11th Annual
2016 Environmental and Occupational Health
Technical Symposium

Health Effects of Chemical Mixtures in
Environmental and Occupational Health
Welcome

• Introduce Symposium Co-Chair Ty Avendano
  – A few administrative items:
    • Registration
    • Restrooms
    • Emergency exits
  – Overview of Agenda
    • Speakers
    • Breaks and lunch
    • Student presentations
• Introduction of EOH Faculty
Symposium Overview

- Concepts related to the topic: Health Effects of Chemical Mixtures
  - Toxicology
  - Epidemiology
  - Risk Assessment of Mixtures
  - Occupational Exposures to Mixtures
  - Carcinogenesis of Chemical Mixtures
  - Panel Discussion
Toxicology of Mixtures: Polycyclic Aromatic Hydrocarbons

- Toxicology of PAHs
- Consideration for PAH-mixture effects
- Predictive modeling of PAH carcinogenesis for:
  - Hazard identification and risk assessment
  - Early biomarkers
- Studies using *in vitro* 3D normal human bronchial epithelial cells

Susan Tilton, Ph.D.
Environmental and Molecular Toxicology Department
Model and Predict Exposure Space

Binary ADHD outcome
Red=cases, Blue=noncases

Bivariate-smoothed mixture surface of risk using GAMs

mapped by exposure
X-axis: PCB levels
Y-axis: DDE levels
Risk Characterization of Mixtures - Component vs. Whole Mixture Approaches

- **Component-based methods (Practical)**
  - simple models describe complex biological processes-based method
  - Need good toxicity and exposure data on individual components
  - Typically additivity is assumed

- **Whole mixture based assessments (Preferred??)**
  - Need good toxicity and exposure data on the whole mixtures
  - Need to evaluate sufficient similarity
  - Can also assess fractions of the whole mixture
  - Not many assessments done to date

Adapted from EPA, 2011
One Scientist’s Journey from a Regulatory…

CHEMICAL

…to a Non-Regulatory…

MIXTURES

…Federal Government Agency

(And his search for scientists who believe there is room for those who want to focus on “simple” mixtures)
2. Chemicals can affect Hallmarks, e.g. BPA

Normally, PTEN is the “brakes”

- Evade Growth Suppression
- Resist Cell Death (Apoptosis Evasion)
- Sustain Proliferation

Tumor-Promoting Inflammation
- Induce Angiogenesis
- Activate Invasion and Metastases
- Replicative Immortality
- Genetic Instability
- Dysregulated Metabolism
- Tumor Microenvironment

Panel Discussion

• Is the assumption of additivity of effects from exposure to chemical mixtures appropriate? Protective?

• What future advances in the study and evaluation of chemical mixtures do you foresee?
Exposure to Environmental Mixtures

Chemical + Physical

Effects of Chemical + Noise Co-Exposure

Michael J. Sullivan, Ph.D., CIH
Measurements of Hearing Impairment

1. Audiology/
   Hearing Thresholds

2. Morphology/
   Cytocochleogram
Examples of Cochlear Pathology

Intact cochlea

Damaged cochlea
Noise Only Hearing Loss
Toluene Only Hearing Loss

Cytocochleogram – Toluene #2

BAER Thresholds – Toluene #2
Toluene + Noise Hearing Loss

**Cytocochleogram**

617.8 mg/kg - 100 dB

**Baer Thresholds**

617.8 mg/kg - 100 dB

**Percent Distance (mm) Basilar Membrane from Apex**
Total length = 9.66 mm

**Frequency (kHz)**

0.5 1 2 4 8 32 64
Conclusions

• 100 dB noise causes hearing loss
• 617.8 mg Toluene/kg (1000 ppm inhalation equivalent) causes hearing loss
• Noise plus Toluene causes additive hearing loss as measured by both audiometric and pathology metrics