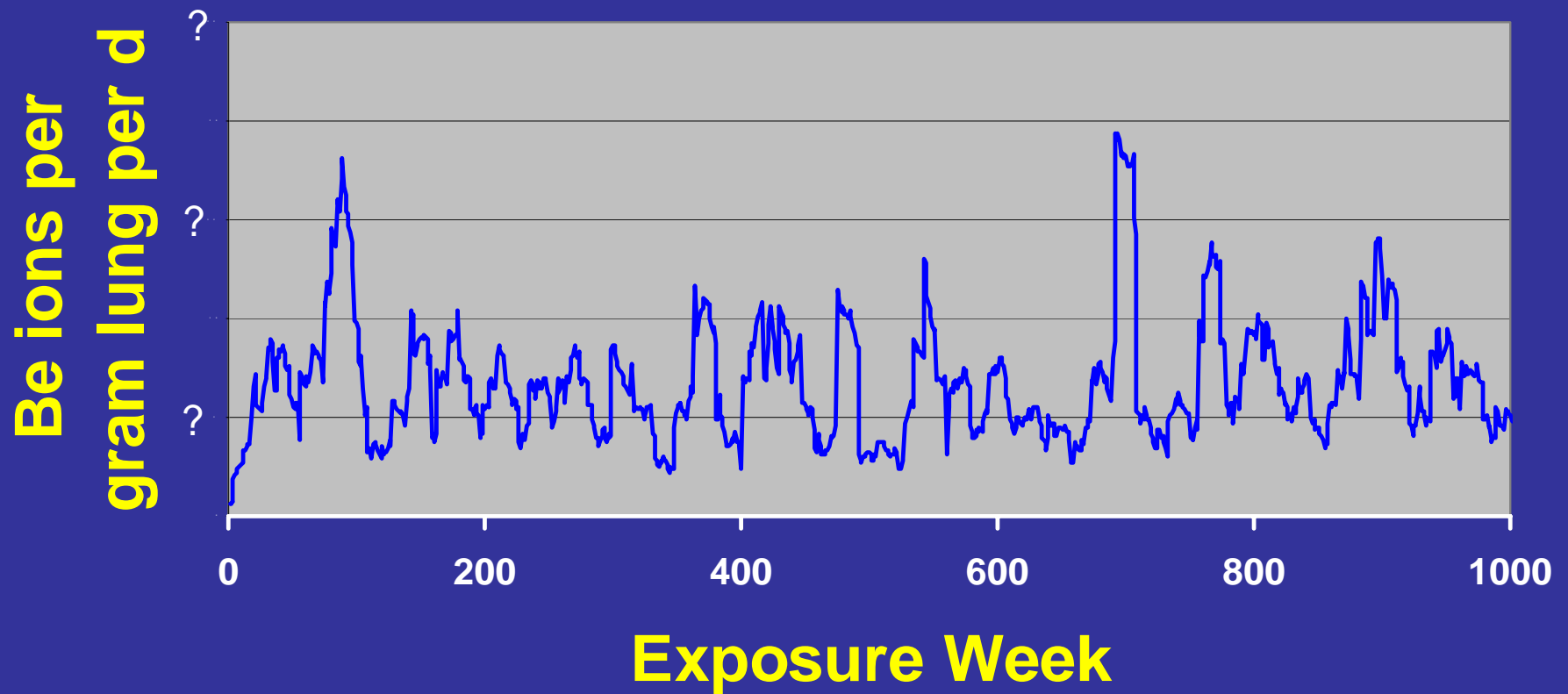
# Lung Burden History - Worker 1 (28 d clearance half-time)



# Lung Burden History - Worker 1 (350 d clearance halftime)



# Lung Dose History - Worker 1 (hypothetical for mod. soluble Be)



# Recommendations

- Understanding the interrelationships of particle size, surface area, bioavailability of Be, and associated risks for CBD may lead to more protective exposure limits
- Particle morphology influences the size-dependent specific surface area
- Direct measurements of particle surface area are needed parts of a comprehensive sampling program
- Both inhalation and dermal routes must be addressed.
- Epidemiology studies, in vitro studies, and studies in genetically-engineered mice must work together

***Questions ?***

session 4

## ***Industrial Hygiene Update***

1:30 – 2:00 pm

### **Critical Gaps and Needed Industrial Hygiene Actions to Understand and Prevent Beryllium Sensitization and CBD**

Keynote Speaker: Mark D. Hoover, PhD, CHP, CIH, NIOSH

2:00 – 2:30 pm

### **Characterization of Beryllium Aerosols**

Aleksandr B. Stefaniak, PhD, CIH, NIOSH

2:30 - 3:00 pm

### **Skin as a Route of Exposure to Beryllium**

Gregory A. Day, PhD, NIOSH

3:00 – 3:15 pm

*BREAK*

3:15 – 3:45 pm

### **Approaches to Control of Beryllium in Production and D&D Workplace Activities**

Robert Bistline, PhD, U.S. DOE

3:45 – 4:15 pm

### **A Comprehensive Worker Protection Program in a Beryllium Ceramics Facility**

Michael Kent, MS, CIH, Brush Wellman Inc.

4:15 – 4:45 pm

### **What is a “safe” level of exposure for return to work?**

John Martyny, PhD, CIH, NJC

4:45 – 5:15 pm

### **Setting Administrative Guidelines and Standards**

Paul F. Wambach, CIH, U.S. DOE

