EPA Review of Completed AHETF Exposure Study for Backpack and Handgun Application of Liquid Spray

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Science Review
AHETF Pesticide Handler Scenarios:
"Backpack and Handgun Rights-of-Way"

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AHETF Submissions and EPA Reviews

Two pesticide handler exposure scenarios, three main AHETF reports/submissions, each with an EPA review

AHETF Report No.	Description
AHE400	Field and Analytical Reports for both scenarios
AHE1012	Backpack Applicator Scenario Monograph
AHE1013	Handgun Applicator Scenario Monograph

Overview

- Issues Common to Both Scenarios
  - Study Objectives
  - Study Design
  - Protocol Amendments & Deviations
  - Exposure Monitoring Methods
  - QA/QC
- Issues Specific to Each Scenario
  - Scenario Characteristics
  - Exposure Monitoring Results
  - Review of Analytical Objectives
- Conclusions

Study Objectives

- To capture the range of expected dermal and inhalation exposures for workers making liquid spray pesticide applications in utilities rights-of-way (ROW) and similar areas…
  - With backpack equipment
  - With handgun equipment
- Meet pre-defined analytical objectives/ benchmarks

Study Objectives

Data Analysis Benchmarks	
Primary	For dermal exposure normalized by the amount of active ingredient handled, estimates of key statistics (GM, AM, P95) should be accurate to within 3-fold
Secondary	Adequate analytical power to distinguish a proportional from an independent relationship between dermal exposure and amount of active ingredient handled

General Study Design

- AHETF "Governing Document" (2010) demonstrated that varying configurations of a clustered sampling approach could satisfy objectives
  - Across all scenarios a '5 x 5' (n = 25) configuration was considered most optimal in satisfying objectives while minimizing costs and number of participants
- Presented to the HSRB in October 2010, the "Backpack and Handgun ROW Applicator Scenario Plan" proposed a '7 x 3' configuration for each scenario
- "Diversity selection" employed, though aspects of recruitment were randomized to minimize selection bias

Exposure Monitoring Methods

Dermal Exposure			Inhalation Exposure
Hands	**Head**	**Body**	
Wash  *Multiple samples analyzed separately*	Face/neck wipe  • *Multiple samples analyzed as one* • *Extrapolation to non-wiped areas*	Whole-Body Dosimeter + Socks  *WBD analyzed in 6 sections*	Air pump (~2 L/min)  OVS tube  *Tube front and back sections analyzed separately*

Exposure Monitoring Methods

Analytical Limits (µg/sample)								
Monitoring Matrix	Limit of Detection				Limit of Quantification			
	2,4-D	Fosamine	Glyphosate	Imazapyr	2,4-D	Fosamine	Glyphosate	Imazapyr
Inner Dosimeter	0.30	0.1701	0.139	0.041	1.0			
Socks	0.060	0.0285	0.011	0.0355	0.25			
Hand Rinse	0.30	0.1278	0.179	0.167	1.0			
OVS air sampler (per section)	0.0015	0.0008	0.0016	0.0005	0.005			
Face/Neck Wipe	0.30	0.3123	0.143	0.317	1.0			

Besides OVS tube back section, very few samples < LOD or LOQ

Protocol Amendments

- Changes to aid in finding potential applicators
  - Same employer allowed (different crew, different site, different year)
  - Don't exclude workers who wear leg protection, hard hats, or boots above mid-calf
  - Additional sites similar to ROWs in terms of foliage density/height and terrain
  - Include contiguous U.S. states with original monitoring areas
- Increase in levels of positive controls (i.e., field fortifications) to accommodate occurrences of high exposures
- Various analytical method amendments

EPA found amendments to be reasonable

Protocol Deviations

- Use of validated/finalized analytical methods prior to protocol amendment
- Unavailability of some test substances for purity analysis
- Instances of less-than-4 hour monitoring times (3 applicators)
- Lack of a hand wash at a break (1 applicator)
- Use of non-AHETF-supplied chemical-resistant gloves (1 applicator)
- Inhalation pump off during (non-exposure) times
- Failure to document changes to analytical facilities

EPA believes the deviations do not undermine or compromise the exposure results

Quality Assurance

- AHETF Quality Assurance Unit (QAU) ensures that studies follow EPA Good Laboratory Practice (GLP) Standards (40 CFR part 160)
  - GLP training of research personnel
  - Site/equipment inspections
  - Protocol and amendment review
  - Report auditing
  - Study report included signed Quality Assurance Statements

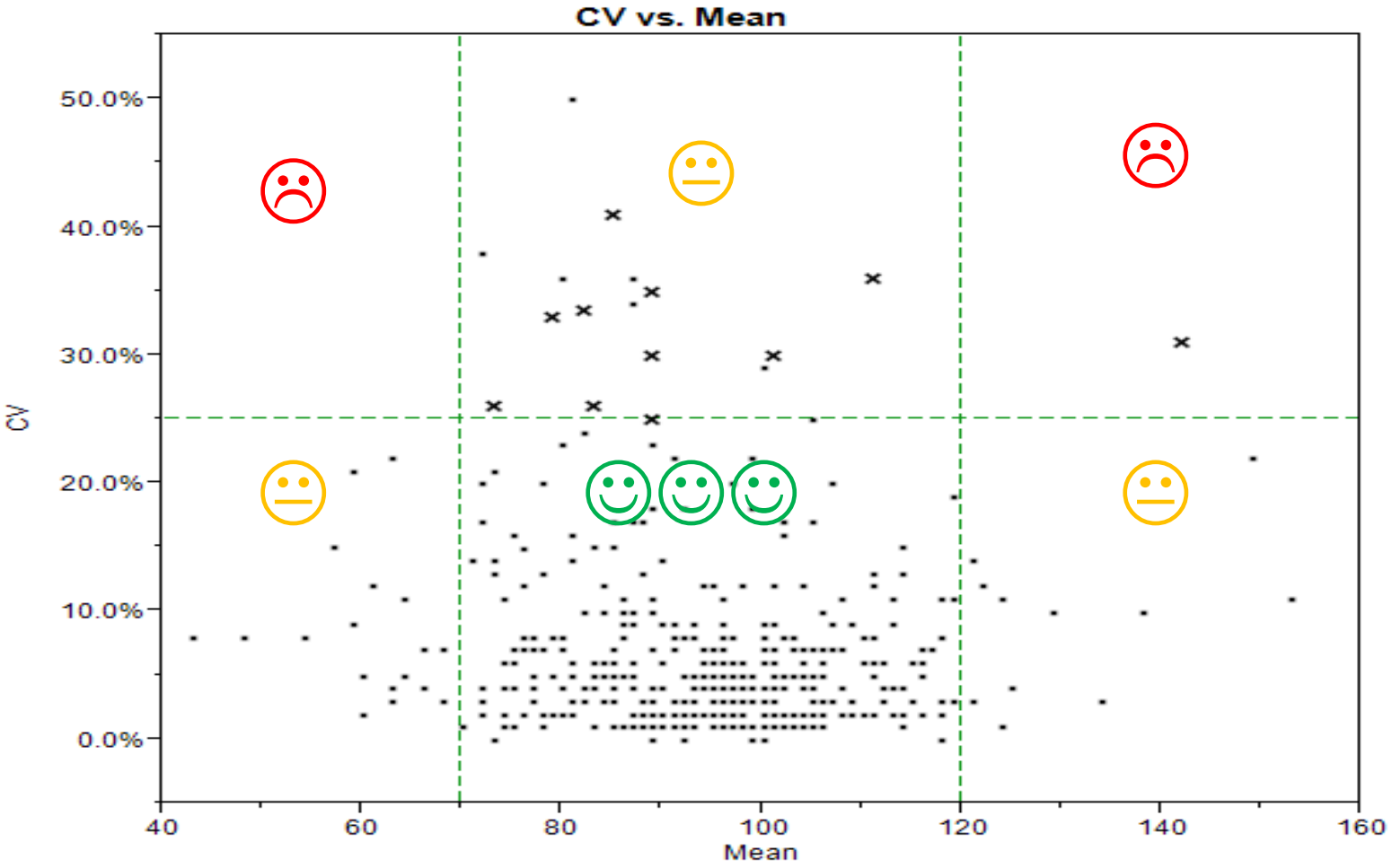
Quality Control Samples

	Negative Controls (blanks)	**Positive Controls (field fortifications or spikes)**

Laboratory	▪ Largely < LOD
	▪ Some detections
	  ▪ Glyphosate: 1 OVS front section
	  ▪ Imazapyr: 16% of WBD and 28% of OVS were between LOD and LOQ
		▪ Average recoveries ranged 89% to 108% (across all fortification levels for each chemical and sampling matrix)

Field	▪ Some detected residues > LOD or LOQ, mostly OVS tubes ▪ No systematic concerns	▪ Average recoveries ranged from 48% to 153% (across all fortification levels for each chemical and sampling matrix) ▪ Unusual results noted
	No corrections to monitoring results for detections in controls	*All monitoring results are corrected up/down to 100% based on field fortification results*

Field Fortification Summary



Displayed: all active ingredients at all fortification levels on all days

Backpack Scenario Characteristics

Scenario Definition:

Application of liquid spray pesticides in utilities rights-of-way (ROW) or areas of similar terrain and foliage density/height/etc. using backpack equipment

Backpack Scenario Characteristics: Activity

- Load backpack (no mixing), manually pressurize, spray foliage
- Walk through area
- "Hack-and-squirt" not excluded (3 of 19 applicators)
- Overhead and below waist spraying

Backpack Scenario Characteristics: Sites

Utility ROW (electric transmission/distribution, pipeline)

Similar areas/treatments (wildlife refuge, park, drainage ditch)

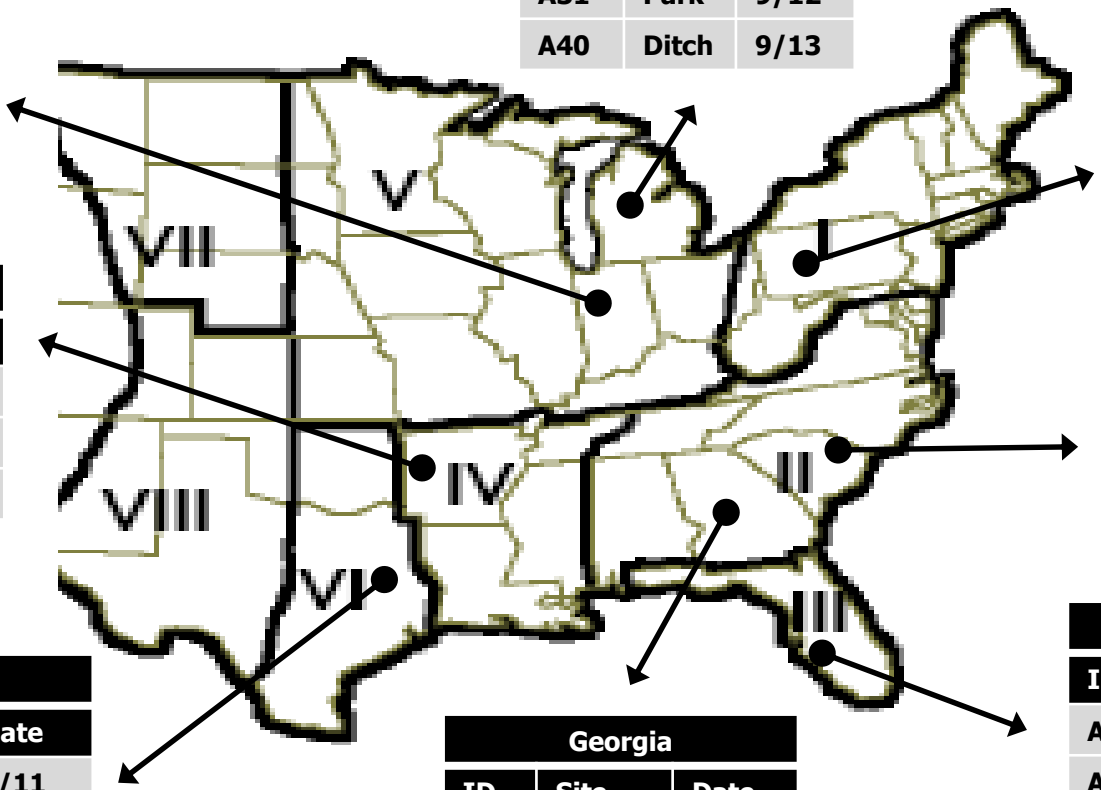
Backpack Scenario Characteristics: Locations/Dates

Indiana		
ID	Site	Date
A16	ROW	5/12
A38	ROW	8/13

Michigan		
ID	Site	Date
A31	Park	9/12
A40	Ditch	9/13

Pennsylvania		
ID	Site	Date
A27	ROW	9/12
A33	ROW	6/13
A34	Park	7/13

Arkansas		
ID	Site	Date
A1	ROW	5/11
A23	ROW	7/12
A24	ROW	8/12



N. & S. Carolina		
ID	Site	Date
A8	ROW	6/11
A20	ROW	6/12

E. Texas		
ID	Site	Date
A2	ROW	5/11
A4	ROW	5/11
A25	ROW	8/12

Georgia		
ID	Site	Date
A10	ROW	10/11

Florida		
ID	Site	Date
A11	Refuge	11/11
A12	ROW	4/12
A13	ROW	4/12

Backpack Scenario Characteristics: Locations/Dates

- Original proposal: 7 'clusters' each with 3 applicators
- To ensure adequate supply of employers and applicators, protocol amendment expanded monitoring areas
  - e.g., WV → WV + DE, MD, OH, PA
- Recruitment difficulties also resulted in "on-demand" style monitoring – many individual applicators were separated significantly in time and place
- Resulting data structure:
  - 9 U.S. states over 3 years
  - 15 'clusters' with 1 or 2 applicators per 'cluster'

Backpack Scenario Characteristics: Workers

N	Gender	Age	Work Experience	Weight	Employment
19*	all male	21 – 53 years	4 months to 15 years	137 – 351 lbs	All commercial applicator employees

*After years of recruitment phase + field phase, AHETF halted monitoring at n=19, instead of 21.

*AHETF anticipated that the data structure – many more clusters than originally planned – would meet objectives, despite not having monitored a total of 21.

*Additional months or years to collect data for two additional applicators potentially of limited value.

Backpack Scenario Characteristics: Equipment

- 9 different makes/models used in monitoring (but no two workers used the same backpack)
- 3-5 gallon tanks
- Hand-pressurized (< 50 psi)
- Spray up to 15-20 feet
- Fan and/or stream pattern

Backpack Scenario Characteristics: Application Info.

	Tank Loads	Spray volume (gals)	Area (acres)	Time (hrs)	AaiH (lb)
Min	2	4.5	0.45	2	0.03
Max	17	64.5	6	10.7	9.65
Avg.	7	22	2.7	6.3	2.6

Backpack Exposure Monitoring Results

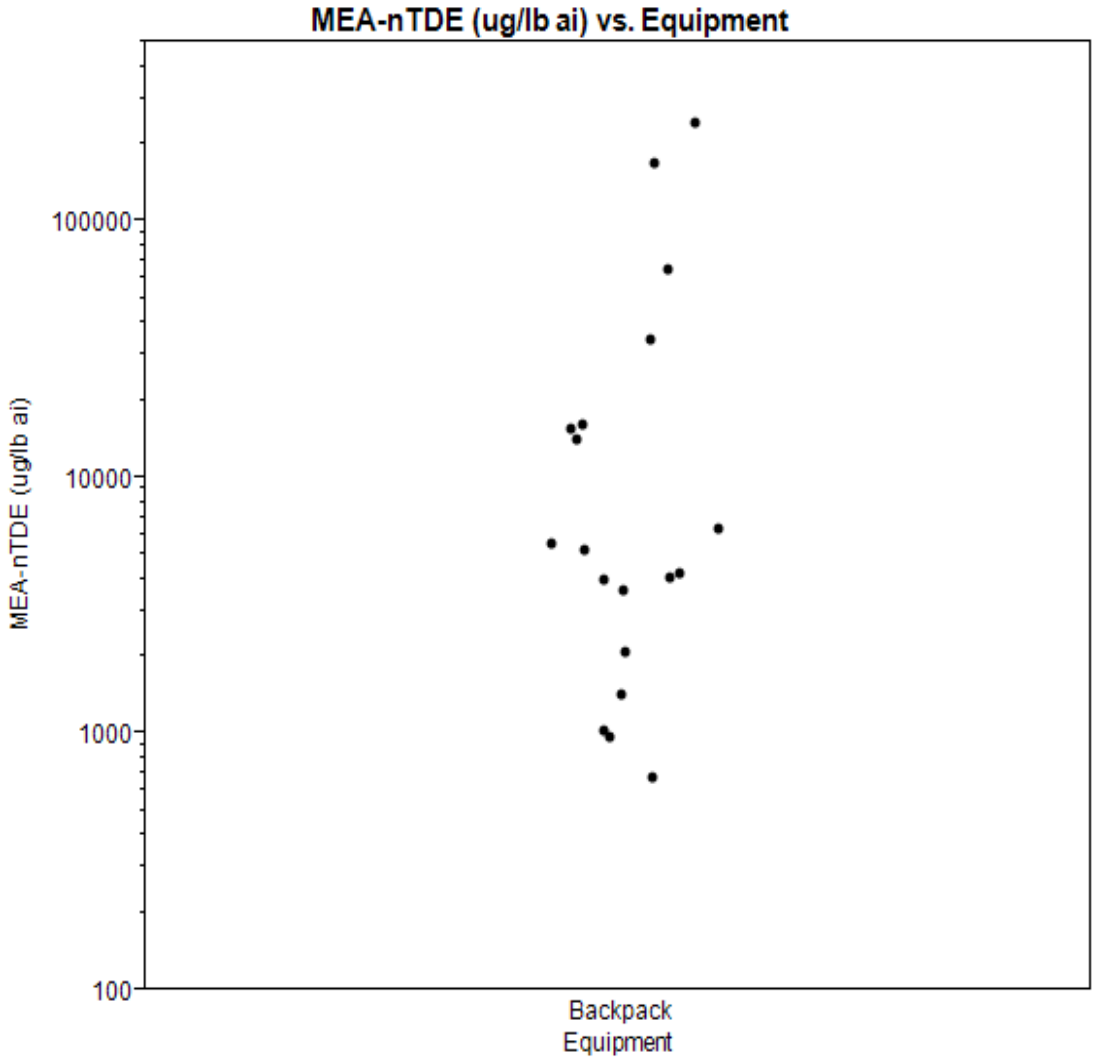
Dermal Exposure (µg)			Inhalation Exposure (µg)
Hands	**Head**	**Body**	
▪ Sum of wash samples ▪ Adjusted upward by a factor of 2 by EPA ("MEA")	Face/neck wipe: ▪ Extrapolated to areas covered by protective eyewear (7 of 19) ▪ Extrapolated to whole head ▪ Adjusted upward by a factor of 2 by EPA ("MEA")	Sum of: ▪ Six WBD sections ▪ Sock dosimeters	▪ Sum of front and back OVS sections ▪ Adjusted by 16.7 LPM breathing rate and pump rate

- Represents workers wearing long-sleeve shirt, pants, chemical-resistant gloves, shoes/socks and no respirator
- All measurements adjusted by average recovery of corresponding field fortification matrix and level
- Left-censored results were few (½ LOD or ½ LOQ used)
- Each worker's total (dermal and inhalation) exposure then divided by the amount of active ingredient they handle (ug/lb ai)

Backpack Exposure Monitoring Results: Dermal

- Adjustment of hand washes and face/neck wipe results
  - Discussed at June 2007 HSRB
  - If measured contribution from hands and face/neck represents between 20% and 60% of the total, measurements are to be adjusted upward by a factor of 2, or provide a validation study supporting the method's efficiency
  - Recent AHETF submission supporting removal of this approach – still in review by EPA
  - Dermal exposure results used by EPA for these scenarios will reflect a 2X adjustment to the hand wash and face/neck wipe measurements - referenced as "MEA"

Backpack Exposure Monitoring Results: Dermal



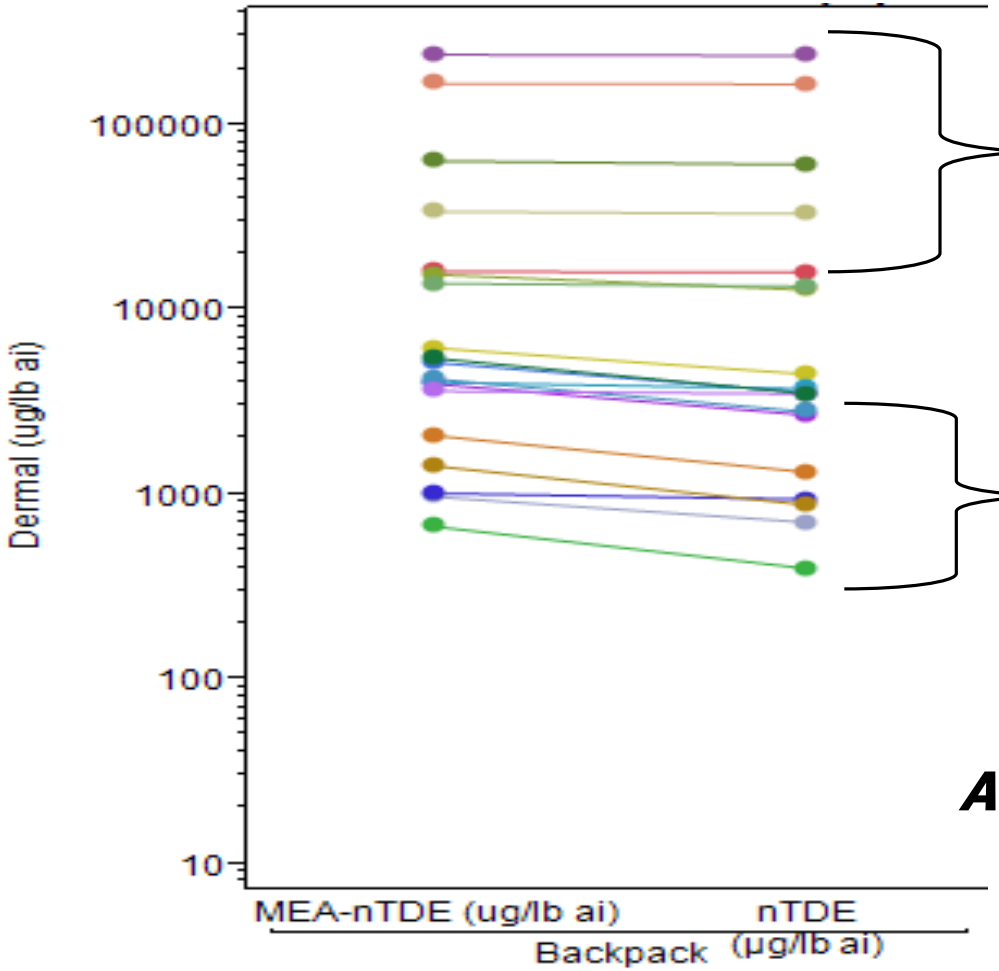
N=19

Simple statistics:

Minimum = 675 ug/lb ai
Maximum = 241,293 ug/lb ai
A. Mean = 31,273 ug/lb ai
P95 = 176,086 ug/lb ai

Backpack Exposure Monitoring Results: Dermal

MEA vs non-MEA

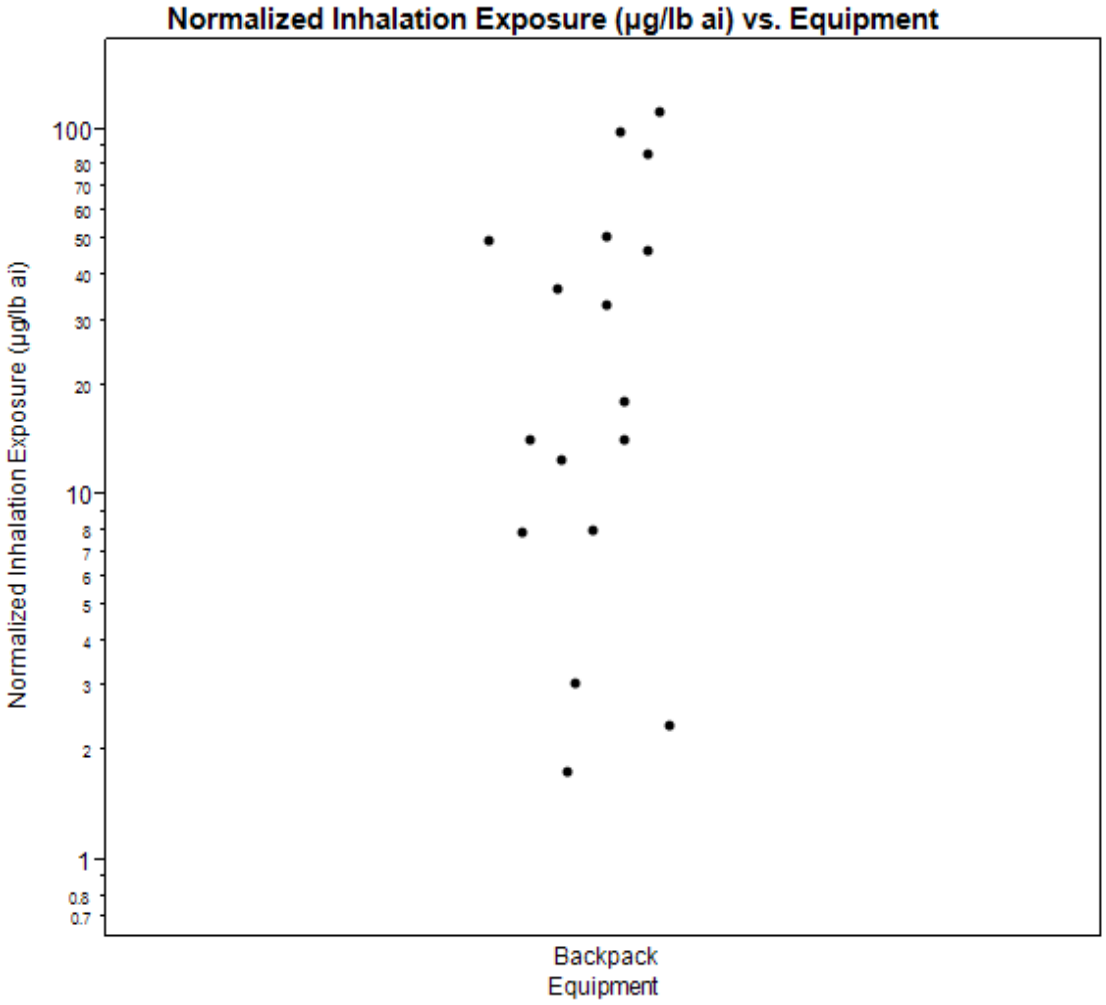


1-4% contribution

47-69% contribution

Average contribution = 27%

Backpack Exposure Monitoring Results: Inhalation



N=17 (two invalid samples)

Simple statistics:

Minimum = 1.74 ug/lb ai
Maximum = 112 ug/lb ai
A. Mean = 35 ug/lb ai
P95 = 101 ug/lb ai

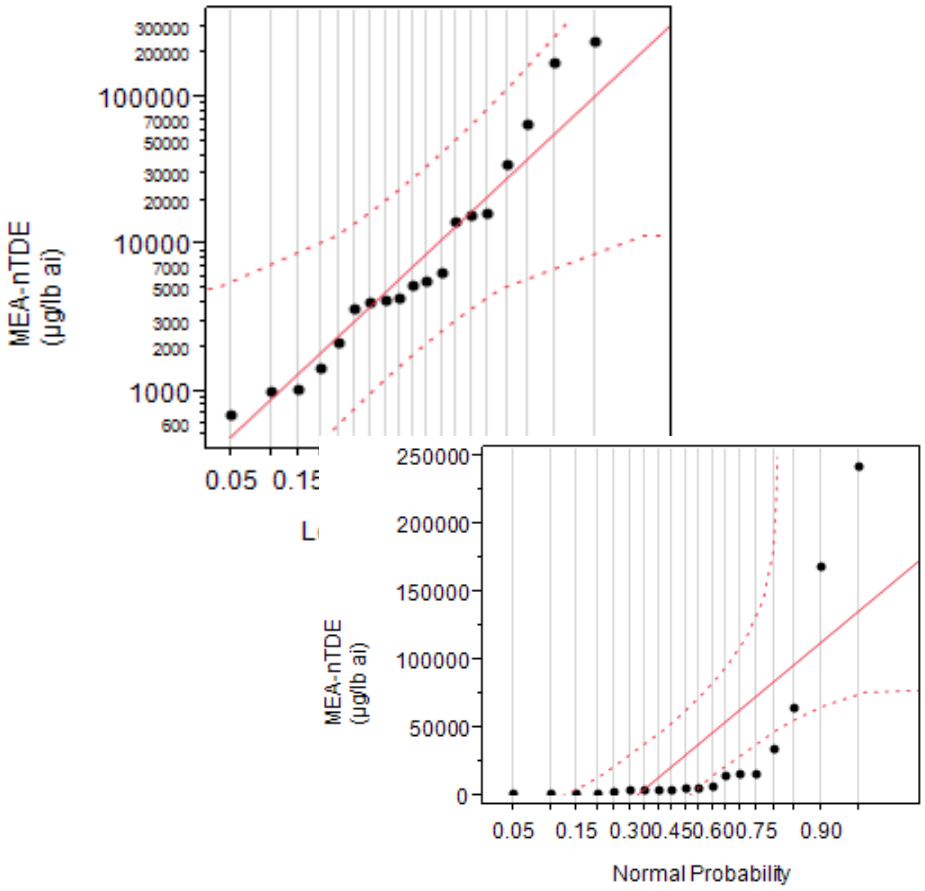
Analysis of Backpack Exposure Monitoring Results

- Estimates of exposures normalized by amount of active ingredient handled ("unit exposures") using three methods
  - Empirical estimates (simple statistics)
  - Simple random sample (lognormal, independent)
  - Mixed model (lognormal, nested)
- Format pertains to primary analytical objective

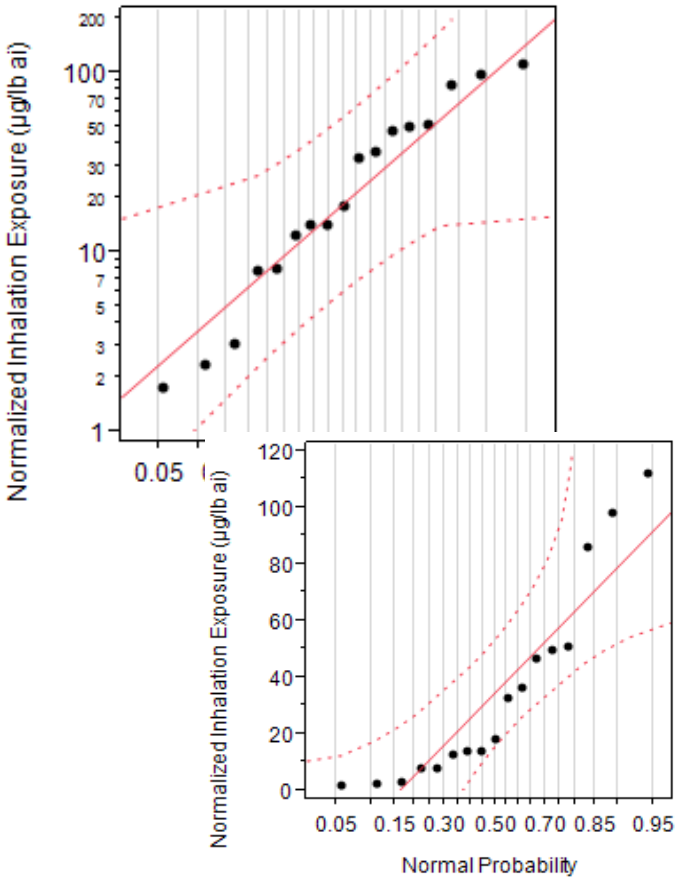
Backpack Exposure Monitoring Results: Distributional Fit

Lognormal Probability Plots

Dermal



Inhalation



Backpack Exposure Monitoring Results: Data Structure

- 15 clusters – 1 or 2 applicators per cluster
- AHETF analysis properly incorporated cluster effect ("ICC")

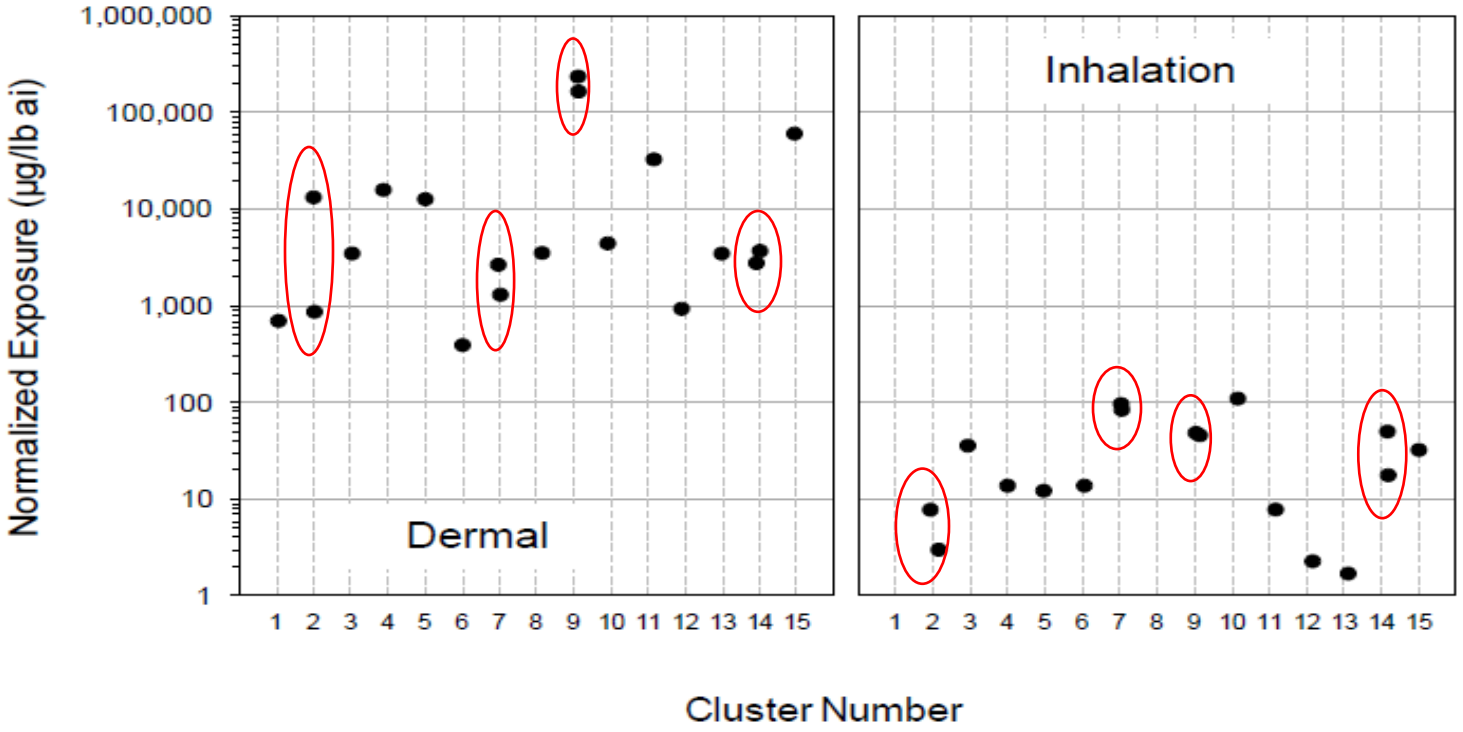


Figure from AHE1012 Appendix D (non-MEA dermal values shown)

Backpack Exposure Monitoring Results: Statistics

- Considering data structure, lognormal mixed-model is most appropriate
  - $AM_M = GM_M * e^{(0.5*(\ln GSD_M)^2)}$
  - $P95_M = GM_M * GSD_M^{(1.645)}$
- Confidence intervals via bootstrapping (10,000 simulations)

	Unit Exposures (µg/lb ai)				
	GSD_M	**ICC**	**GM_M**	**AM_M**	**$P95_M$**
Dermal	5.1 (2.9 – 9.2)	0.75 (0.00 – 0.97)	6,843 (3,006 – 15,664)	26,052 (8,144 – 101,555)	100,769 (28,549 – 347,158)
Inhalation	3.7 (2.3 – 6.2)	0.85 (0.38 – 0.98)	16.8 (8.3 – 34.3)	39.8 (15.8 – 113.1)	145.8 (47.9 – 427.6)

"M" denotes mixed-model estimates
GSD = geometric standard deviation
ICC = intra-class correlation
GM = geometric mean
AM = arithmetic mean
P95 = 95th percentile

Backpack Exposure Analysis: Primary Objective

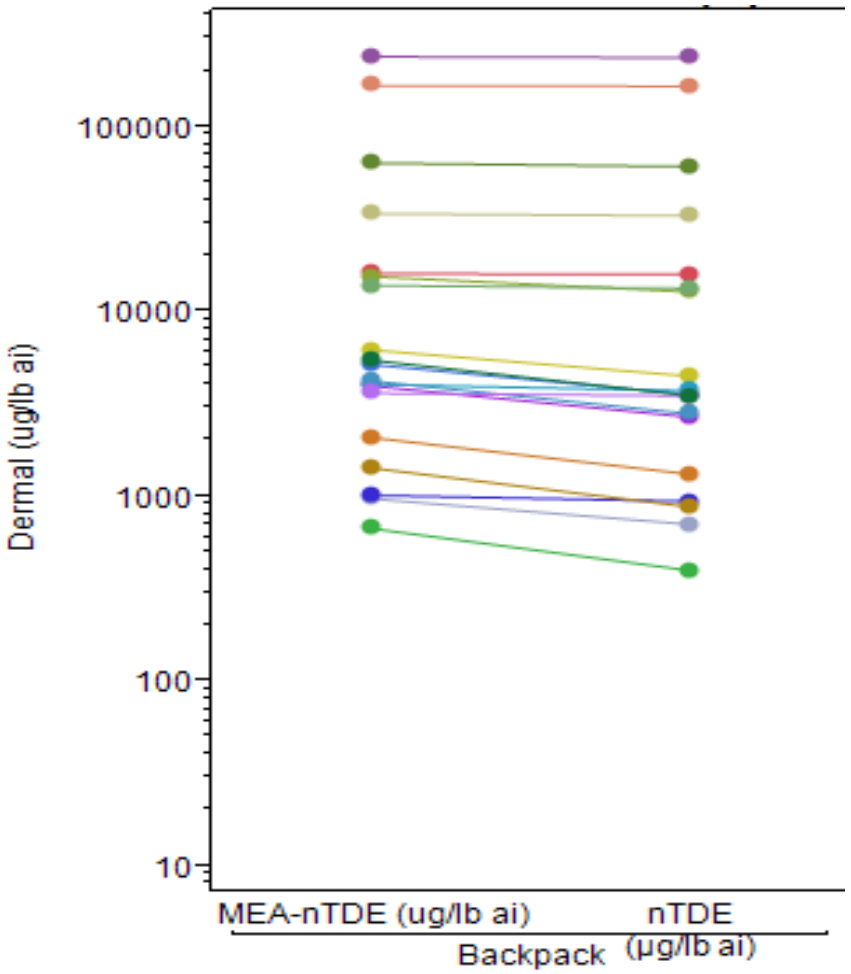
- Accuracy benchmark – no more than 3-fold
  - Described as "fold relative accuracy (fRA)" or "k-factor"

Statistic	fRA ("K factor")	
	Dermal (MEA)	Inhalation
GM_M	2.3	2.0
AM_M	3.5	2.7
$P95_M$	3.5	3.0

- Benchmark not met: dermal k-factors > 3
  - Original '7x3' proposal would have resulted in even less accuracy
- To meet 3-fold benchmark, AHETF demonstrated additional monitoring of 10-16 applicators would be necessary

Backpack Exposure Analysis: Primary Objective

- Effect of MEA
  - For each applicator, double hand washes and face/neck wipes
  - In this case, MEA *decreases* variability
  - Resulting in slightly *smaller* (parametric) arithmetic mean and P95 and *better* accuracy than non-MEA
- EPA will continue to use MEA dermal data



Backpack Exposure Analysis: Secondary Objective

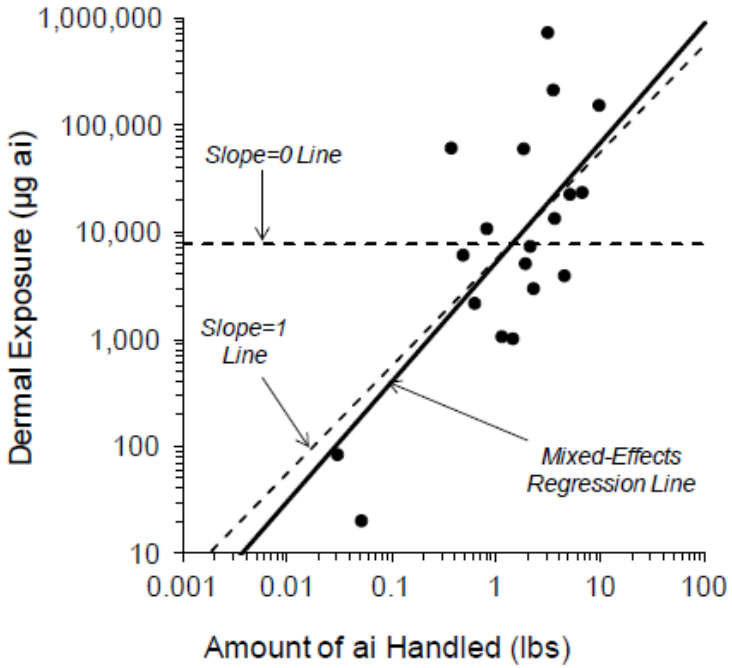
- For routine EPA handler assessments, exposure is predicted from amount of active ingredient handled, which assumes the two are proportional
- Objective: design study such that there is 80% statistical power to distinguish independence from proportionality between *dermal* exposure and amount of active ingredient handled
  - Objective is not whether proportionality is supported – its whether the design provided reasonable power to evaluate the relationship

Backpack Exposure Analysis: Secondary Objective

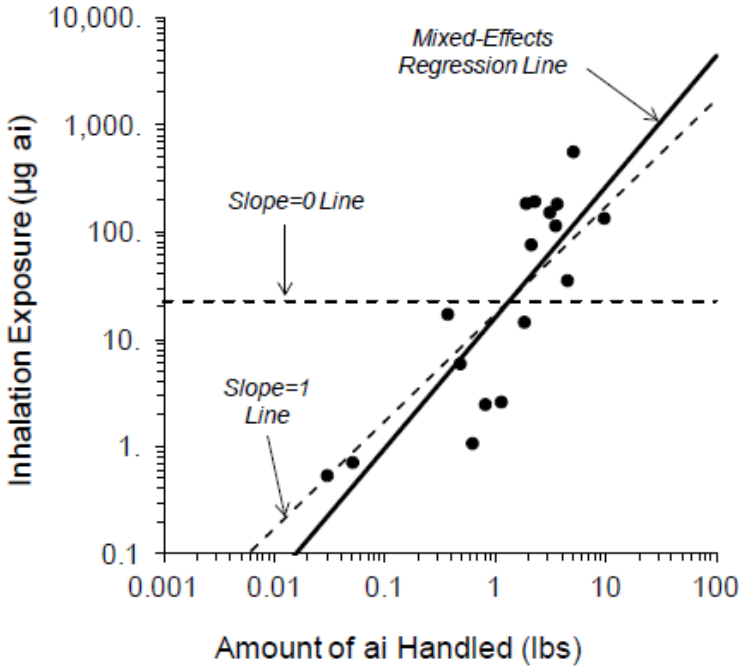
- Mixed-model regression
  - log(exposure) vs. log(AaiH)
  - If width of 95% CI is 1.4 or less, the study design provided at least 80% power
  - EPA is satisfied with proportionality assumption when 95% confidence intervals of regression slope includes 1

Backpack Exposure Analysis: Secondary Objective

Dermal



Inhalation



Figures from AHE1012 Appendix D
(Non-MEA dermal values shown – MEA does not have significant effect)

Backpack Exposure Analysis: Secondary Objective

Mixed-Model Regression Slope Results			
Exposure Route	**Slope Estimate**	**95% CI**	**95% CI Width**
Dermal (MEA)	1.12	0.56 – 1.67	1.11
Inhalation	1.22	1.00 – 1.44	0.44

- Secondary benchmark met: post-hoc analysis shows at least 80% power
- Proportionality with AaiH consistent with dermal and inhalation exposure data

Backpack Exposure Results: Additional Analyses

- EPA visually compared results for certain aspects of the backpack applicator scenario
  - Sites (ROW vs non-ROW)
  - Spraying overhead (no/rarely vs. some vs. yes/often)
  - Inclusion of "hack-and-squirt" (yes/no)
  - Use of (non-chemical) protective leg gear (yes/no)
- No visible differences sufficient to pursue from a regulatory context

Handgun Scenario Characteristics

Scenario Definition:

Application of liquid spray pesticides in utilities rights-of-way (ROW) or areas of similar terrain and foliage density/height/etc. using handgun equipment

Handgun Scenario Characteristics: Activity

- No mixing of solution
- Ride vehicle and spray, sometimes walk through area
- Overhead and below waist spraying
- "Hack-and-squirt" not excluded (but no workers conducted)

Handgun Scenario Characteristics: Sites

Utility ROW (electric transmission/distribution and pipeline)

Similar areas/treatments (airport fence line, roadside, drainage ditch)

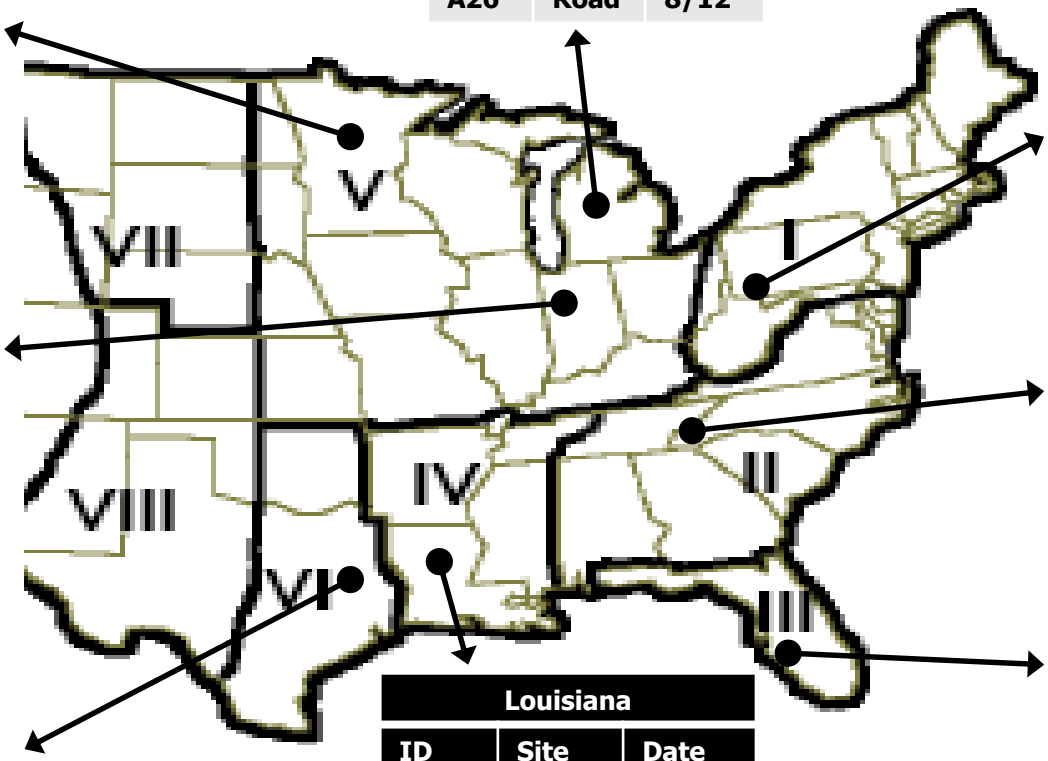
Handgun Scenario Characteristics: Locations/Dates

Minnesota		
ID	Site	Date
A32	ROW	6/13
A37	ROW	7/13

Michigan		
ID	Site	Date
A26	Road	8/12

Penn. & W. Virginia		
ID	Site	Date
A28	ROW	9/12
A29	ROW	9/12
A30	ROW	9/12

Indiana		
ID	Site	Date
A21	ROW	7/12
A22	ROW	7/12
A35	ROW	7/13



N. Carolina & Tenn.		
ID	Site	Date
A9	ROW	6/11
A19	ROW	6/12
A39	ROW	9/13

E. Texas		
ID	Site	Date
A3	ROW	5/11
A5	Ditch	5/11
A18	ROW	5/12

Louisiana		
ID	Site	Date
A14	Fence	4/12
A15	ROW	5/12
A17	ROW	5/12

Florida		
ID	Site	Date
A6	ROW	6/11
A7	ROW	6/11
A36	ROW	7/13

Handgun Scenario Characteristics: Locations/Dates

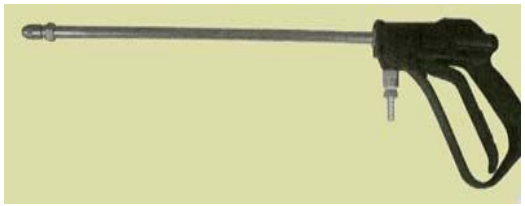
- Original proposal: 7 'clusters' each with 3 applicators
- To ensure adequate supply of employers and applicators, protocol amendment expanded monitoring areas
  - e.g., WV → WV + DE, MD, OH, PA
- Recruitment difficulties also resulted in "on-demand" style monitoring – many individual applicators were separated significantly in time and place
- Resulting data structure:
  - 10 U.S. states over 3 years
  - 13 'clusters' with 1 to 3 applicators per 'cluster'

Handgun Scenario Characteristics: Workers

N	Gender	Age	Work Experience	Weight	Employment
21	all male	19 – 68 years	2 months to 34 years	127 – 251 lbs	• 15 commercial applicator employees • 5 utility company employees • 1 commercial applicator (owner)

Handgun Scenario Characteristics: Equipment

- Handgun



- Hose/reel, mechanical pump, tank

- Vehicle (trucks, ATVs, tractors)

Handgun Scenario Characteristics: Application Info.

	Spray Pressure (psi)	Spray volume (gals)	Area (acres)	Time (hrs)	AaiH (lb)
Min	30	80	0.36	3	0.077
Max	800	2900	52	11	46
Avg.	171	459	12	7	12

Handgun Exposure Monitoring Results

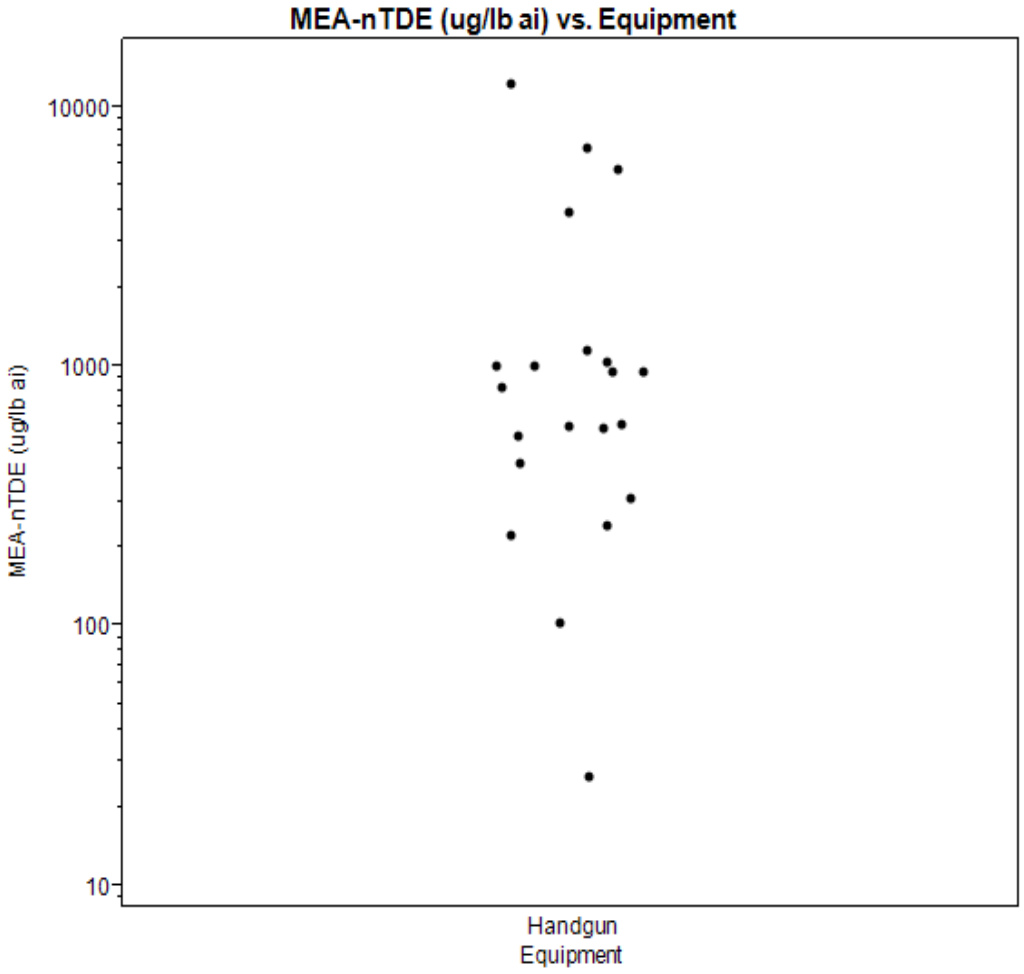
Dermal Exposure (µg)			Inhalation Exposure (µg)
Hands	**Head**	**Body**	
▪ Sum of wash samples ▪ Adjusted upward by a factor of 2 by EPA	Face/neck wipe: ▪ Extrapolated to areas covered by protective eyewear (12 of 21) ▪ Extrapolated to whole head ▪ Adjusted upward by a factor of 2 by EPA	Sum of: ▪ Six WBD sections ▪ Sock dosimeters	▪ Sum of front and back OVS sections ▪ Adjusted by 16.7 LPM breathing rate and pump rate

- Represents workers wearing long-sleeve shirt, pants, chemical-resistant gloves, shoes/socks and no respirator
- All measurements adjusted by average recovery of corresponding field fortification matrix and level
- Left-censored results were few (½ LOD or ½ LOQ used)
- Each worker's total (dermal and inhalation) exposure then divided by the amount of active ingredient they handle (ug/lb ai)

Handgun Exposure Monitoring Results: Dermal

- Adjustment of hand washes and face/neck wipe results
  - Discussed at June 2007 HSRB
  - If measured contribution from hands and face/neck represents between 20% and 60% of the total, measurements are to be adjusted upward by a factor of 2, or provide a validation study supporting the method's efficiency
  - Recent AHETF submission supporting removal of this approach – still in review by EPA
  - Dermal exposure results used by EPA for these scenarios will reflect a 2X adjustment to the hand wash and face/neck wipe measurements - referenced as "MEA"

Handgun Exposure Monitoring Results: Dermal

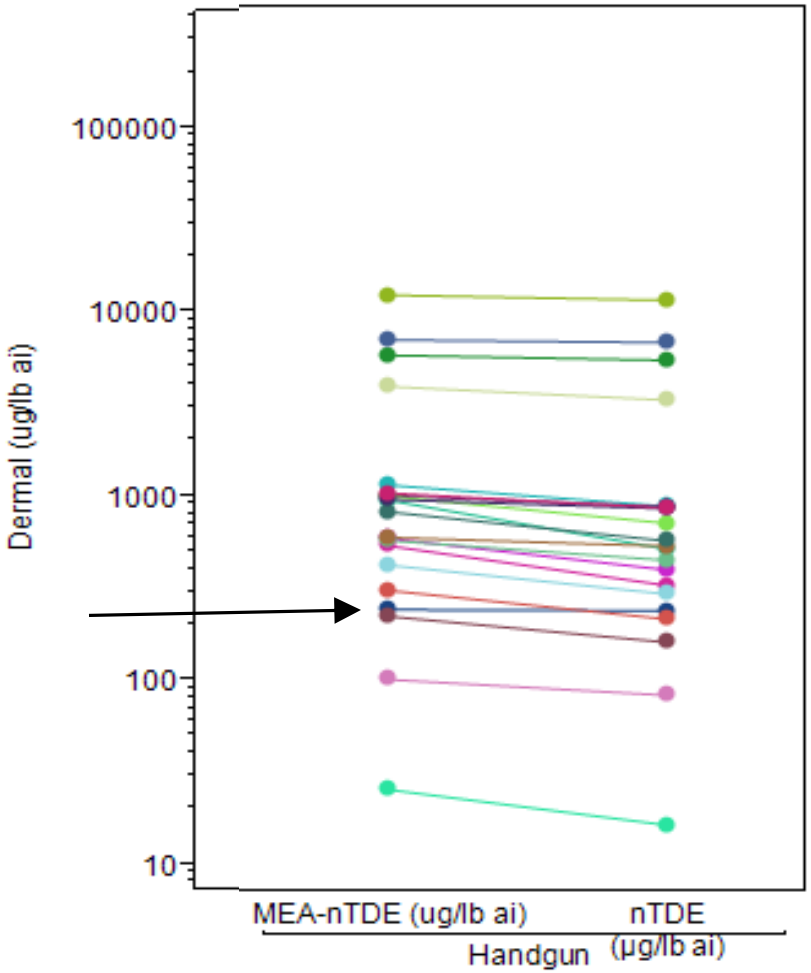


N=21

Simple statistics:

Minimum = 26 ug/lb ai
Maximum = 12,123 ug/lb ai
A. Mean = 1,868 ug/lb ai
P95 = 6,942 ug/lb ai

Handgun Exposure Monitoring Results: Dermal



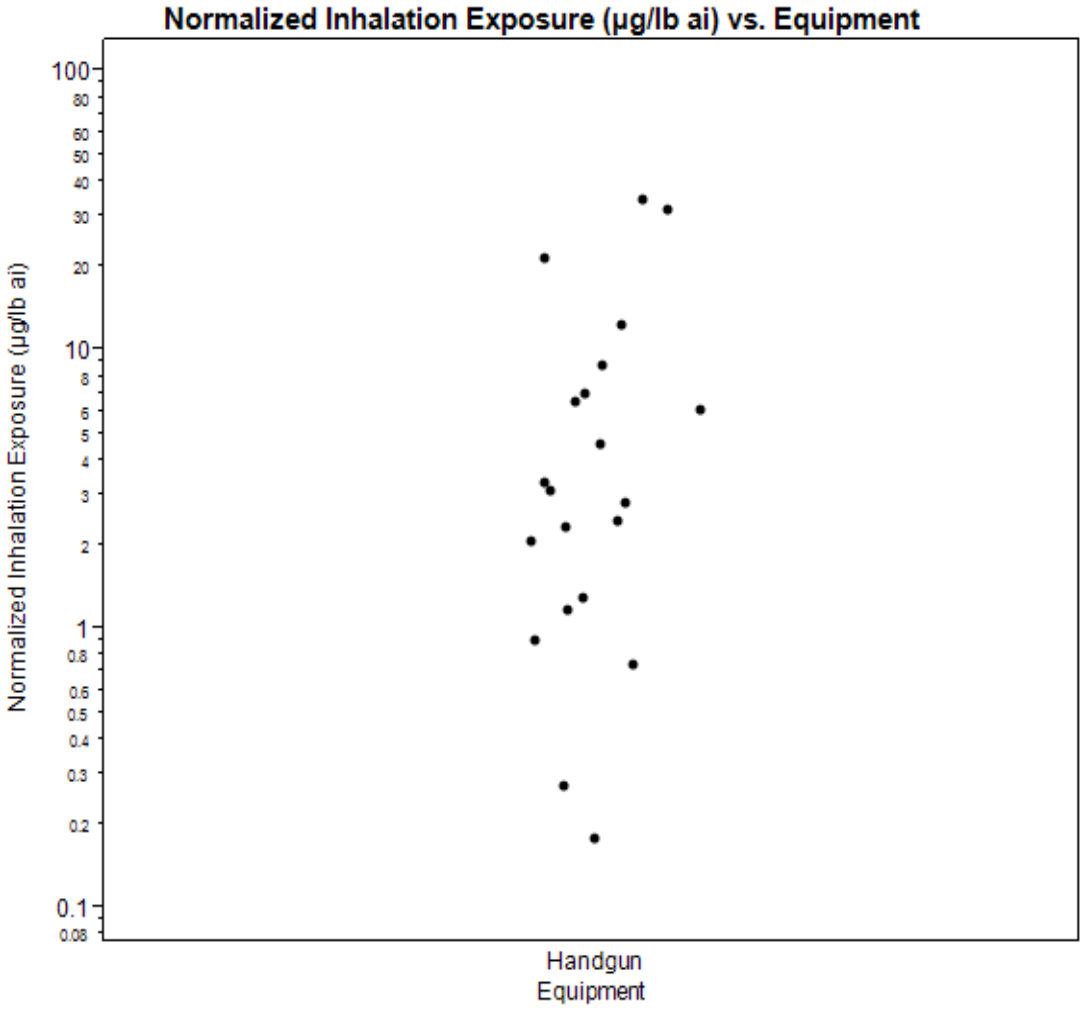
MEA vs non-MEA

1-7% contribution

11-84% contribution

Average contribution = 30%

Handgun Exposure Monitoring Results: Inhalation



N=21

Simple statistics:

Minimum = 0.18 ug/lb ai
Maximum = 35 ug/lb ai
A. Mean = 7 ug/lb ai
P95 = 32 ug/lb ai

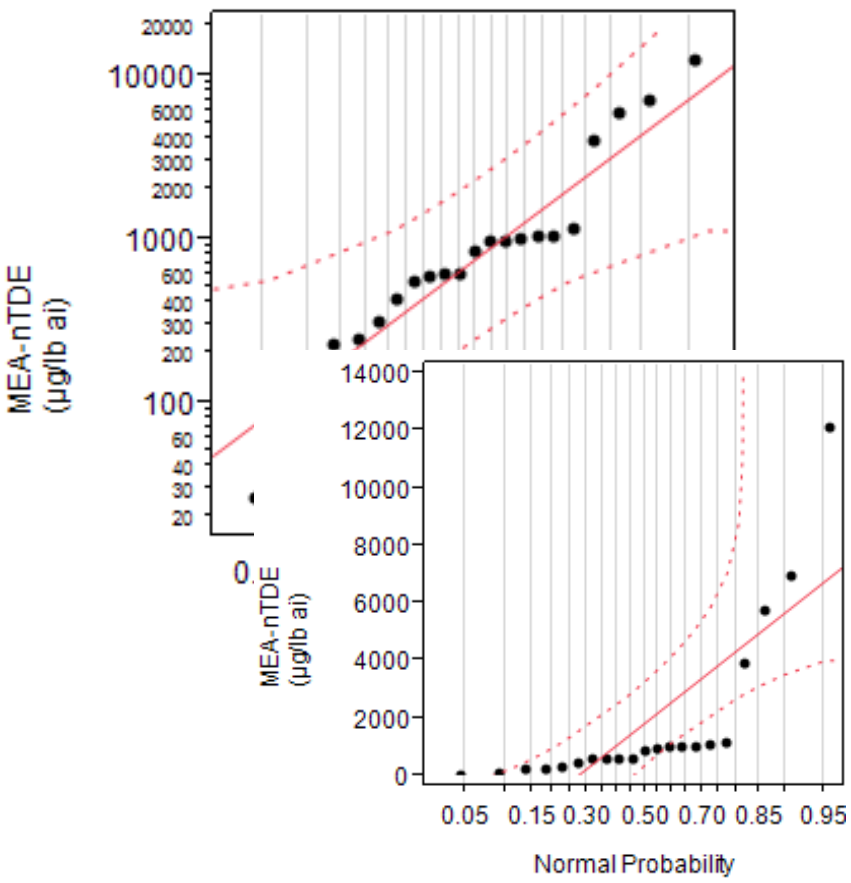
Analysis of Handgun Exposure Monitoring Results

- Estimates of exposures normalized by amount of active ingredient handled ("unit exposures") using three methods
  - Empirical estimates (simple statistics)
  - Simple random sample (lognormal, independent)
  - Mixed model (lognormal, nested)
- Format pertains to primary analytical objective

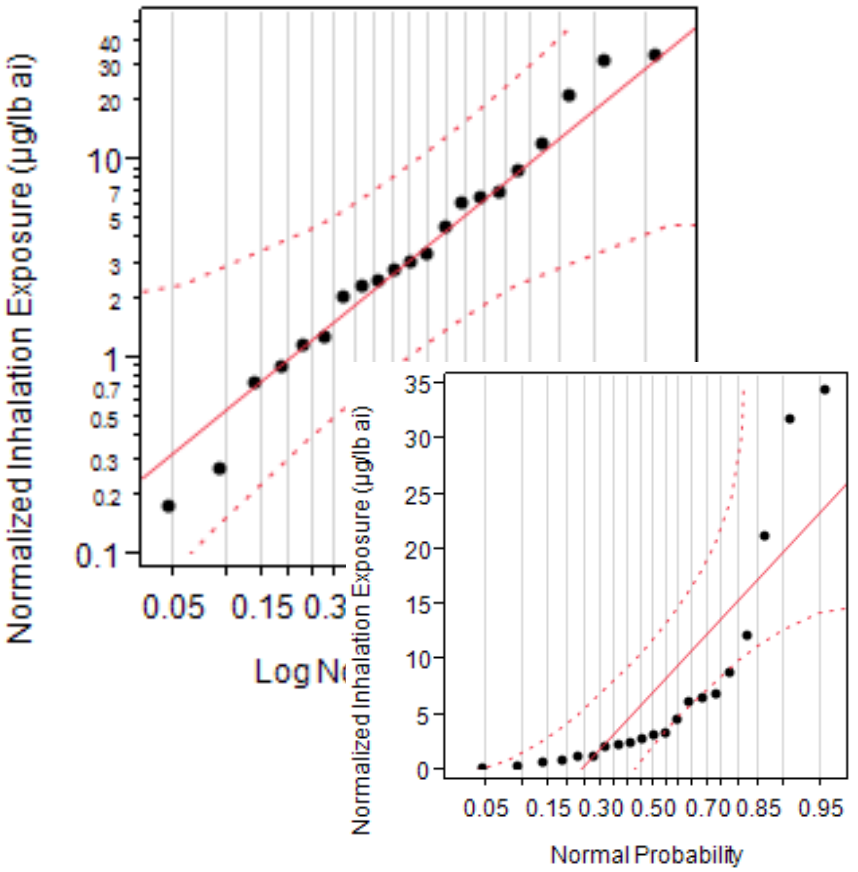
Handgun Exposure Monitoring Results: Distributional Fit

Lognormal Probability Plots

Dermal



Inhalation



Handgun Exposure Monitoring Results: Data Structure

- 13 clusters – 1 to 3 applicators per cluster
- AHETF analysis properly incorporated cluster effect ("ICC")

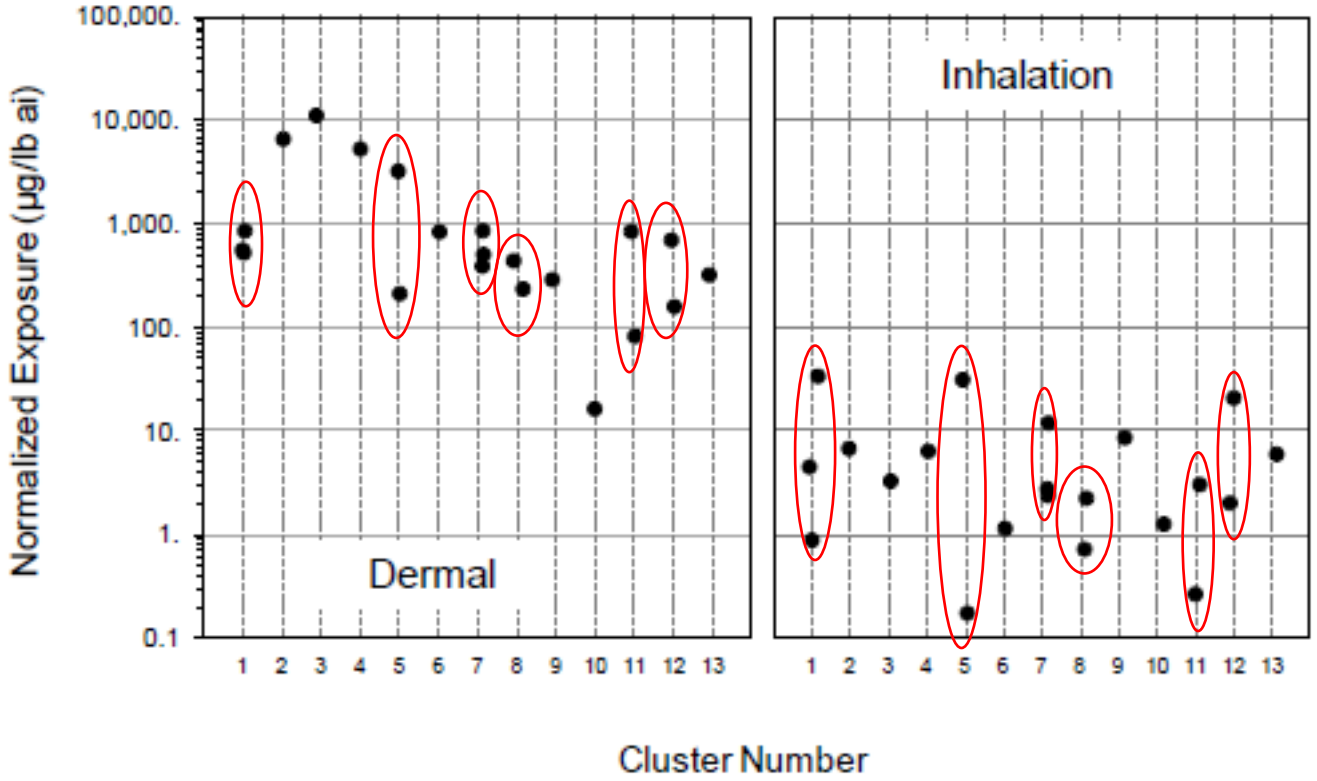


Figure from AHE1013 Appendix D (non-MEA dermal values shown)

Handgun Exposure Monitoring Results: Statistics

- Considering data structure, lognormal mixed-model is most appropriate
  - $AM_M = GM_M * e^{(0.5*(\ln GSD_M)^2)}$
  - $P95_M = GM_M * GSD_M^{(1.645)}$
- Confidence intervals via bootstrapping (10,000 simulations)

	Unit Exposures (µg/lb ai)				
	GSD_M	**ICC**	**GM_M**	**AM_M**	**$P95_M$**
Dermal	4.1 (2.7 – 6.4)	0.00 (0.00 – 0.68)	762 (416 – 1401)	2,051 (906 – 5,317)	7,713 (2,988 – 20,244)
Inhalation	4.1 (2.7 – 6.3)	0.00 (0.00 – 0.68)	3.24 (1.77 – 5.94)	8.68 (3.84 – 22.4)	32.6 (12.7 – 85.4)

"M" denotes mixed-model estimates
GSD = geometric standard deviation
ICC = intra-class correlation
GM = geometric mean
AM = arithmetic mean
P95 = 95th percentile

Handgun Exposure Analysis: Primary Objective

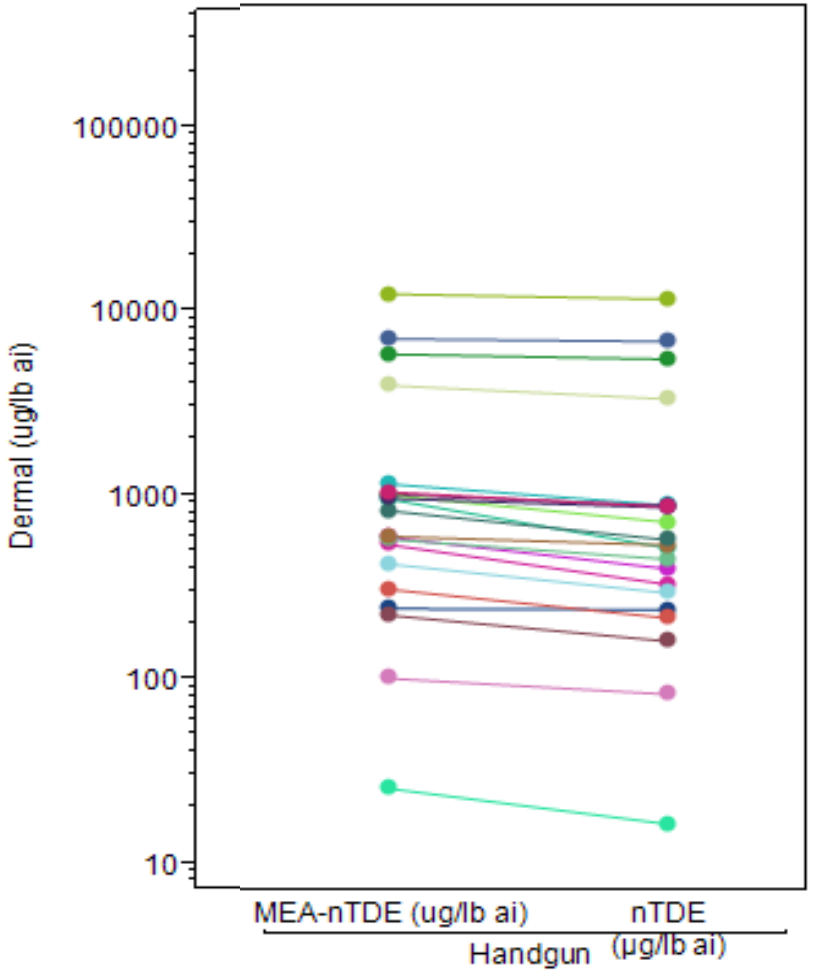
- Accuracy benchmark – no more than 3-fold
  - Described as "fold relative accuracy (fRA)" or "k-factor"

Statistic	fRA ("K factor")	
	Dermal (MEA)	Inhalation
GM_M	1.8	1.8
AM_M	2.4	2.4
$P95_M$	2.6	2.6

- Benchmark met
  - Original '7x3' proposal might not have met benchmark

Handgun Exposure Analysis: Primary Objective

- Effect of MEA
  - For each applicator, double hand washes and face/neck wipes
  - More even distribution of MEA – no meaningful change in variability
- Thus, unlike backpack, MEA parametric statistics are greater than non-MEA results and accuracy is unchanged



Handgun Exposure Analysis: Secondary Objective

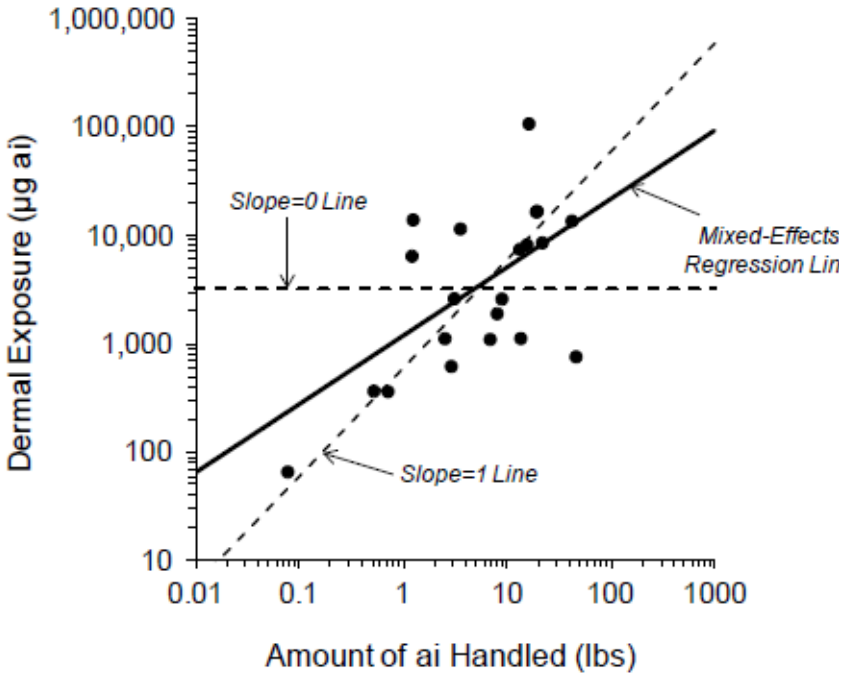
- For routine EPA handler assessments, exposure is predicted from amount of active ingredient handled, which assumes the two are proportional
- Objective: design study such that there is 80% statistical power to distinguish independence from proportionality between *dermal* exposure and amount of active ingredient handled
  - Objective is not whether proportionality is supported – its whether the design provided reasonable power to evaluate the relationship

Handgun Exposure Analysis: Secondary Objective

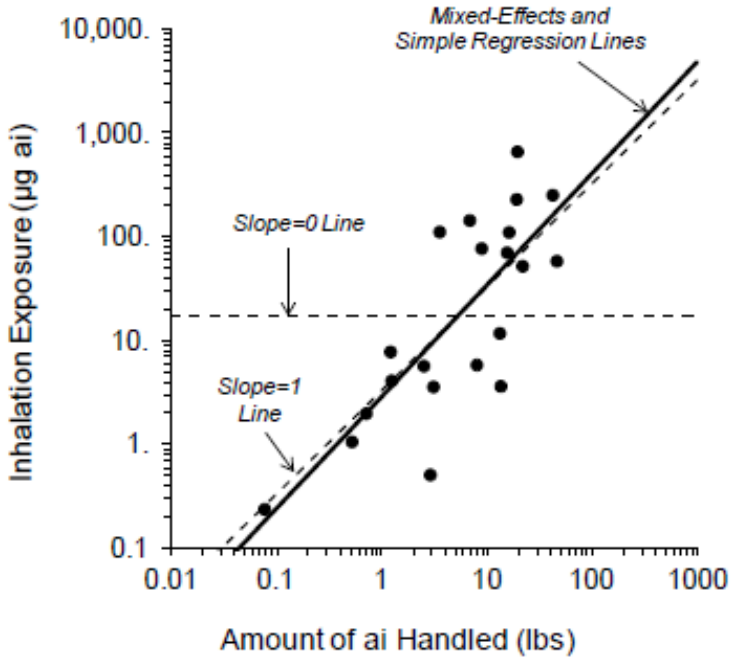
- Mixed-model regression
  - log(exposure) vs. log(AaiH)
  - If width of 95% CI is 1.4 or less, the study design provided at least 80% power
  - EPA is satisfied with proportionality assumption when 95% confidence intervals of regression slope includes 1

Handgun Exposure Analysis: Secondary Objective

Dermal



Inhalation



Figures from AHE1013 Appendix D
(Non-MEA dermal values shown – MEA does not have significant effect)

Handgun Exposure Analysis: Secondary Objective

Mixed-Model Regression Slope Results			
Exposure Route	**Slope Estimate**	**95% CI**	**95% CI Width**
Dermal (MEA)	0.64	0.25 – 1.00	0.75
Inhalation	1.08	0.66 – 1.49	0.83

- Secondary benchmark met: post-hoc analysis shows at least 80% power
- Proportionality with AaiH consistent with dermal and inhalation exposure data

Handgun Exposure Results: Additional Analyses

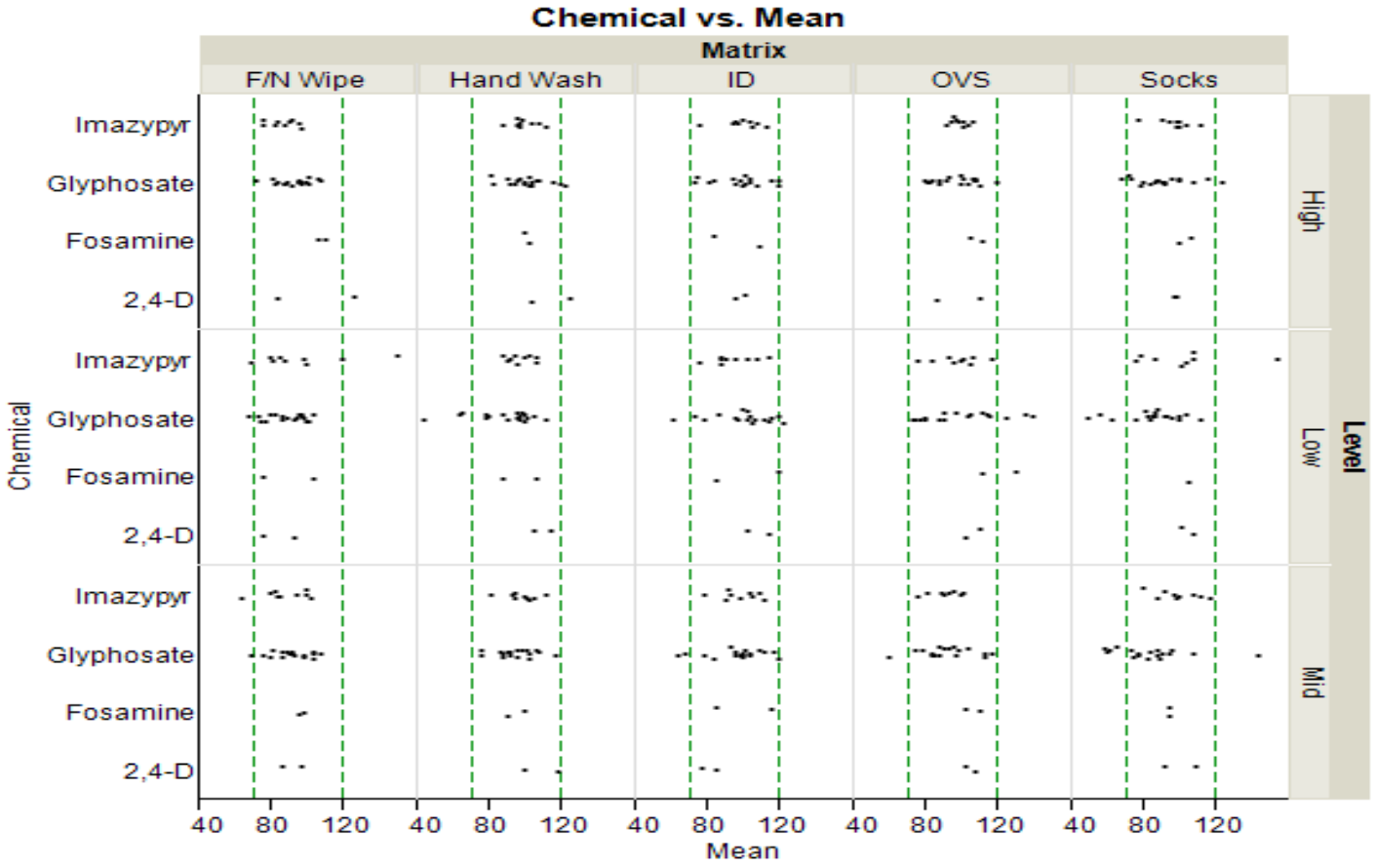
- EPA visually compared results for certain aspects of the handgun applicator scenario
  - Sites (ROW vs non-ROW)
  - Spraying overhead (no/rarely vs. some vs. yes/often)
  - Spraying from vehicle vs. walking (vehicle, both, walk)
  - Use of (non-chemical) protective leg gear (yes/no)
- No visible differences sufficient to pursue from a regulatory context

Conclusions

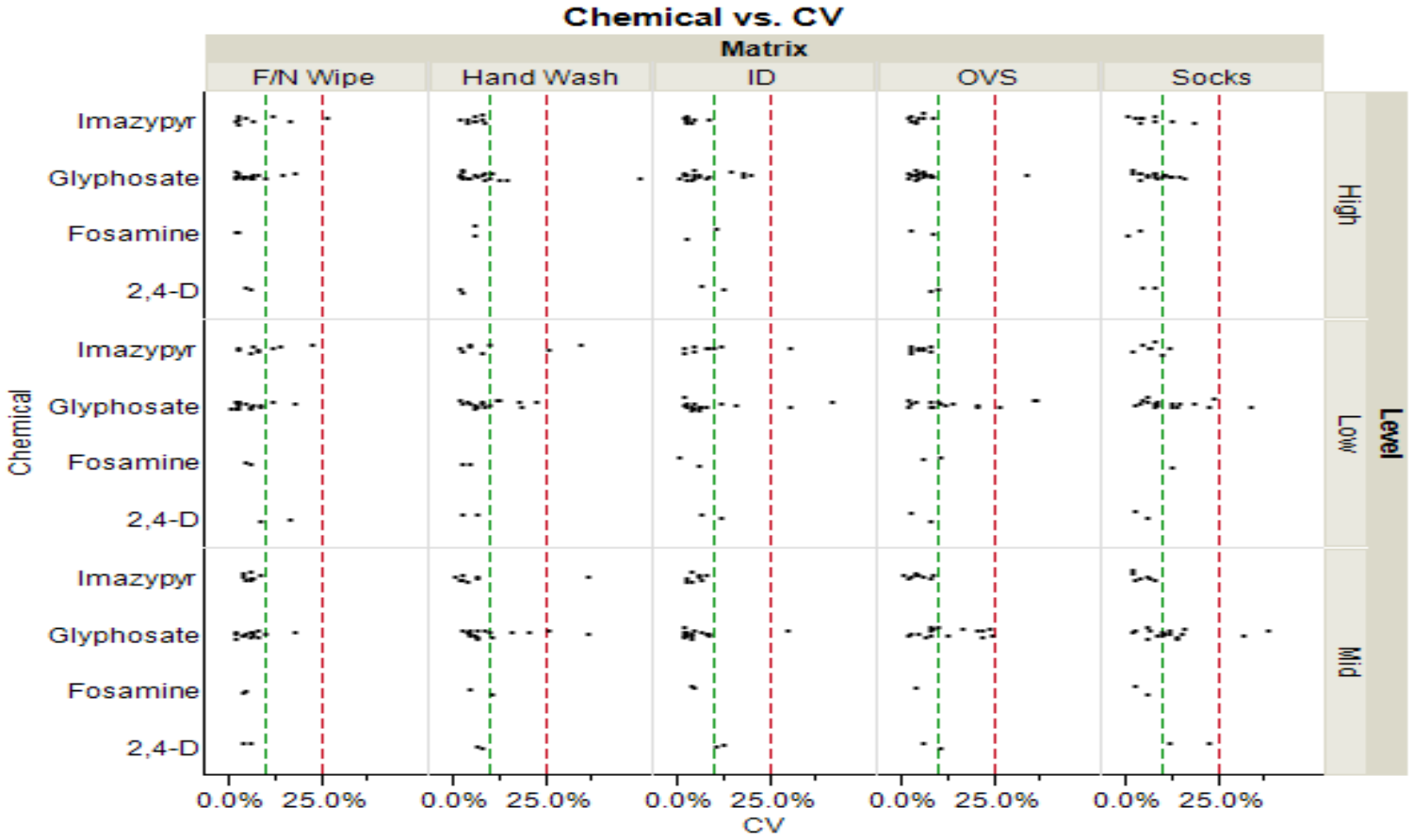
- Acceptable study design, diversity of conditions adequately captured
- Monitoring methods were consistent with EPA guidelines and prevailing research
- EPA recognizes that statistical inference requires assumption that sample is representative of exposure for all U.S. backpack and handgun applicator scenarios in applicable areas
- Acceptable analysis of primary and secondary objectives
  - Primary objective met for handgun applicator scenario but not for backpack applicator scenario
  - EPA does not believe additional backpack monitoring is necessary – formal incorporation of uncertainty will be considered
  - Secondary objective met for both scenarios
- Data recommended for use in regulatory assessments with AaiH normalization as default condition

Supplemental Slides

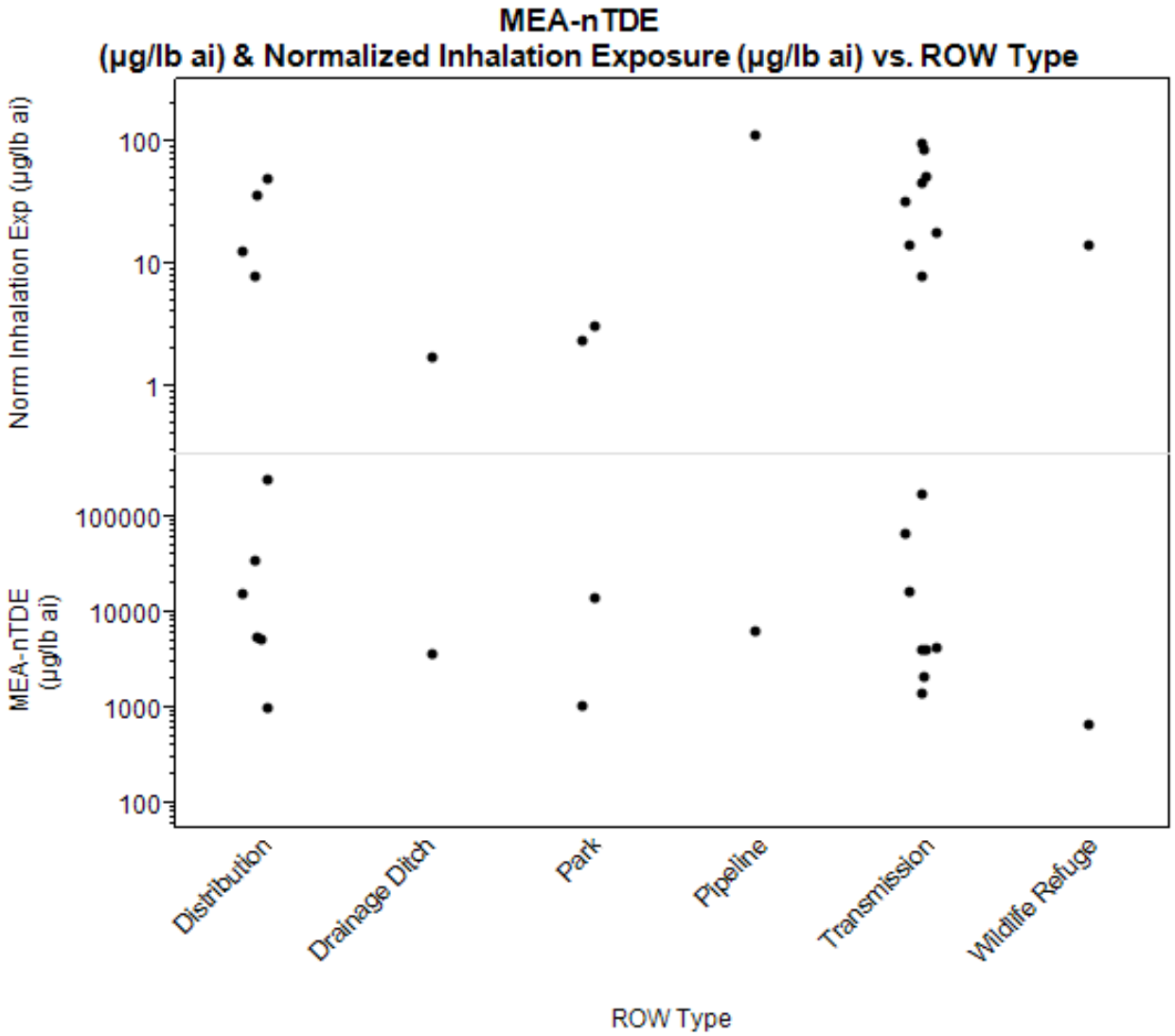
Field Fortification Results – Avg Recovery
Chemical x Matrix x Spike Level



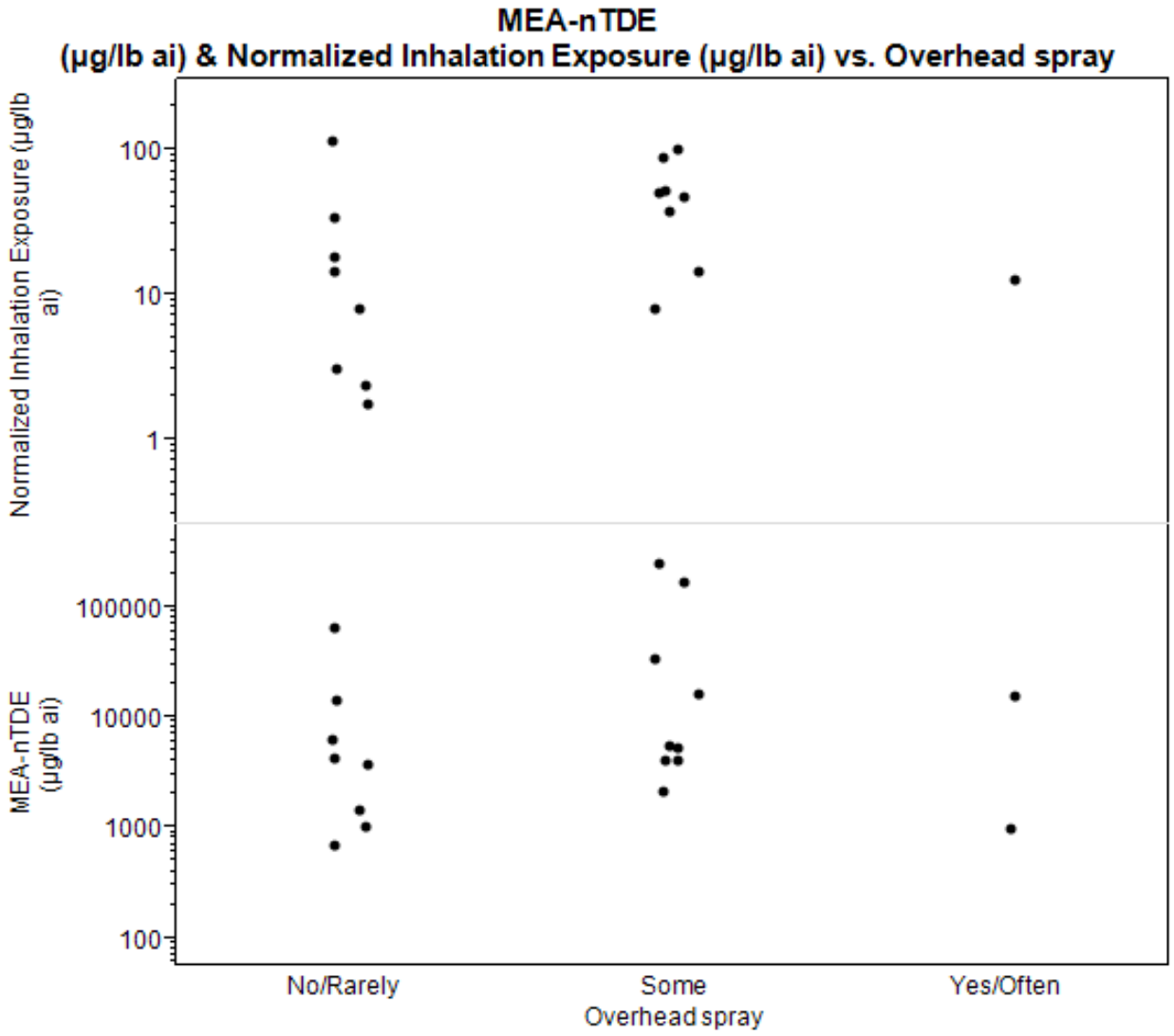
Field Fortification Results – Coeff. of Variation
Chemical x Matrix x Spike Level



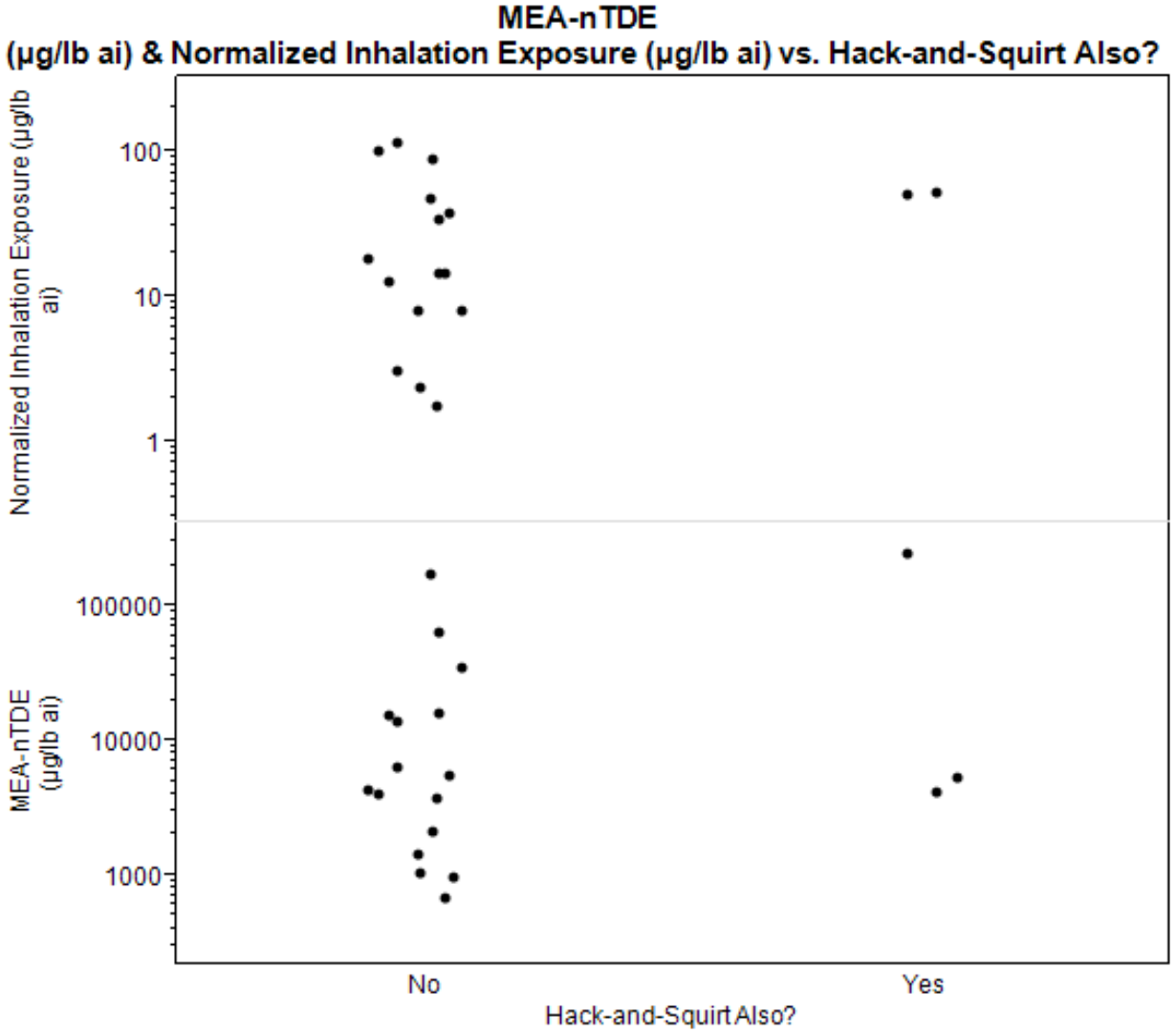
Backpack Exposure Results: Additional Analyses



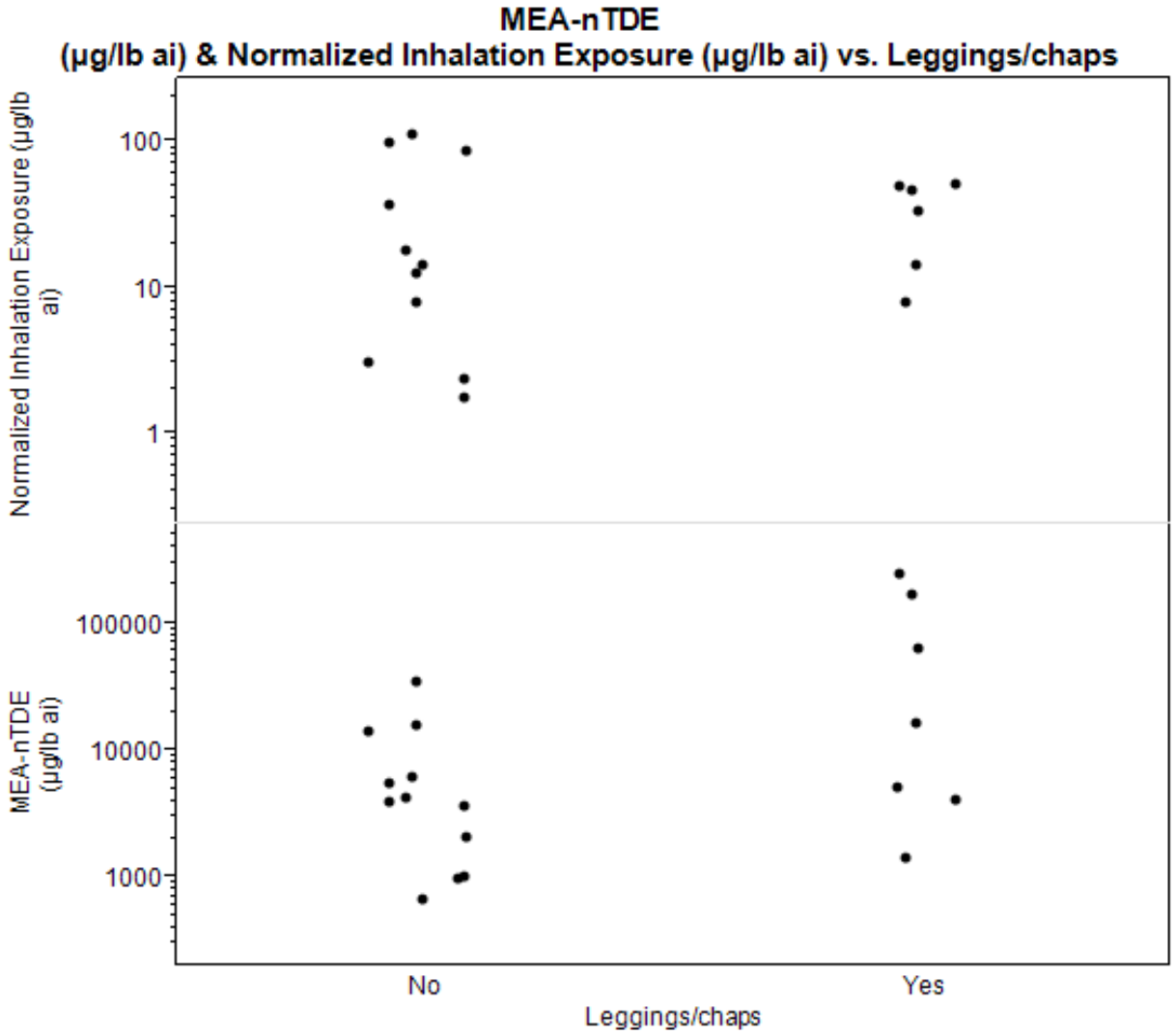
Backpack Exposure Results: Additional Analyses



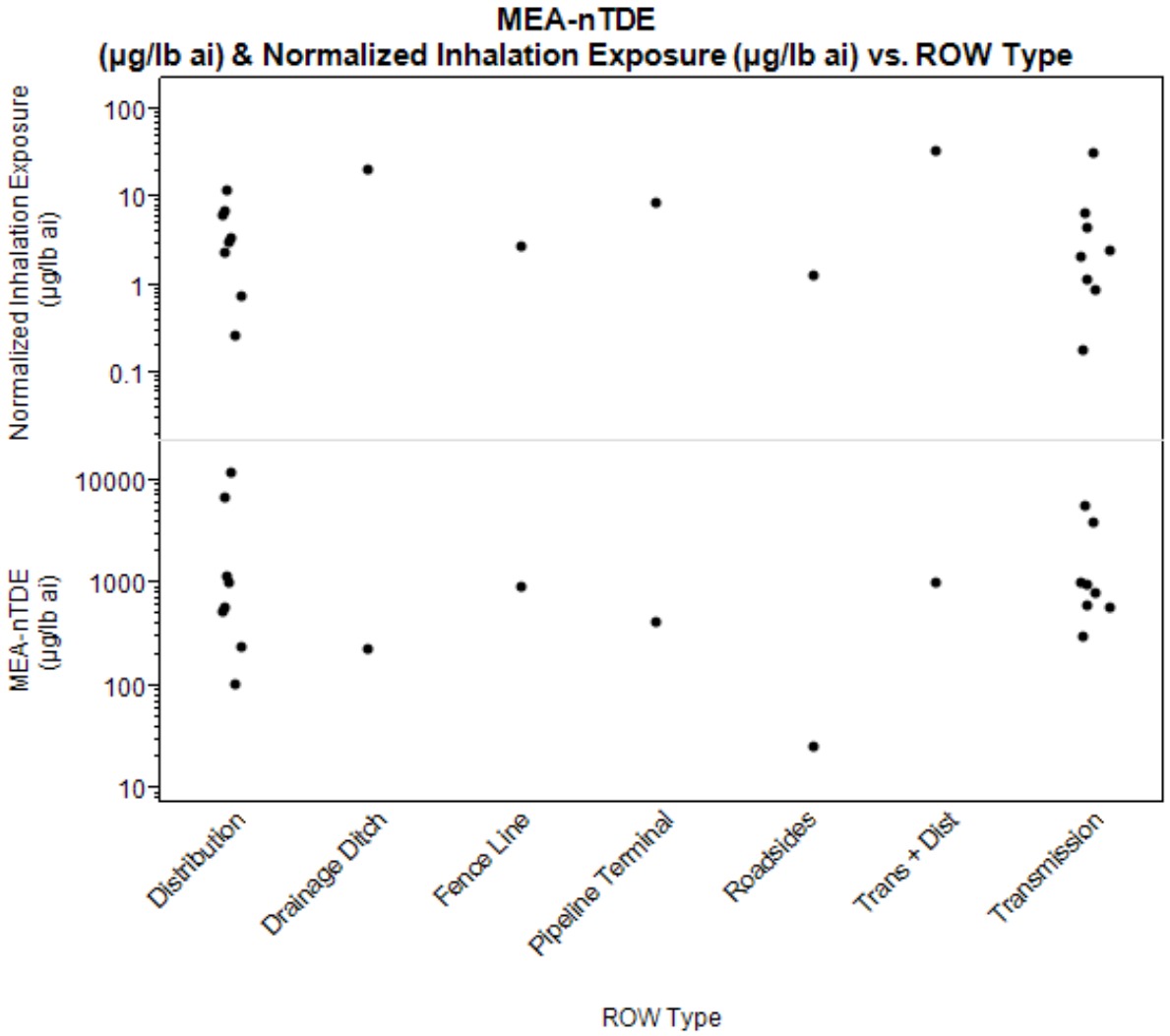
Backpack Exposure Results: Additional Analyses



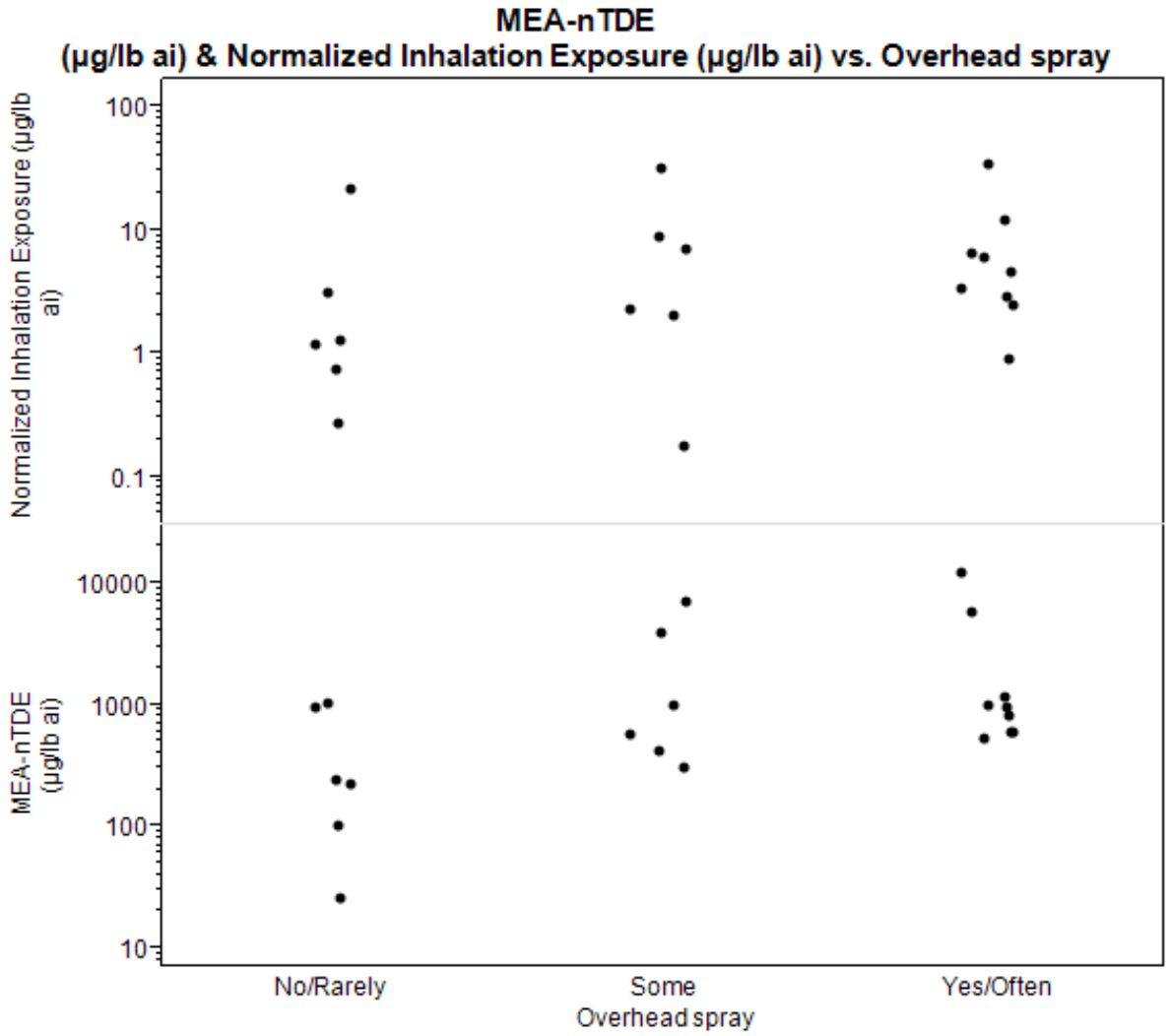
Backpack Exposure Results: Additional Analyses



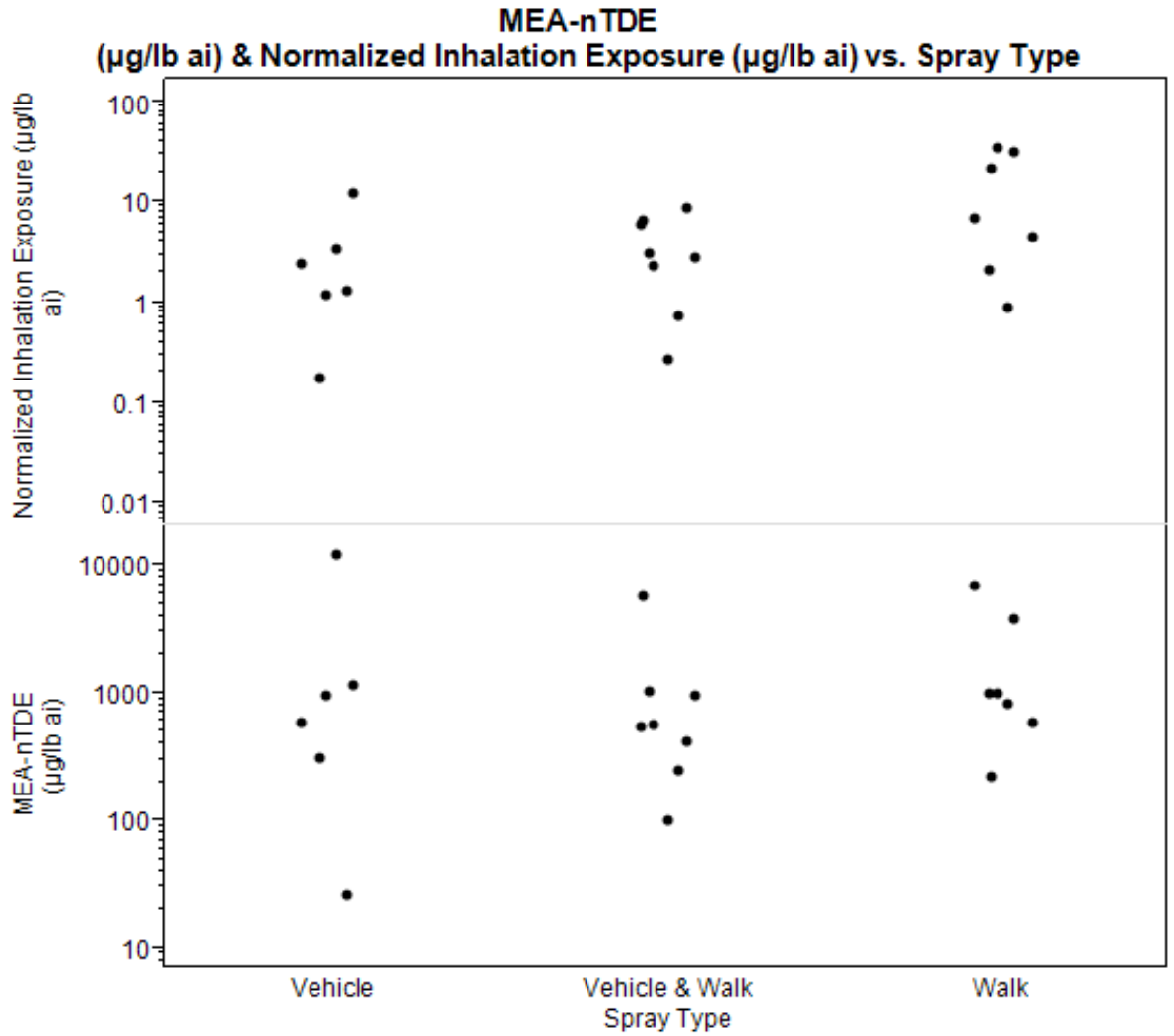
Handgun Exposure Results: Additional Analyses



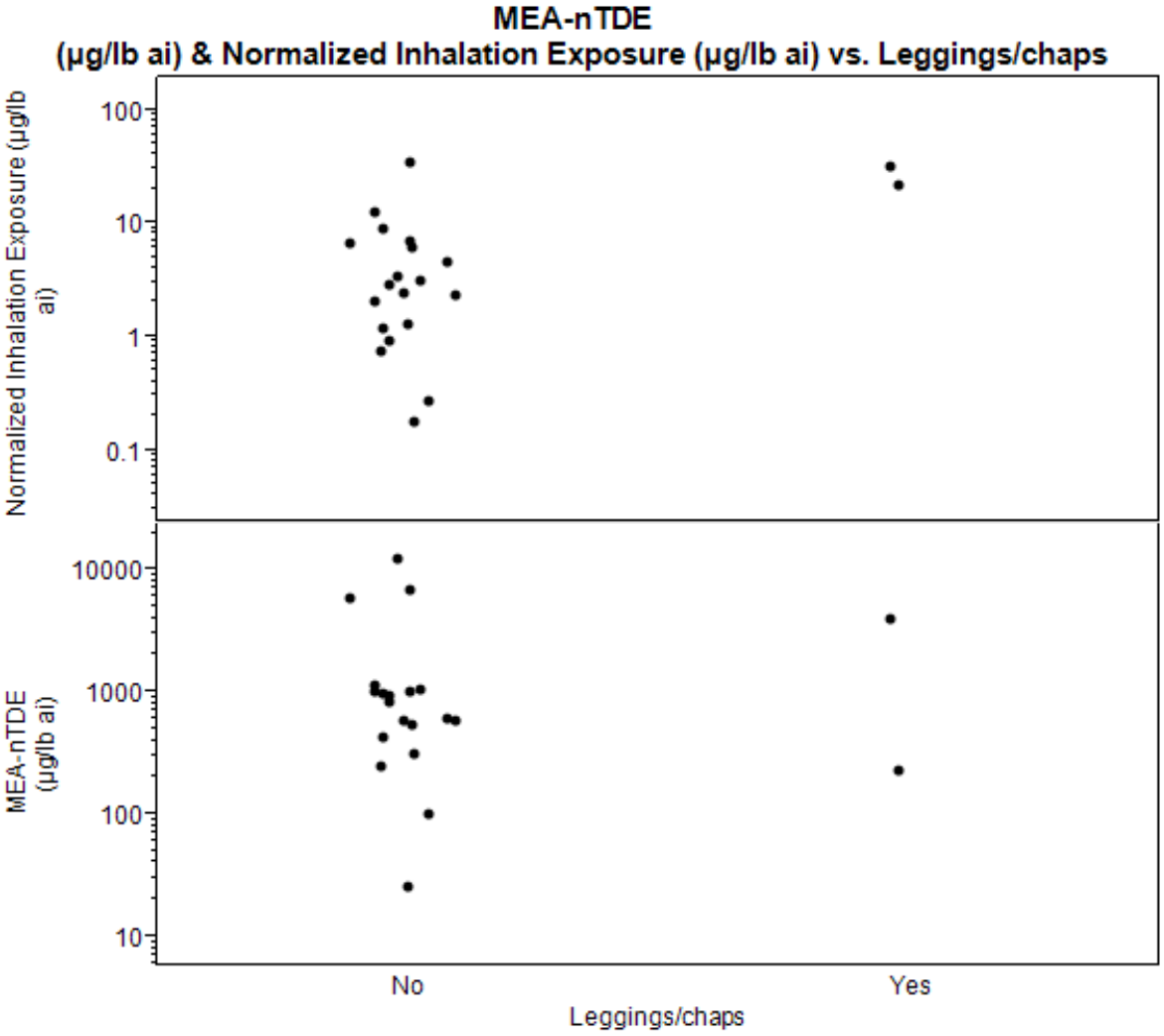
Handgun Exposure Results: Additional Analyses



Handgun Exposure Results: Additional Analyses



Handgun Exposure Results: Additional Analyses



Ethics Review of Completed AHETF Exposure Study for Backpack and Handgun Application of Liquid Spray

Kelly Sherman

Office of the Director
Office of Pesticide Programs

April 22, 2015

Overview

- Recruiting
- Consent process
- Subject demographics
- Monitoring
- IRB oversight
- Protocol amendments and deviations
- Responsiveness to protocol reviews
- Completeness of documentation
- Substantive acceptance standards
- Findings and conclusion

Recruiting

- 3-phase process outlined in the protocols and SOPs was followed
  1) Initial list generated from published lists and databases
  2) List narrowed through phone calls qualifying questions to produce list of potentially eligible employers
  3) Research personnel visited potentially eligible employers, confirmed eligibility, recruited workers, and scheduled monitoring

Recruiting – Protocol Amendments

- Amended protocol to allow three additional sources of employers from which subjects could be recruited:
  - Employers from another monitoring site that indicate they also spray ROWs in the site in question
  - Referrals from other employers
  - Commercial applicators that the AHETF is already aware of

Consent Process

- Process outlined in the protocols and SOPs was closely followed
- No reported deviations related to the consent process
- No unreported deviations noted related to the consent process

Subject Demographics

	Backpack	Handgun
Males	19	21
Females	0	0
Completed consent process in English	17	21
Completed consent process in Spanish	2	0
Self-identified as low or limited literacy and used witness	1	0
Years of experience	0.33 – 15	0.17 – 34
Age Range	21 – 53	19 - 68
Withdrew at own request	0	0
Removed from participation by AHETF	0	0

Monitoring

- Exposure monitoring was conducted without incident
- No subjects withdrew from the research
- No adverse events or incidents of concern were reported

Monitoring: Heat Index

- Greatest risk is heat-related illness
- SOP AHETF-11.G.1 – "Identification and Control of Heat Stress"
- Researchers appear to have closely followed the procedures in SOP
- No reports of heat-related illness
- 5 MUs cut short due to heat index

IRB Oversight

- Initial protocols reviewed by convened IRB
- Subsequent amendments and deviations reviewed under expedited procedures
- 8 amendments approved by IIRB/SAIRB
- 5 deviation reports reviewed and acknowledged by IIRB/SAIRB

Key Protocol Amendments

- Add add'l sources of employers for recruiting
- Modify clothing restrictions to allow chaps, leggings, any type of headgear, and below-the-knee rubber boots
- Allow test locations that are not strictly electric or pipeline utilities as long as foliage height, density, and terrain is similar
- Remove restriction against same employer for a second MU as long as the second MU involves a different year, job site, and crew

Key Deviations

- Shorter monitoring time and/or fewer loads applied due to heat index cutoff being reached
- One subject smoked a cigarette during the monitoring period without first having his hands washed by a researcher
- At his request, one subject wore his own chemical-resistant gloves rather than chemical-resistant gloves provided by the AHETF
- No deviations of ethical significance

Responsiveness to Protocol Reviews

- ☑ Provide information about how subjects will be provided individual exposure information
- ☑ Provide an explanation of the process that the AHETF follows to improve and verify the accuracy of the Spanish translations
- ☑ Describe the risk of toxicity from pesticide handling as a risk of participating in the study
- ☑ The consent form should explain that the pregnancy test will be provided by the researchers, and explain when it will take place.
- ☑ Study participants should undergo hand washes prior to smoking to reduce their risk of accidental ingestion of the surrogate compounds.

Completeness of Documentation

- IIRB correspondence volumes are complete and well-indexed
- Requirements of §26.1303 are satisfied

Substantive Acceptance Standards

- 40 CFR §26.1703
  - Prohibits reliance on data involving intentional exposure of pregnant or nursing women or of children
- 40 CFR §26.1705
  - Prohibits reliance on data unless EPA has adequate information to determine substantial compliance with subparts A through L for 40 CFR 26
- FIFRA §12(a)(2)(P)
  - Makes it unlawful to use a pesticide in human tests without fully informed, fully voluntary consent

Findings

- All subjects were at least 18; pregnant or nursing women were excluded
- No significant deficiencies in the ethical conduct of the research
- Protocol was closely executed; deviations did not compromise safety or consent of subjects
- Subjects were fully informed and their consent was fully voluntary, without coercion or undue influence

Conclusion

- Available information indicates that the AHETF Worker Exposure Monitoring Study: Backpack and Handgun Application of Liquid Spray in Utilities Rights-of-Way (AHE400) was conducted in substantial compliance with subparts K and L of 40 CFR part 26

Charge Questions

1. Was the research reported in the Agricultural Handler Exposure Task Force (AHETF) completed monograph reports and associated field study report for AHE400 faithful to the design and objectives of the protocol, SOPs, and governing documents?

2. Has the Agency adequately characterized, from a scientific perspective, the limitations on these data that should be considered when using the data in estimating exposure of those who apply liquid pesticide sprays to utilities rights-of-way and similar areas using backpack or handgun spray equipment?

3. Does available information support a determination that the studies were conducted in substantial compliance with subparts K and L of 40 CFR Part 26?