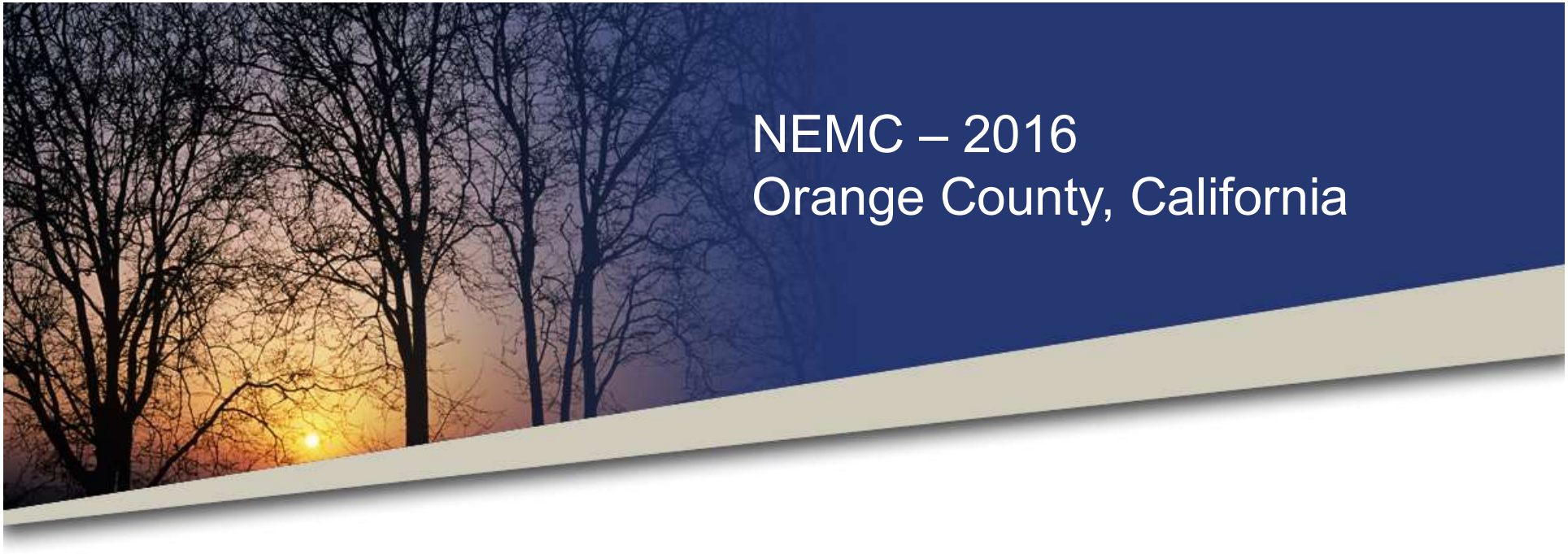

NEMC – 2016
Orange County, California

Overcoming Legacy Obstacles: Validating Methods that Answer Questions

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Agenda

- About Validation and Validity
- Types of Questions Asked
- Types of Methods to Answer
- Some Legacy Obstacles
- A Few Successes
- A Few Challenges

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Definitions

- Success: Validation of methods that answer questions we care about
- Method Validation: More than IDOCs and MDLs …

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Validation

- US EPA – 2005, 2016 Guidance on Validation and Peer Review: General principles for determining and demonstrating that (a) method is suitable for its intended purpose (*i.e.*, yields acceptable accuracy for the analyte, matrix, and concentration range of concern).

- USP/ICH - Analytical Method Validation is the process of demonstrating that an analytical procedure is suitable for its intended purpose.

- ISO 17025 & TNI Validation is the confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled.

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Method Validation Guidance

Validation and Peer Review
of U.S. Environmental Protection Agency
Chemical Methods of Analysis

Prepared for:

The EPA Forum on Environmental Measurements (FEM)

Prepared by:

The FEM Method Validation Team

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Two Grand Divisions …

- This guidance contains recommendations for validating new, rational, quantitative, and chemical methods of analysis, intended for use in analytical laboratories.
- Rational methods' results are not intended to be method dependent. Rational methods determine identifiable chemicals/analytes, for which, several equivalent analytical methods may be available.
- Empirical methods determine a value that can be arrived at only in terms of the method *per se* and serves, by definition, as the only methods for establishing the measurement.

Scope and Applicability - Based on Validation

- Measurement process components validated
- Nature of the analytes and matrices studied
- The range of analyte levels, for which, the method is claimed to be suitable
- Any known limitations and any assumptions, upon which, a method is based
- A description of how the method and analytical parameters chosen meet the data quality objectives for the specific application

Analytical Chemists Want to Know …

- What is the total mass of a contaminant in a given mass of soil/sediment/water, or volume of air?
- What limit of detection (LOD) and limit of quantitation (LOQ) are needed?
- What interferences do I need to overcome?
- When are results due?
- Generally speaking – rational methods

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Data Users Want to Know …

- When will the results be reported, and how much will they cost?
- Are my detections real? Source of contamination?
- Can I use these results for the intended purpose?
- How much impact, if any, do my data indicate?
- What actions are required as a result?
- Very often – Empirical Methods. (*e.g.*, toxicity characteristic leaching procedure [TCLP], particulate, total suspended solids [TSS], hexane extractable material [HEM])

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Method Validation vs. Intended Purpose

- Laboratories and method development efforts focus on rational methods.
- Data users frequently need empirical methods.
- Some empirical methods have been validated and provide important tools for better decision-making.
- Some opportunities for improvement remain.

Some Legacy Obstacles

- Sampling error, especially the nugget-effect in soils and sediments
- Poor knowledge of site-specific uptake of contaminants by terrestrial receptors
- Poor knowledge of site-specific uptake of contaminants by sediment-dwelling fauna and fish
- Poor correlation of measured sediment contamination with toxicity results
- Normalization of results by lipids, total organic carbon (TOC), and solids, with no real consensus on what they are or how to measure

Some Successes

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The Problem of Sampling Error

- Most variability in soil sampling is caused by sampling error - nugget effect of agglomerative organics
- So, MULTI INCREMENT® Sampling (MIS) - combining many increments of soil from points within exposure area was developed by Enviro Stat, and researched by CRREL for surface soil sampling at ranges for energetic compounds
- Differs from normal composites in two ways:
  - Number of increments (grabs) much higher (30 minimum)
  - Entire area of interest (decision unit, exposure area) is represented by each sample
- MIS approach is to overcome single sample variability from:
  - discrete (single-point) sampling
  - composite sampling with limited increments and/or small area of coverage

DOD NDCEE – D. Roote Presentation

Holloman Laboratory Replicates
TNT Results (mg/kg)

Sample Type	Replicates			Corrected Bulk	Mean	Range	Std Dev	% RSD	RPD	Range RPD	
	1	2	3							High	Low
Discrete	1900	230	210	1960	780	210-1900	970	124	86	3	161
Box	1100	1800	1500	3260	1470	1100-1800	351	24	76	58	99
Wheel	0.6	0.37	0.47	0.80	0.48	0.37-0.6	0.12	24	50	29	74
MIS-Ball-HPLC/UV	1700	1700	1600	1600	1670	1600-1700	58	3	4	6	0.2
MIS-Ball-HPLC/MS/MS	1600	1300	1400	1590	1430	1300-1600	153	11	11	0	20
MIS-Puck-HPLC/UV	1500	1400	1700	1890	1530	1400-1700	153	10	21	10	30
MIS-Puck-HPLC/MS/MS	1600	1400	1800	1500	1600	1400-1800	200	13	6	18	7

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DOD NDCEE – D. Roote Presentation

Fort Lewis Live-Fire Laboratory Replicates NG Results Using EVC Tool (mg/kg)

Sample Type	Replicates			Mean	Std Dev	% RSD
	1	2	3			
Discrete	2390	2020	2110	2170	193	9
Box	5320	4730	4950	5000	298	6
Wheel	2470	2380	2550	2470	85	3
MIS-Puck-HPLC/UV	2230	2250	2220	2233	2	0.1

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A Major Success … Using Empirical Methodology

- Drexler, J.W. & Brattin, W.J., An In Vitro Procedure for Estimation of Lead Relative Bioavailability: With Validation, Human and Ecological Risk Assessment 13(2):383-401, March 2007
- Based on Ruby *et al.* TCLP tumbler set up in 40ºC bath at pH < 2. Tumble for 1 h. Filter and analyze for lead.
- Validation! Same soils fed to juvenile swine. Blood analyzed for lead.

Validation Study (of RBALP)

- Performance was evaluated by triplicate analyses of each of 19 test substances by the author and three independent laboratories, and comparison of the results to relative bioavailability (RBA) values measured *in vivo*.
- Measurements were strongly correlated with the *in vivo* RBA values ($r = 0.924$, $p < 0.0001$), with an average absolute error of 10% and an average predictive error of 20%.
- Comparison of results within and between laboratories: inter- and intra-laboratory coefficients of variation (CVs) were 4% and 6%, respectively, and within-sample precision, approximately 7%.
- Based on the results reported here, the RBALP can be effective in providing reliable estimates of lead RBA as predicted by the immature swine model.
- Simple, reproducible, and rapid *in vitro* procedure for estimating the RBA of lead in solid media.

An Empirical Method in Action – US EPA Saving Money on Cleanups

EPA

www.epa.gov/research

science in ACTION

INNOVATIVE RESEARCH FOR A SUSTAINABLE FUTURE

EPA's new testing methods for arsenic and lead in contaminated soil could save millions in cleanup costs

Issue

Cleaning up arsenic and lead at contaminated sites can be an expensive proposition. Currently, if contaminant levels are high, the top layer of soil is removed and transported to a hazardous materials landfill for treatment to isolate and remove toxic metals. The price tag for such remediation activities can reach into the millions of dollars per acre.

However, not all toxic metals present in soil are in a form that can harm humans or animals. Certain forms of arsenic and lead are not fully available, or absorbed by the human body. The amount that is absorbed is referred to as "bioavailable," meaning it is in a form that can enter the bloodstream and affect human health. Improved methods are needed to determine bioavailability of metals to protect human health.

Action

EPA scientists are developing rapid, reliable, inexpensive methods for assessing the bioavailability of arsenic and lead in contaminated soils. This research is part of EPA's Community Public Health Project.

One of these new methods

the mice have absorbed — in other words, the amount that is bioavailable.

EPA scientists are also working on a chemical extraction laboratory method that mimics the human gastrointestinal system. As part of this effort, they are using advanced

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The Receptor's Eye View

To assess exposure to benthic organisms resulting from contaminated sediment evaluation we can:

- Analyze the bulk sediment, model the desorption from sediment to pore water, and model the partitioning to the receptor.

Or …

- Measure uptake by a biomimetic sampler placed in the sediment or pore water.

Success!

- Jonker, Cornellison, Gschwend, Burgess, and many others have demonstrated the predictive validity of polymeric biomimetic equilibrium sampler for predicting uptake by benthic invertebrates and fish.
- SPME (Hawthorne Method, SW-8272, ASTM D7363), Chemical measure of freely dissolved polyaromatic hydrocarbons (PAHs)/APAHs in sediment porewater that predicts toxicity!
- US EPA guidance is here. US EPA is applying the information to refine understanding at Superfund sites nationwide. (Dec 2012, OSWER 9200.1-120 FS)

Success! (Cont.)

New Bedford Harbor – Polychlorinated biphenyls (PCBs). Compared PED, PDMS sheets and SPMD along with caged blue mussels.

Passive sampler and mussel concentrations were related by power regression equations. High PCB Location: r^2 values ranged from 0.83 to 0.97 and all linear relationships were significant ($p <<< 0.05$)

Low PCB Location: r^2 values ranged from 0.75 to 0.91 and all linear relationships were significant ($p < 0.05$)

For agreement w mussel, PED>PDMS>SPMD
Same conference – Hawthorne notes that polyoxymethylene (POM) also fits literature K_{OW}s better than PDMS.

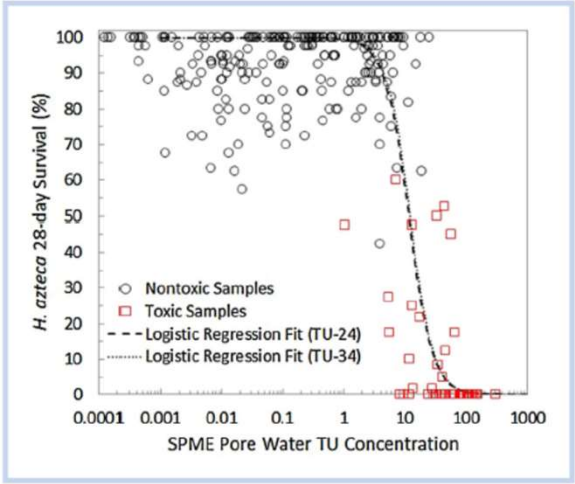

Figure 1. Relationship between freely dissolved porewater toxic units (TU) and *H. azteca* survival when using 24 or 34 PAHs.

Geiger *et al.*

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Boring, but Crucial!

- We must understand why the “quick and dirty” tests like moisture, lipids, and TOC matter the most.
- Lipids – Operationally defined, dependent on solvent, grinder and subsample.
- TOC – No US EPA method for TOC in solid samples. Is it organic? Is it what we should be measuring?
- Do we measure moisture with oven drying or moisture plus volatiles? Are field duplicates evaluated?

Summary

- We have direction, momentum, and progress on:
  - Attacking sampling error
  - Gaining site-specific insight on exposure-uptake in terrestrial receptors
  - Gaining site-specific insight on exposure-uptake in sediment-dwelling receptors and fish
- Let's pay more attention to normalizing factors

Questions?

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