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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

Date: [date placeholder]

SUBJECT: **DRAFT** Review of Agricultural Handler Exposure Task Force (AHETF) Monograph: "Open Pour Loading of Granules" (AHE1017)

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This memorandum presents EPA's review of the occupational handler exposure scenario monograph "Open Pour Loading of Granules" (AHE1017) submitted by the Agricultural Handler Exposure Task Force. It reflects comments and advice provided by the Human Studies Review Board following its review in January 2018[1].

The AHETF satisfactorily followed the study protocols, sampling design, and data analysis plan. EPA considers the open pour loading granules scenario complete and its results are recommended for use in routine regulatory assessment of human health exposure and risk as part of the federal pesticide registration process. Scientific review of the field and analytical reports (AHE170 – Bruce and Holden, 2017) that outline the monitoring data collected to support this scenario can be found in a separate data evaluation review (DER) memorandum (Crowley, [date]).

[1] [placeholder for HSRB report]

1.0 Executive Summary

This document represents the Health Effects Division (HED) review of the Agricultural Handler Exposure Task Force (AHETF) Study AHE1017: Open Pour Loading of Granules Scenario Monograph (Bruce and Holden, 2017). The submission compiles and statistically analyzes dermal and inhalation monitoring for workers who manually open and lift granule pesticide bags/packages and pour them into equipment typically used for agricultural applications. The AHETF study AHE170 (Bruce, 2017) provides the exposure monitoring field and analytical results, including laboratory analyses; details can be found in both the submitted study report and corresponding EPA review (Crowley, [date]).

Overall, the AHETF adequately followed the general study design outlined in the AHETF Governing Document (AHETF, 2008 and 2010) and scenario sampling and data analysis protocol (AHETF, 2014). AHETF efforts represented a well-designed, concerted process to collect reliable, internally-consistent, and contemporary exposure data in a way that takes advantage of and incorporates a more robust statistical design, better analytical methods, and improved data handling techniques. The AHETF data and associated unit exposures are considered superior to the existing data used to assess exposure and risk for this scenario.[2] The data are considered the most reliable data for assessing exposure and risk to individuals open pouring granule pesticides[3] while wearing the following personal protective equipment (PPE): long-sleeved shirts, long pants, shoes, socks, chemical-resistant gloves, and no respirator[4]. Importantly, the data represents exposure during loading only – it does not represent exposure during the application of granule pesticides.

The primary quantitative objective was for dermal exposure results (normalized to the amount of active ingredient handled) to be accurate within 3-fold at the geometric mean, arithmetic mean and 95th percentile. This objective was met: both AHETF-proposed results and EPA-revised results[5] have accuracy of 3-fold or less at the arithmetic mean and 95th percentile. The secondary objective to evaluate proportionality versus independence between dermal exposure and the amount of active ingredient handled – a key assumption in the use of exposure data as "unit exposures" – with 80% statistical power was also met.

Additionally, all estimates of the slope of log dermal exposure-log amount of active ingredient handled (AaiH) regression were approximately 0.7 with confidence intervals including 1 but not zero, demonstrating the data is more consistent with a proportional relationship than an independent one. Thus, for this scenario, HED will continue to use the exposure data normalized by the amount of active ingredient as a default condition for regulatory exposure assessment purposes.

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[2] Pesticide Handlers Exposure Database (PHED) Scenario 2. Granular: Open Mixing

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

[4] 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.

[5] EPA revisions to the AHETF submission include adjustment for the potential inefficiency of the hand wash and face/neck wipe sampling methodologies as well as an alternative data imputation method for missing hand wash samples for workers M1 and M2.

Revisions by EPA include an adjustment for potential inefficiencies of the hand wash and face/neck wipe residue collection methodologies and an alternative data imputation approach for missing hand wash samples for workers M1 and M2. Compared with the AHETF submission, statistical benchmark analyses were not significantly changed by EPA's revisions, however they result in slightly larger estimates of exposure statistics (i.e., means and percentiles) than those calculated by the AHETF. Section 3.3 discusses this in more detail.

Select summary statistics for this scenario are presented in Table 1 below, as well as, for comparison, the value previously used (PHED Scenario 2. Granular: Open Mixing) to assess pesticide human health exposure/risk for open pour loading of granule pesticides.

Table 1. Unit Exposures (µg/lb ai handled): Open Pour Loading Granules

Exposure Route[a]	PHED Scenario #2	AHETF Data[b]		
	"Best fit"	Geometric Mean	Arithmetic Mean[e]	95th Percentile[f]
Dermal[c,d]	6.9	3.88	8.23	29.2
Inhalation	1.7	0.629	0.825	2.11

[a] Exposure values represent long sleeve shirt, pants, shoes/socks, chemical-resistant gloves, and no respirator.
[b] Per current EPA policy, dermal unit exposures reflect 2X adjustment of hand and face/neck measurements to address potential inefficiencies in those exposure monitoring methods since the average percent contribution to total dermal exposure by the hands, face, and neck is greater than 20% (see Section 3.2).
[c] 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 3.3.1.
[d] Reflects imputation of missing hand wash samples for workers M1 and M2. Since the amount of active ingredient handled for each missing hand wash sample was known, imputation was performed using the across-all-worker average AaiH-normalized hand exposure. See Section 3.2.2.
[e] Arithmetic Mean (AM) = GM * exp{0.5*[(lnGSD)^2]}
[f] 95th percentile = GM * GSD^1.645

2.0 Background

The following provides background on the AHETF objectives and review by the Human Studies Review Board (HSRB).

2.1 AHETF Objectives

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

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

Two major assumptions underlie the use of exposure data in this fashion. First, the expected external exposure is unrelated to the identity of the specific active ingredient in the pesticide formulation. That is, the physical characteristics of a scenario such as the pesticide formulation (e.g., formulation type – granule, liquid concentrate, dry flowable, etc.), packaging (e.g., in a bag or jug), 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 loading one chemical formulated as a granule can be used to estimate exposure during loading another chemical also formulated as a granule. Second, dermal and inhalation exposure are assumed proportional to the amount of active ingredient handled. In other words, if one doubles the amount of pesticide handled, exposure is assumed to double.

The AHETF approach for monitoring occupational handler exposure was based on criteria reviewed by EPA and presented to the Human Studies Review Board (HSRB) for determining when a scenario is considered complete and operative. Outlined in the AHETF Governing Document (AHETF, 2008 and 2010), 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 to 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 of the geometric mean, arithmetic mean, and 95^{th} percentile dermal unit exposures. To meet this primary objective AHETF proposed an experimental design with a sufficient number of monitored individuals across a set of monitoring locations. Note that this “fold relative accuracy” (*f*RA) objective does not apply to normalized inhalation exposure, though estimates are provided for reference.

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

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

AHETF developed a study design employing a 'cluster' strategy. A cluster, from a sample size perspective, is defined as a set of workers monitored in spatial and temporal proximity. For AHETF purposes, clusters are generally defined by a few contiguous counties in a given state. Importantly, in terms of a sampling strategy, there is assumed to be some level of correlation within clusters. So, while cluster sampling is logistically more efficient and cost effective, correlation may result in the need to conduct monitoring for more workers overall than if cluster sampling were not employed.

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

2.2 2014 HSRB Protocol Review and Comments

The ability of the EPA to use the AHETF open pour loading granules exposure monitoring data to support 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[6].

The protocol and sampling plan for this exposure data and scenario (AHETF, 2014) was presented to the HSRB in November 2014. The meeting report (HSRB, 2015) stated that the proposed approach would likely generate reliable data for assessing exposure for workers open pouring granule pesticides if performed as described by the protocol and as recommended by the HSRB. However, various issues were raised.

The Board said:

> "Some aspects of the study are commented on below; these provide opportunities to improve the design or identify points that should be considered by the Agency when interpreting and using the data." (page 8 of HSRB, 2015)

The following table outlines issues raised by the HSRB and how/whether the issue was addressed in the protocol or completed study. HSRB issues/comments are quoted directly or paraphrased from the 2015 meeting report with page numbers included for reference.

Table 2. Summary of 2014 HSRB AHE170 Protocol Review

HSRB Comment	Study Outcome
Loss of the active ingredient via volatilization from the granule formulation during the workday is a potential source of underestimation bias with	EPA believes that results of the field fortification sampling, where each exposure collection method/matrix is spiked with a known amount of the test chemical,

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

Table 2. Summary of 2014 HSRB AHE170 Protocol Review	
HSRB Comment	**Study Outcome**
respect to using the exposure results (Issue 1, page 8-9 of HSRB, 2015).	adequately accounts for the HSRB's concern. Should a field fortification show that only 80% of the known spiked amount is recovered in a fortified WBD, hand rinse solution, etc., the actual field sample will be upward-adjusted to reflect this "loss". Importantly, the fortified samples are concurrently in the field under the same conditions as the actual sampling matrices worn/used by the participants.
Loss of the active ingredient via sorption into the skin during the workday is a potential source of underestimation bias with respect to using the exposure results (Issues 1 and 2, page 8-9 of HSRB, 2015).	In theory the exposure matrices are intended to intercept 100% of the product/chemical that otherwise would be deposited on the skin or breathed in through the nose or mouth. In actuality EPA accepts that 100% interception is unlikely. However, the exposure methodologies (WBD, hand washes, face/neck wipes) represent the state of the science for this kind of research. The EPA expressed support for these methods during the 2007 FIFRA SAP (Christian, 2007), including their comparability with biomonitoring, with the Panel ultimately expressing support for the methods. Furthermore, EPA has acknowledged this issue and developed an approach to account for the potential inefficiencies related to the hand rinses and face/wipe methods (see "MEA" elsewhere in this review).
To the extent there is sorption into the skin there are implications for the safety of the workers participating in the study (Issues 1, 2, and 3, page 8-9 of HSRB, 2015).	Though the matrices/methodologies are intended to intercept workers' expected dermal exposure during the study (meaning, in theory, a participant should actually experience no exposure), to the extent there is any actual exposure (and sorption through the skin) during the study, the risk estimates provided by the AHETF in the protocol – as required by the Human Studies rule – are based on EPA risk assessment methodologies, if not directly quoted from EPA risk assessments. Importantly these risk estimates account for dermal absorption, based on studies EPA has reviewed and found acceptable for use in risk assessment. As such EPA does not believe that there are safety concerns related to exposure to the active ingredients as a result of participating in the research.
The protocol provides for use of new gloves for each worker, which avoids exposure to residues in gloves from activities unrelated to the study but is non-conservative in that gloves can be contaminated under normal working conditions and worker are very unlikely to use fresh gloves every day (Issue 2, page 9, HSRB, 2015).	While the HSRB is correct to note that use of fresh gloves introduces a level of uncertainty with respect to the representativeness of the ultimate exposure results, contamination of the exposure sampling from pre-existing chemicals present on workers' gloves is a legitimate consideration in terms of the sample integrity in this research.
Although the Board felt the proposed approach was acceptable given practical constraints, it recommends that, if feasible, some form of classification system be developed that would identify the mechanism by which each MU was recruited and in particular would identify those, if any, that might need to be recruited by "traditional recruitment" in order to provide an after-the-fact (future) indicator of the randomness of the MU selection process (Item 4, page 10 of HSRB, 2015).	The AHETF thoroughly documented the recruitment process which likely can be used to address this concern. In some cases, random sampling from Master lists were used as well as randomization within lists prior to contact attempts.

Table 2. Summary of 2014 HSRB AHE170 Protocol Review	
HSRB Comment	**Study Outcome**
Since the goal is to have each MU in an area have a different AaiH level, with three MUs and three AaiH levels, it appears that there are no replications of AaiH levels within an area. As a result, the variability among humans who would be exposed to a particular scenario cannot be addressed using only the information from this study. While statistical analyses are not the goal of this study, the information will surely be used in some way by someone for that purpose eventually. Lack of replication of the human variability would make it difficult or likely impossible for any user of the database to conduct further statistical analyses (Item 4, page 10 of HSRB, 2015).	It is true that the research is designed to avoid – with the protocol explicitly restricting – repeat exposures using the same person. This is a trade-off in terms of costs of the study and utility of the data. An ideal study where cost is of no concern would obtain measures of both inter- and intra-person variability. However, given the choice, EPA agrees with the AHETF that variability across the exposed population (inter-) is a better first-step than conducting repeat exposures on the same person to obtain measures of intra-person variability. Having a good approximation of the inter-person variability provides an upper bound/extreme measure of the intra-person variability, which can then be reasonably modeled/simulated from there. Conversely, modeling inter-person variability from a dataset more focused on intra-person variability is a difficult and more uncertain exercise.

2.3 2018 HSRB Review and Comments

Along with study protocols, completed studies involving human participants are potentially subject to review by the HSRB to ensure satisfactory adherence to the study protocol and compliance with applicable statutes. The completed study (AHE170) monitoring open pour loading of granules that is the source of information for this monograph was reviewed by the HSRB in January 2018.

[placeholder for additional summary of 2018 HSRB review of the completed study]

3.0 Exposure Study Conduct and Monitoring Results

Field monitoring and analytical results, as well as protocol amendments and deviations, were reported in AHE170 and reviewed by EPA (Crowley, [date]). No existing studies were deemed acceptable by the AHETF, thus AHE170 was designed to supplant previously used data. Additionally, no protocol amendments or deviations were considered to adversely affect the study results.

The following sections summarize the conduct of AHE170, the exposure monitoring results and the scenario benchmark statistical analyses presented in the AHETF scenario monograph (Bruce and Holden, 2017).

3.1 Exposure Study Design and Characteristics

This scenario is defined as manually opening, lifting, and pouring granule pesticide products into in typical agricultural pesticide application equipment while wearing a long-sleeved shirt, long pants, shoes, socks, chemical-resistant gloves, and no respirator. Workers who load granule pesticides using more automated (non-manual) systems such as mini-bulk containers or super sacks were not monitored in this study (Attachment 3 provides example pictures of those systems).

Granules are a particular kind of formulation considered by EPA to include products composed of a high percentage (generally greater than 90%) of granular inert carrier(s) (e.g., corn cobs, clay, limestone, sand, food) and a minimal amount of sticker/binder (generally 5% or less of the formulation). The AHETF adds (AHE1017, p 17):

> Granular formulations differ from dust formulations (which are also applied as a solid) in that the active ingredient (AI) is sorbed onto larger particles. Granule-sized products generally pass through 4-mesh sieves and are retained on 80-mesh sieves. Granules are applied dry and are typically used for in-furrow applications where a metered and controlled application is required, for post-emergence soil applications where their weight allows them to pass through foliage to the ground, and for situations where a larger particle size is necessary for controlled product placement or decreased drift potential. In addition, there is generally a reduced inhalation hazard compared to dust formulations.
>
> Some granular formulations do not fit the descriptions above but are specifically formulated or 'engineered' to achieve some objective. One common reason products are engineered is to reduce dustiness, which further reduces exposure potential. Polymers and Biodac® are examples of carriers used in engineered formulations. However, AHETF believes none of the products used in this study were engineered for special traits such as slow release or reduced dust.

The figures below (from AHE1017 Appendix F; Bruce and Holden, 2017) depict examples of activities for which the exposure data are applicable.

Figure 1: Loading Granules (from abdomen height; worker ID M1)

Figure 2: Loading Granules (from chest height; worker ID M3)

In order to capture the expected range of exposures with a relatively small sample, the monitoring plan/protocol for AHE170 (AHETF, 2014) outlined a strategy to target a diverse set of conditions in terms of geographic areas, types of equipment tanks/containers types, workers, and other potential exposure factors. At the same time, recruiting procedures were developed to minimize bias in the selection of employers and subjects. As described in detail in the study, there were three recruitment phases. The phases involved winnowing down the initial universe list of employers in the monitoring area who may use granule pesticides through processes to identify subsequent lists of "qualified employers" and then "potentially eligible" employers. After confirming eligibility, AHETF scheduled and conducted monitoring of workers. Randomization in the process included creation of a Master Employer List (MEL) – typically about 1,500 names – via sampling from the Employer Universe List (EUL) as well as randomization of the Qualified Employer List (QEL) from which to contact during Phase 2 recruitment. However, in no instance was there an opportunity to randomly select the 3 or 4 workers for a given monitoring area. Non-response (i.e., inability to contact, interview refusals) was approximately 75% across the monitoring areas and still others contacted were deemed not qualified because they didn't use granular pesticides.

The sampling plan for this scenario (AHETF, 2014) outlined a '7x3' design – monitoring of a total of 21 different workers, 3 workers in each of 7 separate 'clusters' or monitoring areas – that the protocol demonstrated would simultaneously be cost-effective and satisfy benchmark data analysis objectives. In actuality, this cost-effective approach was not completely achieved. Though 7 distinct geographical locations were monitored, the temporal differences resulted in an equivalent (and less cost-effective) configuration of 8 clusters. Additionally, 4 workers (instead of 3) were monitored in each of two monitoring areas. This slight change to the data configuration (outlined in protocol amendment 4) was largely due to recruitment difficulties related to significant rainfall in the northeast U.S in the 2016 spring planting season.

Thus, the final dataset consisted of 21 separate workers[7] monitored loading granule pesticide products in 9 U.S. states (Iowa, Florida, Georgia, Nebraska, South Dakota, Pennsylvania, North Carolina, Indiana, and Minnesota) from 2015-2016. Instead of the intended 7 "clusters", the 21 monitored workers ultimately comprised 8 distinct "clusters", when considering spatial proximity as well as a temporal proximity.

As monitoring was conducted across 15 months and 9 different U.S. states, both spatial and temporal diversity is represented in the sample. Per protocol, no worker was monitored twice (no "repeat measures") and, to reduce any potential similarities related to training, all workers were employed by different farms/employers. Though the study protocol did not prescribe certain diversity in the pesticide application equipment, workers loaded granules into a variety of application equipment which also naturally diversified the height from which the loading occurred. The following summary table of loading characteristics was provided in the EPA review of AHE170:

Table 3. AHE170 Loading Summary

Worker ID	Relative Loading Height	Equipment	No. of hoppers	Type of Bag
M1	Abdomen	12-Row Planter	12	Paper
M2	Chin	Twin-Row Planter	6	Plastic
M3	Chest	Drop Spreader	3	Paper
M4	Thigh	Rotary Spreader	1	Plastic
M5	Waist	12-Row Planter	12	Paper
M6	Waist	12-Row Planter	12	Plastic
M7	Waist	6-Row Planter	6	Plastic
M8	Chest	6-Row Planter	6	Plastic
M9	Waist	6-Row Planter	6	Paper
M10	Upper Chest	Rotary Spreader	1	Paper
M11	Face	Drop Spreader	6	Plastic
M12	Waist	24-Row Planter	24	Plastic
M13	Waist	12-Row Planter	12	Plastic
M14	Waist	12-Row Planter	12	Plastic
M15	Waist	6-Row Planter	6	Plastic
M16	Waist	16-Row Planter	16	Plastic
M17	Waist	16-Row Planter	16	Plastic
M18	Waist	12-Row Planter	12	Plastic
M19	Waist	8-Row Planter	8	Plastic
M20	Chest	24-Row Planter	24	Plastic
M21	Waist	12-Row Planter	12	Plastic

Also, per protocol, the amount of active ingredient handled by the workers was diversified – mainly to accommodate the secondary (regression analysis) study objective – but also to potentially add indirect variability to the dataset. Within each monitoring areas the study design called for each of 3 workers to represent (or 'occupy') one of three AaiH strata (from 5 to 15 lbs or 15 to 150 lbs or 150 to 400 lbs), however this was only achieved in 2 of the monitoring areas as only two workers loaded between 150 to 400 lbs of active ingredient. Overall, workers (all males) loaded between 50 and 2,720 pounds of product over 3 to 6 separate loading events in 2

[7] Though two workers (M1 and M2) had incomplete dermal exposure samples – hand wash samples were broken and lost – reasonable data imputation allows for a total of 21 total dermal exposure results. Section 3.2.2 has more information.

to 8 hours, totaling a range of 6 to 175 lbs of active ingredient handled. Thus, ultimately the overall spread of amount of active ingredient handled was approximately 1 to 1.5 orders of magnitude, an adequate range both for enhancing diversity in the dataset and enabling regression analysis.

For more details on worker characteristics and other monitoring conditions, see the monograph submission (AHE1017), the AHE170 report submission and its corresponding EPA review (Crowley, [date]).

3.2 Exposure Monitoring and Calculations

This section briefly describes how exposure was measured, the final dermal and inhalation exposure results used in statistical analyses, and how those results were analyzed.

3.2.1 Monitoring Methods

Dermal exposure was measured using 100% cotton "whole body dosimeters" (WBD) underneath normal work clothing (e.g., long-sleeved shirt, long pants, socks and shoes), hand rinses (collected at the end of the day and during restroom and lunch breaks), and face/neck wipes. Per AHETF goals, monitoring was conducted to represent exposure for workers wearing long-sleeve shirts, pants, shoes/socks, chemical-resistant gloves and no respiratory protection. In order to simulate total head exposure without any eye protection or use of respirators, face/neck wipe samples for those workers who did use eye protection and/or respirators were adjusted to extrapolate to portions of the head covered by protective eyewear and/or hair. Total dermal exposure was then calculated by summing exposure across all body parts for each individual monitored.

Additionally, as presented at a June 2007 HSRB meeting, to account for potential residue collection method inefficiencies[8], EPA follows the rules below to determine whether to adjust the hand and face/neck field study measurements:

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

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

For AHE170 the measurements fell in the second category – on average approximately 30% of total dermal exposure consisted of exposure to the hands and head[9] – thus hand rinse and face/neck wipe measurements have been adjusted upward by a factor of 2 (i.e., multiplied by 2).

Inhalation exposure was measured using a personal air sampling pump and an OSHA Versatile Sampler (OVS) tube. The tube is attached to the worker's shirt collar to continuously sample air from the breathing zone. Total inhalation exposures were calculated by adjusting the measured air concentration (i.e., ug/L) using a breathing rate of 26.7 L/min representing moderate activities such as lifting heavy bags (NAFTA, 1998), and total work/monitoring time[10].

3.2.2 Imputation of Lost Hand Wash Samples

As previously mentioned and outlined in detail in the AHE170 study report, hand wash samples were broken and lost for workers M1 and M2 resulting in incomplete total dermal exposure results for each worker. The table below shows the missing samples for each worker as well as results for hand wash samples that were valid and analyzed.

Worker	Table 4. Hand Wash Result (µg)[1]			
	Sample #1	Sample #2	Sample #3	Sample #4
M1 (3/19/2015 in FL)	broken/lost	broken/lost	6.7	broken/lost
M2 (3/21/2015 in FL)	broken/lost	broken/lost	13.6	*No sample taken*
[1] Reflects adjustment by field fortification results.				

In the monograph submission the AHETF presents analytical results when workers M1 and M2 are completely excluded due to their lack of total dermal exposure results (i.e., a dataset based on 19 workers instead of 21) as well as results when imputing the lost hand wash samples (i.e., a dataset based on all 21 workers). The AHETF states that since each worker had a single valid sample, imputation of the missing results is possible rather than completely excluding the dermal exposure results for these two workers. EPA agrees that imputing these missing values is preferable to excluding M1 and M2 from the dermal exposure dataset for this scenario. EPA supports imputation of the lost hand wash samples to avoid loss of otherwise valuable dermal exposure information; therefore, this review does not consider results based on only 19 workers.

The amount of active ingredient handled for each worker prior to their hand wash sampling can be determined from study AHE170; Attachment 1 summarizes this information. Because monitoring observations show that both M1 and M2 handled the same amount of active ingredient prior to each hand wash – worker M1 handled 22.1 lbs chlorpyrifos prior to each of his 4 hand washes and M2 handled 14.7 lbs chlorpyrifos before each of his 3 hand washes – the AHETF argues that a simple approach would be to assign the valid hand wash result to each of the missing samples, under the assumption that because M1 and M2 each handled the same amount of active ingredient prior to each of their hand wash samples (including prior to the

[9] The contribution is approximately 30% regardless of the data imputations employed for missing M1 and M2 hand washes.

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

known sample's result), each missing sample would be the same as the known result. Thus, by the AHETF's approach, the table above would look like:

Table 5. AHETF Hand Wash Imputation Approach						
Description	**Worker**	**Hand Wash Result (µg)[1]**				
		Sample #1	**Sample #2**	**Sample #3**	**Sample #4**	**Total**
Assume lost hand wash results are identical to valid result	M1 (3/19/2015 in FL)	6.7	6.7	6.7	6.7	26.8
	M2 (3/21/2015 in FL)	13.6	13.6	13.6	*No sample taken*	40.8
[1] Reflects adjustment by field fortification results.						

EPA does not dispute that this approach is simple, nor that its underlying assumption is reasonable. That said, based on review of the AaiH-normalized hand exposures at each hand wash sample across all workers (see Attachment 1), EPA evaluated other approaches including an attempt to bracket the extreme possibilities (i.e., assuming non-detect exposures and assuming high-end exposures). The table below summarizes the results.

Table 6. EPA Hand Wash Imputation Approaches						
Description	**Worker**	**Hand Wash Results (µg)[1]**				
		Sample #1	**Sample #2**	**Sample #3**	**Sample #4**	**Total**
Assume lost hand wash results were < LOD	M1 (3/19/2015 in FL)	0.035	0.035	6.7	0.035	6.8
	M2 (3/21/2015 in FL)	0.035	0.035	13.6	*No sample taken*	13.7
Assume lost hand wash results based on the average AaiH-normalized hand exposure across all workers (1.44 µg/lb ai)[2]	M1 (3/19/2015 in FL)[3]	36.1	36.1	6.7	36.1	115
	M2 (3/21/2015 in FL)[3]	24.1	24.1	13.6	*No sample taken*	61.8
Assume lost hand wash results based on highest-normalized hand exposure (43.3 µg/lb ai for worker M3)[2]	M1 (3/19/2015 in FL)[4]	1088	1088	6.7	1088	3271
	M2 (3/21/2015 in FL)[4]	724	724	13.6	*No sample taken*	1462

[1] Reflects adjustment by field fortification results.

[2] For each worker the amount of active ingredient handled prior to each hand wash sample was available (a total of 45 hand wash samples across the 21 workers). Normalized by the amount of active ingredient prior to each hand wash sample, hand exposures ranged from 0.006 µg/lb ai (M9) to 43.3 µg/lb ai (M3, second hand wash), with a simple average of 1.44 µg/lb ai. See Attachment 1.

[3] Based on the average normalized hand exposure (1.44 µg/lb ai). Missing M1 samples: 1.44 µg /lb ai * 22.1 lb ai = 31.8 µg. M2 = 1.44 µg/lb ai * 14.7 lb ai = 21.2 µg. Field fortification adjustments are then applied.

[4] Based on the maximum normalized hand exposure (43.3 µg/lb ai from worker M3 hand wash sample #2). Missing M1 samples: 43.3 µg /lb ai * 22.1 lb ai = 957 µg. M2 = 43.3 µg/lb ai * 14.7 lb ai = 637 µg. Field fortification adjustments are then applied.

EPA knows of more sophisticated statistical approaches for data imputation (e.g., multiple imputation), however in the interest of simplicity and saving time/resources the approaches outlined above are reasonable and give an overall understanding of the possibilities. While useful as a bounding exercise, EPA rejects both the extreme assumptions of non-detect exposures and hand exposures consistent with the highest hand exposures across the entire dataset. In the case of the AHETF's approach, it assumes that a worker has consistent exposures within their day, while use of the average normalized hand exposure reflects the potential for within-worker variability. EPA prefers the measure that assumes some variability; note, this also results in higher exposure estimates than the AHETF approach. Therefore, data analysis in the following sections, and values recommended for use in exposure/risk assessment reflect the methodology based on the (1.44 µg/lb ai) "per hand wash sample" average normalized hand exposure.

3.2.3 Dermal and Inhalation Exposure Results

Following calculation of total dermal and inhalation exposure as described in Section 3.2.1 above, dermal and inhalation unit exposures (i.e., µg/lb ai handled) are then calculated by dividing the summed total exposure by the amount of active ingredient handled. A summary of the 21 MUs is provided in Table 7 below, with data plots shown in Figures 3 and 4. As previously mentioned:

- Both dermal and inhalation exposure samples are adjusted as appropriate according to recovery results from field fortification samples;
- Dermal exposures reflect EPA's MEA approach;
- Dermal exposures reflect EPA's hand wash sample imputation approach; and,
- Though alternate methods can be applied by data users (e.g., maximum likelihood estimation), residues with results less than analytical limits use the "½ analytical limit" (either ½ LOD or LOQ) convention.

More details on exposure measurements, field fortification sampling, and other laboratory measurements can be found in EPA's study review of AHE170 (Crowley, [date]).

Table 7. Open Pour Loading Granules Exposure Summary

MU ID	State	# Bags handled	# Loads	Work/ Monitoring Time (hours)	Product handled (lbs)	AaiH (lbs)	Unit Exposure (µg/lb ai)		
							Dermal		Inhalation
							Non-MEA	MEA	
M1	FL	12	4	7.0	600	88.5	3.26	5.68	0.689
M2	FL	6	3	5.3	300	44.0	6.13	9.92	0.600
M3	FL	8	3	6.1	388	5.8	96.9	126	5.22
M4	NC	4	3	2.8	200	38.2	1.14	1.72	0.296
M5	IA	21	3	7.0	1025	157.6	0.79	1.05	0.447
M6	IN	6	3	4.6	300	8.7	0.41	0.632	0.406
M7	IA	3	4	3.5	150	22.3	21.6	25.1	0.812
M8	PA	5	3	4.0	250	7.3	5.32	6.67	1.66
M9	IA	1	3	1.9	50	7.4	1.21	1.69	0.251
M10	GA	68	6	3.8	2720	53.3	1.07	1.18	0.409
M11	GA	13	4	4.8	650	93.8	2.68	3.90	0.964
M12	MN	24	3	6.8	1200	36.4	3.13	3.61	0.607

Table 7. Open Pour Loading Granules Exposure Summary									
MU ID	State	# Bags handled	# Loads	Work/ Monitoring Time (hours)	Product handled (lbs)	AaiH (lbs)	Unit Exposure (µg/lb ai)		
							Dermal		Inhalation
							Non-MEA	MEA	
M13	IN	14	3	6.3	700	20.9	1.33	1.80	0.512
M14	MN	23	3	6.2	1150	174.5	2.17	2.57	0.928
M15	MN	6	3	3.9	300	8.6	1.04	1.20	0.251
M16	IN	26	3	6.8	1270	39.0	2.95	4.04	0.267
M17	NE	20	4	7.8	1000	28.5	3.67	4.33	0.611
M18	NE	18	4	7.2	900	26.8	12.96	14.6	1.19
M19	NE	6	3	6.5	300	8.8	5.76	6.98	1.03
M20	NE	18	3	4.7	900	28.4	4.29	4.84	0.873
M21	SD	12	4	7.4	600	17.6	2.60	3.14	0.303
MEA = method efficiency adjustment									

Figure 3: Dermal Unit Exposures (ug/lb ai)

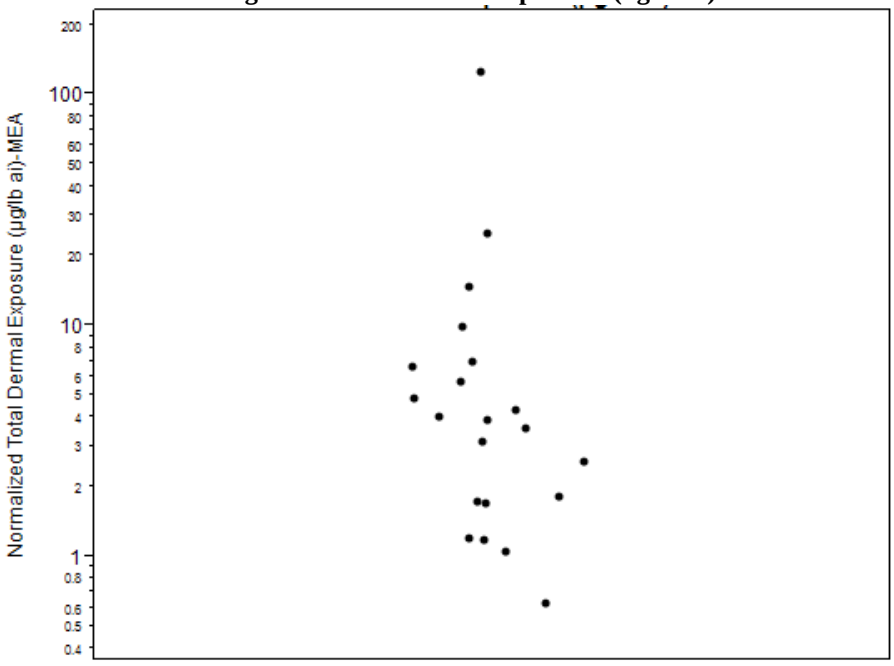
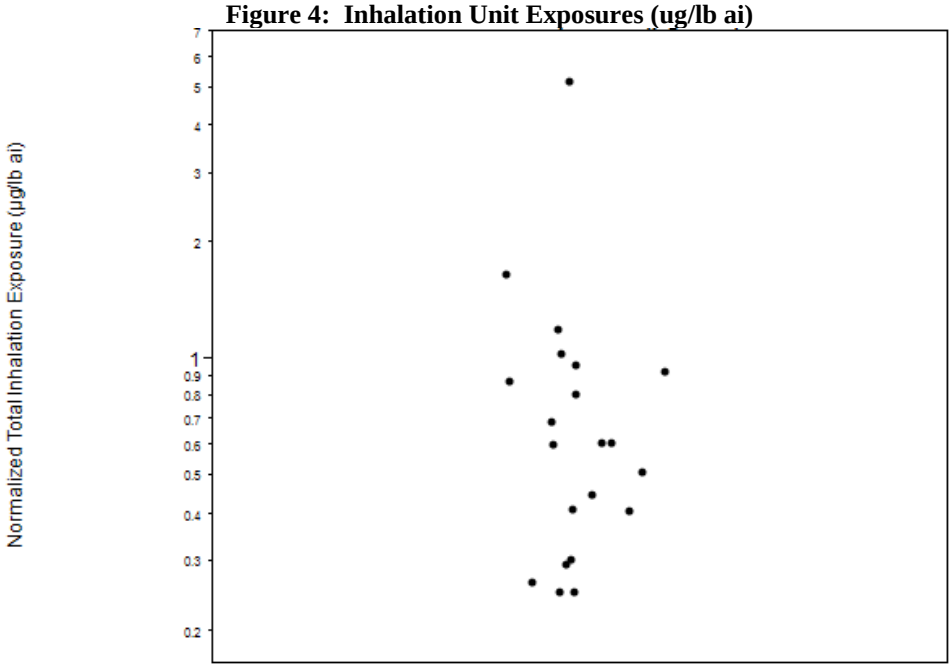


Figure 4: Inhalation Unit Exposures (ug/lb ai)



3.3 Evaluation of Scenario Benchmark Objectives

The AHETF monograph details the extent to which the open pour loading of granules scenario meets objectives described in Section 2.1. The monograph states that both the primary objective (3-fold accuracy) and secondary objective (adequate analytical power to evaluate proportionality) were met. EPA agrees with the methodologies used to assess these objectives (Appendix D of Bruce and Holden, 2017) and has independently confirmed the results by re-analyzing the data with the AHETF-supplied statistical programming code (AHE1017 Appendix E). Furthermore, both objectives are also met with EPA revisions to the exposure results.

3.3.1 Primary Objective: fold Relative Accuracy (fRA)

The primary benchmark objective for AHETF scenarios is for select statistics – the geometric mean (GM), the arithmetic mean (AM), and the 95th percentile (P95) – to be accurate within 3-fold with 95% confidence (i.e., "fold relative accuracy" or fRA).

First, the AHETF evaluated the structure of the final dataset in comparison to the intended study design. The initial study design envisioned a (cost- and analytically-effective) data structure of 7 clusters each with 3 monitored workers, totaling 21 data points. Importantly, as uncertainty can be underestimated if independence is assumed, the AHETF incorporated the potential correlation of monitoring within the same cluster when demonstrating that the planned study design and sample size would satisfy the primary (accuracy) analytical objective. However, when AHE170 was conducted, the AHETF was not able to achieve the intended efficient monitoring configurations due to recruitment difficulties and, from a data analysis perspective resulted in more clusters than intended. While AHE170 utilized the seven monitoring areas as intended (NY/PA, VA/NC/SC/GA/AL, FL, IN/OH, IA, IL MN/ND/SD, ID/WA/OR), they expanded two monitoring areas (NY/PA to include DE and ME; ID/WA/OR to include NE and WY), and, via

protocol amendment, allowed for monitoring more than 3 workers per monitoring area in order to capture the remaining two workers in the 2016 planting season. Ultimately, data analysis included grouping the data from the 7 monitoring areas into 8 (unequally distributed) clusters. Figure 5 below (from AHE1017 Appendix D Table 2) illustrates the clustering used for analysis of the primary objective.

Figure 5: AHE1017 Summary of Data 'Clusters'

Cluster	Monitoring Area Code	Monitoring Unit	Monitoring Date	Nearest Town
1	701	M8	05/14/2015	Kersey PA
2	702	M4	04/04/2015	Dallas NC
		M10	06/02/2015	Tifton GA
		M11	08/18/2015	Irwinville GA
3	703	M1	03/19/2015	Lee FL
		M2	03/21/2015	High Springs FL
		M3	04/02/2015	Mount Dora FL
4	704	M6	05/01/2015	Albion IN
5	704	M13	04/20/2016	Kempton IN
		M16	04/25/2016	La Porte IN
6	705	M5	04/28/2015	Sheldon IA
		M7	05/03/2015	Muscatine IA
		M9	05/19/2015	Lime Springs IA
7	706	M12	04/14/2016	Morgan MN
		M14	04/22/2016	Renville MN
		M15	04/23/2016	Bellechester MN
		M21	05/18/2016	Dell Rapids SD
8	707	M17	05/06/2016	Cairo NE
		M18	05/07/2016	Ravenna NE
		M19	05/07/2016	Gibbon NE
		M20	05/16/2016	Osmond NE

Next, the AHETF demonstrated both dermal and inhalation unit exposures were shown to fit lognormal distributions reasonably well; lognormal probability plots (and normal probability plots, for comparison) are provided as Attachment 2. Finally, 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 noted above.

As presented in Appendix C of the AHETF Governing Document (AHETF, 2008 and AHETF, 2010) and Appendix D of the scenario monograph (Bruce and Holden, 2017), the 95% confidence limits for each of these estimates were obtained by generating 10,000 parametric bootstrap samples. Then, the fRA_{95} 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.

Utilizing both the final datasets and the statistical programming code submitted by the AHETF (in SAS), EPA confirmed the statistical analysis results in the AHETF submission. EPA then used the revised data based on both the method efficiency adjustment outlined in Section 3.2.1

and the lost hand wash sample imputation described in Section 3.2.2, in the same AHETF SAS code, substituting the input data with the EPA-revised data. For both the AHETF data and the EPA-revised dataset, the primary benchmark of 3-fold accuracy for select statistics was met. Accuracy results for inhalation exposure, though not formally part of the primary objective were lower than those for dermal exposure. Results for the AHETF-submitted and EPA-revised dermal exposure data are presented below in Table 8 and inhalation exposure in Table 9.
As can be seen in Table 8, EPA revisions resulted in a slight increase in the magnitude of the dermal exposure estimates, as well as a very slight increase in the fRA_{95} estimates. EPA attributes the latter results to an increase in the 'intra-cluster correlation' (ICC) for each monitoring area. Compared with the EPA revisions, the AHETF's imputation approach results in total dermal exposure results for M1 and M2 that are "farther away" from the total dermal exposure results for the other worker (M3) in their same monitoring cluster (Florida in late March/early April 2015; see Figure 5 above). Thus, because the EPA's revisions result in total dermal exposure estimates for the M1-M2-M3 cluster that are closer together, the ICC increases, which in turn will increase the fRA_{95} estimate.

Table 8. Open Pour Loading Granules – Results of Primary Benchmark Analysis for Dermal Exposure

Statistic	Dermal (EPA-revised)[a]			Dermal (AHETF)		
	Unit Exposure (ug/lb ai)		fRA_{95}	Unit Exposure (ug/lb ai)		fRA_{95}
	Estimate	95% CI		Estimate	95% CI	
GM_S	4.05	2.01 – 7.58	1.9	3.05	1.64 – 5.46	1.8
GSD_S	3.34	2.26 – 4.98	--	3.40	2.31 – 4.98	--
GM_M	3.88	2.02 – 7.49	1.9	2.97	1.63 – 5.45	1.8
GSD_M	3.41	2.28 – 5.18	--	3.43	2.33 – 5.10	--
ICC	0.27	0.00 – 0.70	--	0.13	0.00 – 0.61	--
GM_S = geometric mean assuming SRS = "exp(average of 21 ln(UE)) values". GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 21 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	11.0	3.45 – 17.76	1.9	8.52	2.84 – 13.12	2.2
AM_U	8.37	3.63 – 19.10	2.3	6.47	3.02 – 14.13	2.2
AM_M	8.23	3.67 – 20.06	2.3	6.37	3.05 – 14.55	2.2
AM_S = simple average of 21 unit exposures AM_U = arithmetic mean based on GM_S = GM_S*exp{0.5*((lnGSD_S)^2} AM_M = variance component model-based arithmetic mean = GM_M* exp{0.5*((lnGSD_M)^2}						
$P95_S$	25.09	8.21 – 66.71	3.2	21.60	6.77 – 49.93	3.0
$P95_U$	29.39	11.05 – 71.57	2.6	22.90	9.24 – 53.19	2.4
$P95_M$	29.15	11.32 – 76.42	2.6	22.64	9.37 – 55.20	2.4
$P95_S$ = 95th percentile (i.e., the 20th unit exposure out of 21 ranked in ascending order) $P95_U$ (95th percentile based on GM_S) = GM_S * GSD_S^1.645 $P95_M$ = variance component model-based 95th percentile = GM_M* GSD_M^1.645						

[a] Dermal exposure values reflect 2X default adjustment for hands and face/neck measurements and EPA approach for imputation of lost hand wash samples.

Table 9. Open Pour Loading Granules – Results of Primary Benchmark Analysis for Inhalation Exposure

Statistic	Inhalation		
	Unit Exposure (ug/lb ai)		fRA_{95}
	Estimate	95% CI	
GM_S	0.629	0.439 – 0.907	1.4
GSD_S	2.07	1.65 – 2.60	--

GM_M	0.629	0.438 – 0.907	1.4
GSD_M	2.09	1.65 – 2.65	--
ICC	0.14	0.00 – 0.619	--
GM_S = geometric mean assuming SRS = "exp(average of 21 ln(UE)) values". GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 21 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	0.873	0.547 – 1.22	1.5
AM_U	0.821	0.553 – 1.24	1.5
AM_M	0.825	0.556 – 1.25	1.5
AM_S = simple average of 21 unit exposures AM_U = arithmetic mean based on $GM_S = GM_S*\exp\{0.5*((\ln GSD_S)\text{^}2\}$ AM_M = variance component model-based arithmetic mean = $GM_M* \exp\{0.5*((\ln GSD_M)\text{^}2\}$			
$P95_S$	1.66	1.02 – 3.38	2.0
$P95_U$	2.09	1.23 – 3.52	1.7
$P95_M$	2.11	1.24 – 3.61	1.7
$P95_S$ = 95th percentile (i.e., the 20th unit exposure out of 21 ranked in ascending order) $P95_U$ (95th percentile based on GM_S) = GM_S * GSD_S^1.645 $P95_M$ = variance component model-based 95th percentile = GM_M* GSD_M^1.645			

3.3.2 Secondary Objective: Evaluating Proportionality

The secondary objective of the study design is to be able to distinguish, with 80% statistical power, complete proportionality from complete independence between dermal exposure and amount of active ingredient handled. Upon completion of the study the data can be analyzed to see if it provides a level of precision consistent with that benchmark. Based on analysis of the AHETF submission, as well as results based on EPA revisions to the dermal exposure dataset, this benchmark was met.

To evaluate the relationship for this scenario, the AHETF performed regression analysis of ln(exposure) and ln(AaiH) to determine if the slope is not significantly different than 1 – providing support for a proportional relationship – or if the slope is not significantly different than 0 – providing support for an independent relationship. A proportional relationship would mean that doubling the amount of active ingredient handled would double exposure. Both simple linear regression and mixed-effect regression were performed to evaluate the relationship between dermal exposure and AaiH. A confidence interval of 1.4 (or less) indicates at least 80% statistical power.

As for the primary objective, EPA assessed the secondary objective using both the AHETF-submitted dermal exposure data and using a revised dermal exposure dataset that included the MEA adjustment and the alternative hand wash imputation approach. In comparison to the results from the AHETF submission, there was no substantive effect on the conclusions regarding the secondary objective when using the EPA-revised dataset. For both, the width of the confidence interval for dermal exposure was less than 1.4, indicating the power to detect complete independence from complete proportionality was greater than 80%, and the 95% confidence interval slope of the mixed-effects regression – preferred since it accounts for within-cluster correlation – excludes 0 and includes 1, suggesting a proportional relationship between

exposure and the amount of active ingredient handled is more consistent with the data than an independent one.

The resulting regression slopes and confidence intervals for (AHETF and EPA-revised) dermal exposure and inhalation exposure are summarized in Table 10.

Table 10. Summary Results of log-log Regression Slopes

Model	Dermal Exposure						Inhalation Exposure		
	AHETF			EPA-Revised					
	Est.	95% CI	CI Width	Est.	95% CI	CI Width	Est.	95% CI	CI Width
Simple Linear	0.69	0.125 – 1.25	1.12	0.73	0.172 – 1.28	1.11	0.89	0.552 – 1.24	0.685
Mixed-Effects	0.70	0.115 – 1.28	1.17	0.75	0.205 – 1.29	1.08	0.91	0.557 – 1.26	0.707

Note: results shown using the Kenward-Rogers denominator degrees of freedom method. AHETF statistical analysis (AHE1017 Appendices D and E) provides results using the Containment method as well. Results were not substantially different.

4.0 Data Generalizations and Limitations

The need for an upgraded generic pesticide handler exposure database has been publicly discussed and established (Christian, 2007). No existing exposure data for open pour loading of granules was identified, therefore AHE170 was conducted to supplant data used in regulatory risk assessments. The data will be used generically to assess exposure and risk for workers who manually open, lift, and pour granule pesticide products into in typical agricultural pesticide application equipment while wearing a long-sleeved shirt, long pants, shoes, socks, chemical-resistant gloves, and no respirator. However, certain limitations need to be recognized with respect to collection, use, and interpretation of the exposure data.

4.1 Generic Use in Exposure Assessment

The data comprising this scenario are acceptable for use in assessing exposure for workers who manually open, lift, and pour granule pesticide products into in typical agricultural pesticide application equipment while wearing a long-sleeved shirt, long pants, shoes, socks, chemical-resistant gloves, and no respirator. Though specific active ingredients were monitored, the data is considered reliable for use in a generic fashion (i.e., for any pesticide active ingredient). Importantly, use of the data generically in a regulatory context implies that the pesticide active ingredient being reviewed has a use pattern consistent with the activities and conditions represented by the data for this scenario. Additionally, even for this specific scenario, the availability of this data does not preclude additional consideration or use of acceptable available chemical-specific studies, biomonitoring studies, or other circumstances in which exposure data can be acceptably used in lieu of these data.

4.2 Applicability of AHETF Data for Volatile Chemicals

The data generated in this study are acceptable to use as surrogate data for assessing for workers who handle granule pesticide products which are generally chemicals of low volatility. Since

they are not typically formulated as granule formulations, it is not expected that this dataset would be used to support regulatory decisions for high volatility pesticides (e.g., fumigants).

4.3 Use of "Unit Exposures"

As previously described, statistical analyses demonstrated that the data were more consistent with a proportional relationship between exposure and the amount of active ingredient handled than an independent one. Thus, EPA will continue to recommend use of the exposure data normalized by the amount of active ingredient handled as a default condition.

4.4 Representativeness and Extrapolation to Exposed Population

Targeting and selecting specific monitoring characteristics (i.e., "purposive sampling") as well as certain restrictions necessary for logistical purposes (e.g., selection of certain U.S. states to ensure a large pool of potential granule pesticide users, requiring potential participants to use certain pesticides to ensure laboratory analysis of exposure monitoring matrices, and requiring selection of workers who normally wear the scenario-defined minimal PPE), made the studies comprising this scenario neither purely observational nor random to allow for characterization of the dataset as representative of the population of workers who manually open, lift, and pour granule pesticide products. It is important to recognize this as a limitation when making use of the data.

The final dataset has captured routine behavior as well as limiting the likelihood of "low-end" or non-detect exposures via certain scripting aspects (e.g., monitoring time and tank loading targets), both of which are valuable for regulatory assessment purposes. Construction and use of master lists of potential growers/employers/companies likely mitigated selection bias on the part of participants or recruiters and resulted in diversity of people, equipment, and natural variability in terms of loading granules. Thus, with respect to costs, feasibility, and utility, the resulting dataset is considered a reasonable approximation of expected exposure for this population.

5.0 Conclusions

EPA has reviewed the AHETF Open Pour Loading of Granules 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 data EPA currently uses to estimate dermal and inhalation exposure for open pour loading of granules have been recognized and the need for new data established.
- The primary (quantitative) objective was met: estimates of the arithmetic mean and P95 dermal exposures were shown to be accurate within 3-fold with 95% confidence.
- The secondary (quantitative) objective was met: upon completion of the study, analysis demonstrated that the data provides a level of precision consistent with the pre-study goal of distinguishing complete proportionality from complete independence between dermal exposure and amount of active ingredient handled with 80% statistical power.

- The relationship between both dermal and inhalation exposure and the amount of active ingredient handled was more consistent with a proportional relationship than an independent one. EPA will continue to recommend using exposures normalized by AaiH as a default condition for exposure assessment purposes.
- The AHETF data developed and outlined in the monograph and this review represent the most reliable data for assessing exposure open loading of granule pesticide products.

6.0 References

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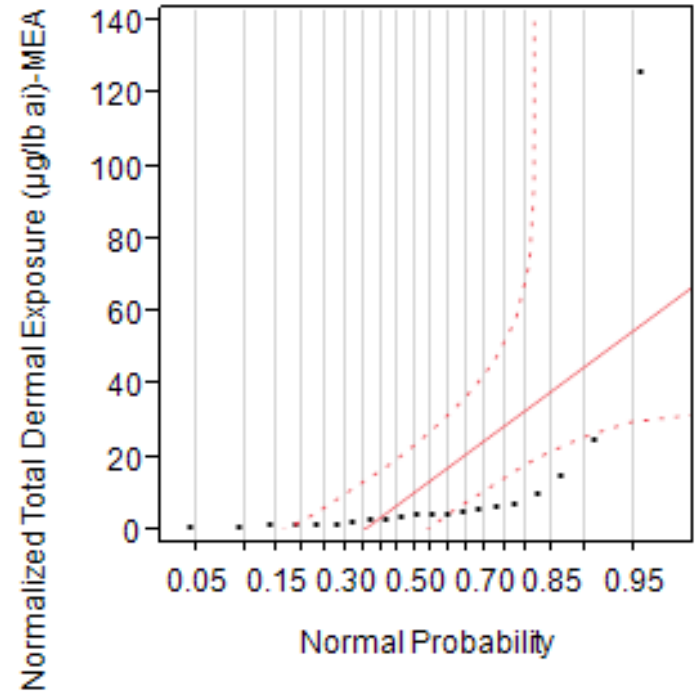
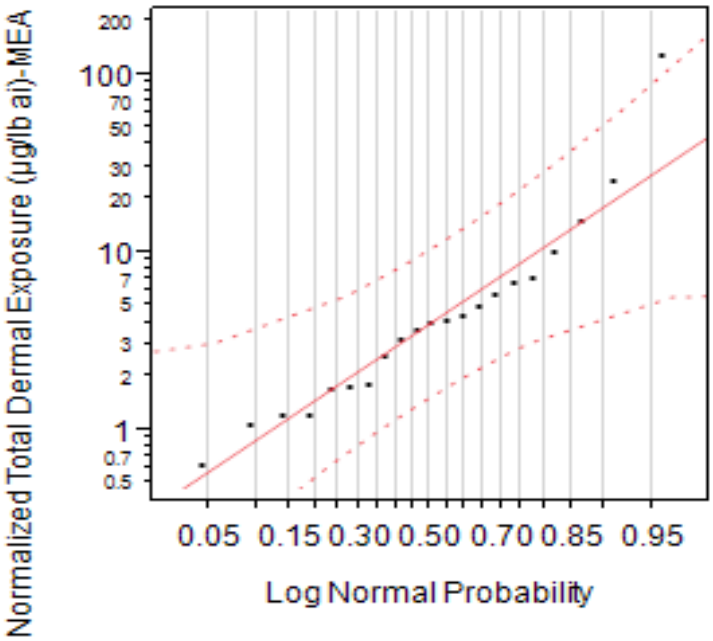
Attachment 1
Table of AaiH-normalized Hand Exposures for each Hand Wash Sample

Worker ID	Hand Wash Sample											
	#1			#2			#3			#4		
	µg	AaiH (lb)	µg/lb ai	µg	AaiH (lb)	µg/lb ai	µg	AaiH (lb)	µg/lb ai	µg	AaiH (lb)	µg/lb ai
1	lost	22.1	unknown	lost	22.1	unknown	5.946	22.1	0.2690	lost	22.1	unknown
2	lost	14.7	unknown	lost	14.7	unknown	11.97	14.7	0.8143			
3	40.2	3.75	10.72	89.7	2.07	43.333						
4	18.9	38.2	0.495									
5	1.5	112.7	0.013	1.6	44.9	0.036						
6	0.06	2.9	0.021	0.5	2.9	0.172	0.5	2.9	0.1724			
7	0.5	5.2	0.096	1.9	5.2	0.365	10.3	11.9	0.8655			
8	9.1	7.3	1.247									
9	0.04	7.2	0.006									
10	4.8	53.3	0.090									
11	49.3	72.1	0.684	9	21.7	0.415						
12	0.5	9.1	0.055	0.5	9.1	0.055	1.4	18.2	0.0769			
13	0.5	5.96	0.084	0.5	5.96	0.084	2.2	8.94	0.2461			
14	4.3	91.2	0.047	11	83.3	0.132						
15	0.06	2.9	0.021	0.06	2.9	0.021	0.5	2.9	0.1724			
16	4.2	12.28	0.342	3.1	12.28	0.252	0.5	14.43	0.0347			
17	0.5	5.7	0.088	0.5	5.7	0.088	1.2	11.4	0.1053	1.3	5.7	0.228
18	10.4	12	0.867	3.4	14.9	0.228						
19	0.5	2.9	0.172	2.8	5.8	0.483						
20	7	28.4	0.246									
21	0.5	4.37	0.114	0.5	5.84	0.086	0.5	4.29	0.1166	2.1	2.86	0.734

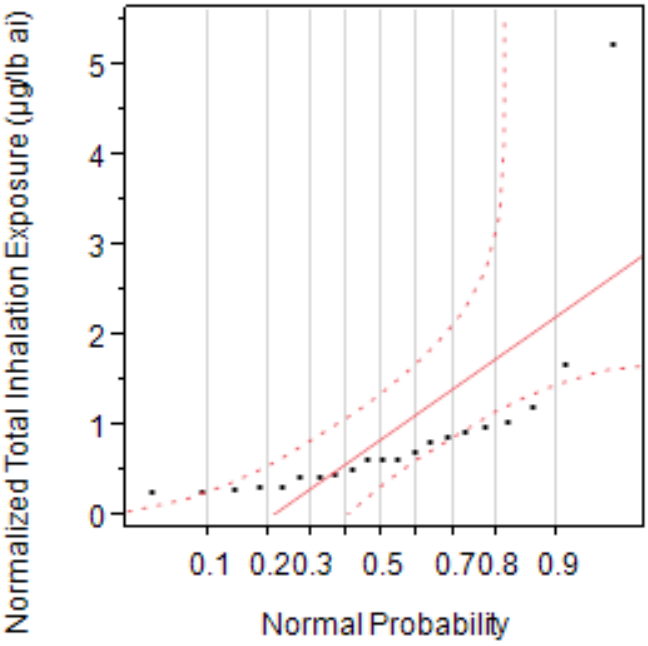
Summary Statistics for AaiH-normalized Hand Exposure (µg/lb ai)	
Count	45
Minimum	0.006
Average	1.44
Maximum	43.3

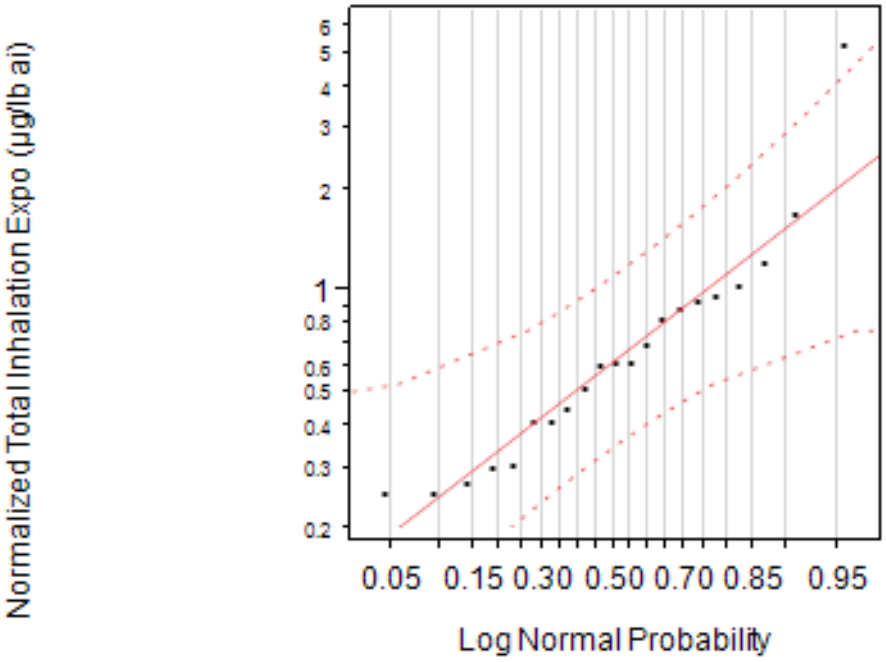
Attachment 2
Normal and Lognormal Probability Plots of (MEA) Dermal Unit Exposures





Normal and Lognormal Probability Plots of Inhalation Unit Exposures





Attachment 3
AHETF-provided pictures of Loading using Bulk Containers, Mini-Bulk Containers, and Super Sacks

Bulk Containers include large containers such as trucks and trailers like those shown below which can hold tons of product. Granules are moved from the bulk container to application equipment (e.g., planters, spreaders, or fixed-wing aircraft) using an auger system, sometimes using an interim container.

Transfer to smaller container for loading into aircraft:

Transfer to application hopper in aircraft:

Mini-Bulk Containers include rigid containers such as the example shown below (several containers on one transfer system trailer) which hold hundreds of pounds of dry product. This particular set-up was used to load treated seed into a planter, but similar systems can be used to load pesticide granules, typically with an auger or conveyor as shown below.

Super Sacks can hold thousands of pounds of granules and are generally lifted by forklifts or other specialized equipment and can be emptied from below into large application hoppers.