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

MEMORANDUM

Date: January 7, 2011

SUBJECT: Review of Agricultural Handler Exposure Task Force (AHETF) Monograph: Closed Cab Airblast Application of Liquid Sprays

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This memorandum presents the Health Effects Division review of the occupational handler exposure scenario monograph "Closed Cab Airblast Application of Liquid Sprays" submitted by the Agricultural Handler Exposure Task Force. Scientific review of the five exposure studies comprising this scenario can be found in a separate data evaluation review (DER) memorandum (Crowley, 2011 – D381148). The AHETF satisfactorily followed the study protocols and satisfied data analysis objectives. EPA considers the closed cab airblast scenario complete and its results are recommended for use in routine assessment of exposure and risk for closed cab airblast applicators.

1.0   Executive Summary

This document represents the Health Effects Division (HED) review of the Agricultural Handler Exposure Task Force (AHETF) Monograph: Closed Cab Airblast Application of Liquid Sprays (AHETF, 2010). HED confirms that the data meets the study design objectives outlined in the AHETF Governing Document (AHETF, 2008) and is considered the most reliable data for assessing exposure and risk to individuals applying liquid spray pesticides[1] with closed cab airblast equipment while wearing the following personal protective equipment (PPE): long-sleeved shirts, long pants, shoes, socks, chemical-resistant gloves, and no respirator[2]. The AHETF data and associated unit exposures are considered superior to the existing closed cab airblast applicator dataset.[3] 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 primary objective 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 was met. The secondary objective to evaluate proportionality between dermal and inhalation 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 not met. Though with less-than-expected statistical power, regression analysis does not reject proportionality between exposure and the amount of active ingredient handled for either the dermal and inhalation routes of exposure. Additional analyses point to incidental exposure sources such as contacts with exterior surfaces having a more substantial impact on exposure. This is not unexpected given the use of the enclosed cab which, as a physical barrier, is intended to prevent exposure from the airblast overspray. Thus, for this scenario, HED will investigate alternative options for use of this data, but continue for the foreseeable future to use the exposure data normalized by the amount of active ingredient as a default condition for exposure assessment purposes.

Select summary statistics for the closed cab airblast applicator scenario "unit exposures" are presented in Table 1 below, as well as the PHED value previously used for comparison.

Table 1. Unit Exposures (ug/lb ai handled): Closed Cab Airblast Applicators				
Exposure Route	**PHED**	**AHETF[a]**		
	"Best Fit"	**Geometric Mean**	**Arithmetic Mean[c]**	**95th Percentile[d]**
Dermal [b]	19	4.1	14.6	56.4
Inhalation	0.45	0.033	0.068	0.240
[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 50% adjustment of hand and face/neck measurements, since the average percent contribution of dermal exposure by the hands, face, and neck is approximately 50%.				

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[1] The data is not applicable to volatile chemicals (e.g., fumigants).

[2] 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.

[3] Pesticide Handlers Exposure Database (PHED) Scenario 12: Airblast Application, Enclosed Cab (APPL)

2.0 Background

The following provides background on the AHETF objectives for this research and also discusses previous reviews of the closed cab airblast 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 define worker exposures associated with major agricultural and non-agricultural handler scenarios. A scenario can be defined as a pesticide handling task based on activity such as mixing/loading or application. Other factors such as formulation (e.g., liquids, granules), tractor type (e.g., open or closed cab), and/or application equipment type (e.g., airblast, aircraft or boom 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, such as the scenario addressed by this monograph, an engineering control (i.e., the closed cabs for this scenario) or additional personal protective equipment/clothing may also be a key element of the scenario (e.g., certain types of headgear to reduce overhead exposures).

AHETF studies use dosimetry methods intended to define pesticide handler dermal and inhalation exposures, which 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" – expressed as exposure per weight-unit chemical 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). Unit exposures are then used generically to predict exposure for other chemicals having the same or 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 closed cab airblast equipment can be used to estimate exposure while spraying another chemical proposed for use with closed cab airblast equipment. 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, one doubles the exposure.

The AHETF approach for monitoring occupational handler exposure was based on criteria reviewed by HED 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), 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 (see Table 6).

- The secondary objective is to evaluate the assumption of proportionality between exposure and amount of active ingredient handled (AaiH) in order to be able to use the AHETF data generically across application rates. 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 contain costs, the AHETF developed a study design employing a 'cluster' strategy. Each cluster is defined by a region. Typically, these regions are defined by a few contiguous counties in a given state(s) within a US EPA growing region. For most handler scenarios a configuration of 5 regional clusters each consisting of 5 participants is used to meet the objectives from a statistical sample size perspective. 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 HED handler risk assessments considerations with respect to amount of area that could be treated in a single work day.

In this case, the scenario is application of liquid spray pesticides using airblast sprayers hauled by trucks or tractors with enclosed cabs while wearing the following personal protective equipment (PPE): long-sleeved shirts, long pants, shoes, socks, chemical-resistant gloves when conducting tasks outside the enclosed cab (e.g., marking treated acreage), and no respirator. Dermal and inhalation exposure monitoring was conducted for 24 workers[4] (referred to as "monitoring units", or MUs) applying liquid spray pesticides using closed cab airblast equipment. Five separate studies were conducted (references in Table 2 below), each monitoring different workers while spraying tree or trellis crops in 5 different states in the U.S. where

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[4] One worker in study AHE59 (WA-apple) was not monitored, reducing the originally planned total from 25 to 24. See Section 3.1 and 3.2.

airblast equipment would typically be used – citrus in Florida, pecans in Georgia, grapes in California, cherries in Michigan, and apples in Washington.

Study ID		Study Title
AHE#	EPA MRID	**Table 2. AHETF Closed Cab Airblast Applicator Studies**
AHE55	48289601	Determination of Dermal and Inhalation Exposure to Workers During Airblast Applications of Liquid Sprays Using Closed Cab Equipment in Florida Citrus
AHE56	48289602	Determination of Dermal and Inhalation Exposure to Workers During Airblast Applications of Liquid Sprays Using Closed Cab Equipment in Georgia Pecans
AHE57	48303501	Determination of Dermal and Inhalation Exposure to Workers During Airblast Applications of Liquid Sprays Using Closed Cab Equipment in Michigan Stone Fruit
AHE58	48289604	Determination of Dermal and Inhalation Exposure to Workers During Airblast Applications of Liquid Sprays Using Closed Cab Equipment in California Trellis Crops
AHE59	48303502	Determination of Dermal and Inhalation Exposure to Workers During Airblast Applications of Liquid Sprays Using Closed Cab Equipment in Washington Pome Fruit

The figures below (from AHETF, 2010) depict examples of this activity for which the exposure data are applicable.

Figure 1: Closed Cab airblast application in GA pecans

Figure 2: Closed Cab airblast application in WA apples

Figure 3: Closed cab airblast application with 2-row tower sprayer with electrostatic nozzles in CA grapes

2.2   HSRB Review and Comments

The ability of the EPA to use the closed cab airblast 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[5]. The following is a timeline of HSRB reviews related to this scenario:

Table 3. Closed Cab Airblast Application Scenario – HSRB Review Timeline	
Date	**HSRB Review**
June 2006	AHE56 (GA-pecan) Protocol (at that time titled "AHE38")
June 2008	Closed Cab Airblast Application Scenario Design
	AHE55 (FL-citrus) Protocol
	AHE56 (GA-pecan) Protocol [2nd review (1st review in June 2006)]
October 2008	Revised Closed Cab Airblast Application Scenario Design
	AHE57 (MI-cherry) Protocol
	AHE58 (CA-grape) Protocol
	AHE59 (WA-apple) Protocol

Execution of the field studies followed favorable reviews by the HSRB; however, throughout the review process, numerous comments and suggestions were noted and incorporated when possible. Throughout the review process a number of significant comments and suggestions were noted by the HSRB which were incorporated into the research whenever possible. Appendix D of the AHETF scenario monograph (AHETF, 2010) outlines both scientific and ethical issues related to the closed cab airblast scenario that were addressed. The following summarizes the more substantive scientific HSRB review comments related to this process and how the AHETF responded.

2.2.1 Characterization of non-respondents and responders who declined to participate (11/14/08 and 12/30/08 HSRB Meeting Reports)

The HSRB was concerned with the inability to evaluate study participants against the universe of closed cab airblast applicators, considering the AHETF indicated they would experience a very low response rate. Continued AHETF attempts to contact non-responders was unsuccessful, thus comparison with those eligible for participation was not possible. However, AHETF did attempt to address the HSRB comment by comparing study participants with those eligible non-participants via an informal survey of local agricultural experts.

The surveyed experts were asked to evaluate how the selected employers and equipment compares to the local population of airblast applicators, using the following characteristics to determine whether they were typical of other growers/applicators in the area where the monitoring was conducted:

- Whether the participant was the grower, employed by a grower or was a commercial applicator;
- The total acres of target crop (for grower MUs only)
- # of employed experienced airblast applicators
- Equipment type

It appears based on this informal survey/poll of local experts that the participants in these 5 studies were not atypical of the population of closed cab airblast applicators. EPA believes that

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this methodology, however, could be improved for future AHETF studies, perhaps via a more systematic database compilation of the information obtained during the recruitment phase. A summary of the findings is provided in Table 3 below.

Table 4. Synopsis of Experts Used to Evaluate the Representativeness of Monitored Workers			
Study ID	Recruited	Responded	Response
AHE55 (FL-citrus)	5 USDA agricultural extension agents	4	All agreed that the study participants were typical in the counties monitored
	1 vocational agricultural teacher	0	--
AHE56 (GA-pecan)	4 USDA agricultural extension agents	3	All agreed that the study participants were typical in the counties monitored
	2 vocational agricultural teachers	1	
AHE57 (MI-cherry)	5 USDA agricultural extension agents	5	All agreed that the study participants were typical in the counties monitored
AHE58 (CA-grape)	5 USDA agricultural extension agents	5	4 of 5 agreed that the study participants were typical in the counties monitored
			1 of 5 did not feel knowledgeable enough to comment
AHE59 (WA-apple)	5 USDA agricultural extension agents	4	3 of 4 agreed that the study participants were typical in the counties monitored
			1 of 4 did not agree – farm sizes were low and newer spray technologies were not included
	1 commissioner from Washington Apple Commission	0	--

2.2.2 Documented Survey Implementation Expertise (11/14/08 and 12/30/08 HSRB Meeting Reports)

Given the admittedly difficult attempts at recruitment for occupational pesticide exposure monitoring studies, the HSRB advised the AHETF to employ individuals with expertise in survey implementation. As a result, the AHETF abandoned use of so-called Local Site Coordinators for recruitment purposes and employed individuals familiar with survey methodology.

2.2.3 No more than 1 worker from the same employer (11/14/08 and 12/30/08 HSRB Meeting Reports)

The HSRB noted that to accurately represent the assumptions of the statistical model and "nested" sample design, the AHETF could utilize no more than 1 worker per employer due to potential exposure correlations for workers of the same employer (e.g., training similarities, etc.). The AHETF responded by indicating that, for the airblast studies, no more than 1 employee of a grower or commercial applicator would be monitored. This was accurately reflected in the executed exposure monitoring.

2.2.4 Better Characterization of the Recruitment Process (11/14/08 HSRB Meeting Report)

The HSRB recommended that the AHETF better define the recruitment process so as to identify the individuals or organizations contacted. Specifically, this arose from concerns that the recruitment will focus on growers with multiple workers at the expense of those who employ only 1 pesticide operator or growers who treat their own farm. The AHETF responded by producing a full set of recruitment-related standard operating procedures (SOPs). Among other issues, for the purposes of contacting growers on the "call" list, no distinction is made between a single grower working his own farm, a grower with a single employee, and a grower with multiple employees.

2.2.5 Capturing Applicator Behavior (11/14/08 and 12/30/08 HSRB Meeting Reports)

The HSRB was concerned that the scripted nature of the exposure monitoring would not capture the extent of exposures typical of closed cab airblast applicator behavior under normal circumstances, such as exiting the cab, opening windows, or non-adherence to label PPE requirements. Per protocol, the AHETF employed observers who recorded applicator behavior throughout the workday. All manner of behaviors were captured, from specifics of the application procedures (i.e., sequence of row treatments) to worker behaviors such as cab exits/entrances, brief window openings, and contact with exterior surfaces with bare hands. Notable observations and their potential impact on use of the data, including additional statistical analyses to evaluate their impact, are presented in Section 3.3.

2.2.6 Exclusion of Monitoring Exposure During Applications to Dormant Crops and Hops

The HSRB expressed concern with the exclusion of monitoring exposure for both dormant crops as well as hops, despite pesticide applications made to both using closed cab airblast applications. The AHETF noted that with consultation with EPA, that the monitoring conducted for the array of non-dormant crops would be considered sufficiently adequate for assessment of closed cab airblast exposures to dormant crops and hops – as well as other crops not specifically monitored. Given the logistical considerations of the sampling design (i.e., the increased chances of finding willing participants for more common pesticide applications), HED agrees that for the purposes of the generic database, the proposed studies are adequate for assessment of closed cab airblast exposure.

2.2.7 Effect of Product and Packaging (11/4/08 HSRB Meeting Report)

The HSRB noted that a rationale was not provided for the statement that neither the product nor packaging would have any influence on exposure, citing the potential for increased exposure due to cleaning spray nozzles clogged from use of solid formulations diluted in water. The AHETF recognized that formulation could potentially affect exposure during applications of liquid sprays if a solid formulation were to clog nozzles and require cleaning by the applicator. In these studies, it is apparent that workers did interact with the spray nozzles; however, since all formulations used in these studies were liquid concentrates, attribution of these interactions to use of solid formulations cannot be made.

2.2.8 Consideration of Alternative Study Design (11/4/08 HSRB Meeting Report)

Due to statistical concerns with the AHETF sampling design expressed by the HSRB during earlier review meetings, including selection of workers and sample representativeness, the HSRB outlined an alternative sampling approach, which included a more robust approach at identifying and recruiting potential participants. With respect to recruitment procedures such as developing the universe of potential participants, writing recruitment letters, employing experienced interviewers, and comparing participant characteristics with those of the applicator population, the AHETF believes, and EPA agrees that, they have followed the fundamental principles of the HSRB recommendations. The changes in recruitment procedures also satisfied the EPA requirement to incorporate "random elements" whenever feasible in the sampling process.

3.0 Results

Exposure results were reported in reports for each of the 5 studies and reviewed in Crowley, 2011 (D381148). The following sections summarize the exposure monitoring results and the scenario benchmark statistical analyses presented in the AHETF scenario monograph (AHETF, 2010).

3.1 Exposure Monitoring and Calculations

Monitored on actual days of work, participants handled between 7 to 90 lbs of active ingredient (carbaryl, malathion, or chlorothalonil), spraying 4 to 30 acres in 2 to 9 hours. Dermal exposure was measured using 100% cotton "whole body dosimeters" (WBD) underneath normal work clothing (i.e., 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).

Additionally, as presented at a June 2007 HSRB meeting, in order to account for potential residue collection method inefficiencies[6], EPA has directed the AHETF to make adjustments 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 50%, 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.

For these studies, the measurements fell in the second category and hand rinse and face/neck wipe measurements have been adjusted upward by 50% (i.e., multiplied by 2).

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

Inhalation exposure is measured using a personal air sampling pump and an OSHA Versatile Sampler (OVS) tube with a glass fiber filter and Chromosorb 102 solvent. 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 8.3 liters per minutes (LPM; converted from 1.0 m^3/hr), representing light activities such as mixing/loading light packages (NAFTA, 1998), and total work/monitoring time.[7] Dermal unit exposures (i.e., ug/lb ai handled) are then calculated by dividing the summed total exposure by the amount of active ingredient handled. Results represent dermal exposure while wearing a long-sleeved shirt, pants, shoes/socks and chemical-resistant gloves and inhalation exposure without respiratory protection.

A summary of the 24 closed cab airblast applicator MUs is provided in Table 5 below, with data plots shown in Figures 4 and 5. More detailed exposure data are provided in Appendix A, Table A-1. 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 23 (rather than 25) measurements due to unknown sampling time invalidating MU A2 in AHE59 (WA-apple). All field measurements were adjusted by their corresponding field fortification recovery values.

Table 5. Closed Cab Airblast Application MU Summary									
Study ID	MU ID	State	Crop	Work/ Monitoring Time (hours)	Area Treated (acres)	AaiH (lbs)	Unit Exposure (ug/lb ai)		
							Dermal		Inhalation
							Non-MEA	MEA	
AHE55	A1	FL	Orange	4.6	12	8	43.9	70.4	0.151
	A2	FL	Tangerine	4.3	6	15	8.9	14.7	0.0396
	A3	FL	Orange	4.6	9	24	20.1	37.2	0.245
	A4	FL	Orange	4.9	20+	40	0.33	0.63	0.0115
	A5	FL	Orange	7.8	30+	75	1.2	1.9	0.0187
AHE56	A1	GA	Pecan	4.4	12	7.9	5.3	5.6	0.0188
	A2	GA	Pecan	4.8	18	15.8	3.2	4.5	0.0628
	A3	GA	Pecan	5.9	30	24.6	2.2	2.5	0.0759
	A4	GA	Pecan	4.4	20	50.5	0.83	1.5	0.002
	A5	GA	Pecan	6.5	30	75.7	31.1	41.8	0.0254
AHE57	A1	MI	Cherry	2	4	10.8	1.9	2.6	0.0144
	A2	MI	Cherry	3.6	7.5	16.9	0.50	0.55	0.0078
	A3	MI	Cherry	4	12	27.6	2.0	2.5	0.0042
	A4	MI	Cherry	4.25	19.75	40.7	0.85	1.3	0.0173
	A5	MI	Cherry	4.7	24	90.3	0.92	1.2	0.0177
AHE58	A1	CA	Grape	5.75	35	63.5	2.2	3.7	0.0557
	A2	CA	Grape	5	20	34.4	1.1	2.0	0.186
	A3	CA	Grape	4.25	16	23.0	0.31	0.43	0.0187
	A4	CA	Grape	6	35	59.2	0.38	0.60	0.0855

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

	A5	CA	Grape	3.1	15	7.3	18.9	21.8	0.0414
	A1	WA	Apple	5	8.5	15.8	0.67	1.2	0.0840
	A2	WA	Apple	3.9	6	9.4	2.5	5.0	--[a]
	A3	WA	Apple	5.3	12	15.9	12.7	20.0	0.0848
	A4	WA	Apple	9.4	23.5	34.5	38.5	76.6	0.0347
AHE59	A5	Worker monitoring planned but not executed because: • On the scheduled monitoring day, only one field studies team was available and was already monitoring another worker • A replacement worker from another eligible grower was not monitored because the grower did not need to spray the surrogate chemical (carbaryl) • An identified backup grower did not have a cab with fully-functional air conditioning • The application window for surrogate chemical (carbaryl) ended before recruitment was possible.							
[a] Air sampling pump time unknown – sample is invalid.									

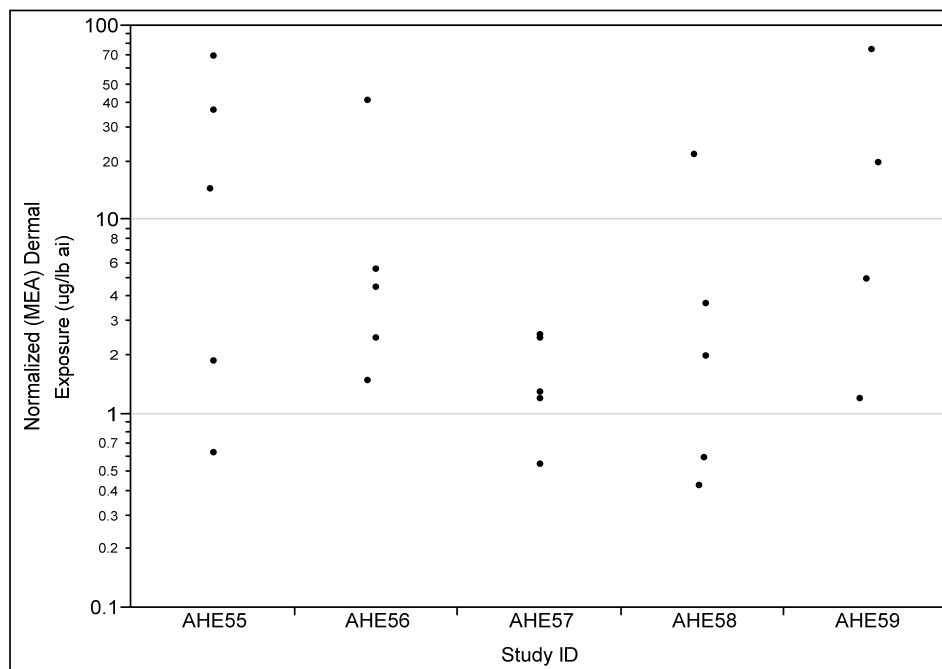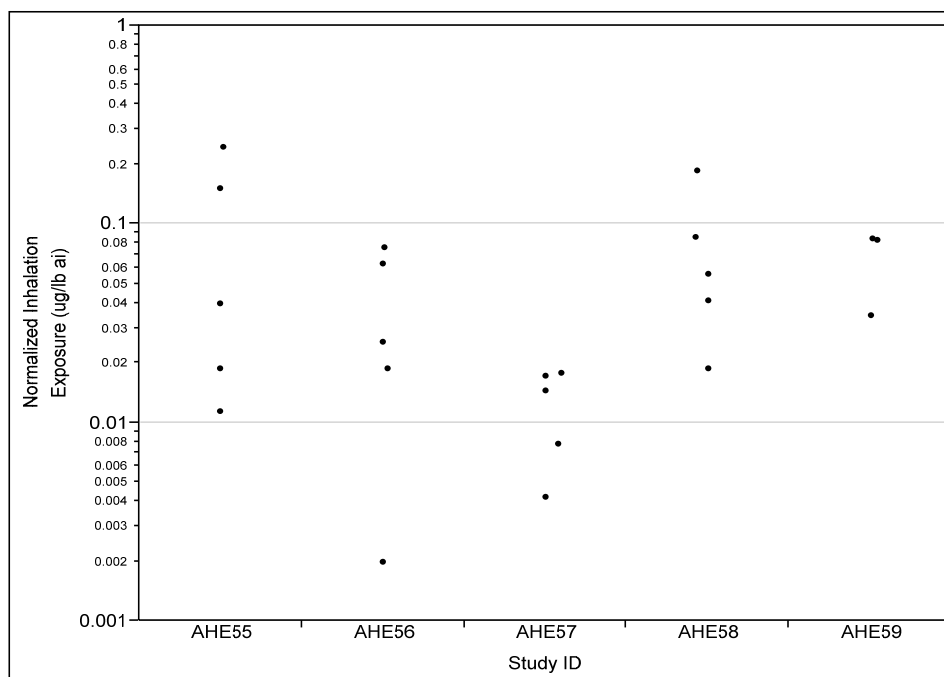**Figure 4: Dermal Unit Exposures (ug/lb ai)**

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

3.2   Evaluation of Scenario Benchmark Objectives

The AHETF monograph details the extent to which the closed cab airblast applicator scenario meets objectives described in Section 2.1. The monograph states that while the primary objective was met, the secondary objective was not. EPA (OPP/HED/CEB) has independently confirmed these results.

3.2.1   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. First, both dermal and inhalation unit exposures were shown to fit lognormal distributions reasonably well. Normal and lognormal probability plots are provided as Appendix B.

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), 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. The primary benchmark of 3-fold accuracy for select statistics was met for dermal exposure data unadjusted for hand rinse and face/neck wipe method inefficiencies. However, as shown in Table 6 below, because the adjustments for hand rinse and face/neck wipe method inefficiencies increased the sample variation, fRA values for the adjusted dermal unit exposures are slightly larger than those for the unadjusted dermal unit exposures – and in some cases, causes the fRA to rise slightly above the 3-fold accuracy threshold. Despite this result, HED considers the primary objective satisfied. Note, though not applicable to the benchmark, the fRA values for inhalation are also presented and generally are below 3-fold.

Table 6. Closed Cab Airblast Application Scenario – Results of Primary Benchmark Analysis						
	Dermal Unit Exposure (ug/lb ai)[a]			Inhalation Unit Exposure (ug/lb ai)		
Statistic	Estimate	95% CI	fRA	Estimate	95% CI	fRA
GM_S	4.1	1.9 – 8.8	2.2	0.032	0.016 – 0.064	2.0
GSD_S	4.86	3.06 – 7.69	1.6	3.28	2.27 – 4.84	1.5
GM_M	4.1	1.9 – 8.8	2.2	0.033	0.017 – 0.064	2.0
GSD_M	4.92	3.08 – 7.99	1.6	3.36	2.29 – 5.14	1.5
ICC	0.10	0.00 – 0.48	--	0.24	0.00 – 0.63	--
GM_S = geometric mean assuming SRS = "exp(average of 24 ln(UE)) values". GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 24 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	13.3	4.6 – 39.7	3.0	0.057	0.028 – 0.146	2.6
AM_U	14.1	5.2 – 43.4	3.1	0.065	0.029 – 0.154	2.4
AM_M	14.6	5.3 – 46.1	3.2	0.068	0.030 – 0.166	2.4
AM_S = average of 24 unit exposures AM_U = arithmetic mean based on GM_S = $GM_S*exp\{0.5*(ln(GSD_S)^2\}$ AM_M = variance component model-based arithmetic mean = $GM_M* exp\{0.5*(ln(GSD_M)^2\}$						
$P95_S$	70.4	13.3 – 172.6	5.3	0.186	0.071 – 0.576	3.1
$P95_U$	54.6	18.6 – 158.5	2.9	0.225	0.090 – 0.573	2.5
$P95_M$	56.4	19.0 – 168.2	3.0	0.240	0.092 – 0.624	2.6
$P95_S$ = 95th percentile (i.e., the 23rd unit exposure out of 24 ranked in ascending order) $P95_U$ = 95th percentile based on GM_S = $GM_S * GSD_S\text{^}1.645$ $P95_M$ = variance component model-based 95th percentile = $GM_M* GSD_M\text{^}1.645$						
[a] Dermal exposure values reflect 50% default adjustment for hands and face/neck measurements.						

3.2.2   Secondary Objective: Testing 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 not met.

3.2.2.1   AHETF Analysis

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 7.

Model	Dermal Exposure						Inhalation Exposure		
	Standard (non-MEA)[a]			MEA					
	Est.	95% CI	CI Width	Est.	95% CI	CI Width	Est.	95% CI	CI Width
Simple Linear[b]	0.32	-0.52 – 1.17	1.69	--	--	--	0.67	-0.02 – 1.36	1.39
Mixed-Effects	0.32	-0.52 – 1.17	1.69	0.41	-0.47 – 1.28	1.75	0.70	0.06 – 1.33	1.27

Table 7. Summary Results of log-log Regression Slopes

[a] Note because the correlation estimate (i.e., the "intra-class correlation", or ICC) is 0, the slope estimates for the simple linear regression and the mixed model are identical.
[b] Confidence intervals based on a simple linear regression are only valid if between-MU correlations are absent.

For dermal exposure, the slope of the mixed-effects regression is 0.32 with 95% confidence intervals including both 0 and 1, suggesting that an independent or a proportional relationship is consistent with the data. For inhalation exposure the mixed-effects regression slope is 0.70, with 95% confidence intervals including 1 while excluding 0, suggesting that a proportional relationship is consistent with the data. In terms of the secondary objective, the width of the confidence interval for dermal exposure was greater than 1.4, indicating the power to detect complete independence from complete proportionality was less than 80%. The AHETF suggests, and EPA concurs, that this may be the result of the range of AaiH may being small relative to the range in exposure observed.

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

3.2.2.2 Additional ICC Considerations (EPA Analysis)

Considering discussions from a meeting of the HSRB in October 2010, where a similar analysis was done for exposure to antimicrobial pesticides, EPA conducted additional analysis with respect to statistical procedures and the intra-class correlation coefficient (ICC) for the close cab airblast applicator dataset. The AHETF statistical analysis for proportionality used the Kenward-Rogers denominator degrees of freedom (DDF) method to calculate confidence intervals for the log-log regression slope[8]. However the Kenward-Rogers method in PROC MIXED in SAS 9.2 ignores covariance parameters with zero variances, suggesting that other methods should be used when the ICC is zero – such as the case for the non-MEA dermal exposure (ICC estimates for both inhalation and MEA-dermal exposure are non-zero). Under contract with EPA/OPP, ICF,

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[8] Note that the choice of denominator degrees of freedom method does not affect the estimated slope and its standard error. Since a bootstrap method was used to compute confidence intervals and fold relative accuracy for the normalized exposure summary statistics (arithmetic mean, 95th percentile, etc.), this issue does not impact those calculations.

Inc. investigated the alternate approaches to calculate the DDF for a similar set of exposure monitoring studies conducted by the Antimicrobial Exposure Assessment Task Force II (AEATF-II)[9]. The ICF memo reviewed the different methods for calculating the DDF for fixed effects in a mixed model using the SAS MIXED procedure based on an article by Schaalje, et al[10]. Table 8 below summarizes the five available methods outlined in the ICF memo.

Table 8. Summary of SAS Methods for Computing Fixed-Effects DDF in PROC MIXED[a]		
DDF Method	**SAS Abbreviation**	**Comments**
Residual	residual	Uses residual degrees of freedom. Ignores covariance structure as defined by the RANDOM and REPEATED statements. This method is not recommended.
Containment	contain	Default method when RANDOM statements are present. Accounts for the minimum contribution of the random effects that syntactically contain the fixed effects of interest.
Between-Within	bw	Default method when REPEATED statements are present and RANDOM statements are not present. Only exact when the data are balanced and the design is a repeated measures design with compound symmetry, and where the levels of the within-subjects effects are not replicated within any of the subjects. Otherwise the method is at best approximate and can be unpredictable.
Satterthwaite / Fai-Cornelius	satterth	Designed to approximate the denominator degrees of freedom for split-plot designs with complicated covariance structures and/or unbalanced data sets.
Kenward-Rogers	kr	Designed to approximate the denominator degrees of freedom for designs with complicated covariance structures and/or unbalanced data sets. Results from simulations suggest better performance than the Satterthwaite method. If a covariance parameter has zero variance then this method ignores that covariance.
[a] RANDOM statement used to define the cluster effect.		

For dermal exposure not adjusted for potential measurement collection inefficiencies (non-MEA), there are 5 workers in 4 of the clusters – AHE59 (WA-apple) had only 4 monitored workers. A simple linear model without the cluster effect gives 22 error degrees of freedom (24-2 = 22). If the mixed model and the kr method are used, the estimated cluster variance is zero and the kr method also treats the true cluster variance as zero, giving 22 error degrees of freedom. This ignores the fact that the cluster variance was estimated, so there should be some uncertainty in that parameter. If the mixed model and the containment method are used, the estimated cluster variance is again zero, but the containment method includes 4 degrees of freedom for the cluster covariance (5 – 1 = 4 clusters), giving 18 error degrees of freedom and a slightly wider confidence interval.

The containment method is better in this case because the method accounts for the uncertainty in the estimated cluster effects – though the cluster variance was estimated to be zero, it does not mean it truly is zero. For instance, if the true cluster variance was very close, but not quite, zero (e.g., 0.000000001), the kr method would either give 22 or 18 error degrees of freedom depending upon whether or not the estimated cluster variance is zero. The containment method,

[9] "Additional statistical issues for the AEATF Mop Study Statistical Review for HSRB". Contract No.: EP-W-06-091.

[10] Schaalje, G. B., J. B. McBride, G. W. Fellingham. "Approximations to Distributions of Test Statistics in Complex Mixed Linear Models Using SAS® Proc MIXED" *Proceedings of the Twenty Sixth Annual SAS Users Group International Conference*. April 2001. Long Beach, CA. ISBN 1-58025-864-6. SAS Institute, Cary, NC 27513.

on the other hand, would give 18 error degrees of freedom in either case. If the true and estimated cluster variances are zero, then the kr method is correct and the containment method is incorrect. However, since it is impossible to know for certain the true cluster variance, the recommended methods are the containment method for the mixed models when the ICC estimate is zero, and the Kenward-Rogers method for the mixed models where the ICC estimate is non-zero.

For both the dermal exposure adjusted for potential method inefficiencies and inhalation exposure the ICC estimates were not zero, thus the AHETF use of Kenward-Rogers is appropriate. For unadjusted dermal exposure data, the ICC estimate is zero for which the "containment" method is recommended. Using this method, however, does not alter the overall conclusions for the unadjusted dermal exposure with respect to the secondary study objective. That is, the 95% confidence interval still includes both 0 and 1 (-0.532 – 1.18) – with a width of 1.71, very slightly larger than the 1.69 reported by the AHETF using the Kenward-Rogers method. Additional details for this analysis are provided as Appendix A, Table A-2. The SAS code for this analysis is provided in Appendix C.

3.2.3 Applicator Behavior and Evaluation of Exposure Determinants (EPA Analysis)

Based on the analysis in Section 3.2.2.1, which showed regression slope confidence intervals failing to reject either a proportional or independent relationship, the relationship between dermal exposure and the amount of active ingredient handled is inconclusive for this scenario. While a proportional relationship seems reasonable for standard exposure scenarios (i.e., if one doubles the amount handled, that exposure would double as well seems plausible), a weak relationship for this scenario is not surprising. The engineering control defining this scenario (i.e., closed tractor cabs) appears to be very effective at reducing the opportunity for routine exposures and may limit exposure potential to sporadic events such as contacts with exterior surfaces during entry or egress from the application vehicle.

Considering this result, a closer look and additional analyses could result in more appropriate uses and interpretation of the data. As discussed in Section 2.2.5, observers recorded both typical application procedures as well as events that potentially could affect exposure. Appendix A, Table A-3 presents notable detailed observations. For example, AHE56 (GA-pecan) MU A5 was observed to have a shirt sleeve button missing, exposing his forearm skin (i.e., the upper body dosimeter at the forearm) while cleaning and reaching into the airblast sprayer. This worker had the highest inner body measurement by an approximate 10X margin (1540 ug) and the second highest hand measurement by an approximate 2X margin (1626 ug, method efficiency adjusted) – combining to result in the highest total dermal exposure measurement by an approximate 2X margin (3168 ug). The next highest dermal exposure measurement (2641 ug) was for AHE59 (WA-apple) MU A4. This worker was frequently observed not wearing chemical-resistant gloves while contacting surfaces outside the enclosed cab. Likely not coincidentally, this worker had the highest hand exposure measurement by an approximate 1.5X margin (2624 ug, method efficiency adjusted). The third highest total dermal exposure measurement (892 ug), was substantially lower than the first two, but was also observed touching

exterior surfaces with bare hands. This worker, AHE55 (FL-citrus) MU A3, in turn had the third highest hand measurement (804 ug, method efficiency adjusted) by an approximate 2X margin.

Because the exposure for these three workers potentially result from incidental contacts, a sensitivity analysis was conducted to determine whether the results showing an inconclusive relationship between dermal exposure and the amount of active ingredient handled would change if these workers were excluded. In other words, did these unusual observations obscure a proportional relationship between dermal exposure and amount of active ingredient handled? Table 9 below presents the regression slopes for the initial case (where all observations were included) and the results when each of the top 3 exposures is excluded. After excluding these exposures, the relationship between dermal exposure and the amount of active ingredient remains inconclusive (i.e., the confidence intervals still include 0).

Table 9. Dermal Exposure and Amount Handled – Sensitivity of Regression Slopes to Data Exclusion					
Model	Exposure Data Configuration	Dermal Exposure			
		Standard (non-MEA)		MEA	
		Est.	95% CI	Est.	95% CI
Mixed-Effects	All observations included (same as Table 7)	0.32	-0.52 – 1.17	0.41	-0.47 – 1.28
	Highest exposure excluded	0.027	-0.78 – 0.84	0.13	-0.71 – 0.97
	1st and 2nd highest exposures excluded	-0.073	-0.80 – 0.65	-0.006	-0.73 – 0.72
	1st, 2nd, and 3rd highest exposures excluded	-0.079	-0.74 – 0.58	-0.023	-0.69 – 0.65
Detailed results including regression plots, as well as the SAS 9.2 code, are provided in Appendix D.					

Another behavior, more quantifiable than those descriptive events just discussed, that could impact exposure is entering and exiting the vehicle hauling the airblast equipment, potentially contacting with pesticide residues as they climb on the machinery. This factor was also analyzed for its potential effect on dermal exposure. The field observations were reviewed to tally the number of times workers entered or exited the cab (including at the start and end of the workday), and ranged from 4 to 26. Most cab entrances/exits were for routine purposes such as lunch or restroom breaks or waiting during tank mixing/loading. For those getting out of the cab many times, they appeared to do so for a number of reasons including marking sprayed rows, fixing malfunctioning rigs, or cleaning or adjusting spray nozzles.

An analysis similar to the evaluation of the relationship between dermal exposure and amount of active ingredient handled was conducted for the number of cab entrances/exits – with the hypothesis that those workers who exit the cab more will have higher dermal exposures. When including all observations (adjusted for potential method inefficiencies), the results show a log-log regression slope of 1.29 with 95% confidence intervals excluding a slope of 0 and including a slope of 1 (results are similar for unadjusted dermal exposure data). This result appears to demonstrate a stronger relationship between dermal exposure and the number of times a worker exits and enters the cab than that with the amount of active ingredient handled. The same sensitivity analysis as previously done does not substantially change this conclusion either. In fact, the model fits best with all observations, with confidence intervals including zero, indicating a weaker relationship, when the highest exposures are excluded. Table 10 below summarizes these results.

Table 10. Dermal Exposure and # Cab Entrances/Exits – Sensitivity of Regression Slopes to Data Exclusion					
		Dermal Exposure			
Model	Exposure Data Configuration	Standard (non-MEA)		MEA	
		Est.	95% CI	Est.	95% CI
Mixed-Effects	All observations included	1.26	0.24 – 2.27	1.29	0.13 – 2.44
	Highest exposure excluded	0.92	-0.18 – 2.02	0.97	-0.15 – 2.10
	1st and 2nd highest exposures excluded	0.44	-0.70 – 1.59	0.44	-0.71 – 1.59
	1st, 2nd, and 3rd highest exposures excluded	0.33	-0.67 – 1.33	0.32	-0.70 – 1.33
Detailed results including regression plots, as well as the SAS 9.2 code, are provided in Appendix D.					

It appears based on these additional analyses that incidental contacts have a significant impact on exposure. This was apparent when comparing the field observations with the corresponding exposure measurements and potentially confirmed via the analysis of the relationship between dermal exposure and cab entrances/exits – more cab exits increases the likelihood for exposure via contacts with exterior surface residues. EPA intends to further evaluation the implications of this for exposure assessment, including consideration of alternate uses of the data from the default normalization by amount of active ingredient handled.

3.3   Data Generalizations and Limitations

The need for an upgraded generic pesticide handler exposure database has been publicly discussed and established (Christian, 2007). No existing closed cab airblast applicator exposure data met AHETF criteria for inclusion in an updated database, thus the 5 exposure monitoring studies were proposed to complete the closed cab airblast applicator scenario. The data will be used generically to assess exposure for applicators applying any conventional chemical applied as a spray using airblast equipment hauled by trucks or tractors with an enclosed cab. However, certain limitations need to be recognized with respect to collection, use, and interpretation of the exposure data.

3.3.1   Generic Use in Exposure Assessment

The data comprising this scenario are acceptable for use in assessing exposure for applicators applying pesticides to any crop using any type of closed cab airblast equipment, while wearing a long-sleeve shirt, pants, shoes/socks, and chemical resistant gloves. This 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.

3.3.2   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 closed cab airblast equipment, which are generally chemicals of low volatility. Since they are not typically used in airblast sprayers, it is not expected that this dataset would be used to support regulatory decisions for high volatility pesticides (e.g., fumigants).

3.3.3   Use of "Unit Exposures"

As previously shown, statistical analyses provide only limited, at best minimal, support for use of the exposure data normalized by the amount of active ingredient handled. In fact, a closer look at the data and additional analyses may potentially show that episodic, incidental exposures may ultimately have the most consequence on exposure than other factors. As a result, alternative uses of the data and/or additional exposure 'models' will be investigated. However, HED will continue to recommend use of the exposure data normalized by the amount of active ingredient handled as a default condition for the foreseeable future.

3.3.4 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 major crops that use closed cab airblast application methods to ensure a large pool of potential applicators; requiring potential applicators to use certain pesticides due 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 closed cab airblast applicators. Thus, it is important to recognize these limitations in considering this dataset as representative of all closed cab airblast applicators.

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-detect exposures), 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.

3.4 Conclusions

HED has reviewed the AHETF Closed Cab Airblast 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 closed cab airblast application scenario dataset (i.e., PHED) 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 closed cab airblast application exposure. Alternative data sources or special circumstances will be considered on a case by case basis.
- Per stated objectives, estimates of the GM, AM, and P95 were shown to be accurate within 3-fold with 95% confidence, however, the data did not provide 80% statistical power to distinguish complete proportionality or 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, though additional analyses suggest

incidental contacts with residues exterior to the enclosed cab may impact exposure more than the amount of active ingredient handled. As a result, HED will consider alternative uses of the data, but continue using exposures normalized by AaiH as a default condition for exposure assessment purposes for the foreseeable future.

4.0   References

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Appendix A
Supplemental Tables 1-4

Table A-1. Closed Cab Airblast Application – Dermal and Inhalation Exposures													
Study ID	MU ID	AaiH (lbs)	Inner WBD (µg)	Dermal								Inhalation	
				Hand (µg)		Head (µg)		Total Exposure (µg)		Unit Exposure (µg/lb ai)		Total (ug)	Unit Exposure (µg/lb ai)
				Non-MEA	MEA	Non-MEA	MEA	Non-MEA	MEA	Non-MEA	MEA		
AHE55 (FL-citrus)	A1	8	139.1	211.2	422	0.89	1.78	351	563	43.9	70.4	1.21	0.151
	A2	15	47.9	85.09	170	0.89	1.78	134	220	8.9	14.7	0.59	0.0396
	A3	24	73.7	402.1	804	7.17	14.40	483	892	20.1	37.2	5.88	0.245
	A4	40	1.0	11.88	23.8	0.27	0.54	13.2	25.3	0.33	0.63	0.46	0.0115
	A5	75	39.0	50.67	101	0.89	1.78	90.5	142	1.2	1.9	1.41	0.0187
AHE56 (GA-pecan)	A1	7.9	40.2	1.67	3.4	0.24	0.48	42.1	44.1	5.3	5.6	0.15	0.0188
	A2	15.8	31.6	18.93	37.8	0.8	1.60	51.3	71.0	3.2	4.5	0.99	0.0628
	A3	24.6	44.7	7.49	15	0.8	1.60	52.9	61.2	2.2	2.5	1.87	0.0759
	A4	50.5	10.6	31.28	62.6	0.24	0.48	42.1	73.7	0.83	1.5	0.10	0.002
	A5	75.7	1540	812.8	1626	0.8	1.60	2354	3168	31.1	41.8	1.92	0.0254
AHE57 (MI-cherry)	A1	10.8	12.7	7.16	14.4	0.24	0.48	20.1	27.6	1.9	2.6	0.16	0.0144
	A2	16.9	7.5	0.65	1.3	0.24	0.48	8.4	9.3	0.50	0.55	0.13	0.0078
	A3	27.6	43.8	9.29	18.6	2.66	5.40	55.8	67.8	2.0	2.5	0.12	0.0042
	A4	40.7	17.5	16.88	33.8	0.24	0.48	34.6	51.8	0.85	1.3	0.71	0.0173
	A5	90.3	61.3	20.62	41.2	0.8	1.60	82.7	104	0.92	1.2	1.60	0.0177
AHE58 (CA-grape)	A1	63.5	43.8	91.89	184	4.79	9.60	141	237	2.2	3.7	3.54	0.0557
	A2	34.4	6.7	29.59	59.2	0.80	1.60	37.1	67.5	1.1	2.0	6.39	0.186
	A3	23.0	4.3	2.63	5.2	0.24	0.48	7.1	10.0	0.31	0.43	0.43	0.0187
	A4	59.2	9.3	10.67	21.2	2.45	4.80	22.3	35.3	0.38	0.60	5.06	0.0855
	A5	7.3	115.4	21.31	42.8	0.24	0.48	138	159	18.9	21.8	0.30	0.0414
AHE59 (WA-apple)	A1	15.8	1.8	8.61	17.2	0.24	0.48	10.6	19.5	0.67	1.2	1.33	0.0840
	A2	9.4	0.7	22.35	44.6	0.80	1.60	23.8	46.9	2.5	5.0	Sample invalid	
	A3	15.9	85.8	114.9	230	0.80	1.60	202	318	12.7	20.0	1.35	0.0848
	A4	34.5	15.7	1312	2624	0.80	1.60	1329	2641	38.5	76.6	1.20	0.0347

Exposure	GSD	ICC	Parameter	DDF Method	Estimate	95% CI			DF
						LCL	UCL	Width	
Dermal Exposure (MEA)	4.7	0.054	Slope	residual	0.406	-0.442	1.254	1.70	22
				contain	0.406	-0.453	1.265	1.72	18
				bw	0.406	-0.442	1.254	1.70	22
				satterth	0.406	-0.448	1.260	1.71	19.55
				kr	0.406	-0.469	1.281	1.75	19.55
			Intercept	residual	3.310	0.494	6.127	5.63	22
				contain	3.310	-0.461	7.082	7.54	4
				bw	3.310	0.494	6.127	5.63	22
				satterth	3.310	0.487	6.134	5.65	21.10
				kr	3.310	0.431	6.189	5.76	21.10
Dermal Exposure (non-MEA)	4.53	0	Slope	residual	0.323	-0.521	1.171	1.69	22
				contain	0.323	-0.532	1.182	1.71	18
				bw	0.323	-0.521	1.171	1.69	22
				satterth	0.323	-0.521	1.171	1.69	22
				kr	0.323	-0.521	1.171	1.69	22
			Intercept	residual	3.159	0.364	5.953	5.59	22
				contain	3.159	-0.583	6.900	7.48	4
				bw	3.159	0.364	5.953	5.59	22
				satterth	3.159	0.364	5.953	5.59	22
				kr	3.159	0.364	5.953	5.59	22
Inhalation Exposure	3.34	0.220	Slope	residual	0.695	0.070	1.320	1.25	21
				contain	0.695	0.061	1.329	1.27	17
				bw	0.695	0.070	1.320	1.25	21
				satterth	0.695	0.063	1.328	1.27	17.51
				kr	0.695	0.059	1.331	1.27	17.51
			Intercept	residual	-2.431	-4.580	-0.282	4.30	21
				contain	-2.431	-5.300	0.438	5.78	4
				bw	-2.431	-4.580	-0.282	4.30	21
				satterth	-2.431	-4.584	-0.277	4.31	20.25
				kr	-2.431	-4.591	-0.270	4.32	20.25

Table A-2. EPA Analysis of AHETF Secondary Objective Analysis using Alternate DDF Methods

| Table A-3. Select Closed Cab Airblast Applicator Field Observations			
Study ID	MU ID	Cab ents./exits (#)	Observation
AHE55 (FL-citrus)	A1	4	1113: "Worker in cab while mix/load is performed."
			1231: "…brushes up against treated foliage due to narrow rows"
			1322: "…again brushing up against treated foliage."
			1422: "…again brushing up against treated foliage…"
	A2	16	1207: "…exits cab with gloves on, then turns valve…"
			1232: "…exits cab with gloves on, picks up a plastic pipe…"
			1245: "…exits cab after putting gloves on…"
			1412: "…exits cab wearing gloves…"
	A3	10	1032: "…exits cab…no gloves worn since no contact with equipment."
			1144: "…exits cab without gloves…shuts the door…contacting the side edge."
			1214: "…opens door with bare hands…"
	A4	4	1032: "Mixing completed. Worker did not exit cab."
			1124: "Worker remains inside cab as water was added, then test substance."
			1213: "Puts gloves on, then exits cab."
	A5	8	1032: "…exits cab wearing gloves. Opens up back of sprayer…"
			1529: "…exits cab. Not wearing gloves."
AHE56 (GA-pecan)	A1	12	0833: "Donning gloves while exiting cab…"
			0911: "Out of tractor with gloves on…"
			0934: "Donned gloves while exiting tractor…"
	A2	14	1119: "…exited cab, donned gloves."
			1149: "Exited cab, wearing fresh gloves…"
	A3	16	1137: "Climbed out of truck with gloves on…"
			1141: "Climbed up on flat bed…"
			1322: "…donned clean gloves, exited cab."
			1335: "Out of truck and puts on gloves to jump start the sprayer engine."
			1340: "Exited cab with gloves on…leaning against sprayer"
			1347: "Out of cab, gloves on…holds onto…other application equipment."
	A4	6	0134: "…at mixing/loading site. Stays inside cab…"
			0300: "Exited tractor with gloves donned."
			0346: "Waits inside the cab…during M/L."
			0405: "Donned gloves and exited cab."
			0447: "Donned gloves before exiting tractor."
	A5	22	0640: "Waited inside truck during M/L."
			0710: "…gets out of the truck to adjust spray pressure while wearing gloves."
			0742: "Rain had started…"

			Table A-3. Select Closed Cab Airblast Applicator Field Observations
Study ID	**MU ID**	**Cab ents./exits (#)**	**Observation**
			0835-0843: "Donned clean gloves. Left shirt sleeve cuff is open…states that the button popped off…clean out spray nozzles…reached down into nozzle area with right arm up to arm pit…lean on fan casing…clean the top spray nozzles"
			1017: "…out of truck wearing gloves."
			1025: "…continued to blow out spray nozzles…left shirt sleeve opening near mid-forearm, exposing the dosimeter."
			1059: "With only left glove on, climbed on flat-bed near sprayer…"
			1230: "…left lower sleeve was soiled and the edge of the right lower sleeve was soiled."
AHE57 (MI-cherry)	A1	4	1430: "Arrived at mix/load area and got out of the cab with fresh gloves."
			1528: "Put on clean gloves when he left the tractor…"
	A2	4	0710: "…stayed inside cab…"
			0829: "Dons gloves before entering cab and discards gloves outside the cab."
	A3	6	1403: "…shirts sleeve unbuttoned…also unbuttoned…above waist."
			1534: "…exited the cab with clean gloves on."
			1648: "…drop of spray…landed on his hand…wiped his hand on right pant leg."
	A4	8	1534: "Donned nitrile gloves and stood near tractor…"
			1710: "Exited tractor with clean gloves…reentered cab…again exited tractor…inner dosimeter is exposed on his back…near his waist…"
	A5	6	0630: "…exited tractor with clean gloves."
			0806: "…got out of the cab with clean gloves."
AHE58 (CA-grape)	A1	14	1005-1012: "A1 stepped out of tractor…donned face mask and glove and goggles."
			1035: "…got out to adjust nozzles."
			1122: "A1 occasionally opened back window of cab to give instructions to mixer."
			1315: "Donned glove, goggles. Turned off nozzles…"
	A2	8	0948: "Mixer overfilled tank. Two-three gallons spilled at top of tank. Re-entered tractor. Did not step in spill."
	A3	10	Nothing noteworthy.
	A4	12	0330: "Entered field for bathroom break. Refused hand wash."
			0338: "Adjusted agitation…after donning gloves."
			0345: "…got out of cab…to check pressure and agitation…Wore safety glasses and gloves."
	A5	4	0814: "Turned off water near tank with bare hand…"
			0930: "Touched inner dosimeter (cuff) with bare hand."
AHE59 (WA-apple)	A1	10	Gen. obs.: "…did not wear the chemical resistant gloves during the mixing/loading process…"
			0858: "Climbed back into cab, opened door with bare hands."
			0951: "Opened cab door and tied ribbon marker to tree (observer unable to determine whether gloves worn during this process)."
	A2	4	Gen. obs.: "The applicator was not observed to handle anything except the door and door handle…Door opened

Study ID	MU ID	Cab ents./exits (#)	Observation
**Table A-3. Select Closed Cab Airblast Applicator Field Observations**
			with bare hand."
			1000: "Arrives at mixing/loading station remained sitting inside cab."
	A3	12	0821: "Put on chemical resistant gloves and goes to airblast sprayer…"
			0828: "Remained in cab during loading."
			0956: "Opened truck door with bare hands…"
			1209: "Exited tractor cab and wiped nose with bare hand."
			1248: "Placed gloved hand on lever...Touched another valve on spray tank with gloved hand."
	A4	26	Gen. obs.: "Exchange of tractor and sprayer…"
			0822: "Inner dosimeter cuff is observed at right wrist, out from right shirt sleeve. Long sleeve shirt is not tucked into pants.
			0833: "Spoke to mixer loader through opened back window of tractor cab. Closed window"
			1102: "…exited cab and with bare hands picked up a marker from ground…"
			1320: "Exited cab, walked back to sprayer and with bare hands, turned lever…"
			1432: "Walked to front of spray tank and with bare hand turned lever…"
			1500: "Opened rear window…"
			1549: "…walked back to sprayer and with bare hands, turned off a couple nozzles…"

Appendix B

Normal and Lognormal Probability Plots of Dermal and Inhalation Unit Exposures

Normal Quantile Plot

Log Normal Probability
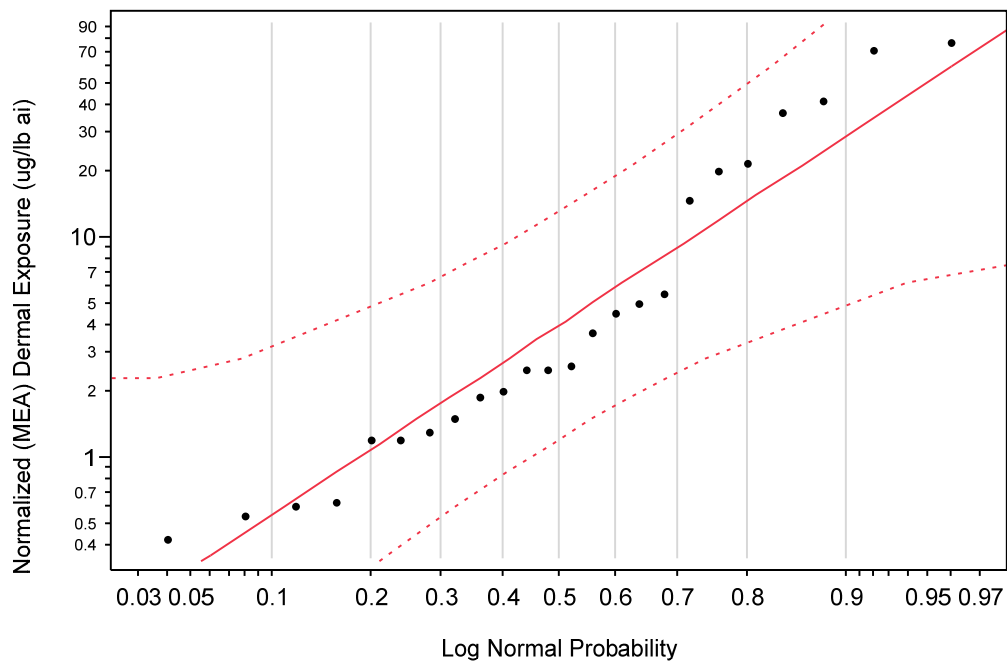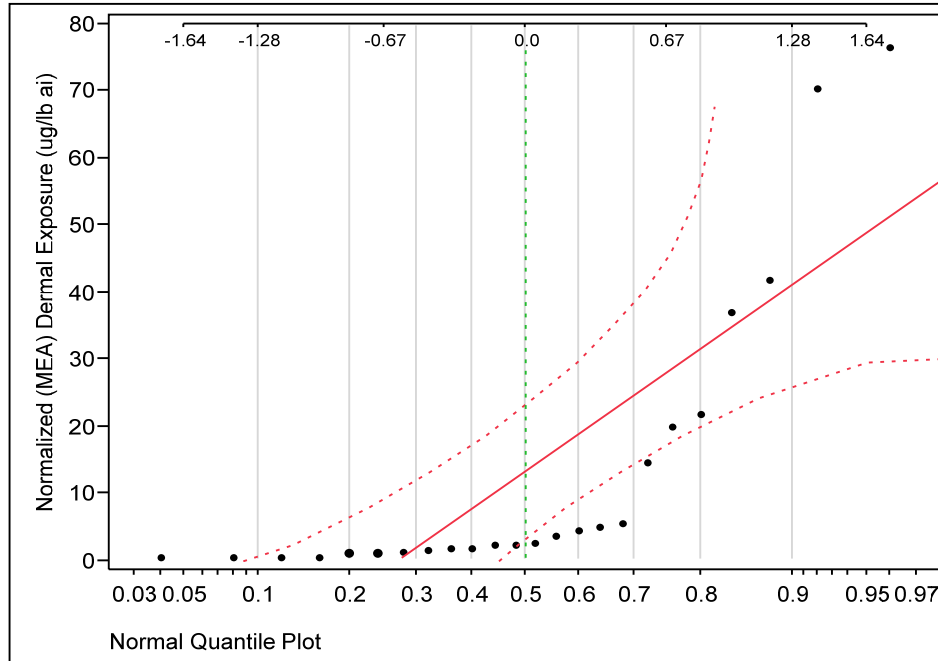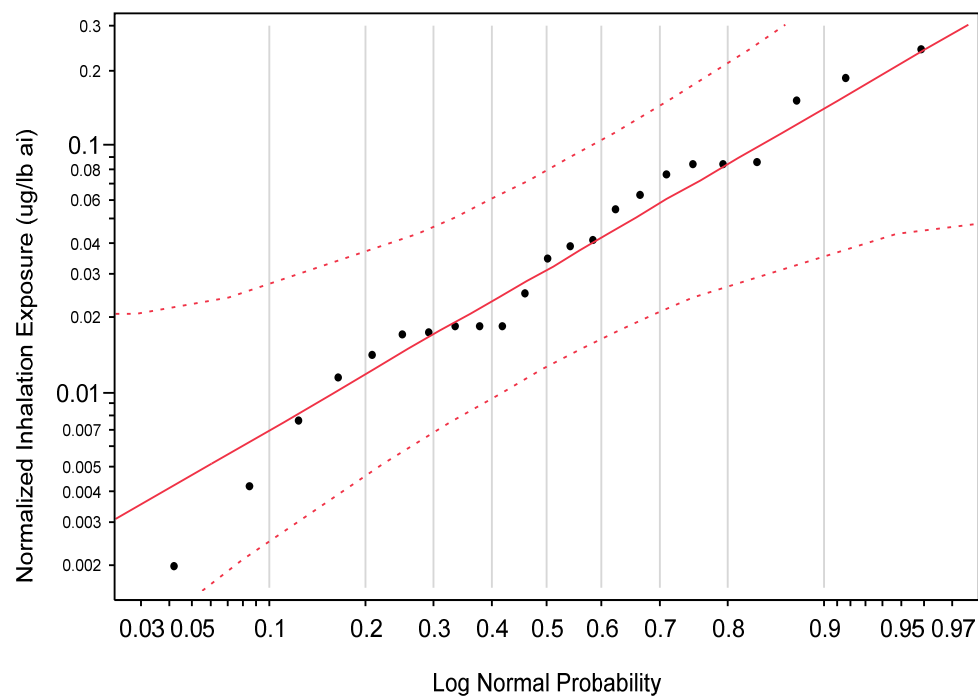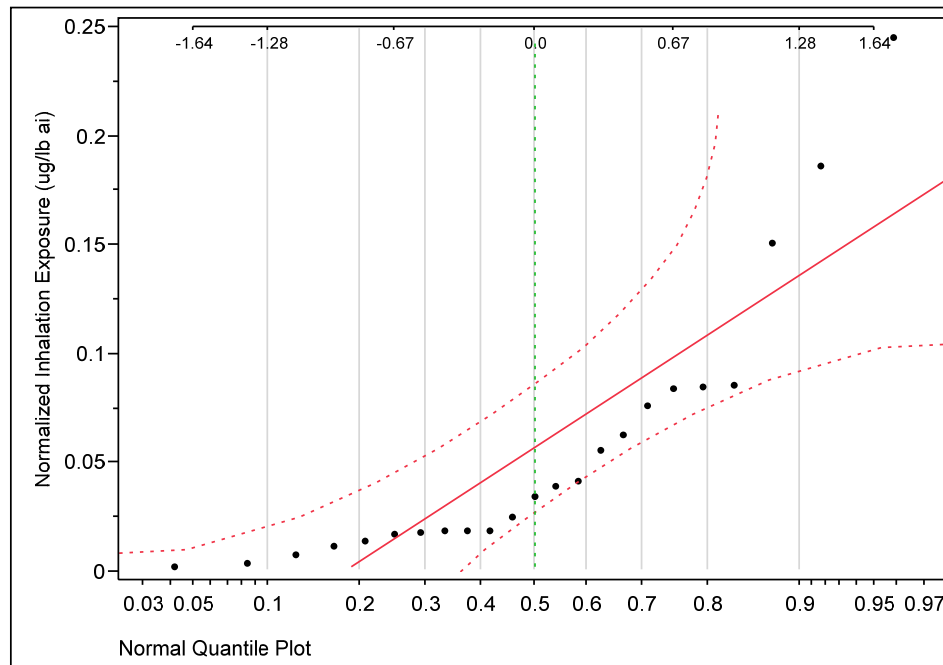
Appendix C
SAS Code for "Different Denominator Degrees of Freedom Analysis" (Section 3.2.2.2)

Note – the code below references the following ".csv" files to be housed in the same folder/directory:

"CCAB-QAd-Final – 11-8-10.csv"
"CCAB-with MEA-QA'd_FINAL 6-10-10 - EPA vers 6-15-10.csv"

1. Name file with code below as "Eval_CCAB_HED.sas"

```
Options LS=93 PS=59 NoDate NoNumber FormDLIM='-' Mprint;

Title1 "CCAB Scenario: Benchmark Evaluation Analyses";

LibName Here '.';
%Let DataSet=CCABData;

  ** Identify Excel spreadsheets with data (saved in CSV format) **;

FileName _DermInh "CCAB-QAd-Final - 11-8-10.csv";
FileName _MEADerm "CCAB-with MEA-QA'd_FINAL 6-10-10 - EPA vers 6-15-10.csv";

  *** Read in the non-MEA dermal and the inhalation data  ***;

Data DermInh;
  Infile _DermInh Delimiter=',' lrecl=300 dsd FirstObs=64;

      Length MUID $8 Study $10 MU $4 Town $40 Crop $16;
      Length c1-c26 cInh cNrmInh $16;
      InFormat MonDate mmddyy10.;
      Format MonDate mmddyy10.;

  Input Study MU AaiH
        c1-c5 Derm NrmDerm
        c6-c8 cInh cNrmInh
        c9-c14 MonDate c15-c26 Crop;
  If Study=' ' then delete;

    *--> Create an MU ID variable from Study and MU code --;
  MUID = Trim(Study) || "-" || Trim(MU);

    *--> Put nearest town and state together --;
  Town = Trim(c17) || " " || Trim(c15);

    *--> Handle missing inhalation exposures --;
  If cInh="---"
      then Inh=.;
      else Inh=Input(cInh,16.);
  If cNrmInh="---"
      then NrmInh=.;
      else NrmInh=Input(cNrmInh,16.);

  Keep Study MUID MonDate Crop Town AaiH Derm NrmDerm Inh NrmInh ;
```

```
Run;

   *** Read in the MEA Dermal data  ***;

Data MEADerm;
   Infile _MEADerm Delimiter=',' lrecl=300 dsd FirstObs=33;

        Length MUID $8 Study $10 MU $4;
        Length c1-c5 $16;

   Input Study MU AaiH c1-c5 Derm_MEA NrmDerm_MEA;
   If Study=' ' then delete;

   MUID = Trim(Study) || "-" || Trim(MU);

   Drop MU c1-c5;
   Keep MUID Derm_MEA NrmDerm_MEA;

Run;

   *** Combine all exposure data into a single SAS dataset ***;

Proc Sort Data=DermInh;
        By MUID;
Run;
Proc Sort Data=MEADerm;
        By MUID;
Run;
Data &DataSet;
        Merge DermInh MEADerm;
        By MUID;
Run;

    ** List the dataset for documentation purposes **;

Proc print data=&DataSet;
   Title2 "Listing of Dataset &DataSet";
   ID Study MUID;
Run;

    ** Save as a permanent SAS dataset for possible future use **;

Data Here.&DataSet;
        Set &DataSet;
Run;




   *** Perform benchmark objective evaluations ***;



%Include "Macro_ObjEval_REG.sas";
%ObjEvalREG(&DataSet,Study,MUID,AaiH,Derm,NrmDerm);
```

```
%ObjEvalREG(&DataSet,Study,MUID,AaiH,Inh,NrmInh);
%ObjEvalREG(&DataSet,Study,MUID,AaiH,Derm_MEA,NrmDerm_MEA);
*EndSAS;
```

2.   Name file with code below as "Macro_ObjEval_REG.sas"

```
%Macro ObjEvalREG(Dset,Clus,MU,AaiH,Exp,NrmExp);

  *---> Extract Needed Data ---;

Data AnaSet;
  Set &Dset;
  Clus=&Clus;
  MU=&MU;
  Exp = &Exp;
  If Exp=. then delete;
  AaiH = &AaiH;
  NrmExp = &NrmExp;
  LnAaiH = Log(AaiH);
  LnExp = Log(Exp);
  LnNrmExp = Log(NrmExp);
  Keep Clus MU Exp AaiH NrmExp LnAaiH LnExp LnNrmExp;
Run;



Proc Sort Data=AnaSet; By Clus MU;
Proc Print Data=AnaSet NoObs Label;
   By Clus; ID Clus;
   Var MU AaiH Exp NrmExp;

Run;

proc datasets library=work;
delete misc1 misc2;
run;

%do meth=1 %to 5;

%if &meth=1 %then %let method=residual;
%if &meth=2 %then %let method=contain;
%if &meth=3 %then %let method=bw;
%if &meth=4 %then %let method=satterth;
%if &meth=5 %then %let method=kr;



Proc Mixed Data=AnaSet Method=REML;
Title2 "Mixed Model Regression of Ln Exposure on Ln ";
Class Clus;
Model LnExp =  LnAaiH  / DDFM = &method;
Random Clus;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope' LnAaiH 1 / CL ;

ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
```

```sas
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Clus=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper ddfmethod df;
Run;

proc Print data=misc;
run;

proc append base=misc2 data=misc;
run;




%end;

proc export data=misc2 file="F:\AHTEF Monograph\CCAB study\mixed model with
only linear term.xls" dbms=excel2000 replace;
sheet="Mixed Linear model Exp &Exp";
run;




%Mend ObjEvalREG;
*=========================================================;
```

Appendix D

Results and SAS 9.2 Code for:

Regression Sensitivity to Dermal Exposure Data Exclusion

and

Statistical Evaluation of "Cab Entrances/Exits"

Note: The following analyses were conducted for dermal exposure (MEA corrected): If ICC is zero then containment method was used for calculating 95% C.I for slope and intercept, else KR method was used.

A. Use of all observations (no exclusions).

Regression model: ln(dermal exposure)=Intercept + ln(number of Exits)

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	1.8549	18.5	-0.7082	4.4180	3.95169	.004764165	5.12624
2	Slope_ln(number_exits)	1.2853	20.2	0.1316	2.4390	.	.	2.30735
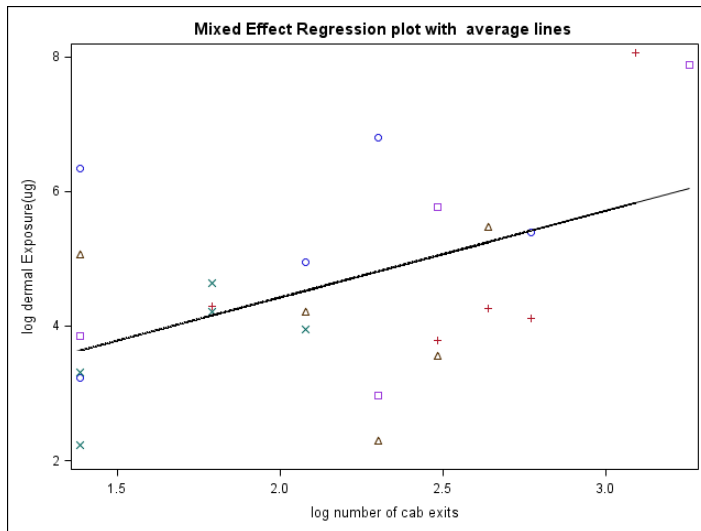
B. Removing the observation with maximum dermal exposure: Study ID: AHE56 ; MUID: A5.
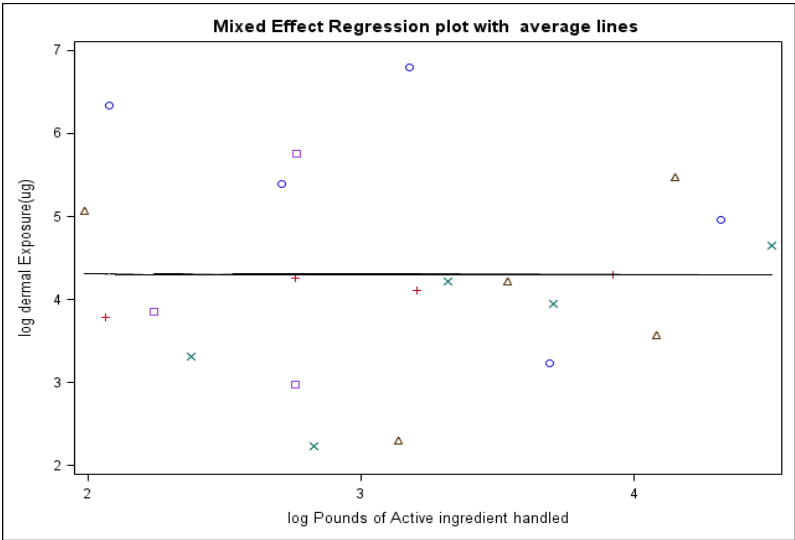
Regression model: ln(dermal exposure)=Intercept + ln(Ai)
16
                                        09:27 Tuesday, December 14,
2010

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	4.0466	20.3	1.3275	6.7658	4.12162	0.085456	5.43824
2	Slope_ln(ai)	0.1322	18.9	-0.7060	0.9703	.	.	1.67638
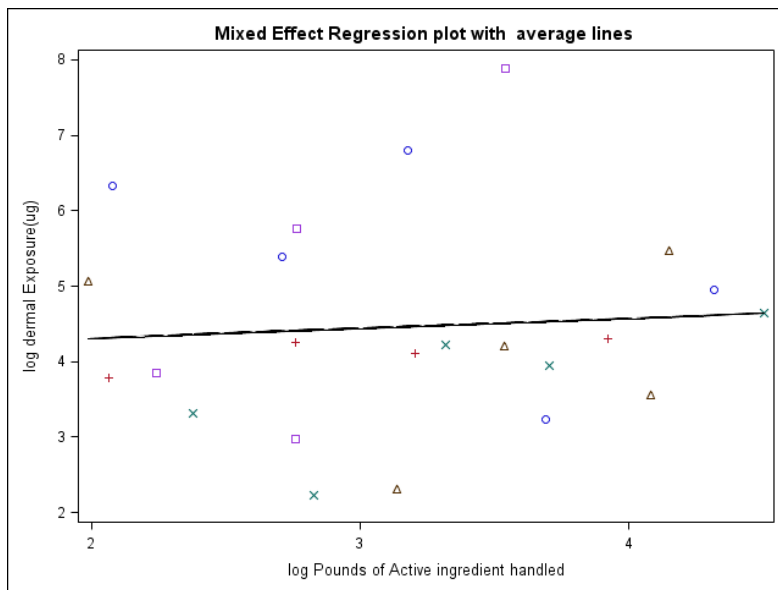
Mixed Effect Regression plot with average lines

Regression model: ln(dermal exposure)=Intercept + ln(number of
exits)   21

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	2.4112	20.3	-0.07201	4.8943	3.71350	0.10173	4.96634
2	Slope_ln(number_exits)	0.9730	21	-0.1513	2.0973	.	.	2.24864
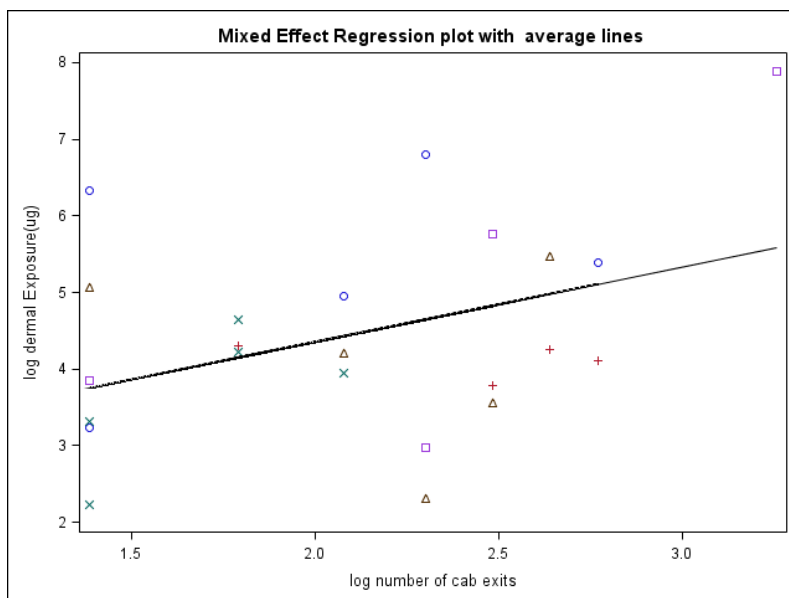
Mixed Effect Regression plot with average lines

C. Removing the first and second highest observations in terms of dermal exposure:

Study ID: AHE56 ; MUID: A5 ; Study ID: AHE59 MUID: A4

Regression model: ln(dermal exposure)=Intercept + ln(Ai)

09:27 Tuesday, December 14, 2010

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	4.3180	19.6	1.9769	6.6591	3.39500	0.11084	4.68224
2	Slope_ln(ai)	-0.00569	18.7	-0.7315	0.7201	.	.	1.45155

Mixed Effect Regression plot with average lines

Regression model: ln(dermal exposure)=Intercept + ln(number of exits)

09:27 Tuesday, December 14, 2010

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	3.3912	19.7	0.9295	5.8529	3.33272	0.12368	4.92339
2	Slope_ln(number_exits)	0.4417	20	-0.7081	1.5915	.	.	2.29952
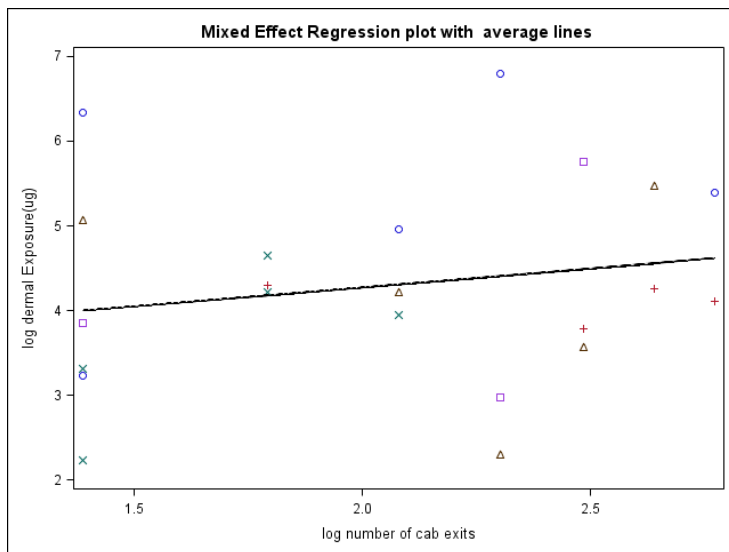
Mixed Effect Regression plot with average lines

D. Removing the first three highest observations in terms of dermal exposure: **Study ID: AHE56 ; MUID: A5 ; Study ID: AHE59 MUID: A4 ; Study ID: AHE55 MUID: A3**

Regression model: ln(dermal exposure)=Intercept + ln(Ai)
                                          09:27 Tuesday, December 14,
2010

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	4.2580	4	1.4308	7.0851	3.00727	0	5.65434
2	Slope_ln(ai)	-0.02250	15	-0.6922	0.6472	.	.	1.33932
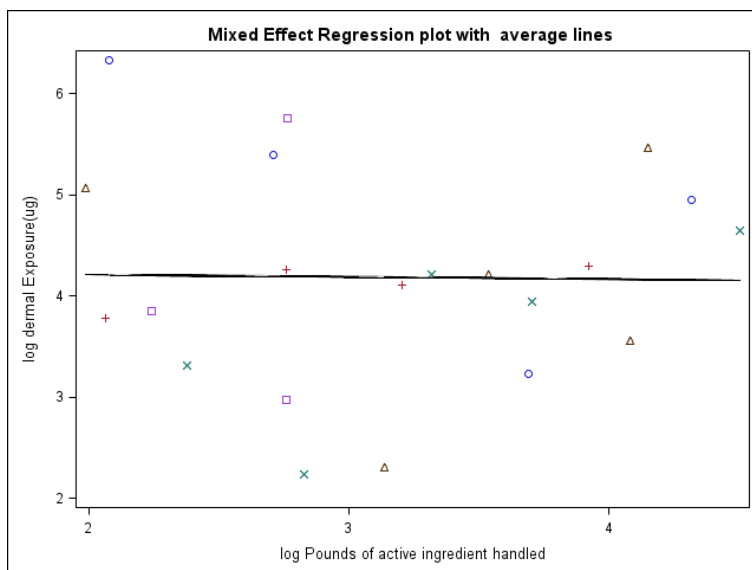
Mixed Effect Regression plot with average lines

Regression model: ln(dermal exposure)=Intercept + ln(number of exits)   52

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Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	3.5449	4	0.7824	6.3075	2.97011	0	5.52507
2	Slope_ln(number_exits)	0.3150	15	-0.6952	1.3251	.	.	2.02026

Mixed Effect Regression plot with average lines
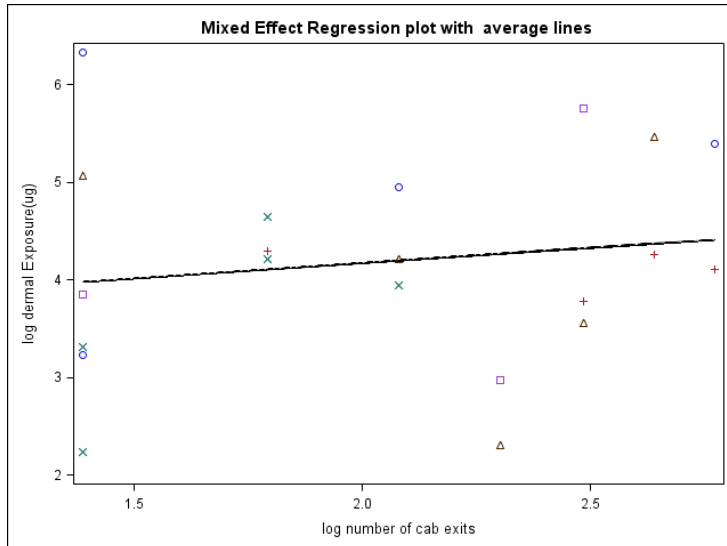
SAS Code

```
/* MEA corrected */

data monograph;
input   StudyID $ MUID $ ai    number_cab_exits  Total_residue     Cluster
; datalines;
AHE55 A1    8      4      563   1
AHE55 A2    15     16     220   1
AHE55 A3    24     10     892   1
AHE55 A4    40     4      25.3  1
AHE55 A5    75     8      142   1
AHE56 A1    7.9    12     44.1  2
AHE56 A2    15.8   14     71    2
AHE56 A3    24.6   16     61.2  2
AHE56 A4    50.5   6      73.7  2
AHE56 A5    75.7   22     3168  2
AHE57 A1    10.8   4      27.6  3
AHE57 A2    16.9   4      9.3   3
AHE57 A3    27.6   6      67.8  3
AHE57 A4    40.7   8      51.8  3
AHE57 A5    90.3   6      104   3
AHE58 A1    63.5   14     237   4
AHE58 A2    34.4   8      67.5  4
AHE58 A3    23     10     10    4
AHE58 A4    59.2   12     35.3  4
AHE58 A5    7.3    4      159   4
AHE59 A1    15.8   10     19.5  5
```

```
AHE59 A2      9.4    4       46.9   5
AHE59 A3      15.9   12      318    5
AHE59 A4      34.5   26      2641   5
;

*/case 1 No observation is deleted*/;
data monograph;
set monograph;
ln_ai=log(ai);
ln_number_exits=log(number_cab_exits);
ln_total_residue=log(Total_residue);
run;


proc mixed data=monograph;
class cluster;
model ln_total_residue=ln_ai/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(ai)' ln_ai 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;


data covout;
set covout ;
run;


*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " No observation has been removed ";
Title " Regression model: ln(dermal exposure)=Intercept + ln(Ai)";
proc Print data=misc;
run;


 proc mixed data=monograph;
   class cluster;
   model ln_total_residue=ln_ai/ outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_ai="log Pounds of Active ingredient handled";
run;
```

```
Title "Mixed Effect Regression plot  ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_ai/group=cluster;
   series y=pred x= ln_ai/group=cluster ;
run;




proc mixed data=monograph;
class cluster;

model ln_total_residue=ln_number_exits/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(number_exits)' ln_number_exits 1 / CL ;

ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " No observation has been removed ";
Title " Regression model: ln(dermal exposure)=Intercept + ln(number of
Exits)";
proc Print data=misc;
run;

proc mixed data=monograph;
   class cluster;
   model ln_total_residue=ln_number_exits/ outp=pred1 outpm=pred2;
   random cluster;
Label
```

```
  ln_total_residue= "log dermal Exposure(ug)"
ln_number_exits="log number of cab exits";
run;


Title "Mixed Effect Regression plot ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_number_exits/group=cluster;
   series y=pred x=ln_number_exits;
run;




*/case 2 deleting one observation*/;
data monograph1;
set monograph;
If total_residue=3168  then delete;
run;


proc mixed data=monograph1;
class cluster;

model ln_total_residue=ln_ai/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(ai)' ln_ai 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
```

```sas
Run;
Title " Removing the highest observation ranked by dermal exposure";
Title1 " Regression model: ln(dermal exposure)=Intercept + ln(Ai) ";
proc Print data=misc;
run;


proc mixed data=monograph1;
   class cluster;
   model ln_total_residue=ln_ai/ outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_ai="log Pounds of Active ingredient handled";
run;



Title "Mixed Effect Regression plot  ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_ai/group=cluster;
   series y=pred x= ln_ai ;
run;




proc mixed data=monograph1;
class cluster;

model ln_total_residue=ln_number_exits/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(number_exits)' ln_number_exits 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing the highest observation ranked by dermal exposure";
```

```sas
Title " Regression model: ln(dermal exposure)=Intercept + ln(number of exits)
";
proc Print data=misc;
run;
proc mixed data=monograph1;
    class cluster;
    model ln_total_residue=ln_number_exits/ outp=pred1 outpm=pred2;
    random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_number_exits="log number of cab exits";
run;


Title "Mixed Effect Regression plot  ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
    scatter y=ln_total_residue x=ln_number_exits/group=cluster;
    series y=pred x=ln_number_exits;
run;



*/case 3 deleting two observations*/;
data monograph2;
set monograph;
If total_residue=3168 or total_residue=2641 then delete;
run;


proc mixed data=monograph2;
class cluster;

model ln_total_residue=ln_ai/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(ai)' ln_ai 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
```

```sas
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing two highest observation ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(Ai) ";
proc Print data=misc;
run;

proc mixed data=monograph2;
   class cluster;
   model ln_total_residue=ln_ai/ outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_ai="log Pounds of Active ingredient handled";
run;



Title "Mixed Effect Regression plot  ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_ai/group=cluster;
   series y=pred x= ln_ai ;
run;




proc mixed data=monograph2;
class cluster;

model ln_total_residue=ln_number_exits/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(number_exits)' ln_number_exits 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
```

```sas
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing two highest observations ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(number of exits)
";
proc Print data=misc;
run;
proc mixed data=monograph2;
   class cluster;
   model ln_total_residue=ln_number_exits/ outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_number_exits="log number of cab exits";
run;


Title "Mixed Effect Regression plot  ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_number_exits/group=cluster;
   series y=pred x=ln_number_exits;
run;

*/case 4 deleting three observations*/;

*---> Additional Calculations from Regression ---;
data monograph3;
set monograph;
If total_residue=3168 or total_residue=2641 or total_residue=892 then delete;
run;


proc mixed data=monograph3;
class cluster;

model ln_total_residue=ln_ai/ddfm=contain;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(ai)' ln_ai 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
```

```
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing all three highest observation ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(Ai) ";
proc Print data=misc;
run;
proc mixed data=monograph3;
   class cluster;
   model ln_total_residue=ln_ai /ddfm=contain outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"

ln_ai="log Pounds of active ingredient handled";
run;


Title "Mixed Effect Regression plot  ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_ai/group=cluster;
   series y=pred x=ln_ai;
run;


proc mixed data=monograph3;
class cluster;

model ln_total_residue=ln_number_exits/ddfm=contain;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(number_exits)' ln_number_exits 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
```

```sas
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing all three highest observation ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(number of exits)
";
proc Print data=misc;
run;
proc mixed data=monograph3;
    class cluster;
    model ln_total_residue=ln_number_exits/ ddfm=contain outp=pred1
outpm=pred2;
    random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_number_exits="log number of cab exits";
run;


Title "Mixed Effect Regression plot  ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
    scatter y=ln_total_residue x=ln_number_exits/group=cluster;
    series y=pred x=ln_number_exits;
run;
```

2 – Non-MEA-Dermal Exposure Data

Note: The following analyses were conducted for dermal exposure without MEA correction: If ICC is zero then containment method was used for calculating 95% C.I for slope and intercept, else KR method was used.
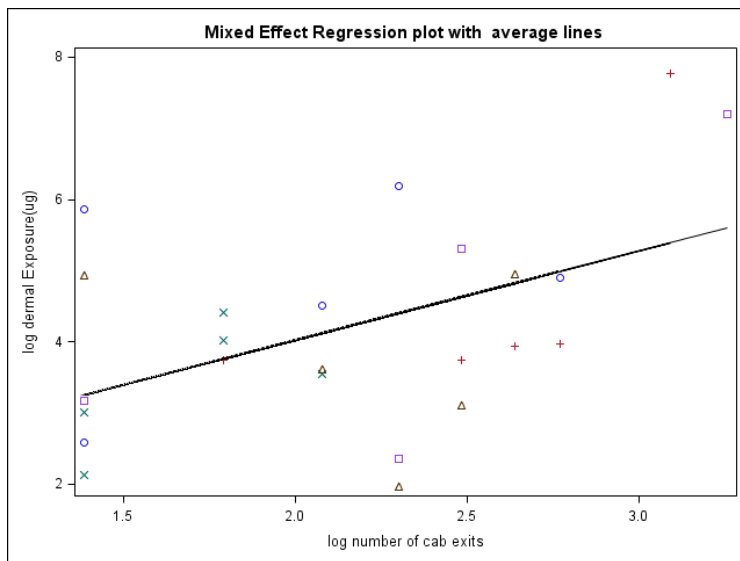
A. Use of all observations (no exclusions).

Regression model: ln(dermal exposure)=Intercept + ln(number of Exits)   11
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Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	1.5073	4	-1.4722	4.4868	3.82025	0	5.95903
2	Slope_ln(number_exits)	1.2570	18	0.2404	2.2736	.	.	2.03325

Mixed Effect Regression plot with average lines

B. Removing the observation with maximum dermal exposure: Study ID: AHE56 ; MUID: A5.
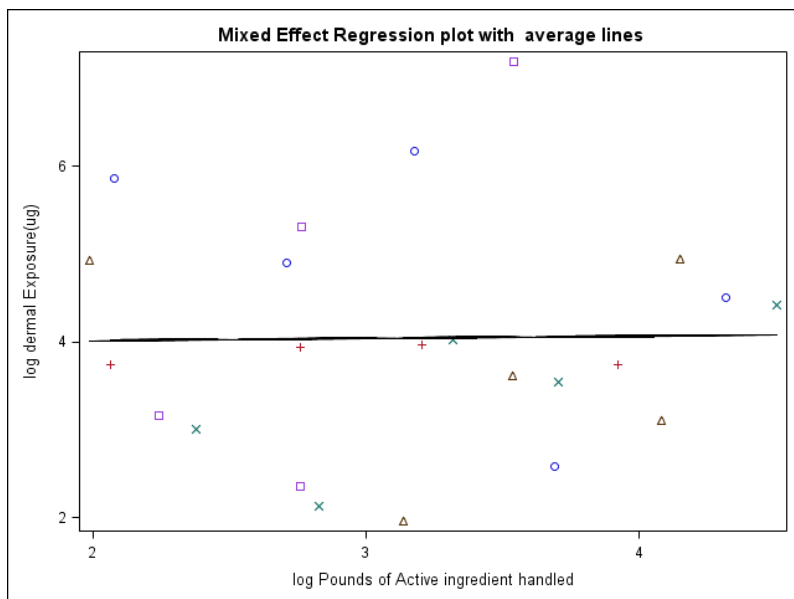
Regression model: ln(dermal exposure)=Intercept + ln(Ai)
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                                                        12:16 Tuesday, December 14, 2010

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	3.9652	4	0.5016	7.4287	3.86635	0	6.92701
2	Slope_ln(ai)	0.02617	17	-0.7832	0.8355	.	.	1.61867

Regression model: ln(dermal exposure)=Intercept + ln(number of exits)   30

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	2.1227	19.4	-0.2847	4.5301	3.49880	0.017230	4.81472
2	Slope_ln(number_exits)	0.9151	20.7	-0.1849	2.0150	.	.	2.19992
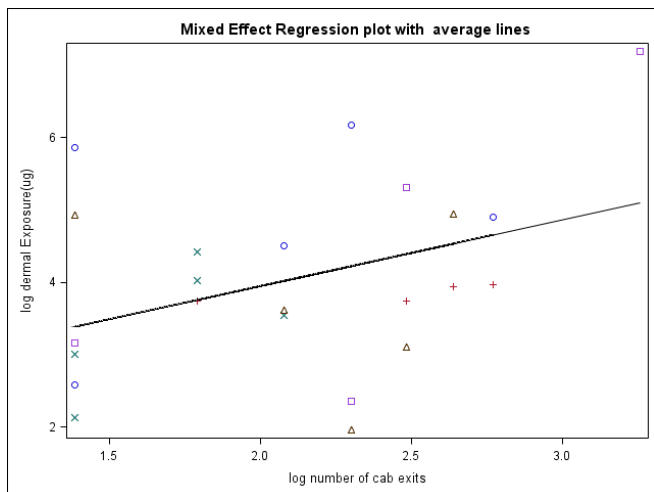
c. Removing the first and second highest observations in terms of dermal exposure: Study ID: AHE56 ; MUID: A5 ; Study ID: AHE59 MUID: A4
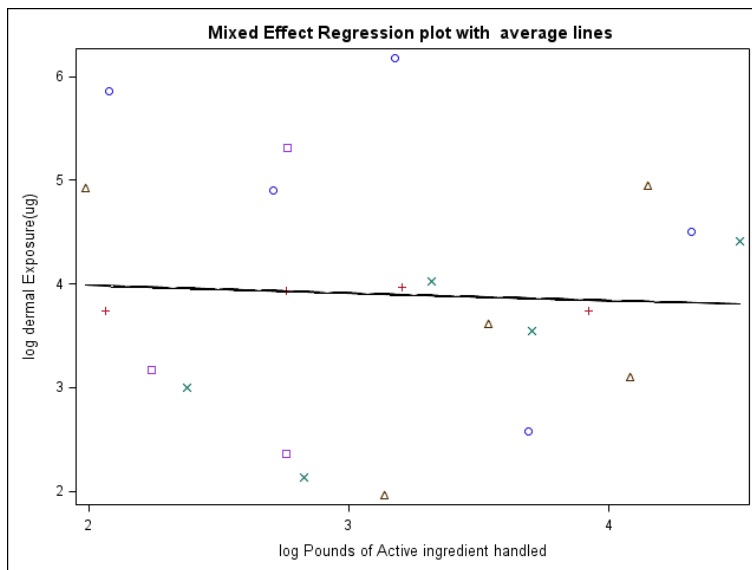
Regression model: ln(dermal exposure)=Intercept + ln(Ai)

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	4.1303	19.6	1.7995	6.4612	3.27514	0.035975	4.66168
2	Slope_ln(ai)	-0.07255	19	-0.7991	0.6540	.	.	1.45304

Mixed Effect Regression plot with average lines

Regression model: ln(dermal exposure)=Intercept + ln(number of exits)

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	2.9928	19.2	0.5561	5.4295	3.21497	0.049222	4.87340
2	Slope_ln(number_exits)	0.4423	19.9	-0.7034	1.5881	.	.	2.29150
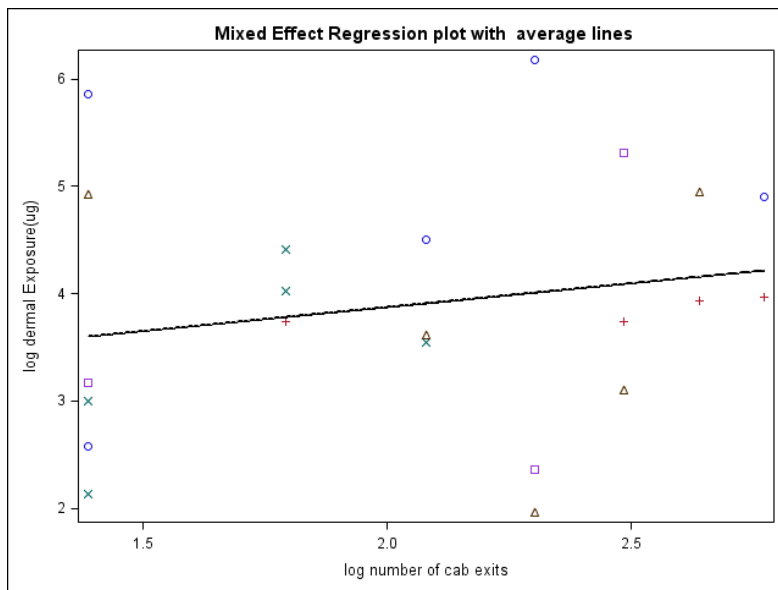
Mixed Effect Regression plot with average lines

D. Removing the first three highest observations in terms of dermal exposure: **Study ID: AHE56 ; MUID: A5 ; Study ID: AHE59 MUID: A4 ; Study ID: AHE55 MUID: A3**
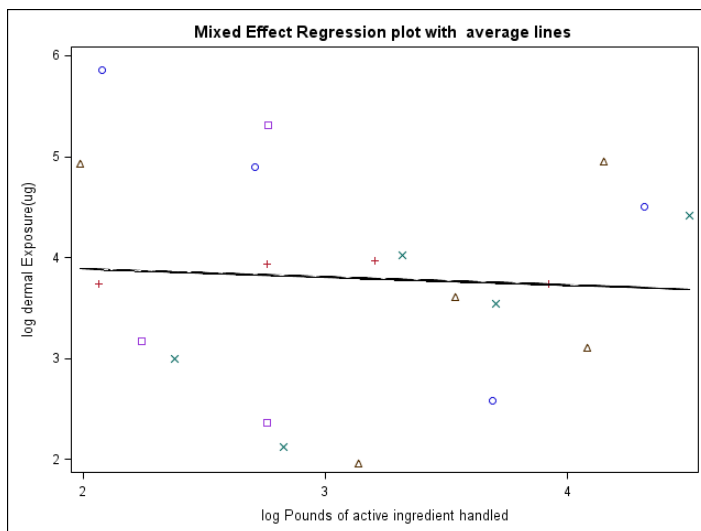
Regression model: ln(dermal exposure)=Intercept + ln(Ai)
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Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	4.0446	4	1.2454	6.8438	2.97471	0	5.59843
2	Slope_ln(ai)	-0.07868	15	-0.7417	0.5844	.	.	1.32608

Mixed Effect Regression plot with average lines

Regression model: ln(dermal exposure)=Intercept + ln(number of exits)   56

Obs	Label	Estimate	DF	Lower	Upper	GSD	ICC	WidthCI
1	Intercept	3.1282	4	0.3920	5.8644	2.93944	0	5.47238
2	Slope_ln(number_exits)	0.3279	15	-0.6726	1.3284	.	.	2.00099

Mixed Effect Regression plot with average lines
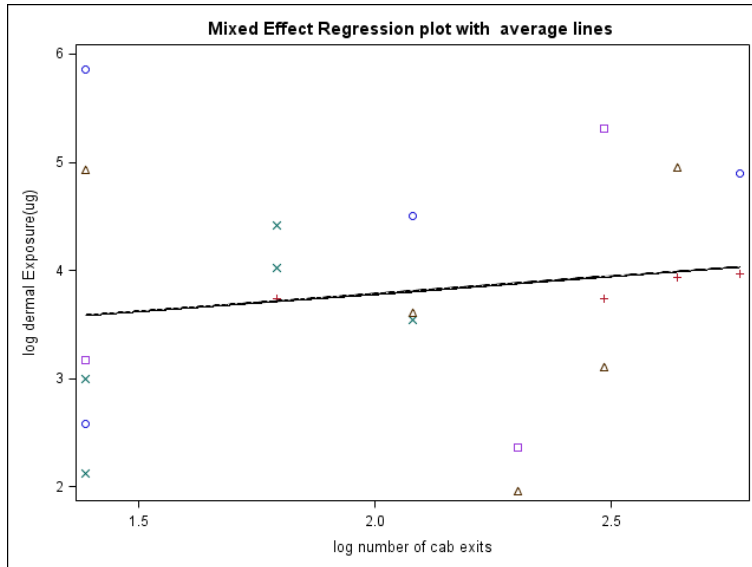
SAS Code

```
/* No_ MEA correction is made */

data monograph;
input  StudyID $ MUID $ ai    number_cab_exits  Total_residue    Cluster
; datalines;
AHE55 A1    8     4     351   1
AHE55 A2    15    16    134   1
AHE55 A3    24    10    483   1
AHE55 A4    40    4     13.2  1
AHE55 A5    75    8     90.5  1
AHE56 A1    7.9   12    42.1  2
AHE56 A2    15.8  14    51.3  2
AHE56 A3    24.6  16    52.9  2
AHE56 A4    50.5  6     42.1  2
AHE56 A5    75.7  22    2354  2
AHE57 A1    10.8  4     20.1  3
AHE57 A2    16.9  4     8.4   3
AHE57 A3    27.6  6     55.8  3
AHE57 A4    40.7  8     34.6  3
AHE57 A5    90.3  6     82.7  3
AHE58 A1    63.5  14    141   4
AHE58 A2    34.4  8     37.1  4
AHE58 A3    23    10    7.1   4
AHE58 A4    59.2  12    22.3  4
```

```
AHE58 A5     7.3    4       138    4
AHE59 A1    15.8   10      10.6    5
AHE59 A2     9.4    4      23.8    5
AHE59 A3    15.9   12       202    5
AHE59 A4    34.5   26      1329    5

;

*/case 1 No observation is deleted*/;
data monograph;
set monograph;
ln_ai=log(ai);
ln_number_exits=log(number_cab_exits);
ln_total_residue=log(Total_residue);
run;

proc mixed data=monograph;
class cluster;
model ln_total_residue=ln_ai/ddfm=contain;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(ai)' ln_ai 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " No observation has been removed ";
Title " Regression model: ln(dermal exposure)=Intercept + ln(Ai)";
proc Print data=misc;
run;

 proc mixed data=monograph;
   class cluster;
   model ln_total_residue=ln_ai/ddfm=contain outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
```

```sas
   ln_ai="log Pounds of Active ingredient handled";
run;


Title "Mixed Effect Regression plot with  average lines ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_ai/group=cluster;
   series y=pred x= ln_ai ;
run;




proc mixed data=monograph;
class cluster;

model ln_total_residue=ln_number_exits/ddfm=contain;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(number_exits)' ln_number_exits 1 / CL ;

ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " No observation has been removed ";
Title " Regression model: ln(dermal exposure)=Intercept + ln(number of
Exits)";
proc Print data=misc;
run;

proc mixed data=monograph;
   class cluster;
```

```
    model ln_total_residue=ln_number_exits/ddfm=contain outp=pred1
outpm=pred2;
    random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_number_exits="log number of cab exits";
run;


Title "Mixed Effect Regression plot with  average lines ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
    scatter y=ln_total_residue x=ln_number_exits/group=cluster;
    series y=pred x=ln_number_exits;
run;




*/case 2 : 1 observation is deleted*/;

data monograph1;
set monograph;
If total_residue=2354  then delete;
run;


proc mixed data=monograph1;
class cluster;

model ln_total_residue=ln_ai/ddfm=contain;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(ai)' ln_ai 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
```

```sas
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing the highest observation ranked by dermal exposure";
Title1 " Regression model: ln(dermal exposure)=Intercept + ln(Ai) ";
proc Print data=misc;
run;

proc mixed data=monograph1;
   class cluster;
   model ln_total_residue=ln_ai/ ddfm=contain outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_ai="log Pounds of Active ingredient handled";
run;


Title "Mixed Effect Regression plot with  average lines ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_ai/group=cluster;
   series y=pred x= ln_ai ;
run;



proc mixed data=monograph1;
class cluster;

model ln_total_residue=ln_number_exits/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(number_exits)' ln_number_exits 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
```

```sas
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing the highest observation ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(number of exits)
";
proc Print data=misc;
run;
proc mixed data=monograph1;
    class cluster;
    model ln_total_residue=ln_number_exits/ddfm=kr outp=pred1 outpm=pred2;
    random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_number_exits="log number of cab exits";
run;


Title "Mixed Effect Regression plot with  average lines ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
    scatter y=ln_total_residue x=ln_number_exits/group=cluster;
    series y=pred x=ln_number_exits;
run;



*/case 3 two observations have been deleted*/;
data monograph2;
set monograph;
If total_residue=2354 or total_residue=1329 then delete;
run;


proc mixed data=monograph2;
class cluster;

model ln_total_residue=ln_ai/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(ai)' ln_ai 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
```

```
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing two highest observation ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(Ai) ";
proc Print data=misc;
run;


proc mixed data=monograph2;
   class cluster;
   model ln_total_residue=ln_ai/ outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_ai="log Pounds of Active ingredient handled";
run;


Title "Mixed Effect Regression plot with  average lines ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_ai/group=cluster;
   series y=pred x= ln_ai ;
run;




proc mixed data=monograph2;
class cluster;

model ln_total_residue=ln_number_exits/ddfm=kr;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(number_exits)' ln_number_exits 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;


data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
```

```sas
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing two highest observations ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(number of exits)
";
proc Print data=misc;
run;
proc mixed data=monograph2;
    class cluster;
    model ln_total_residue=ln_number_exits/ outp=pred1 outpm=pred2;
    random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_number_exits="log number of cab exits";
run;


Title "Mixed Effect Regression plot with  average lines ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
    scatter y=ln_total_residue x=ln_number_exits/group=cluster;
    series y=pred x=ln_number_exits;
run;

*/case 4 three observations have been deleted*/;

*---> Additional Calculations from Regression ---;
data monograph3;
set monograph;
If total_residue=2354 or total_residue=1329 or total_residue=483 then delete;
run;



proc mixed data=monograph3;
class cluster;

model ln_total_residue=ln_ai/ddfm=contain;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(ai)' ln_ai 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;
```

```sas
*---> Additional Calculations from Regression ---;
Data Misc;
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing all three highest observation ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(Ai) ";
proc Print data=misc;
run;
proc mixed data=monograph3;
   class cluster;
   model ln_total_residue=ln_ai /ddfm=contain outp=pred1 outpm=pred2;
   random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
/*ln_number_exits="log number of cab exits"; */
ln_ai="log Pounds of active ingredient handled";
run;


Title "Mixed Effect Regression plot with  average lines ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
   scatter y=ln_total_residue x=ln_ai/group=cluster;
   series y=pred x=ln_ai;
run;


proc mixed data=monograph3;
class cluster;

model ln_total_residue=ln_number_exits/ddfm=contain;
random cluster;
Estimate 'Intercept' Intercept 1 / CL ;
Estimate 'Slope_ln(number_exits)' ln_number_exits 1 / CL ;
ODS Output CovParms=CovOut
Estimates=EstOut(keep=Label Estimate Lower Upper df);
Run;
Proc Transpose Data=CovOut
Out=Covout(drop=_Name_ rename=(Cluster=Vc Residual=Vw));
ID CovParm;
Var Estimate;
Run;

data covout;
set covout ;
run;

*---> Additional Calculations from Regression ---;
Data Misc;
```

```
*length ddfmethod $ 20;
Merge CovOut EstOut;
V = Vc+Vw;
GSD = exp(Sqrt(V));
ICC = Vc/V;
WidthCI = Upper-Lower;
*ddfmethod="&method";
Keep GSD ICC WidthCI Label Estimate Lower Upper  df;
Run;
Title " Removing all three highest observation ranked by dermal exposure";
Title " Regression model: ln(dermal exposure)=Intercept + ln(number of exits)
";
proc Print data=misc;
run;
proc mixed data=monograph3;
    class cluster;
    model ln_total_residue=ln_number_exits/ ddfm=contain outp=pred1
outpm=pred2;
    random cluster;
Label
 ln_total_residue= "log dermal Exposure(ug)"
ln_number_exits="log number of cab exits";
run;


Title "Mixed Effect Regression plot with  average lines ";
/**scatter plot and the average regression line **/
proc sgplot data=pred2 noautolegend;
    scatter y=ln_total_residue x=ln_number_exits/group=cluster;
    series y=pred x=ln_number_exits;
run;
```