UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

MEMORANDUM (DRAFT)

Date: March 24, 2015

SUBJECT: Review of Agricultural Handler Exposure Task Force (AHETF) Monograph: "Backpack Application of Liquid Sprays in Utilities Rights-of-Way" (AHE1012)

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This memorandum presents EPA's review of the occupational handler exposure scenario monograph "Backpack Application of Liquid Sprays in Utilities Rights-of-Way" (AHE1012) submitted by the Agricultural Handler Exposure Task Force. Scientific review of the field and analytical report (AHE400 – Bruce, E., 2014) that outlines the monitoring data collected to support this scenario can be found in a separate data evaluation review (DER) memorandum (Crowley, 2015).

The AHETF satisfactorily followed the study protocols, sampling design, and data analysis plan. Though data analysis objectives/benchmarks were not fully met, EPA considers the backpack rights-of-way scenario complete and its results are recommended for use in routine assessment of exposure and risk.

1.0 Executive Summary

This document represents the Health Effects Division (HED) review of the Agricultural Handler Exposure Task Force (AHETF) Study AHE1012: Backpack Application of Liquid Sprays in Utilities Rights-of-Way (Bruce, et al, 2014). AHETF Report AHE400 (Bruce, E., 2014), "Determination of Dermal and Inhalation Exposure to Workers during Backpack and Handgun Application of Liquid Sprays in Utilities Rights-of-Way", provides the exposure monitoring field and analytical results, including laboratory analyses; details can be found in both the submitted study report and its corresponding EPA review (Crowley, 2015). The scenario monograph (AHE12012) subject to this review compiles the exposure monitoring results as outlined in the submitted AHE400 into a formal generic exposure scenario which can be utilized by pesticide regulatory agencies for exposure assessment purposes.

Overall, the AHETF adequately followed the general study design outlined in the AHETF Governing Document (AHETF, 2008 and 2010a) and specific scenario sampling and data analysis plan (AHETF, 2010b). AHETF efforts represented a well-designed, concerted process to collect reliable, internally-consistent, and contemporary exposure data in a way that takes advantage of and incorporates a more robust statistical design, better analytical methods, and improved data handling techniques. The AHETF data and associated unit exposures are considered superior to the existing used to assess exposure and risk for this scenario.[1] The data are considered the most reliable data for assessing exposure and risk to individuals applying liquid spray pesticides[2] via backpack sprayer, including frill applications, in utility rights-of-ways (ROW) or areas of similar terrain and foliage/vegetation characteristics while wearing the following personal protective equipment (PPE): long-sleeved shirts, long pants, shoes, socks, chemical-resistant gloves, and no respirator[3]. Importantly, the data represents exposure during loading and application only – it does not represent exposures during the mixing of pesticide spray solutions.

The primary quantitative objective was for dermal exposure results (normalized to the amount of active ingredient handled) to be accurate within 3-fold at the geometric mean, arithmetic mean and 95th percentile. This objective was not met: AHETF results showed an accuracy of approximately 4-fold. The secondary objective to evaluate proportionality versus independence between dermal exposure and the amount of active ingredient handled with 80% statistical power – a key assumption in the use of exposure data as "unit exposures" – was met. Additionally, the AHETF estimate of the slope of log dermal exposure-log amount of active ingredient handled (AaiH) was 1.12 (95% CI: 0.56 – 1.67) – a result consistent with the assumption of proportionality. Thus, for this scenario, HED will continue to use the exposure data normalized by the amount of active ingredient as a default condition for exposure assessment purposes.

[1] Beard, K.K. (1997). Evaluation of Applicator Exposures to SURFLAN® A.S. During Mixing, Loading, and Application with Backpack Sprayers. EPA MRID 44339801. See: http://www.epa.gov/opp00001/science/handler-exposure-data.html
[2] The data are not applicable to volatile chemicals (e.g., fumigants).
[3] Adjustments to this dataset would be required to represent alternative personal protective equipment (e.g., applying a protection factor to represent exposure when using a respirator or additional protective clothing). These types of adjustments would be used in risk assessments as appropriate, given the availability of reliable factors, and are not addressed in this review.

After adjustments by EPA for potential inefficiencies of the hand wash and face/neck wipe residue collection methodologies, results of the benchmark objective analyses were nearly identical to those described above. That is, the adjustments did not alter the outcomes of the benchmark analyses and conclusions were unaffected. However, as would be expected, the adjustments to the data result in slightly different estimates of exposure statistics (i.e., means and percentiles) than those calculated without the adjustments. Section 3.2.1 discusses this in more detail.

Select summary statistics for this backpack applicator scenario are presented in Table 1 below, as well as the value previously used (Beard, 1997 – EPA MRID 44339801) to assess pesticide exposure/risk for this scenario for comparison.

Table 1. Unit Exposures (µg/lb ai handled): Backpack Applicators

Exposure Route	Beard, K.K., 1997 (EPA MRID 44339801)	AHETF[a]		
	Arithmetic Mean	Geometric Mean	Arithmetic Mean[c]	95th Percentile[d]
Dermal[b]	8,260	6843	30,394	117,564
Inhalation	2.58	16.8	39.8	146

[a] Statistics are estimated using a variance component model accounting for correlation between measurements conducted within the same field study (i.e., measurements collected during the same time and at the same location). Additional model estimates (e.g., empirical and simple random sample assumptions) are described in Section 3.0.
[b] Per current EPA policy, dermal unit exposures reflect 2X adjustment of hand and face/neck measurements to address potential inefficiencies in those exposure monitoring methods since the average percent contribution to total dermal exposure by the hands, face, and neck is greater than 20% (see Section 3.1).
[c] Arithmetic Mean (AM) = GM * exp{0.5*((lnGSD)^2)}
[d] 95^{th} percentile = GM * GSD^1.645

2.0 Background

The following provides background on the AHETF objectives and also discusses review of the backpack rights-of-way applicator scenario by the Human Studies Review Board (HSRB).

2.1 AHETF Objectives

The AHETF is developing a database (Agricultural Handlers Exposure Database or AHED) which can be used to estimate worker exposures associated with major agricultural and non-agricultural handler scenarios. A scenario is defined as a pesticide handling task based on activity such as mixing/loading or application. Other factors such as formulation (e.g., liquids, granules) application equipment type (e.g., tractor-mounted boom sprayers, backpack sprayers) are also key criteria for defining scenarios. AHETF-sponsored studies are typically designed to represent individuals wearing long-sleeved shirts, long pants, shoes, socks, chemical-resistant gloves as appropriate, and no respirators. In some cases, an engineering control (e.g., enclosed cabs on tractors) or additional personal protective equipment/clothing may also be a key element of the scenario.

AHETF studies use dosimetry methods intended to define pesticide handler dermal and inhalation exposures, attempting to represent the chemical exposure "deposited on or to-the-skin" or “in the breathing zone.” For the purposes of pesticide handler exposure assessment, dermal and inhalation exposures are expressed as “unit exposures” – exposure per the weight-based amount of pesticide handled. Mathematically, unit exposures are expressed as exposure normalized by the amount active ingredient handled (AaiH) by participants in scenario-specific exposure studies (e.g., mg exposure/lb ai handled). Scenario-specific unit exposures are then used generically to predict exposure for other chemical and/or application conditions such as different application rates.

Two major assumptions underlie the use of exposure data in this fashion. First, the expected external exposure is unrelated to the identity of the specific active ingredient in the pesticide formulation. That is, the physical characteristics of a scenario such as the pesticide formulation (e.g., formulation type – wettable powder, liquid concentrate, dry flowable, etc.), packaging (e.g., bottle or water-soluble packet), or the equipment type used to apply the pesticide, influence exposure more than the specific pesticide active ingredient (Hackathorn and Eberhart, 1985). Thus, for example, exposure data for spraying one chemical using a backpack sprayer in a utility right-of-way can be used to estimate exposure for another chemical used in the same manner. Second, dermal and inhalation exposure are assumed proportional to the amount of active ingredient handled. In other words, if one doubles the amount of pesticide handled, exposure is expected to double.

The AHETF approach for monitoring occupational handler exposure was based on criteria reviewed by EPA and presented to the Human Studies Review Board (HSRB) for determining when a scenario is considered complete and operative. Outlined in the AHETF Governing Document (AHETF, 2008 and 2010a), the criteria can be briefly summarized as follows:

- The primary objective of the study design is to be 95% confident that key statistics of dermal exposure (normalized to the amount of active ingredient handled, i.e., dermal “unit exposures”) are accurate within 3-fold. Specifically, the upper and lower 95% confidence limits should be no more than 3-fold higher or lower than the estimates for each the geometric mean, arithmetic mean, and 95th percentile dermal unit exposures. To meet this primary objective AHETF proposed an experimental design that provides a sufficient number of field trials and a sufficient number of monitored individuals. Note that this “fold relative accuracy” (*f*RA) objective does not apply to normalized inhalation exposure, though estimates are provided for reference.

- The secondary objective is to evaluate the assumption of proportionality between dermal exposure and amount of active ingredient handled (AaiH) in order to be able to use the AHETF data generically across application conditions. To meet this objective, the AHETF proposed a log-log regression test to distinguish complete proportionality (slope = 1) from complete independence (slope = 0), with 80% statistical power, achieved when the width of the 95th confidence interval of the regression slope is 1.4 or less. Note, again, that this objective does not apply to normalized inhalation exposure; however the tests are performed for informational purposes.

To simultaneously achieve both the primary and secondary objectives described above and maximize logistical/cost efficiently while minimizing the number of participating workers, the

AHETF developed a study design employing a 'cluster' strategy. A cluster, from a sample size perspective, is defined as a set of workers monitored in spatial and temporal proximity. While cluster sampling is logistically more efficient and cost effective, importantly, in terms of a sampling strategy, there is assumed to be some level of correlation within clusters. For AHETF purposes, clusters are generally defined by a few contiguous counties in a given state(s) within a US EPA agricultural growing region.

Though other configurations may also satisfy study objectives, for most handler scenarios the optimal configuration for the AHETF is 5 regional clusters each consisting of 5 participants. The 25 total participants together with the conditions under which the worker handles the active ingredient are referred to as monitoring units (MUs). Within each cluster, the AHETF partitions the practical AaiH range handled by the participants in each cluster appropriate to a given scenario. In general, the strata of AaiH for any given scenario is commensurate with typical commercial production agriculture and EPA handler risk assessment with respect to amount of area that could be treated or amount of dilute solution that could be sprayed in a work day.

2.2 Previous HSRB Review and Comments

The ability of the EPA to use the backpack ROW applicator exposure monitoring studies to develop regulatory decisions is contingent upon compliance with the final regulation establishing requirements for the protection of subjects in human research (40 CFR Part 26), including review by the Human Studies Review Board[4].

The protocol and sampling plan for this exposure data and scenario (AHETF, 2010b) was presented to the HSRB in October 2010. The meeting report (HSRB, 2010) stated that the proposed approach would generate reliable data for assessing exposure for backpack sprayers applying pesticides in utility rights-of-way. The Board agreed that the proposal had clear scientific objectives and a reasonable experimental design to meet the objectives, including appropriate justification of and analytical plan for measuring test substances as well as justification for sample size and study site selection.

However, the HSRB also commented about some potential weaknesses of the study. The HSRB was concerned that exposure variability would be extremely high so as to be unrepeatable as well as potentially preventing evaluation of proportionality with amount of active ingredient handled. The Board also recommended that the field notes be adequate such that "time-on-task" could be estimated as a fraction of total monitored time, particularly if a minimum of 4 hours was required.

While the data did prove highly variable, it did not appear to hamper evaluation of proportionality (see Section 3.2.2), and since the study is unlikely to be repeated it is unknown whether such results could be reproduced. However, given the very high variability observed, it is unlikely that a repeat study would demonstrate even higher variability. While a 4-hour minimum was included in the protocol (to ensure detectable residues – with the additional effect of skewing the data to higher exposures), a few workers did work less than 4 hours and were noted as protocol deviations. However, even with less-than-4 hour monitoring, there were very

[4] http://www2.epa.gov/programs-office-science-advisor-osa/human-studies-review-board

few non-detect results on the exposure matrices. Should additional analysis be desired to address concerns with the time requirement, the field notes/observations are fairly detailed and could be used to estimate time-on-task.

3.0 Exposure Study Conduct and Monitoring Results

Field monitoring and analytical results, as well as protocol amendments and deviations, were reported in AHE400 and reviewed by EPA (Crowley, 2015). The following sections summarize the conduct of the study, the exposure monitoring results and the scenario benchmark statistical analyses presented in the AHETF scenario monograph (Bruce, et al, 2014).

3.1 Exposure Study Design and Characteristics

This scenario is application of liquid spray pesticides via backpack sprayer, including frill applications[5], in rights-of-ways or areas of similar terrain and foliage/vegetation characteristics such as a public park or drainage ditches while wearing the following work clothing/PPE: long-sleeved shirts, long pants, shoes, socks, chemical-resistant gloves, and no respirator. Dermal and inhalation exposure monitoring was conducted for 19 different workers[6] and reported in the AHETF submission "Determination of Dermal and Inhalation Exposure to Workers during Backpack and Handgun Application of Liquid Sprays in Utilities Rights-of-Way" (AHE400; Bruce, E., 2014).

The figures below (from AHE1012 Appendix C; Bruce, et al, 2014) depict examples of activities for which the exposure data are applicable.

[5] A frill application, also known as "hack and squirt", consists of workers using machetes or hatchets to make slices at the base of trunks of trees or bushes (forming a "frill") in which to spray pesticide.

[6] The original sampling plan called for monitoring 21 workers. The AHETF terminated sampling at 19 workers due to logistical difficulties and the duration of the study at that point. Additionally, only 17 of the 19 workers had valid inhalation monitoring due to lack of analyte or pump malfunction.

Figure 1: Application in Distribution Right-of-Way

Figure 2: Frill Application ("hack-and-squirt") in addition to Backpack Spraying

Figure 3: Application to invasive grass in a public park

In order the capture the expected range of exposures within this scenario (with a small sample), the monitoring plan outlined a strategy to target a diverse set of conditions in terms of application sites, equipment, workers, and other potential exposure factors. For each targeted area, the AHETF developed lists of potential utility companies and application companies that might be able to provide eligible workers to monitor. From a universal list of all companies who may conduct rights-of-way applications, AHETF constructed additional lists of "qualified employers" and then "potentially eligible" employers via randomized telephone calls and questionnaires, from which they would schedule monitoring. When multiple workers in a given area/time were available, the monitored workers were selected at random.

The sampling plan for this scenario (AHETF, 2010b) intended for a '7x3' design – monitoring of a total of 21 different workers, 3 workers in each of 7 separate 'clusters' or monitoring areas represented by the U.S. states: WV, NC, FL, AR, IN, MN, and eastern TX. Monitoring locations were all places where undesirable vegetation such as shrubs, vines, or bushes were meant to be controlled. Most of the monitoring was in utility rights-of-ways, such as areas where electric transmission and distribution lines or pipelines run through. These are areas where controlling vegetation is important so as to provide easy access to utility personnel and vehicles, but also because the vegetation can damage utility distribution equipment.

Following recruitment difficulties, some monitoring areas were expanded to include additional states, as well as to expand beyond strictly rights-of-way areas to additional use sites of similar terrain and foliage/vegetation such as wildlife refuges, parks, and drainage ditches. While these are not rights-of-way, both the purpose of the application (i.e., controlling undesirable vegetation) and location characteristics such as terrain were similar to the right-of-way locations that constituted the bulk of the monitoring. Additionally, monitoring was conducted over an extended period of time from May 2011 to September 2013.

Thus, the actual conduct of the study utilized the (expanded) 7 monitoring areas, but because of temporal differences, effectively constituted of 15 clusters, with 1 or 2 workers per cluster, totaling 19 monitored workers. Because of the length of time and cost expended to conduct monitoring for 19 workers – and the belief that study objectives would be met with 19 – AHETF elected to terminate the monitoring at 19 total workers instead of 21. Section 3.2.1 provides more discussion on this issue.

Monitoring was conducted across 3 years and 9 different U.S. states, providing both spatial and temporal diversity in the sample. Additionally, there were no repeat measurements on the same worker, and only two of those workers worked for the same employer. In the same-employer case, the workers were monitored in different calendar years, at different job sites, and were part of different application crews. By diversifying locations, employers and workers, as well as the amount of active ingredient handled (to accommodate the secondary objective), brands/types of backpacks and configurations and spray techniques were also indirectly varied. For more details on these conditions see the monograph submission (AHE1012), the data submission (AHE400) and EPA review of AHE400 (Crowley, 2015).

3.2 Exposure Monitoring and Calculations

Monitored on actual days of work, participants handled between 0.03 to 9.65 lbs of active ingredient (fosamine, glyphosate, or imazapyr), spraying 4.5 to 64.5 gallons of solution in 2 to 11 hours. Dermal exposure was measured using 100% cotton "whole body dosimeters" (WBD) underneath normal work clothing (e.g., long-sleeved shirt, long pants, socks and shoes), hand rinses (collected at the end of the day and during restroom and lunch breaks), and face/neck wipes (adjusted to extrapolate to portions of the head covered by protective eyewear, respirators, and/or hair). Per AHETF goals, monitoring of these backpack applications was conducted to represent exposure for workers wearing long-sleeve shirts, pants, shoes/socks, chemical-resistant gloves and no respiratory protection. While this was largely the case, because of the nature of the terrain and environment nearly all workers wore (company-required) hard hats and 7 of 19 wore additional leg coverings to protect from thorns or snakes. Additional evaluation of some of this additional clothing is reviewed in Section 3.3.

Additionally, as presented at a June 2007 HSRB meeting, in order to account for potential residue collection method inefficiencies[7], EPA made adjustments in the AHETF-supplied data to hand and face/neck field study measurements as follows:

- if measured exposures from hands, face and neck contribute less than 20% as an average across all workers, no action is required;
- if measured exposure contribution from hands and face/neck represents between 20% and 60% of total, the measurements shall be adjusted upward by a factor of 2, or submission of a validation study to support the residue collection method;
- if measured exposure contribution from hands and face/neck represents is greater than 60%, a validation study demonstrating the efficiency of the residue collection methods is required.

[7] The terminology used to describe this are "method efficiency adjusted" (MEA) or "method efficiency corrected" (MEC).

For these studies, the measurements fell in the second category – on average a contribution of 27% to total dermal exposure – and hand rinse and face/neck wipe measurements have been adjusted upward by a factor of 2 (i.e., multiplied by 2).

Inhalation exposure is measured using a personal air sampling pump and an OSHA Versatile Sampler (OVS) tube. The tube is attached to the worker's shirt collar to continuously sample air from the breathing zone. All samples are adjusted as appropriate according to recovery results from field fortification samples.

Total dermal exposure was calculated by summing exposure across all body parts for each individual monitored. Total inhalation exposures were calculated by adjusting the measured air concentration (i.e., ug/L) using a breathing rate of 16.7 liters per minutes, representing light activities (NAFTA, 1998), and total work/monitoring time.[8] Dermal and inhalation unit exposures (i.e., ug/lb ai handled) are then calculated by dividing the summed total exposure by the amount of active ingredient handled.

A summary of the 19 backpack applicator MUs is provided in Table 2 below, with data plots shown in Figures 4 and 5. All field measurements were adjusted by their corresponding field fortification recovery values. In additional, though alternate methods can be applied by data users (e.g., maximum likelihood estimation), residues with results less than analytical limits use the "½ analytical limit" (either ½ LOD or LOQ) convention.

For dermal exposure, both hand rinse and face/neck wipe method efficiency adjusted (MEA) data and unadjusted results are presented. Note for inhalation exposure, there were a total of 17 (rather than 19) measurements due to sampling pump malfunction or lack of remaining sample for analysis (MU A1 – sample extract was used up from previous analysis with an improper analytical method).

[8] Inhalation Exposure (ug) = collected air residue (ug) x [breathing rate (L/min) ÷ average pump flow rate (L/min)]

Table 2. Backpack Application MU Summary								
MU ID	State	Application Site	Work/ Monitoring Time (hours)	Solution Sprayed (gallons)	AaiH (lbs)	Unit Exposure (ug/lb ai)		
						Dermal		Inhalation
						Non-MEA	MEA	
A27	PA	Distribution	3.5	4.5	1.44	712	978	--
A33	PA	Transmission	9	28.5	4.49	884	1436	7.95
A34	PA	Park	2	13.5	0.81	13485	13977	3.07
A8	NC	Distribution	4	12.25	2.11	3541	5502	36.5
A10	GA	Transmission	6.4	64.5	9.65	16096	16195	14.1
A20	SC	Distribution	5.1	48	0.48	12896	15628	12.5
A11	FL	Wildlife Refuge	8.2	22.5	0.051	400	675	14.1
A12	FL	Transmission	5	16.5	1.9	2710	3990	98.4
A13	FL	Transmission	5	20	2.27	1329	2095	85.9
A1	AR	Distribution	10.7	33.25	6.65	3586	5209	--
A23	AR	Distribution	6	14.5	3.11	238799	241923	49.5
A24	AR	Transmission	4.3	33	0.37	167305	168771	46.8
A16	IN	Pipeline	10.2	15.875	5.08	4507	6255	112
A38	IN	Distribution	8.8	14.75	1.83	33279	34234	7.98
A31	MI	Park	6.3	16.5	1.13	949	1024	2.33
A40	MI	Drainage Ditch	7.8	7.5	0.62	3537	3654	1.74
A2	TX	Transmission	7.5	16.5	3.62	3763	4075	51.1
A4	TX	Transmission	6.1	16	0.03	2823	4250	18.1
A25	TX	Transmission	3.6	19.5	3.51	61489	64311	33

Figure 4: Dermal Unit Exposures (MEA) (ug/lb ai)

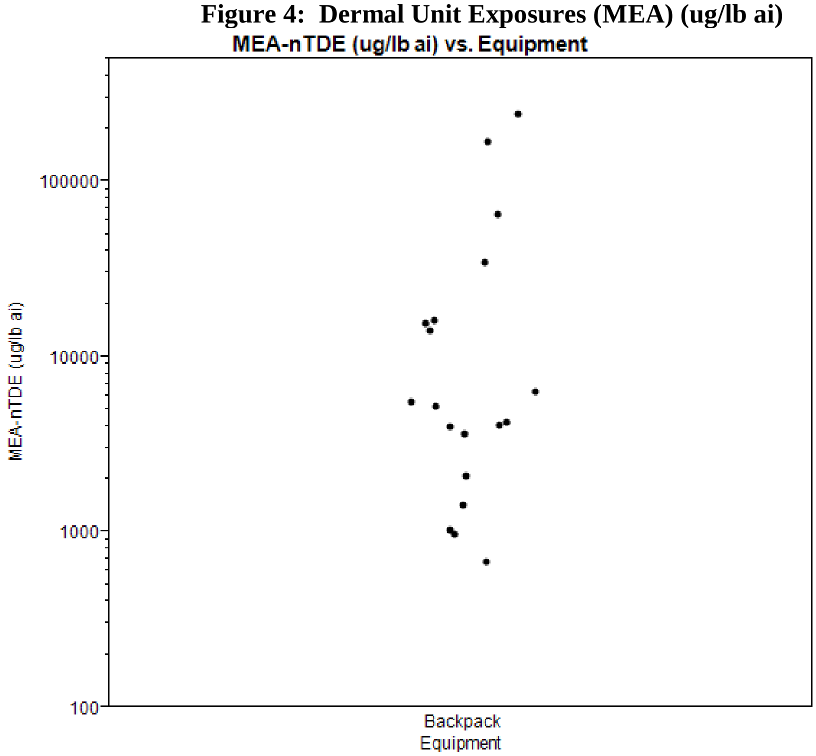
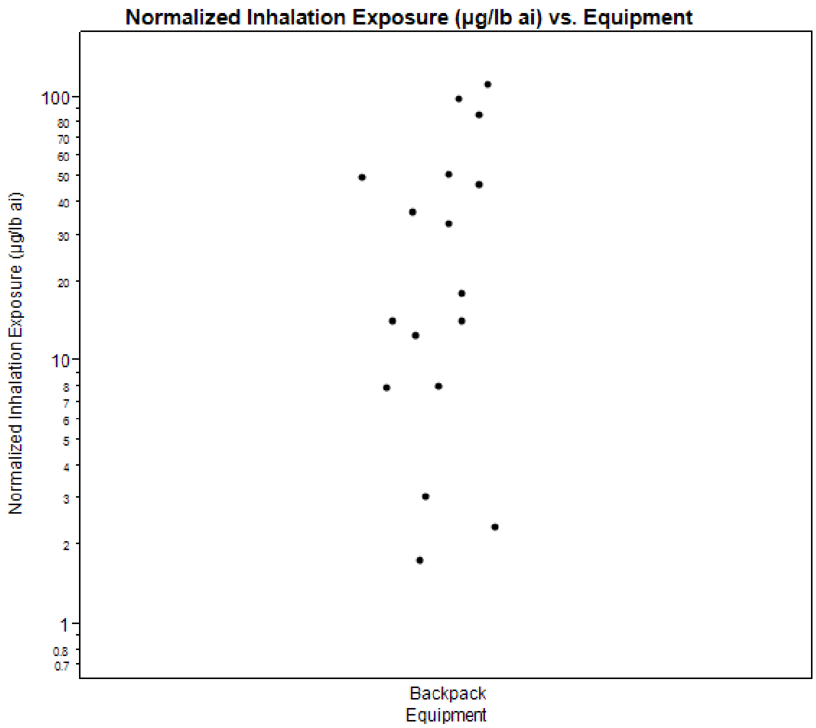


Figure 5: Inhalation Unit Exposures (ug/lb ai)



3.3 Evaluation of Scenario Benchmark Objectives

The AHETF monograph details the extent to which the backpack ROW applicator scenario meets objectives described in Section 2.1. The monograph states that while the primary objective (3-fold accuracy) was not met, the secondary objective (adequate analytical power) was met. EPA agrees with the methodologies used to assess these objectives (Appendix E of Bruce, et al, 2014) and has independently confirmed the results by re-analyzing the data with the AHETF-supplied statistical programming code.

3.3.1 Primary Objective: fold Relative Accuracy (fRA)

The primary benchmark objective for AHETF scenarios is for select statistics – the geometric mean (GM), the arithmetic mean (AM), and the 95th percentile (P95) – to be accurate within 3-fold with 95% confidence (i.e., "fold relative accuracy"). The AHETF analyzed the data using various statistical techniques to evaluate this benchmark. Importantly, the AHETF presented results in the monograph without the MEA factors previously described. As described in previous sections of this review, EPA applied the MEA factor to the AHETF results. This section discusses results with and without the EPA-incorporated MEA factors.

First, both dermal and inhalation unit exposures were shown to fit lognormal distributions reasonably well. Normal and lognormal probability plots are provided as Appendix A. Next, the AHETF calculated estimates of the GM, AM and P95 based on three variations of the data:

- Non-parametric empirical (i.e., ranked) estimates;
- Assuming a lognormal distribution and a simple random sample (SRS); and,
- Hierarchical variance component modeling to account for potential MU correlations.

As presented in Appendix C of the AHETF Governing Document (AHETF, 2008 and AHETF, 2010a) and Appendix E of the scenario monograph (Bruce et al, 2014), the 95% confidence limits for each of these estimates were obtained by generating 10,000 parametric bootstrap samples. Then, the fRA for each was determined as the maximum of the two ratios of the statistical point estimates with their respective upper and lower 95% confidence limits.

EPA performed the method efficiency adjustments on the dermal exposure, utilizing the same (SAS) statistical programming code submitted by the AHETF, except substituting the input data with the MEA data. The primary benchmark of 3-fold accuracy for select statistics was not met for dermal exposure data both adjusted and unadjusted for potential hand rinse and face/neck wipe method inefficiencies. Results for the unadjusted and adjusted dermal exposure data are presented below in Table 3 and inhalation exposure in Table 4.

Both the means and percentiles and fRA_{95} values for the MEA dermal exposure data are slightly lower than the unadjusted data. The adjustments have the (obvious) effect of increasing the exposure estimates on an individual level – and non-parametric statistics reflect that result (e.g., the simple MEA arithmetic mean is 31,273 ug/lb ai while the non-MEA arithmetic mean is 30,110 ug/lb ai). But on the sample level, due to the relative effect of the adjustments on individual workers (workers with larger total exposures were relatively unaffected by the adjustment) and the resulting decrease in variability, parametric statistics are lower than the unadjusted data. Despite this result, in order to apply consistent policy, EPA will rely on the data adjusted for potential inefficiencies for the hand rinse and face/neck wipes.

Table 3. Backpack ROW Application – Results of Primary Benchmark Analysis for Dermal Exposure

Statistic	Dermal (MEA) [a]			Dermal (non-MEA)		
	Unit Exposure (ug/lb ai)		fRA_{95}	Unit Exposure (ug/lb ai)		fRA_{95}
	Estimate	95% CI		Estimate	95% CI	
GM_S	7,356	2,924-15,976	2.3	5,886	2,222-13,785	2.5
GSD_S	5.33	2.87-9.11	--	6.09	3.14-10.89	--
GM_M	6,843	3,006-15,664	2.3	5,508	2,270-13,386	2.4
GSD_M	5.13	2.88-9.15	--	5.86	3.17-10.91	--
ICC	0.75	0.00-0.97	--	0.70	0.00-0.96	--
GM_S = geometric mean assuming SRS = "exp(average of 19 ln(UE)) values". GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 19 ln(UE)) values" GM_M = variance component model-based geometric mean GSD_M = variance component model-based geometric standard deviation ICC = intra-cluster correlation						
AM_S	31,273	6,949-78,821	3.5	30,110	5,980-88,678	4.1
AM_U	29,784	7,891-101,565	3.5	30,096	6,973-121,370	4.1
AM_M	26,052	8,144-101,555	3.5	26,317	7,166-122,551	4.1
AM_S = simple average of 19 unit exposures						

AM_U = arithmetic mean based on GM_S = GM_S*exp{0.5*((lnGSD_S)^2} AM_M = variance component model-based arithmetic mean = GM_M* exp{0.5*((lnGSD_M)^2}						
$P95_S$	241,923	27,500-917,904	6.4	238,799	25,195-1,097,817	7.5
$P95_U$	115,166	27,639-351,621	3.6	114,902	25,093-383,796	3.9
$P95_M$	100,769	28,549-347,158	3.5	101,020	26,148-382,338	3.8
$P95_S$ = 95th percentile (i.e., the 18th unit exposure out of 19 ranked in ascending order) $P95_U$ = 95th percentile based on GM_S = GM_S * GSD_S^1.645 $P95_M$ = variance component model-based 95th percentile = GM_M* GSD_M^1.645						
[a] Dermal exposure values reflect 2X default adjustment for hands and face/neck measurements.						

Table 4. Backpack ROW Application – Results of Primary Benchmark Analysis for Inhalation Exposure			
Statistic	**Inhalation**		
	Unit Exposure (ug/lb ai)		**fRA_{95}**
	Estimate	**95% CI**	
GM_S	18.9	8.0-35.6	2.1
GSD_S	3.65	2.22-6.19	--
GM_M	16.8	8.3-34.3	2.0
GSD_M	3.72	2.25-6.21	--
ICC	0.85	0.38-0.98	--
GM_S = geometric mean assuming SRS = "exp(average of 17 ln(UE)) values". GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 17 ln(UE)) values" GM_M = variance component model-based geometric mean GSD_M = variance component model-based geometric standard deviation ICC = intra-cluster correlation			
AM_S	35	14.5-100.3	2.7
AM_U	43.7	15.3-113.7	2.7
AM_M	39.8	15.8-113.1	2.7
AM_S = simple average of 17 unit exposures AM_U = arithmetic mean based on GM_S = GM_S*exp{0.5*((lnGSD_S)^2} AM_M = variance component model-based arithmetic mean = GM_M* exp{0.5*((lnGSD_M)^2}			
$P95_S$	112	45.1-836.1	4.4
$P95_U$	158.9	46.3-431.1	3.1
$P95_M$	145.8	47.9-427.6	3.0
$P95_S$ = 95th percentile (i.e., the 16th unit exposure out of 17 ranked in ascending order) $P95_U$ = 95th percentile based on GM_S = GM_S * GSD_S^1.645 $P95_M$ = variance component model-based 95th percentile = GM_M* GSD_M^1.645			

As shown in the tables above, for AHETF-calculated dermal exposures, while estimates of the geometric mean were accurate to approximately 2-fold, both the arithmetic mean and 95th percentiles are accurate to only approximately 4-fold. For MEA dermal exposures calculated by EPA the mean and 95th percentiles were accurate to within 3.5-fold. Though not of primary interest for the accuracy benchmark, mixed-model estimates of inhalation data were accurate to within 3-fold.

The AHETF recognized the failure to meet the accuracy benchmark (3-fold) for dermal exposure and addressed it in the monograph report. This outcome could be the result of several reasons: small sample size, extreme variability, or a high ICC. Prior to study conduct, study design analysis utilized estimates of 4 and 0.3 for the geometric standard deviation (a measure of variability) and the ICC, respectively, to determine the sample size. While the ICC was higher-than-expected at approximately 0.7, there were fewer workers within clusters than originally planned. Due to recruiting/logistical difficulties, 19 workers in 15 clusters, compared with the original 7x3 design; thus, the effect of the high ICC is muted. However, the observed variability (GSD ≈ 6) was much higher than that assumed in the sampling plan, and is the prime reason for not meeting the within 3-fold accuracy benchmark.

Due to the high variability, the AHETF demonstrated through simulations that it would take 8 more clusters of 2 workers each (totaling 16) or 10 more clusters of 1 worker to meet the goal of 3-fold accuracy[9]. They also conclude that while accuracy may be improved it is unlikely exposure estimates would be greatly affected. Finally the AHETF believes that it would not be worth the multi-year delay – nor ethically justifiable – to monitor these additional workers to meet the accuracy benchmark.

3.3.2 Secondary Objective: Evaluating Proportionality

The secondary objective of AHETF studies is to be able to distinguish, with 80% statistical power, complete proportionality from complete independence between dermal exposure and amount of active ingredient handled. Based on the AHETF analysis this benchmark was met.

To evaluate the relationship for this scenario the AHETF performed regression analysis of ln(exposure) and ln(AaiH) to determine if the slope is not significantly different than 1 – providing support for a proportional relationship – or if the slope is not significantly different than 0 – providing support for an independent relationship. Both simple linear regression and mixed-effect regression were performed to evaluate the relationship between dermal exposure (both standard and adjusted for exposure method collection inefficiencies) and AaiH. A confidence interval of 1.4 (or less) indicates at least 80% statistical power. The resulting regression slopes and confidence intervals are summarized in Table 5.

Table 5. Summary Results of log-log Regression Slopes

Model	Dermal Exposure						Inhalation Exposure		
	Standard (non-MEA)			MEA					
	Est.	95% CI	CI Width	Est.	95% CI	CI Width	Est.	95% CI	CI Width
Simple Linear	1.22	0.63 – 1.82	1.19	1.20	0.64 – 1.75	1.11	1.20	0.76 – 1.65	0.89
Mixed-Effects	1.12	0.56 – 1.67	1.11	1.06	0.56 – 1.58	1.01	1.22	1.00 – 1.44	0.44

Note: results shown using the Kenward-Rogers denominator degrees of freedom method. AHETF statistical analysis (AHE1012 Appendices E and F) provides results using the Containment method as well. Results were not substantially different.

For dermal exposure, the slope of the mixed-effects regression – preferred since it accounts for within-cluster correlation – is 1.12 with a 95% confidence interval that excludes 0 and includes 1, suggesting a proportional relationship is more consistent with the data than an independent relationship. For inhalation exposure, the mixed-effects regression slope is 1.22, with a 95% confidence intervals that excludes 0 and includes 1, suggesting a proportional relationship is more consistent with the data than an independent relationship. In terms of the secondary

[9] Note that the AHETF terminated sampling at 19 workers, two short of the original plan for 21 monitored workers. It can be concluded from the results and additional AHETF analysis that had 21 workers been monitored this would also have been inadequate to meet the accuracy target.

objective, the width of the confidence interval for both dermal and inhalation exposure was less than 1.4, indicating the power to detect complete independence from complete proportionality was greater than 80%.

Adjustments for hand rinse and face/neck wipe inefficiencies do not alter these conclusions. For MEA dermal exposures, the 95% confidence intervals for the mixed-effects log-log regression slope also excludes 0 and includes 1 and the width of the interval is less than 1.4.

3.4 Additional EPA Analysis of Scenario Characteristics

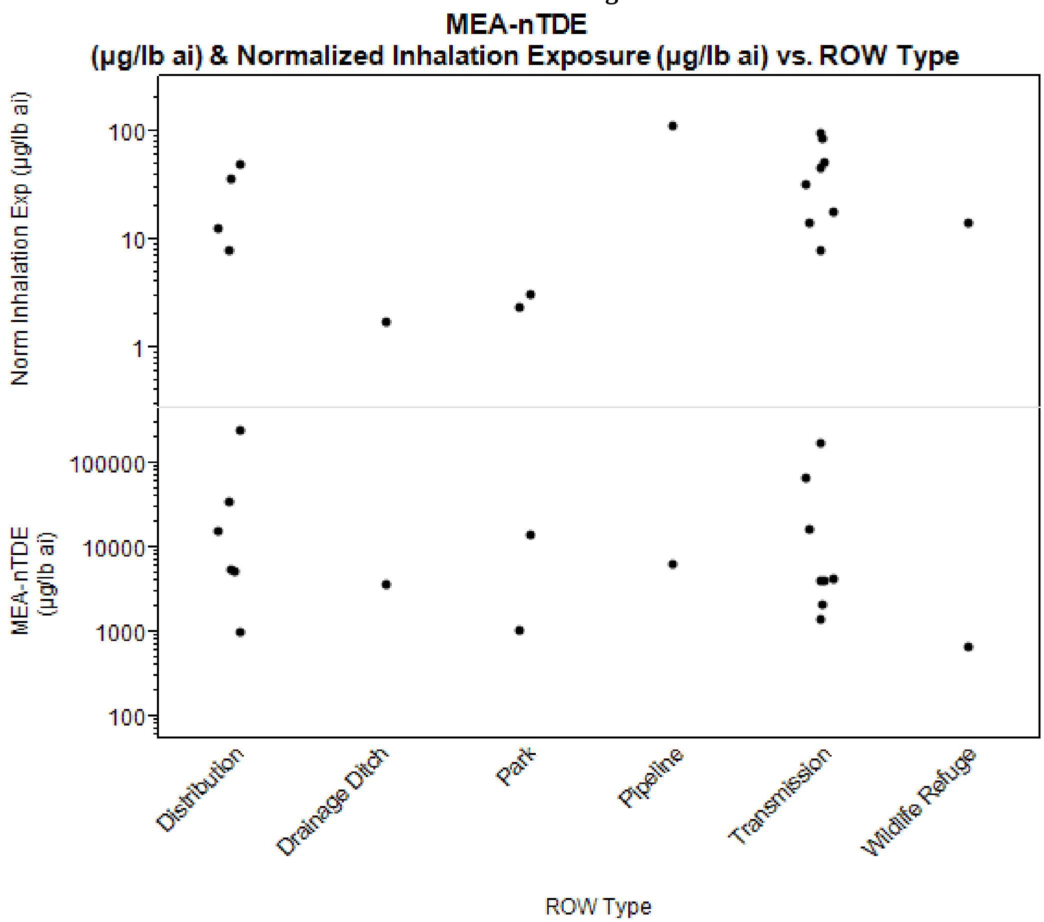
While exposure normalized to active ingredient handled is the preferred format of the data for use in exposure assessment, it is worth evaluating other aspects of the backpack ROW applicator dataset. Due to routine application and worker characteristics observed during recruitment and monitoring, some aspects of the data were further evaluated for potential effects on the data. For example, the use of additional application sites considered similar to rights-of-way in terms of terrain and vegetation type/density; the inclusion of workers who wear leggings/chaps for physical protection; prevalence of overhead spraying; and employment of the frill ("hack-and-squirt") methodology. In this scenario the extreme variability in itself warrants examination of the data.

It is important (and incumbent upon anyone analyzing this data) to note that the data were not collected in a way to be able to, with any meaningful analytical power (with the exception of amount of active ingredient handled), detect or determine any differences due to any particular factors. In fact, with a primary goal of capturing variability and diversity within the scenario, the sampling methodology use by the AHETF runs counter to the methodology (i.e., holding parameters equal) that would be employed to evaluate the significance of certain exposure factors. Nevertheless, it is still worthwhile to at least visually examine the data for any trends for further evaluation, particularly in a regulatory context.

Site of Application

As previously described, the AHETF amended the protocol to include additional sites that were not strictly rights-of-way (such as pipeline or electricity rights-of-way), but similar in terms of terrain and the undesirable target vegetation. For this backpack scenario, this included areas such as a drainage ditch, parks, and a wildlife refuge. Figure 4 below shows the normalized (unit) exposures for each site-category monitored.

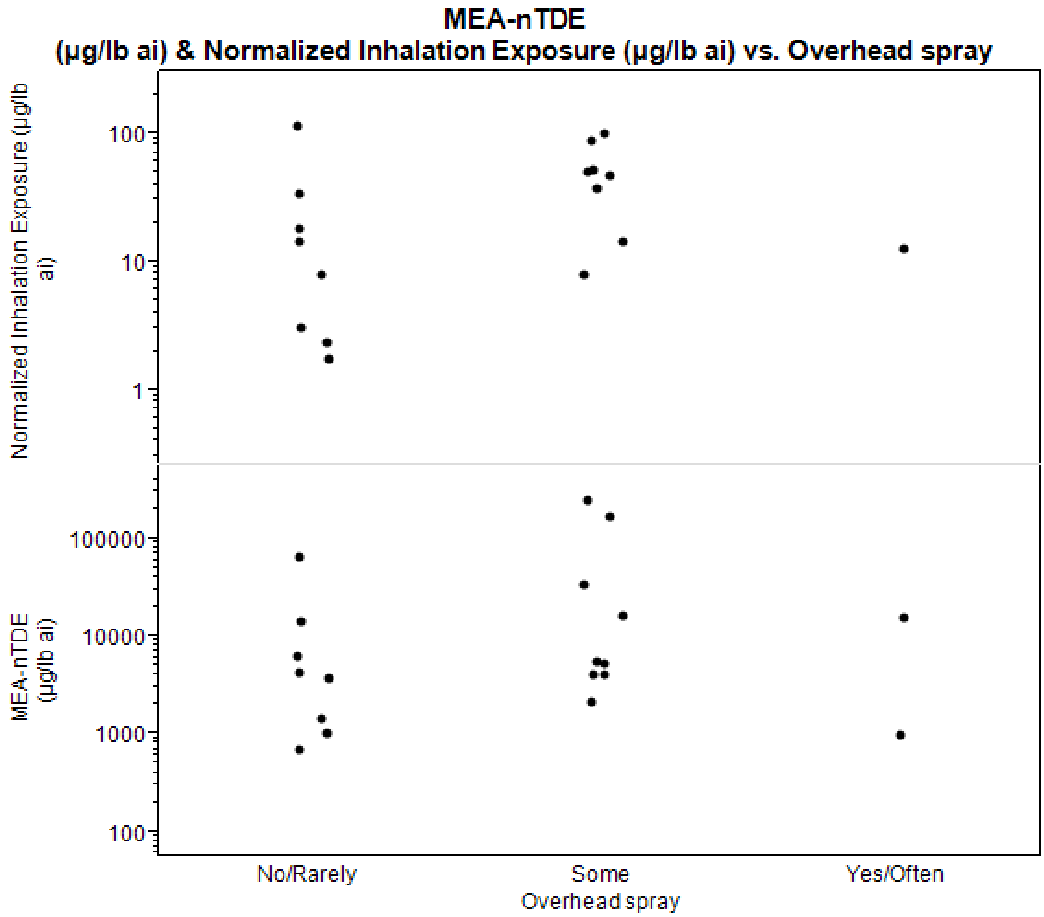
Figure 4



Prevalence of Overhead Spraying

Overhead spraying is often thought to yield higher exposures than downward spraying simply due to the potential for the spray plume/droplets to settle down upon the worker. For this backpack monitoring data the worker observations were reviewed for occurrences of overhead spraying and (crudely) quantified into the categories "Yes/Often", "Some", and "No/Rarely". Figure 5 below presents these results. It should not be surprising that frequent overhead spraying with backpacks in rights-of-way areas is infrequent (only 2 of 19 workers), since they are generally low-pressure sprayers. Should significant overhead spraying be required (to reach higher trees or foliage) another application method or equipment would likely be used.

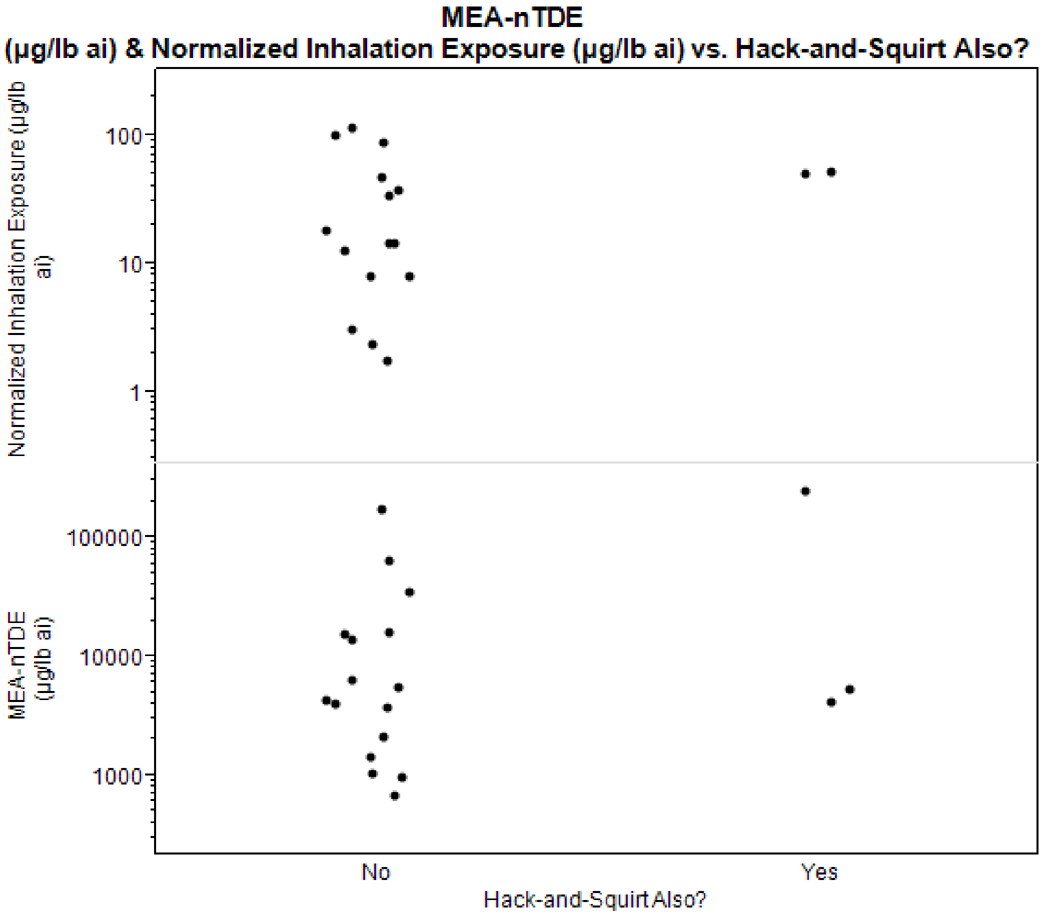
Figure 5



Frill ("Hack-and-Squirt") Applications

Because it is sometimes a routine practice of backpack applications in rights-of-way areas, workers who, in addition to their backpack spraying, employed frill applications were not excluded from the dataset. However, users of the data aware of this practice may wish to know whether that method has the potential to result in higher exposures. Figure 6 below displays exposure results for backpack applicators who did (3 of 19) and did not (16 of 19) make frill applications.

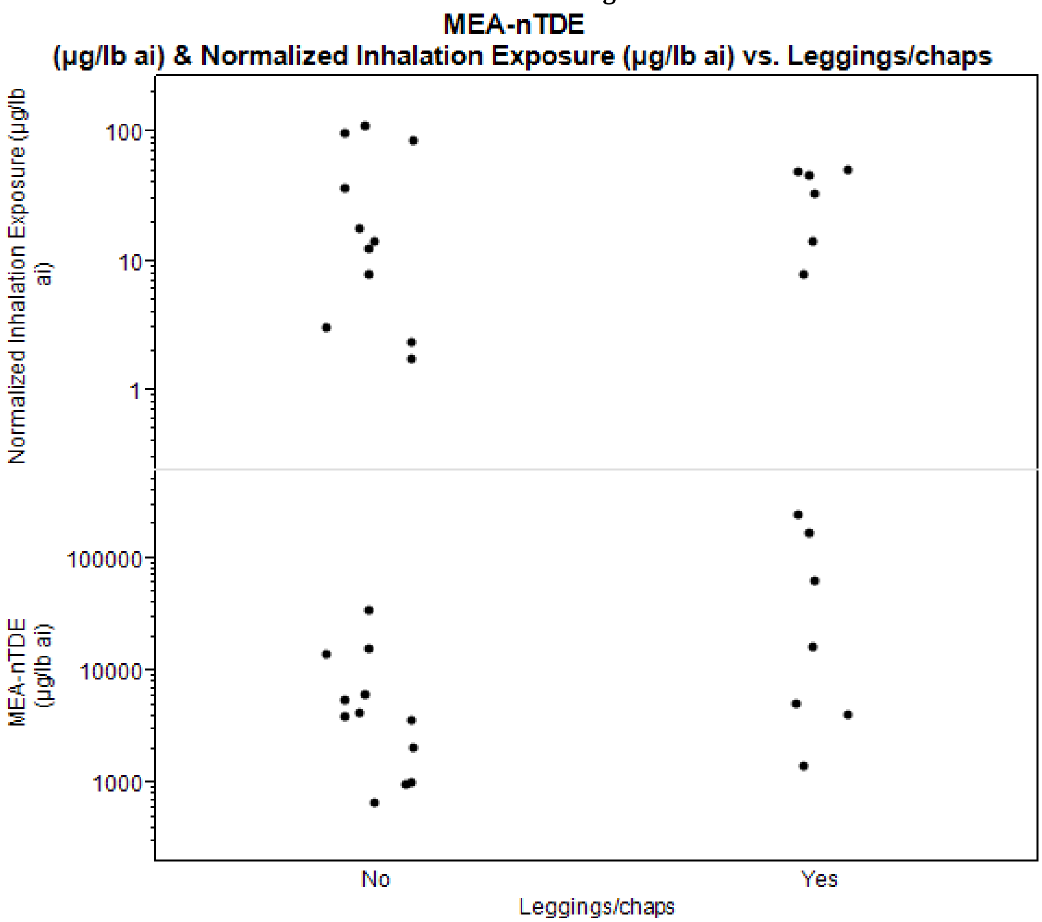
Figure 6



Use of Protective Leggings/Chaps

During recruitment it became obvious that excluding workers who wear protective leggings/chaps (to protect against snakes and thorns) from the monitoring (in order to avoid confounding) would significantly reduce the pool of available workers. Thus the AHETF amended the protocol to relax this restriction. Ultimately, slightly less than half (7 of 19) of the backpack applicators used protective leg gear. Users of the data may wish to evaluate whether there is any potential for the protective leg gear to reduce (or increase) exposure. Figure 7 below presents the data.

Figure 7



Overall, it does not appear from simple visual observations of the particular variables above, that any would be particularly useful in a regulatory context. But, again, because of the exposure sampling methodology and lack of analytical power, there could be a (true) effect, but it is not observable in the data. In addition, while difficult to quantify, a read through the worker observations also does not provide much more additional information than that which has been quantified above.

4.0 Data Generalizations and Limitations

The need for an upgraded generic pesticide handler exposure database has been publicly discussed and established (Christian, 2007). No existing exposure data for backpack applicators in rights-of-way areas met AHETF criteria for inclusion in an updated database; thus the data outlined in AHE400 (field study) and AHE1012 (scenario monograph) will serve to complete the scenario.

The data will be used generically to assess exposure for applicators applying any conventional pesticide applied as a spray using backpack sprayers to areas containing undesirable vegetation such as shrubs/bushes/vines in rights-of-way or similar areas. However, certain limitations need to be recognized with respect to collection, use, and interpretation of the exposure data.

4.1 Generic Use in Exposure Assessment

The data comprising this scenario are acceptable for use in assessing exposure for applicators applying any conventional pesticide applied as a spray using backpack sprayers to areas containing undesirable vegetation such as shrubs/bushes/vines in rights-of-way or similar areas while wearing a long-sleeve shirt, pants, shoes/socks, and chemical resistant gloves. This includes additional practices in backpack applications such as the use of frill applications and protective leg gear, as described in Section 3.3.

Importantly, use of the data generically in a regulatory context implies that the pesticide active ingredient being reviewed has a use pattern consistent with the activities and conditions represented by the data for this scenario. In other words, other pesticides may be used in rights-of-way areas for a particular purpose, but that does not automatically mean this dataset would apply for that pesticide. If, for example, a pesticide has more limited use as a spot treatment or does not require workers to fully immerse in the target vegetation, another dataset might be a better surrogate.

Additionally, even for this specific scenario, the availability of this data does not preclude additional consideration or use of acceptable available chemical-specific studies, biomonitoring studies, or other circumstances in which exposure data can be acceptably used in lieu of these data.

4.2 Applicability of AHETF Data for Volatile Chemicals

The data generated in this study are acceptable to use as surrogate data for assessing applicator exposure to other conventional pesticides used in backpack sprayers, which are generally chemicals of low volatility. Since they are not typically used in backpack sprayers, it is not expected that this dataset would be used to support regulatory decisions for high volatility pesticides (e.g., fumigants).

4.3 Use of "Unit Exposures"

As previously shown, statistical analyses provide general support for use of the exposure data normalized by the amount of active ingredient handled. Thus, EPA will continue to recommend use of the exposure data normalized by the amount of active ingredient handled as a default condition.

4.4 Representativeness and Extrapolation to Exposed Population

Targeting and selecting specific monitoring characteristics (i.e., "purposive sampling") as well as certain restrictions necessary for logistical purposes (e.g., selection of certain U.S. states to ensure a large pool of potential applicators; requiring potential applicators to use certain pesticides to ensure laboratory analysis of exposure monitoring matrices; and requiring selection of workers who normally wear the scenario-defined minimal PPE), made the studies comprising this scenario neither purely observational nor random to allow for characterization of the dataset as representative of the population of backpack applicators in rights-of-way areas.

It is important to recognize this as a limitation when making use of the data.

It appears however, that the dataset has captured routine behavior as well as limiting the likelihood of "low-end" exposures via certain scripting aspects (e.g., monitoring time requirements to avoid non-detects), both of which are valuable for regulatory assessment purposes. Also, the random elements incorporated into the recruitment process likely mitigated selection bias on the part of participants or recruiters. Thus, with respect to costs, feasibility, and utility, the resulting dataset is considered a reasonable approximation of expected exposure for this population.

5.0 Conclusions

EPA has reviewed the AHETF Backpack ROW Application scenario monograph and concurs with the technical analysis of the data as well as the evaluation of the statistical benchmarks objectives. Conclusions are as follows:

- Deficiencies in the existing scenario dataset have been recognized and the need for new data established.
- The AHETF data developed and outlined in the monograph and this review represent the most reliable data for assessing backpack application exposure in rights-of-way or similar areas.
- The primary (quantitative) objective was not met: estimates of the GM, AM, and P95 dermal exposures were not shown to be accurate within 3-fold with 95% confidence.
- The secondary (quantitative) objective was met: the dataset provided adequate statistical power to distinguish proportionality from independence between dermal exposure and AaiH.
- The assumption of proportionality between both dermal and inhalation exposure and the amount of active ingredient handled was not rejected. As a result, EPA will continue using exposures normalized by AaiH as a default condition for exposure assessment purposes for the foreseeable future.

6.0 References

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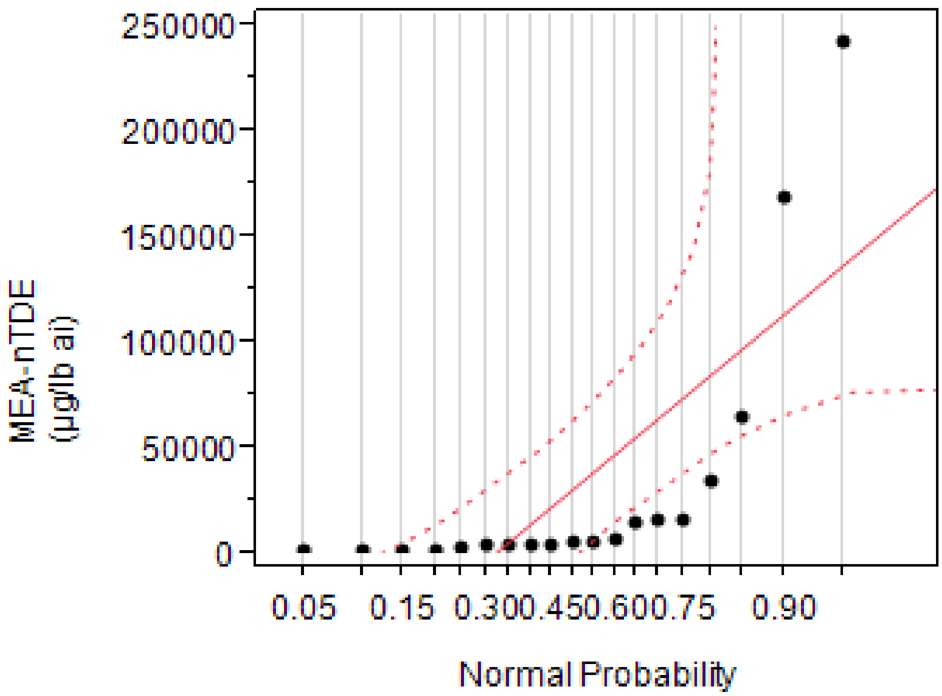
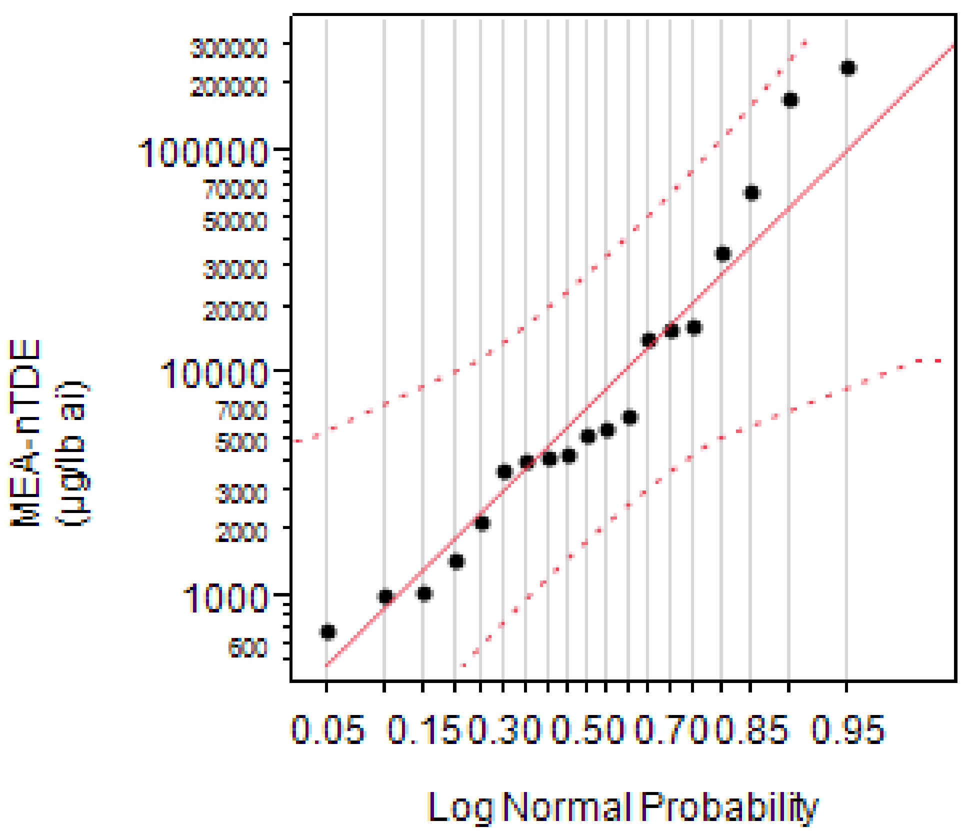
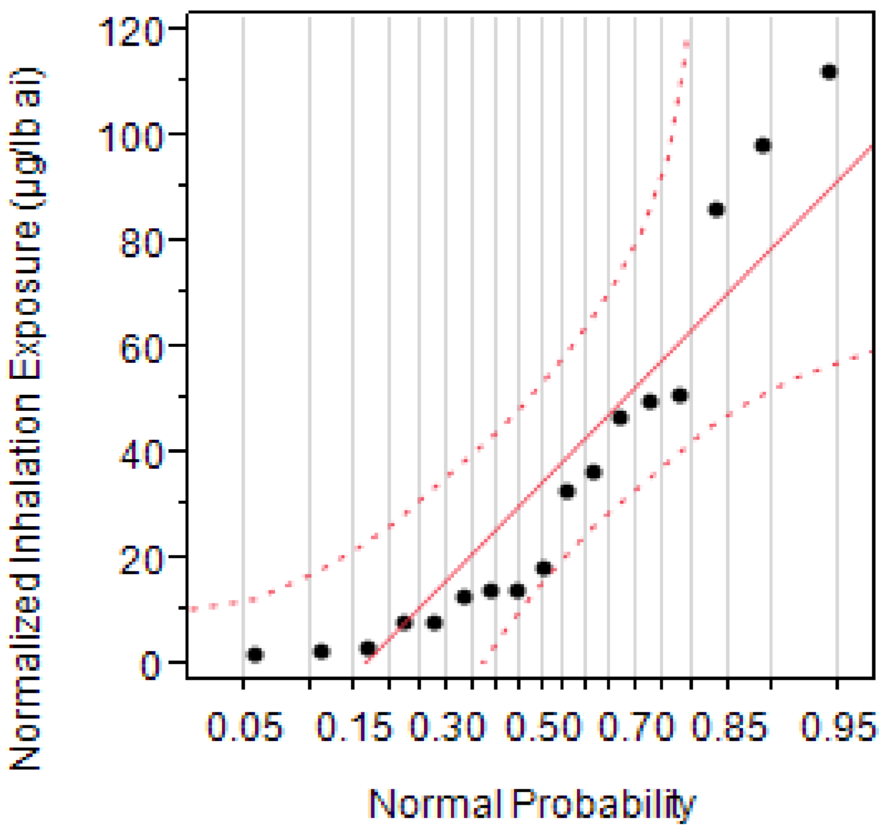
Appendix A

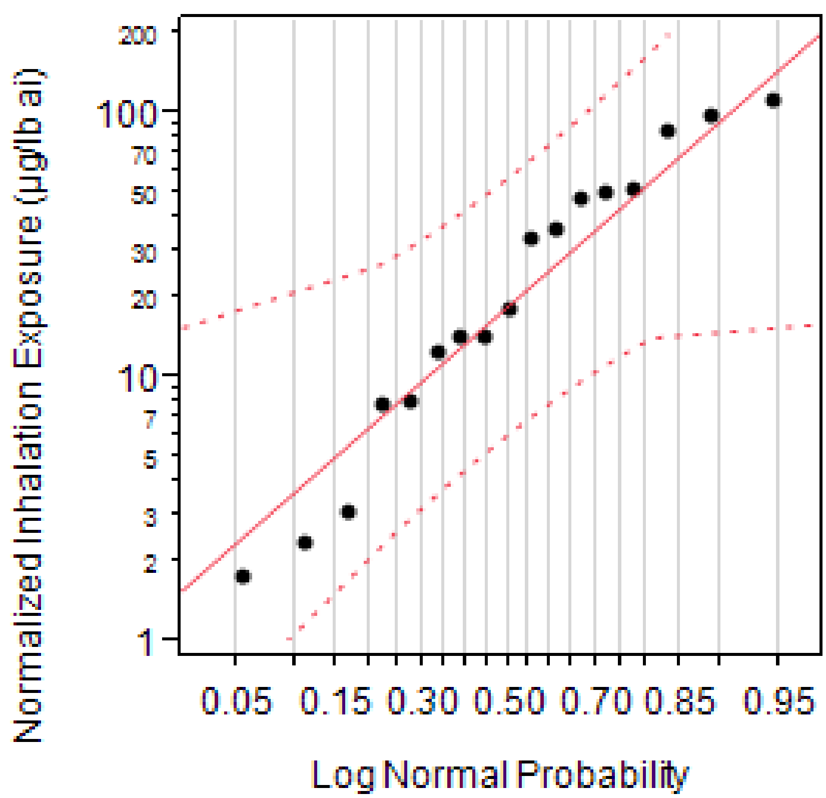
Normal and Lognormal Probability Plots of Dermal and Inhalation Unit Exposures







Normalized Inhalation Exposure (µg/lb ai)
120
100
80
60
40
20
0
0.05
0.15
0.30
0.50
0.70
0.85
0.95
Normal Probability



Normalized Inhalation Exposure (µg/lb ai)
200
100
70
50
30
20
10
7
5
3
2
1
0.05
0.15
0.30
0.50
0.70
0.85
0.95
Log Normal Probability