UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

DATE: September 27, 2016

SUBJECT: Science Review of the AEATF II Solid Pour (Powder & Granule) Human Exposure Monitoring Study (AEATF II Study AEA07; MRID 49905201).

PC Code(s): Not Applicable (NA)	DP Barcode(s)/No(s): NA
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Petition No(s).: NA	Regulatory Action: Human Health
Risk Assess Type: Surrogate Handler Exposure Data	Case No(s).: NA
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This memorandum presents the EPA/OPP Antimicrobials Division (AD) science review of the human exposure solid pour (powder & granule) study submitted by the Antimicrobial Exposure Assessment Task Force II (AEATF II). The dermal and inhalation exposure data as represented in this review are acceptable and, subject to the considerations described below, are recommended for use for pesticide handler exposure assessments.

EXECUTIVE SUMMARY

This document represents the USEPA, Office of Pesticides Program, Antimicrobials Division (AD) review of the Antimicrobial Exposure Assessment Task Force II (AEATF II) solid pour study. The protocol for this completed study was previously reviewed by the EPA and the Human Studies Review Board (HSRB) for ethical and scientific design. Both EPA and HSRB approved the protocol and provided recommendations for some minor modifications (discussed within this memo). This memo contains the scientific review, recommended unit exposures, and study limitations to be considered by users. The ethics review is contained in a separate memo. Both of these reviews are to be presented to the HSRB on October 20, 2016.

The AEATF II designed the study to develop unit exposures for (1) consumer open pour of powder, (2) consumer open pour of granules, (3) occupational open pour of powder, and (4) occupational open pour of granules. The results of the study are reported herein.

The solid pour study investigators monitored inhalation and dermal exposures to 18 different test subjects for the worker scenarios and a different set of 18 test subjects for the consumer scenarios. The 18 test subjects for the worker portion of the study were used for both the pouring of the powder scenario and then again for the pouring of the granules scenario. The 18 test subjects for the consumer portion of the study were also used both for the pouring of the powder scenario and the pouring of the granules scenario. Cyanuric acid (CYA) was the active ingredient in the products used for all four scenarios. Various size product containers, different receiving containers for consumers versus occupational, amounts poured, and pour heights were employed. Also varied for the consumers were the use of a scoop and the pre-dissolving of the solids. Also varied for the occupational workers was the pre-measuring and pre-weighing of the CYA. EPA confirms that the data are considered the most reliable data for assessing handler exposures from pouring solid antimicrobial products. The reader is referred to Section 3.0 for a discussion on the data limitations and use of the data as surrogate.

EPA intends to use this AEATF II solid pour dataset instead of the Chemical Manufacturers Association (CMA) and/or the Pesticide Handlers Exposure Database (PHED) datasets to assess exposure for persons pouring a solid antimicrobial product in various settings. The exposure data in the AEATF II solid pour scenarios represent the pouring of a powder and granule antimicrobial products by consumers and workers. The scenario does not cover the subsequent application of the treatment solution. The total potential exposure from pouring and the subsequent application of the treatment solution can be determined by combining the results of this study with the results of the studies AEATF II has previously conducted or plans to conduct. There are also antimicrobial uses of solid pour that require no additional application (e.g., pouring products into a swimming pool or into paint during the manufacturing process).

Select summary statistics for the “unit exposures” (i.e., exposures normalized to pounds active ingredient handled) are presented in Tables 1a and 1b for the dermal and inhalation routes of exposure. Each test subject wore both inner and outer whole body dosimeters (WBD) that were sectioned and analyzed separately for each body part (e.g., lower leg, upper leg, lower arm, upper arm, etc). This WBD sectioning allows for estimating unit exposures for various clothing combinations of long/short pants and/or long/short sleeved shirts. Note: The AEATF II

corrected the dermal hand/face/neck exposures using an 85% sampling efficiency factor which was subsequently removed by EPA (see Section 2.2 for details). Therefore, the dermal results herein differ slightly from the AEATF II's study report.

For comparison, results from the PHED studies used in prior risk assessments for solid pour are also presented in Tables 1a and 1b. The summary statistics from the new AEATF study reported in Tables 1a and 1b are estimated using the lognormal simple random sampling model while the PHED results are empirical estimates.

Table 1a. Unit Exposures (UE) for the AEATF Open Pour Powder Occupational and Consumer Scenarios

Exposure Route	Setting	Clothing	PHED ("best fit")[a]	AEATF II[b, c] (n= 18 per scenario)	
				Arithmetic Mean[d]	95th Percentile[e]
Dermal (mg/lb ai)	Occupational	Long pants/long-sleeves, gloves	0.17	0.226	0.631
	Consumer	Long pants/long-sleeves, no gloves	3.7	3.43	12.2
		Short pants/short-sleeved, no gloves	Not Available	9.6	34.6
Inhalation Inhalable <100 µm (Respirable <4 µm)	Occupational	Breathing Zone (mg/lb ai)[f]	0.043	0.224 (0.00178)	0.708 (0.00587)
	Consumer			0.0436 (0.00013)	0.142 (0.00040)
	Occupational	Breathing Zone (8 hr TWA mg/m^3/lb ai)[g]	0.0078	0.0280 (0.00022)	0.0885 (0.00073)
	Consumer			0.00545 (0.00002)	0.0177 (0.00005)

[a] Historically PHED data has been used to assess the open pour powder exposures to antimicrobial products. The PHED "best fit" measure is the sum of the median and/or geometric mean for the various individual body parts. PHED inhalation dose estimates were calculated assuming a breathing rate of 1.7 m^3/hour. PHED inhalation UE represent inhalable (total) particulates. The PHED TWA estimate is based on the arithmetic mean.

[b] Dermal and inhalation UEs are corrected for field recoveries. Each UE contains all 18 MEs monitored, no outliers.

[c] Statistics are estimated using a lognormal simple random sampling model. Details are described in Appendix A.

[d] Arithmetic Mean (AM) = GM * exp{0.5*(lnGSD)^2}

[e] 95th percentile = GM * GSD$^{1.645}$

[f] Inhalation (mg/lb ai) = air conc ((mg/m^3) / lb ai) * breathing rate (1 m^3/hour) * pouring duration (hours/day)

[g] 8-Hour Time Weighted Average (TWA) (mg/m^3/lb ai) = air conc ((mg/m^3) / lb ai) * pouring duration (hours/day) / 8 (hours)

Table 1b. Unit Exposures (UE) for the AEATF Open Pour Granule Occupational and Consumer Scenarios					
Exposure Route	**Setting**	**Clothing**	**PHED ("best fit")[a]**	**AEATF II[b, c] (n= 18 per scenario)**	
				Arithmetic Mean[d]	**95th Percentile[e]**
Dermal (mg/lb ai)	Occupational	Long pants/long-sleeves, gloves	0.0069	0.049	0.118
	Consumer	Long pants/long-sleeves, no gloves	0.0084	0.91	3.49
		Short pants/short-sleeved, no gloves	Not Available	1.87	7.25
Inhalation Inhalable <100 µm (Respirable <4 µm)	Occupational	Breathing Zone (mg/lb ai)[f]	0.0017	0.0784 (0.00324)	0.255 (0.0105)
	Consumer			0.00284 (0.000060)	0.00941 (0.00018)
	Occupational	Breathing Zone (8 hr TWA mg/m^3/lb ai)[g]	0.00043	0.0098 (0.00040)	0.0319 (0.00131)
	Consumer			0.00036 (0.000008)	0.00118 (0.00002)

[a] Historically PHED data has been used to assess the open pour granule exposures to antimicrobial products. The PHED "best fit" measure is the sum of the median and/or geometric mean for the various individual body parts. PHED inhalation dose estimates were calculated assuming a breathing rate of 1.7 m^3/hour. PHED inhalation UE represent inhalable (total) particulates. The PHED TWA estimate is based on the arithmetic mean.

[b] Dermal and inhalation UEs are corrected for field recoveries. Each UE contains all 18 MEs monitored, no outliers.

[c] Statistics are estimated using a lognormal simple random sampling model. Details are described in Appendix A.

[d] Arithmetic Mean (AM) = GM * exp{0.5*(lnGSD)^2}

[e] 95th percentile = GM * GSD$^{1.645}$

[f] Inhalation (mg/lb ai) = air conc ((mg/m^3) / lb ai) * breathing rate (1 m^3/hour) * pouring duration (hours/day)

[g] 8-Hour Time Weighted Average (TWA) (mg/m^3/lb ai) = air conc ((mg/m^3) / lb ai) * pouring duration (hrs/day) / 8 (hrs)

The following important points with respect to these data are noted:

- The AEATF II data and associated unit exposures are considered superior to the existing solid (powder and granules) pour datasets for antimicrobial uses (i.e., CMA and PHED data). AEATF II efforts represented a well-designed, concerted process to collect reliable 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 dermal unit exposures recommended in Table 1a and 1b for occupational scenarios are based on the long sleeved shirt, long pants, and chemical resistant gloves. For consumer scenarios, the typical clothing scenario is the short sleeves, short pants, and no gloves.

- Estimates of the geometric mean (GM), arithmetic mean (AM), and 95th percentile (P95) were shown to be accurate within 3-fold with 95% confidence for all scenarios except for the consumer granules scenario for dermal exposure where the accuracy goal is 2.2 for GM, 3.6 for AM, and 3.3 for P95. At this time, no additional monitoring for the solid pour scenarios is required.
- The statistical analysis (Section 2.4) provides evidence for or against log-log-linearity with a slope of 1[1] between exposure and pounds of active ingredient (ai) handled. An ideal result of the log-log-linearity test is an estimated slope between 0 and 1 with a confidence interval that includes 1 but not zero indicating that independence between exposure and pounds of active ingredient (a slope of zero) is rejected and that log-log-linearity with a slope of 1 is not rejected. The results of this analysis indicate the following:
    - The analyses of log-log-linearity in Section 2.4, Tables 9 and 10, show that dermal and inhalation exposure tend to increase with pounds of active ingredient handled (AaiH) for all the scenarios.
    - For both of the occupational granules and powder dermal scenarios, the confidence intervals include 1 but not zero, indicating that independence is rejected and log-log-linearity with a slope of 1 is not rejected.
    - For the occupational and consumer, granules and powder inhalation scenarios (Section 2.4, Table 10), the confidence intervals include 1 but not zero, indicating that independence is rejected and log-log-linearity with a slope of 1 is not rejected.
    - For the consumer granules dermal scenario, the confidence intervals for the slope include both zero and 1, indicating that independence is not rejected and log-log-linearity with a slope of 1 is not rejected.
    - For the consumer powder dermal scenario the confidence interval does not include zero or 1. Thus the log-log-linearity with a slope of 1 was rejected. However, the upper confidence bound for the slope was a little less than 1, indicating that the evidence against log-log-linearity with a slope of 1 is not highly statistically significant.

To assess the risks resulting from solid pour exposures, EPA will combine appropriate unit exposure (UE) values with chemical-specific inputs (e.g., maximum labeled application rates, dermal absorption, toxicological endpoints of concern) and default inputs (high end volume mixed, loaded, and/or applied) in the standard pesticide handler exposure algorithm: Potential exposure = UE (mg/lb ai or mg/m^3/lb ai) x absorption (%) if applicable x maximum label rate (% ai by weight) x Weight of treated product/article (pounds).

[1] The statistical analysis of log-log-linearity tests whether the slope of log exposure against log ai is 1, which supports the use of the data in the "unit exposure" formats. We now refer to these analyses as the log-log-linearity analyses. In the Governing Documents and in previous reviews of the AEATF II studies we have referred to these analyses as a "proportionality" analysis, but this has caused some confusion because the statistical models do not assume that the exposure is directly proportional to the AI but instead assume that the logarithm of the exposure is linear in the logarithm of AI with a slope of 1, which is a related finding but a very different model, as explained in more detail in Appendix A. We have therefore changed the terminology from "proportionality" to "log-log-linearity with a slope of 1."

1.0 Background

The AEATF II is developing a database representing inhalation and dermal exposure during a number of antimicrobial handler scenarios. A scenario is defined as a pesticide handling task based on activity (e.g., application or mixing/loading) and equipment type (e.g., aerosol cans, ready-to-use wipes, mop & bucket, pressure treatment of wood facilities, painting, etc). The AEATF II is monitoring residues on both inner and outer dosimeters, which will allow the EPA to estimate exposures to various clothing configurations (e.g., long pants, long-sleeved shirt or long pants, short-sleeved shirt or short pants, short-sleeved shirts, plus shoes, socks, and no gloves). Prior to conducting intentional exposure studies in humans, the protocols are reviewed by the Human Studies Review Board (HSRB). The HSRB reviewed this solid pour exposure study protocol in April 2014.

1.1 Solid Pour Scenarios Defined

The solid pour scenarios in this study are defined as manually pouring a pesticide formulated as a powder or granules from various types of containers (pouches, cans, drums) of various sizes from various heights into receiving containers (swimming pool or manufacturing-type “vats” simulated by 180 gallon tank with hatch), with and without pre-measurements of the product being poured. Subjects poured as they normally would do. Subjects wore whole body dosimeters (WBD) underneath long-sleeved shirts, and long pants (plus a personal air sampler). The test subjects representing consumers wore no gloves and the subjects representing occupational workers wore a pair of new nitrile chemical resistant gloves. The conditions under which the study participants handle the pesticide as they are monitored are referred to as the scenario. Both inner and outer dosimeters were worn by the monitored study participants, and both inner and outer dosimeters were analyzed for residues.

1.2 Study Objective

The AEATF II’s study objective is to monitor inhalation and dermal exposures to be used as inputs in exposure algorithms to predict future exposures to persons manually pouring powder and granule antimicrobial products packaged in open pour containers. Dermal and inhalation exposure monitoring was conducted while study participants poured powder and granule products using various methods (containers, heights, pre-measurements or not, etc) for use in exposure assessments, as “unit exposures”. The study was designed to provide results for two distinct unit exposures: powders and granules.

“Unit exposure” (UE) is defined as the expected external chemical exposure an individual may receive (i.e., "to-the-skin" or “in the breathing zone”) per weight-unit of chemical handled and is the default data format used in pesticide handler exposure assessments. Mathematically, unit exposures are expressed as "handler" exposure normalized by the amount of active ingredient (ai) handled by participants in scenario-specific exposure studies (e.g., mg ai exposure/lb ai handled). EPA uses these UEs generically to estimate exposure for other chemicals having the same or different application rates.

Criteria for determining when a scenario is considered complete and operative have been developed (SAP 2007). Outlined in the AEATF II Governing Document, the criteria can be briefly summarized as follows:

- The AEATF II's objective for this study design is to be 95% confident that key statistics of normalized exposure are accurate within 3-fold. Specifically, the upper and lower 95% confidence limits should be no more than 3-fold (K=3) higher or lower than the estimates for each of the geometric mean, arithmetic mean, and 95th percentile unit exposures. To meet this objective, AEATF II proposed an experimental design with 18 monitoring events (MEs) for each of the occupational and consumer subjects each pouring powder and granule formulated products (total of 72 MEs).

A secondary objective for EPA is for meeting 80% power for detecting log-log-linearity with a slope of 1. This objective is approximately met if the widths of the confidence intervals for the slope based on the lognormal model are at most 1.4.

1.3 Protocol Modifications, Amendments, and Deviations

1.3.1 Protocol Modifications Based on EPA and HSRB Reviews

EPA required four science-based modifications to the solid pour protocol (EPA 2013). The AEATF-II provided changes to their protocol based on these four EPA review comments which are summarized as follows (AEATF-II 2014):

- The number of scoops and pours from the containers are not provided; only the range of the total amount of active ingredient handled (AaiH) in each subgrouping is specified in the protocol. Therefore, individual MEs have not yet been assigned AaiH. The AEATF II will need to assign specific AaiH, scoop sizes, and containers before proceeding with the research.

  AEATF-II responded… "*The total amount of AI that each subject will pour and the size of the source containers will be randomly selected using a computer program. A choice of a few different scoops will provided to allow subjects to use what they are familiar with and to correspond to the amount of product that needs to be transferred. The people in the consumer pouring will have a choice of two scoops. The people in the occupational monitoring will have a choice of three different sized scoops. The number of scoops will not be defined for the occupational monitoring – instead, they will be told how much product on a weight basis needs to be scooped. The container will weighed to determine the amount scooped. The number of scoops will be counted and recorded. The container size(s) and total amount to be transferred (poured or poured and scooped) will be randomly allocated to each ME before the protocol is finalized. For consumer monitoring, the number of scoops will be predetermined and specified, along with the container size(s) and total amount of product to be transferred. The amount of product that each scoop holds (i.e. one pound) will be marked on the scoop. Using a scoop of known volume is a fairly standard method that homeowners use when measuring out*

their own pool chemicals." (AEATF-II 2014) EPA is in agreement to this approach. Container sizes used in the study are summarized in Table 3 below.

- The protocol should be revised to specify that subjects in the consumer portion of the study are required to wear particulate dust masks to provide additional respiratory protection. The protocol currently states that subjects in the occupational portion will be required to wear dust masks but that subjects in the consumer portion will be "given the option" to wear one.

  AEATF-II agreed.

- The AEATF-II should provide additional details about how the airflow in the indoor environment is oriented between the pouring of the solids and the test subject (e.g., is the airflow blowing powder in the direction of the test subject as they pour?).

  AEATF-II responded to EPA's, and a similar HSRB comment (to add variability), by varying the positioning of the subjects around the receiving container; air velocity and direction within the warehouse is fixed.

- The AEATF-II will need to provide hand wash removal efficiency information, possibly a hand wash removal efficiency study, to allow EPA to correct for incomplete residue removal from the hand sampling.

  AEATF-II used an 85% correction factor based on a dermal absorption study (Inokuchi et al, 1978) to correct the hand and face/neck sampling results for method removal efficiency. Upon further review, EPA decided not to use the correction factor (see Section 2.2 for further discussion).

In addition to the EPA comments noted above, the HSRB also provided written discussion on a number of issues pertaining to the review of the solid pour study. AEATF II provided EPA with their responses to the HSRB inquiries. The science-based issues raised by HSRB, and the AEATF II responses, are reproduced in Table 2 below from AEATF II's correspondence to EPA (verbatim) (AEATF-II 2014):

Table 2. HSRB Protocol Comments and AEATF II's Responses.

Issue Raised by HSRB[1]	**AEATF Response[2]**
Page 10 – potential limitation with respect to pouring distance for occupational monitoring due to using a single receiving container	To incorporate diversity in pouring height, a platform of about 18 to 24 inches will be built. Nine subjects will pour from the platform while nine will pour while standing on the ground. This will allow for about a 2 foot difference in pouring distance. In addition, the height of each subject will be measured as this would also impact pouring distance. EPA Note: In the completed study, the "platform" was a stand with two steps, the first step was 7 inches from the

	ground and the second step was 13 inches from the ground (with the subjects themselves selecting which step to stand on).
Page 11 – the impact of a partial lid	It is not clear whether the partial lid would reduce potential exposure by reducing the plume of dust that might occur when the product hits the water or if it might increase exposure due to increasing the likelihood of spillage because of the smaller opening. Because solid antimicrobial products may be added to open tanks and to more narrow chutes or access ports, the use of a round hinged lid provides a compromise. EPA Note: See Figure 1 for picture of tank and lid.
Page 11 - the subsequent time spent in the immediate vicinity of the pour for occupational subjects	There is no physical mixing done by workers adding antimicrobial products to industrial and manufacturing processes; the products are added to mixing vats that are mechanically stirred or mixed, no manual effort is involved. To keep the worker in the pour area for a few minutes immediately following his task, a simple routine reflective of what is seen in an industrial setting will be implemented. This will consist of the worker inspecting for spillage, making sure the tank water is circulating, closing the tank lid, and putting the lids back on the empty or partially empty product container(s). If there is a spill, he will be asked to clean up as he normally would (supplies such as broom, dust pan, and rags will be available). All of this will be documented in the observations.
Pages 11-12 – adding variability to the effect of ventilation in the indoor setting	The AEATF will vary the positioning of the subjects around the receiving container. This will be done by turning the lid by approximately 45 degrees with each subject (over the range available, since some access to the tank may be blocked by piping) to get this variation since the air velocity and direction will be fixed. EPA Note: In the completed study, the author indicated the following procedure was used (study report page 17) *"To add variability to the effect of airflow in the indoor setting, the positioning of subjects around the tank was varied by having each subject pour from a different side of the tank."*
Page 12 – discussion of new versus old gloves	As standard practice both the AEATF and the AHETF [Agricultural Handler Exposure Task Force] provide new gloves to test subjects when the protocol or label requires the use of gloves. The purpose of this is to eliminate the potential for chemical interferences that could occur from

	other residues on or in the workers' gloves and to ensure that the gloves worn meet Worker Protection Standards. As such per standard procedure, new gloves will be provided to the occupational test subjects.
Pages 12-13 - potential for wet hands, especially during the residential pouring events	The AEATF will not have any preventative steps in place to prevent a subject from getting their hands wet during the pouring/scooping process. The observer will be requested to look out for wet hands and will ask the subject afterwards if he/she got their hands wet during their task. EPA Note: Study results indicate that consumer, granule, ME1 had visible residues (wet granules) on wet hands; ME9 had the highest hand residues in the study and that… *"…the tips of his fingers contacted the solution, and solution splashed out of the bucket and onto the deck* (observational notes on page 226 of study report).", and page 80 of study report further indicated…. "*At the end of monitoring, his hands, lower legs, and lower arms were visibly wet*." In the consumer powder scenario, ME3 and ME12 had wet finger tips. For the occupational scenarios, only one subject's glove was reported as "wet" (ME11).
Page 13 – discussion of solid pour studies done by AHETF and AEATF	The AEATF is pleased that the detailed information regarding the two on-going AHETF studies and one planned AEATF study was helpful to demonstrate that the proposed AEA07 study is not duplicating data that already exists. The AEATF wants to emphasize that pouring indoors and scooping product from drums are key differences between how occupational solid antimicrobial products are handled and how agricultural pesticides are handled.
Pages 13-14 – evaluation of linearity between amount handled and exposure	The range of product handled for the consumer scenario is 1 to 50 pounds and 5 to 90 pounds for the occupational scenario. Within each scenario, this range is divided into 3 levels, with 6 MEs assigned to each level. The amount of CYA to be handled by each subject will be randomly determined within the constraints of each level; a provision that no two subjects within a level can handle the same amount of product will be added.

[1] HSRB final report for the review of the Solid Pour protocol (June 25, 2014).
[2] AEATF-II 2014.

1.3.2 Protocol Amendments

The study report (pages 92-94) lists 16 protocol amendments. The amendments range from minor changes such as reporting format requirement updates; change adding another

newspaper to use for recruitment of test subjects; change analytical principal investigator, etc to more substantive changes such as to include consumers who do not own pools and no experience pouring products into pools; removal of the 25 lb bucket for powders; and allowing for the inclusion of AEATF employees/spouses for occupational test subjects. The bias of including test subjects who do not have experience with pool chemicals most likely would lead to more exposure from an inexperienced handler rather than less exposure, assuming experience may influence efficiency/cleanliness. The removal of the 25 lb buckets for powders was done after it was observed that two of the MEs encountered (page 66-67 of study report) "*…poor pouring characteristics of powder and dust that is generated when handling large volumes of powder, as was observed during MEs 14 and 15*." According to the study report, "*biocides formulated as powders are normally not sold to consumers in large containers because of the poor pouring characteristics…*". The three other MEs that were to be assigned the 25 lb buckets were switched to other containers. The AEATF consulted with EPA prior to the change and EPA agreed; with a caveat that EPA would include in the characterization for consumers pouring powders from large container sizes (e.g., 25 lb buckets) indicated "high" exposure and are not recommended. The change in the inclusion criteria of allowing employees of AEATF member companies (or their spouses) resulted in two employees recruited from two regional manufacturing plants owned by two of the task force member companies; no spouses of employees of member companies were recruited. One of the member company employees was randomly assigned as an alternate and was not monitored. The other employee is coded as ME 4 for the occupational granule scenario and as ME 10 for the occupational powder scenario (individual results for these two MEs can be viewed/compared to the other MEs in Tables 4c and 4d below).

1.3.3 Protocol Deviations

A total of 10 protocol and two SOP deviations were noted in the study (study report pages 94 & 95). The 10 protocol deviations included the following: travel spike deviations; dosimeter cut short; poured a differing amount of ai than planned for one ME; scoop rather than pour for two MEs; for the analytical method and sample analysis of the occupational face/neck wipe, the sample extracts were not evaporated to dryness and reconstituted, rather aliquots were diluted with the internal standard solution and analyzed. The two SOP deviations included not calibrating two balances on Day 2 of consumer monitoring; and minor dosimeter removal deviations (e.g., did not remove button, sample label placed on bag rather than aluminum foil, etc). For a detailed description of each of the protocol and SOP deviations the reader is referred to the study report. EPA accepts the study author's conclusion that these deviations did not adversely affect the outcome of the study.

EPA also notes additional protocol deviations that were not mentioned in the study report. First, the protocol plan was to have the subjects work as they normally would do; but the observational notes for ME 14 in the consumer powder scenario (study report page 249) indicates "*we did recommend that he not toss it* [powder] *out across the pool*" because the subject did not have experience with pouring powders. ME 14's unit exposure is below the mean for the scenario. Second, the pool deck was planned to be flush with the pool but ended up being slightly above the pool rim. Third, the protocol did not mention the use of a sump pump in the pool to aid in dissolving the CYA. Fourth, weather data were recorded at 15 minute intervals rather than the

planned 5 minute intervals. Lastly, although not a protocol deviation, in the original protocol (dated April 2013, pages 19 and 23), the plan was to randomly select the order in which the granule and the powder were to be poured first for each test subject to avoid a potential systematic bias of someone becoming more proficient with pouring. However, the final protocol (page 708 of the completed study) modified the order to have all of the subjects pour the granules first and the powders second. According to page 35 of the completed study report, "*all test subjects conducted the granular pouring ME first and the powder pouring ME second. This was done to minimize the potential for cross-contamination…*". The effect of this modification may introduce potential biases due to learning experience from the first task (i.e., pouring granules). The actual effect on the unit exposures is unknown; exposure to powders would be expected to be higher than exposures to granules, and they were.

1.4 Material & Methods

Table 3 summarizes some of the key field aspects of the study.

Table 3. Summary of Key Study Design Parameters.

Parameter	Consumer Scenarios		Occupational Scenarios	
	Powder	**Granule**	**Powder**	**Granule**
Site location	Outdoor pool; Concord, Ohio		Indoor warehouse; Concord, Ohio	
Weather	Temp 62 to 76 F %RH 44 to 84 Wind 0 to 10 mph		Temp 62 to 76 F %RH 27 to 46	
Receiving container	Swimming pool (18ftx9ftx52inches)		180 gal tank with 24x24 inch hinged lid	
Product containers	(1) Plastic bag (2) 1 lb can (3) 4.5 lb can (4) 25 lb bucket	(1) Plastic bag (2) 1.75 lb can (3) 6 lb can (4) 25 lb bucket	(1) 25 lb bucket (6 gallons) (2) 50 lb drum (14 gallons) (3) 90 lb drum (30 gallons)	
Sampling dates	August 13 to 17, 2014		March 26 to April 1, 2015	
Sampling durations	Avg 4.1 min (1 to 19 min)	Avg 5.1 min (1 to 20 min)	Avg 9.8 min (2 to 22 min)	Avg 6.5 min (2 to 10 min)
AaiH (lb ai)	Avg 9.41 (0.476 to 47.5)	Avg 17.1 (0.98 to 48.7)	Avg 37.1 (5.1 to 71.8)	Avg 42.0 (11.1 to 97.0)
Particle size	98% < 250 µm and 45% < 45 µm	>98% >250µm, 64% > 600 µm, 4.6% > 1700 µm	45% < 45 µm and 45% < 45 µm	>98% >250µm, 64% > 600 µm, 4.6% > 1700 µm

- ***Study Location:*** The solid pour study was conducted both indoors (occupational) and outdoors (swimming pool) at the Ricerca Biosciences LLC in Concord, Ohio. Photos and schematics of the swimming pool and test rooms are located in Appendix D starting on page 204 of the study report.

- ***Substance Tested:*** The test substance monitored was cyanuric acid (CYA) as 100% active ingredient; CAS number 108-80-5. Note: CYA itself is not a registered pesticide (CYA can be used to stabilize chlorine in a swimming pool). Chlorinated CYA is a registered pesticide (but not used in this study).
- ***Test System:*** The study was designed to monitor exposures to consumers and occupational workers while open pouring powder and granules (tested separately) using different size and types of packaging containers. Figure 1 below provides several photos from the study showing the various test systems. The occupational scenarios were performed in a warehouse using a 180 gallon tank with a hinged lid. Test subjects poured or scooped the powder/granule using various size containers and stood on the ground or on the two steps as illustrated in Figure 1. The consumer scenarios used various size containers to pour as they normally would do into the outdoor swimming pool as illustrated in the photos in Figure 1. As described in the study report, *"Each of the thirty-six test subjects conducted two consecutive monitoring events, one using a set of containers containing granular CYA and one monitoring event using containers of powder CYA. The granular monitoring event was conducted first, samples collected and the subject re-dressed, and the powder monitoring event was conducted second."*

Figure 1a. Occupational Scenario Tank/Lid/Step Configuration in Warehouse.

Figure 1b. Occupational Powder Pour from Bucket (Nitrile Gloves).

Figure 1c. Occupational Powder Pour, Dust Plume (Air Sampling Tube, Respirator).

Figure 1d. Occupational Scenario, Using Scoop to Weigh/Transfer Product.

Figure 1e. Consumer Pouring/Broadcasting Directly into Swimming Pool (Respirator).

Figure 1f. Consumer Scooping Product into Swimming Pool.

- ***Sample Size:*** The study consisted of 18 monitoring events (ME) for each of the consumer and occupational scenarios for both powder and granule scenarios (e.g., n=18 for consumer powder; n=18 for consumer granule; n=18 for occupational powder; and n=18 for occupational granule). Each ME within a scenario is a different subject; but each subject designated as a consumer and an occupational subject performed both a powder and a granule pour (i.e., there were 18 different people selected to be monitored as consumers and another 18 different people selected to be monitored as occupational).

- ***Duration:*** The sampling times for the consumer granules averaged 5.1 minutes and ranged from 1 to 20 minutes; for the consumer powder the sampling time averaged 4.1 minutes and ranged from 1 to 19 minutes. The sampling times for the occupational granules averaged 6.5 minutes and ranged from 2 to 13 minutes; for the occupational powder the sampling time averaged 9.8 minutes and ranged from 2 to 35 minutes. Each individual ME sampling duration is reported on pages 114 & 155 of the AEATF study report. The duration of the sampling pump run times were used as the duration of the ME and to calculate the volume of air sampled (m^3) and the corresponding air concentration (mg/m^3). Each individual ME air sampling pump flow rates and start/stop sampling times are reported on pages 116-119 of the AEATF study report.

- ***AaiH:*** The specific AaiH for each individual ME is reported in Tables 4a, 4b, 4c and 4d below and pages 123 & 124 of the AEATF study. The amount of active ingredient

handled (AaiH) was measured by weighing the containers prior to and subsequent to the monitoring event. The average and range of AaiH are as follows:

- Consumer granules averaged 17.1 lbs ai ranging from 0.98 to 48.7 lb ai.
- Consumer powder averaged 9.41 lb ai with a range of 0.476 to 47.5 lb ai.
- Occupational granules averaged 42.0 lb ai with a range of 11.1 to 97.0 lb ai.
- Occupational powder averaged 37.1 lb ai with a range of 5.1 to 71.8 lb ai.

- ***Pouring Procedures***: The following encompasses a summary of the pouring procedures:
  - "*The consumer test subjects were taken up the steps of the deck with the observer and were free to position themselves and pour as they normally would do relative to the swimming pool."* (page 42 of study report)
  - "*Subjects in the occupational monitoring phase were brought into the warehouse by either the Study Director or the observer and provided instruction on which tank to pour into and how much product from which containers to add."* (page 42 of study report)
  - *"…the subject was given basic instruction of what needed to be poured, whether a scoop was required, whether pre-dissolving was required (consumer monitoring), and for the occupational monitoring, which tank to pour into, which side to pour from, which scale to use, and whether pouring should be done from the step. Instructions on cleanup tasks were also given."* (page 42-43 of study report)
  - In the two consumer scenarios, some of the subjects poured the powder or granule product directly into the pool; some used a combination of scooping and pouring the product directly into the pool; and some pre-dissolved the product in a small 2 and 5 gallon buckets, stirred the slurry and then poured it into the pool. The size of containers, number of scoops, and pre-dissolving product for each of the individual MEs are provided on pages 110 and 111 of the study report.
  - In the two occupational scenarios, "*three subjects were assigned to pour directly from one or more 25 pound buckets; the rest either weighed and scooped product or did a mixture of pouring directly from one or more 25-pound buckets as well as weighing and scooping product and then adding it to the tank. The amount to be weighed (in pounds) and the container to scoop from, was told to the subject. The task of weighing and scooping involved opening a container, transferring product from that container using a scoop to a receiving bucket until the correct weight was reached, and then pouring the contents of the bucket into a tank of water. Depending on how much product needed to be transferred, sometimes multiple buckets were filled, weighed, and poured. Nine of the 18 MEs per formulation were instructed to stand on a step while pouring."* (page 67 of study report) The size of containers, number of scoops, and use of the step for each of the individual MEs are provided on pages 112 and 113 of the study report.
  - For the consumer scenarios, approximately 2 hours elapsed between monitoring of different test subjects and 2 to 4 test subjects were monitored per day. For the occupational scenarios, test subjects were scheduled 3 hours apart and 1 to 3 subjects were monitored per day. The time that elapsed from the end of an

individual's granule pour and the start of the powder pour ranged from 12 to 21 minutes.
    - Observational notes for each monitoring event for the consumers are provided in Appendix E, starting on page 217 of the study report; and for occupational in Appendix F starting on page 254 of the study report.

- ***Environmental Conditions*:** Environmental conditions (humidity, temperature indoors and outdoors as well as wind speed and direction outdoors) are reported for each individual ME on pages 125-127 of the study report. Environmental conditions outdoors were collected with a Kestrell 3000 meter and indoor measurements were collect with a HOBO Pro V2 data logger. The humidity ranged from 44 to 84% outdoors and 27 to 46% indoors. Outdoor and indoor temperatures both ranged from 62 to 76º F. The outdoor wind speed ranged from 0 to 10 mph; for ME 10 the wind gusted to 10 mph. Air flow measurements indoors for the occupational scenarios were measured, however, the air flow measurements were sampled prior to the study and conditions changed during the study. According to the study report (pages 32), *"Airflow measurements in the warehouse were performed on March 23, 2015, by HZW Environmental Consultants LLC using an Alnor Velometer (Model 6000AP). The direction of airflow was observed using SKC Smoker Tubes. At the time that air flow measurements were taken a small wall-mounted heater suspended on the west wall in line with the tanks was operating due to the cold temperatures in the warehouse. Air flow at Tank 2 (closest to the heater) was 0 to 10 feet per minute, moving from east to west. Airflow at Tank 1 was 0 to 5 feet per minute, moving from east to west. At the time of the air flow measurements, it was assumed that this heater would be operating when test subjects were present; however, the operations department had turned off the heater so it was not in operation during the study. Without the heater on, the airflow around the tanks was less than the measured flow since all warehouse doors were closed during monitoring."*

2.0 Results

2.1 QA/QC Recovery Results

Controls. The non-fortified field and laboratory control samples (blanks) were as follows: hand wash and face/neck were all less than the limit of quantification (LOQ); slightly above LOQ for 6 inner dermal dosimeters, 2 glass fiber and 8 foam plugs of the inhalation samplers. The field recoveries were corrected for the positive controls (page 72 of study report). The LOQs for the various matrices are air sampling glass fiber filters and foam plugs 10 ng/each sample, neck/face wipe 10 ug/sample, WBD sections 3 µg/section, and hand wash 20 ng/mL (hand wash samples were 600 mL per sample).

Method Validation. The method validation consisted of 7 samples for each monitoring matrix at 3 fortification levels. The results of the method validation of CYA for the 6 matrices ranged from 99.6±6.5 to 103±6.7 percent.

Laboratory Recoveries. The concurrent laboratory recovery values for all of the matrices ranged from 103.6±7.1 to 115±17.8 percent. The number of laboratory recovery samples ranged

from 20 for face/neck wipes to 80 for inner dosimeters. Actual field samples were not corrected for concurrent laboratory results.

Field Recoveries. The field recovery values for all of the matrices ranged from 97.0±13.3 to 114±12.1 percent. The number of field fortification levels ranged from 3 to 5 per matrix with ~50 fortification samples per matrix. Only the face/neck wipe actual field samples were corrected for the field recovery results since the results were <100 percent. Results of each individual field recovery are provided on pages 142 to 151 of the study report.

2.2 Calculating Unit Exposures

Dermal Unit Exposure. Dermal exposure is measured using 100% cotton inner and outer whole body dosimeters (WBD). The inner WBDs were worn underneath normal work clothing (i.e., long-sleeved shirt and long pants). The normal work clothing worn over the inner WBDs were also analyzed and reported as outer dosimeters. In addition, dermal exposures also included hand washes and face/neck wipes. The occupational subjects work nitrile chemical resistant gloves, consumers wore no gloves. For the occupational subjects, the hand washes were conducted on their bare hands after the subjects removed their own chemical resistant gloves (outer gloves not sampled). The inner and outer WBDs are sectioned and analyzed by body part (i.e., upper and lower arms, front and rear torso, and upper and lower legs). Samples are adjusted, as appropriate, according to recovery results from field fortification samples (i.e., only the face/neck samples needed to be corrected since the field recovery results were <100%).

A hand wash removal efficiency study was not conducted with human subjects for CYA. Instead, the AEATF II corrected the results of the hand and face/neck exposures for sampling method efficiency using the results from rat skin wipes in a rat dermal absorption study (Inokuchi et al. 1978). The hand & face/neck exposures were initially corrected by the AEATF II for the 85% sampling efficiency (Inokuchi et al. 1978) but that correction was subsequently removed by EPA. EPA removed the 85% sampling efficiency correction because we interpreted the reported wipe removal of CYA from the rat skin (reported by Inokuchi et al. (1978), page 54, Table VI as the "*pieces of gauze and rinsing water*") as a combination of residues from both the gauze covering used to dose the rat plus the gauze used to wipe the skin at the varying post-application time periods. Unfortunately, the gauze used to wipe the rat skin after removal of the gauze covering used to dose the rat was not analyzed separately. The AEATF II subsequently agreed to EPA's interpretation. The results reported within this EPA review do not include a hand wash (or face/neck) sampling method removal efficiency correction. EPA has developed recommended default correction values to account for hand/face/neck method sampling inefficiencies. These defaults include: no correction if the hands/face/neck are less than 20% of the total dermal; a correction of 2x if the hands/face/neck are between 20% and 60% of total dermal exposure; and a method efficiency study if the hands/face/neck are greater than 60% of total exposure. The results of this solid pour study fall into the second category. However, at this time, EPA does not recommend that the AEATF II conduct a separate hand wash removal efficiency study using additional human subjects nor the default correction factor of 2x for the hand/face/neck prior to the use of these data by EPA for regulatory purposes. EPA's recommendation is based on the following attributes of the study that would tend to allow for efficient sampling using hand washes and face/neck wipes:

- The sampling duration for the solid pour study is very short, averaging only 5 to 10 minutes (maximum duration 20 minutes), which allows less time for dermal absorption of CYA by the hands/face/neck;
- The dermal absorption of CYA is very low *("…percutaneous absorption of the compound to body was regarded as very scarce, detecting no radioactivity in blood and only less than 0.01% of dose in total urine in 21 hours after application.*" Inokuchi et al. (1978));
- Inokuchi et al. (1978) reported that "*…the radio-activities remained in the rinsed skin were 1 – 3% of applied dose…*" after 6 hr, 9 hr, and 12 hrs of CYA exposure time ("*rinsed skin*" refers to the applied skin section of the rat that was removed 21 hrs after dosing and *"…the surface* [of the excised rat skin] *was rinsed repeatedly with about 100 ml in total of water."*)*;*
- CYA is very water soluble (2 g/L); and
- The test substance in the AEATF exposure study is formulated as powders and granules. The physical mechanisms of the hand wash procedure (i.e., pouring 400 mL of distilled water over both of the subject's hands while they scrubbed them followed by a 100 ml distilled water rinse) and face/neck wipes will likely dislodge the particles from the skin.

If EPA determines at a later date to correct the hand and face/neck residue data for sample method efficiency, it would be a simple process to complete.

The various analyses of residues on the dosimeters worn by each individual subject allow for the estimation of exposure for the following 3 clothing configurations:

(1) "Long-Long" or "Long Long Dermal" = long pants, long-sleeved shirt, and no gloves for consumers and chemical resistant gloves for occupational;
(2) "Long-Short" or "Long Short Dermal"= long pants, short-sleeved shirt, and no gloves for consumers and chemical resistant gloves for occupational; and
(3) "Short-Short" or "Short Dermal" = short pants, short-sleeved shirt, no gloves for consumers and chemical resistant gloves for occupational.

Total dermal exposure is calculated by summing exposure across all body parts for each individual monitored. The following WBD sections are summed to calculate the clothing configuration of long pants, long-sleeved shirts (Long-Long) plus face/neck wash and hand wash:

- inner lower and inner upper arms,
- inner front and inner rear torso, and
- inner lower and inner upper legs.

The following WBD sections are summed to calculate the clothing configuration of long pants, short-sleeved shirts (Long-Short) plus face/neck wash and hand wash:

- outer and inner lower arms,

- inner upper arms,
- inner front and inner rear torso, and
- inner lower and inner upper legs.

The following WBD sections are summed to calculate the clothing configuration of short pants, short-sleeved shirts (Short-Short) plus face/neck wash and hand wash:

- outer and inner lower arms,
- inner upper arms,
- inner front and inner rear torso,
- inner upper legs, and
- inner and outer lower legs.

Dermal unit exposures (i.e., mg/lb ai handled) are calculated by dividing the summed total exposure by the amount of active ingredient handled.

Inhalation Exposure. Inhalation exposure is measured using a personal air sampling pump and an "…*IOM* [Institute of Occupational Medicine] *personal inhalable particulate sampler (SKC catalog number 225-70A) containing a cassette holding a 25 mm 1 micron pour* [pore] *size glass fiber filter and a MultiDust polyurethane foam plug was placed on each subject. The IOM sampler contains a reusable two-part cassette designed for airborne particle collection and when fitted with a filter and the MultiDust foam plug allowed for sampling of both inhalable and respirable fractions simultaneously.*" The IOM cassette was attached to the worker's collar to continuously sample air at a target rate of 2.0 Lpm from the breathing zone.

The results from the IOM cassettes are reported herein as the "total" or "inhalable" air concentration monitored from the glass fiber filter (<100 µm) and "respirable" from the foam plug (<4 µm).

Inhalation unit exposures for both the inhalable and respirable portions are provided using the three following methods:

(1) Air concentration normalized by AaiH (i.e., mg/m^3/lb ai handled) is calculated by dividing the air concentrations by the amount of ai handled.
(2) Air concentration expressed as an 8 hour time weighted average (TWA) and normalized by AaiH (i.e., mg/m^3/lb ai handled) is calculated as the air concentration ((mg/m^3) / lb ai) * sampling duration (hours/day) / 8 (hours / day).
(3) Inhalation exposure (mg/lb ai) or dose is calculated as the air concentration ((mg/m^3) / lb ai) * breathing rate (1 m^3/hour) * sampling (hours/day).

2.3 Dermal and Inhalation Exposure Results

Results. A summary of the individual and mean dermal and inhalation results of the *consumer* granule and powder scenarios are presented in Tables 4a and 4b, respectively. The results for the *occupational* granule and powder scenarios are presented in Tables 4c and 4d, respectively. Both empirical means and the results of the lognormal simple random sample

means are provided for comparison; the latter being the recommended values summarized in Tables 1a and 1b. For the consumer scenarios, the clothing configuration of long pants, long sleeved shirts (Long-Long) as well as short pants, short-sleeved shirts (Short-Short), and no gloves (in both scenarios) are provided. The clothing configurations of long pants, long sleeved-shirts (Long-Long) as well as long pants, short sleeved-shirts (Long-Short), and chemical resistant gloves (for both scenarios) are provided for the occupational scenarios. Also shown for comparison to the total dermal exposure are the dermal results for the hand exposures only. These tables report the results for each individual worker along with empirical and lognormal simple random sampling method statistical summaries.

Appendix A provides statistical models to estimate the unit exposure summary statistics, including:

- Empirical simple random sampling model (see Appendix A, Tables 1 through 14 for detailed summaries);
- Lognormal simple random sampling model (see Appendix A, Tables 15 through 18, and for more details, Tables 21 through 36).

The results of the lognormal simple random sampling model have been selected to best represent the summary statistics for the unit exposures (for summary results of recommended unit exposures see Tables 1a and 1b above). For a detailed discussion of the lognormal simple random sampling model calculations and results the reader is referred to Appendix A (along with a discussion of the HSRB-suggested quadratic models on pages 88 & 89 of Appendix A).

Study Observations. The solid pour study includes the recorded individual participant activities by observers. Detailed observations recorded during each ME capturing the notable events that occurred during the solid pouring can be viewed in the study report's Appendices E and F starting on page 217. Although a review of these observations indicate that the pouring of granules and powders resulted in the creation of dust plumes (to varying degrees) and some visible residue on hands and/or dosimeters, these types of exposures are expected based on the task and are not considered outliers in the data. Appendix A presents statistical results using all the data and compare those results with results calculated after excluding some of these potential outliers. The following observations are highlighted:

- **Consumer Granules:** As illustrated in Table 4a, ME 1 and ME 9 showed higher hand exposures relative to the other MEs. Both of these MEs included the step of pre-dissolving the granules in a bucket of water prior to addition into the pool. ME 4 also conducted this step without appreciable hand exposure relative to ME 1 and ME 9. ME 9 did not own a pool and the observation was noted that the subject was "messy" when stirring the solution in the bucket. ME 9 was identified in the study report as a potential outlier; EPA also reviewed ME 9 as a potential outlier but has decided to include this ME in the recommended unit exposures.

- **Consumer Powder:** ME 17 had the highest hand unit exposure as illustrated in Table 4b. The observations noted a small dust plume but minimal contact with the subject, however, residue was observed on the hands; it was noted that there was no

apparent issue with the bag. ME 17 did not own a pool. ME 17 was identified in the study report as a potential outlier; EPA also reviewed ME 17 as a potential outlier but has decided to include this ME in the recommended unit exposures. ME 6 also showed high unit exposure for the short-sleeve clothing configuration. ME 6 tossed the powder across the pool with wind gusts to 9 mph. For ME 10 it was noted that it was "quite windy"; scooping was suspended for 2 minutes during the ME (sampling pump was not turned off). MEs 3, 5, 10, and 12 pre-dissolved the powder in a bucket with water prior to transferring to the pool.

- **Occupational Granules:** Dust plumes were observed during many of the MEs. MEs 5, 12, 13, 15 removed the chemical resistant glove at what appears to be the end of the ME. ME 5 had the highest hand unit exposure.

- **Occupational Powders:** Dust plumes were observed during many of the MEs. ME 1 used his hand (with gloves) to compress the powder in the scoop; hand exposure for this ME is less than the mean hand unit exposure for the scenario. ME 11 reported *"…he felt irritation on his cheeks, below his eyes but the irritation went away after washing his face with water and Ivory soap.*" ME 11 had a face exposure of 641 µg. ME 16 also reported "*…that he felt some irritation under the left eye (on upper cheek), but it went away after washing.*" Face/neck wipes were taken prior to subject washing their face again. ME 16 had a face exposure of 825µg. The average face exposure for this scenarios was 975 µg. The observational notes for ME 14 indicates "*we did recommend that he not toss it* [powder] *out across the pool*" because the subject did not have experience with pouring powders. ME 14's unit exposure is below the mean for the scenario.

- **Individual Test Subject (W24):** The results of this individual's exposure is highlighted because this individual visited the emergency room complaining of stomach pain, vomiting, and sweating (see Appendix H of the study for additional details). Test subject W24 corresponds to occupational powder ME 18 and occupational granule ME 6. The observational notes indicate nothing remarkable about the exposure during the pouring tasks and it was noted that the individual had good technique and seemed experienced. Subject W24's inhalation 8-hr TWA exposure was lower than the average of the other subject's exposure (i.e., 0.184 mg/m^3 compared to scenario average of 0.898 mg/m^3 for the powder scenario and 0.0181 mg/m^3 compared to scenario average of 0.464 mg/m^3 for the granule pouring). Also note, all subjects in the study wore respiratory protection (N95 Filtering Facepiece Respirator, 3M model 8210) so the actual exposure received would be less than breathing these air concentrations. The dermal exposure for the long pants, long sleeved shirt, and gloves for ME 18 (powder) is 3.11 µg compared to the scenario average of 7.02 µg; and for ME 6 (granule) the dermal exposure is 0.51 µg compared to the scenario average of 2.25 µg. Note: the dermal exposure reported here is not normalized to AaiH and is not the absorbed dose, rather the amount of chemical sampled from the skin of the hands and found on the inner whole-body dosimeter that was used to intercept the chemical that either penetrated or otherwise circumvented the outer clothing. Therefore, these sampling results are being reported to provide

some relative ranking of this subject compared to the other subjects within the scenario, it is not meant to depict the actual absorbed dose.

Impact of Non-detects. All of the hand samples were above the limit of quantification (LOQ). All but one of the face/neck samples were above the LOQ. All of the outer dermal dosimeters were above the LOQ. All of the inner dermal dosimeters were above the LOQ except for the consumer granule scenario where six of the inner dosimeter measurements were below the LOQ. The impact of the non-detects are reviewed in Appendix A (page 26), including the statistical methods of substituting NDs with ½ LOQ, full LOQ, zero, and censored data maximum likelihood (MLE). The dermal unit exposures for the consumer granule scenario have the only non-detect dermal samples. The dermal unit exposures for the consumer granule scenario using the four substitution methods described above are 1.87, 1.87, 1.88, and 1.74 mg/lb ai, respectively. The inhalation exposure measurements were also mostly above the LOQ, exceptions are 5 of the glass fiber filter measurements for consumers that were below the LOQ. Likewise, the inhalation unit exposures using the four substitution methods for handling non-detects are virtually identical (see Appendix A page 28). The unit exposures provided in the summary Tables 1a and 1b and Tables 4a, b, c and d are based on ½ LOQ for non-detects.

Table 4a. Summary of Consumer Granules dermal and inhalation unit exposure estimates for pouring solids.

Monitoring Event (ME)	AaiH (lb)	Unit exposure (mg/lb AaiH)			Unit exposure ((mg/m^3)/lb AaiH)	
		Hands	Long-Long	Short-Short	Inhalation TWA	Respirable Inhalation TWA
1	0.977	5.520	5.671	19.277	0.001127	0.0000214
2	5.855	0.099	0.111	0.251	0.000376	0.0000059
3	1.710	0.030	0.129	0.732	0.000254	0.0000030
4	1.710	0.519	0.586	0.928	0.000227	0.0000030
5	3.419	0.046	0.058	0.076	0.000067	0.0000099
6	0.976	0.468	0.547	0.616	0.000135	0.0000053
7	15.968	0.251	0.262	0.467	0.000169	0.0000038
8	16.660	0.760	0.785	1.339	0.000234	0.0000048
9	9.943	14.965	15.162	26.788	0.002221	0.0000451
10	11.710	0.041	0.052	0.334	0.000053	0.0000025
11	17.557	0.068	0.077	0.237	0.000118	0.0000017
12	11.709	0.344	0.374	0.609	0.000534	0.0000213
13	22.253	0.178	0.201	0.386	0.000283	0.0000038
14	30.985	0.040	0.049	0.244	0.000198	0.0000031
15	34.212	0.041	0.044	0.213	0.000150	0.0000038
16	24.314	0.022	0.030	0.097	0.000018	0.0000013
17	48.629	0.025	0.027	0.048	0.000109	0.0000033
18	48.700	0.079	0.091	0.230	0.000187	0.0000039
Empirical Mean	17.072	1.305	1.348	2.937	0.000359	0.0000082
Empirical SD	15.292	3.639	3.686	7.431	0.000528	0.0000110
Lognormal Simple Random Sample Mean	22.236	0.890	0.906	1.874	0.000355	0.0000076
Lognormal Simple Random Sample SD	46.433	4.794	4.037	6.913	0.000534	0.0000087

Table 4b. Summary of Consumer Powder dermal and inhalation unit exposure estimates for pouring solids.

Monitoring Event (ME)	AaiH (lb)	Unit exposure (mg/lb AaiH)			Unit exposure ((mg/m^3)/lb AaiH)	
		Hands	Long-Long	Short-Short	Inhalation TWA	Respirable Inhalation TWA
1	4.274	0.404	0.985	8.815	0.001782	0.0000026
2	0.477	1.534	1.983	5.223	0.023192	0.0000254
3	0.951	5.664	5.845	7.176	0.004274	0.0000215
4	0.950	0.204	0.450	1.331	0.004034	0.0000201
5	0.476	3.841	4.291	6.470	0.001244	0.0000229
6	2.843	2.786	4.262	80.527	0.012839	0.0000599
7	12.810	0.299	0.328	0.639	0.000932	0.0000027
8	8.541	0.490	0.514	0.786	0.000882	0.0000027
9	15.538	0.768	0.826	2.728	0.002595	0.0000051
10	7.620	2.409	2.609	5.790	0.003342	0.0000119
11	9.374	0.341	0.372	0.956	0.001239	0.0000026
12	8.549	2.309	2.436	5.253	0.008165	0.0000173
13	0.951	5.409	5.752	8.434	0.004205	0.0000055
14	38.956	0.570	0.648	2.280	0.003890	0.0000072
15	47.543	0.487	0.517	1.514	0.001064	0.0000041
16	8.550	0.821	0.934	3.535	0.002880	0.0000037
17	0.476	27.854	30.022	40.886	0.021785	0.0000459
18	0.477	3.245	3.523	6.551	0.000843	0.0000109
Empirical Mean	9.409	3.302	3.683	10.494	0.005510	0.0000151
Empirical SD	13.251	6.371	6.834	19.672	0.006863	0.0000160
Lognormal Simple Random Sample Mean	12.118	3.109	3.431	9.595	0.005446	0.0000157
Lognormal Simple Random Sample SD	39.315	6.537	6.409	19.142	0.007817	0.0000216

Table 4c. Summary of Occupational Granules dermal and inhalation unit exposure estimates for pouring solids.

Monitoring Event (ME)	AaiH (lb)	Unit exposure (mg/lb AaiH)			Unit exposure ((mg/m^3)/lb AaiH)	
		Hands	Long-Long	Long-Short	Inhalation TWA	Respirable Inhalation TWA
1	11.126	0.017	0.036	0.270	0.005287	0.0002001
2	11.712	0.016	0.033	1.534	0.002910	0.0000815
3	17.568	0.003	0.020	0.145	0.005097	0.0001646
4	18.349	0.004	0.015	0.057	0.003014	0.0000467
5	23.814	0.048	0.096	1.037	0.013424	0.0005955
6	24.400	0.008	0.021	0.034	0.000740	0.0000338
7	29.475	0.003	0.009	0.287	0.000640	0.0000485
8	34.355	0.018	0.071	0.642	0.014999	0.0004799
9	38.845	0.012	0.054	0.225	0.004503	0.0002312
10	25.181	0.014	0.057	0.663	0.018331	0.0006925
11	39.821	0.007	0.030	0.909	0.010380	0.0006439
12	48.605	0.020	0.033	0.128	0.004828	0.0002340
13	70.858	0.020	0.128	0.346	0.010714	0.0004567
14	56.608	0.016	0.072	0.231	0.004969	0.0002592
15	58.950	0.007	0.044	0.290	0.005959	0.0003181
16	65.782	0.013	0.052	0.508	0.014211	0.0008252
17	84.131	0.002	0.028	0.144	0.002064	0.0000913
18	97.014	0.014	0.057	0.445	0.035618	0.0010021
Empirical Mean	42.033	0.013	0.048	0.439	0.008761	0.0003558
Empirical SD	25.350	0.011	0.030	0.393	0.008518	0.0002929
Lognormal Simple Random Sample Mean	43.101	0.014	0.049	0.481	0.009803	0.0004048
Lognormal Simple Random Sample SD	31.201	0.014	0.037	0.619	0.014025	0.0005758

Table 4d. Summary of Occupational Powder dermal and inhalation unit exposure estimates for pouring solids.

Monitoring Event (ME)	AaiH (lb)	Unit exposure (mg/lb AaiH)			Unit exposure ((mg/m^3)/lb AaiH)	
		Hands	Long-Long	Long-Short	Inhalation TWA	Respirable Inhalation TWA
1	5.130	0.045	0.409	1.048	0.012077	0.0000544
2	14.060	0.067	0.228	5.576	0.032144	0.0001765
3	9.880	0.159	0.311	1.886	0.030855	0.0001911
4	16.340	0.012	0.063	0.823	0.006595	0.0000628
5	20.330	0.013	0.143	3.055	0.034154	0.0001315
6	23.750	0.007	0.031	0.172	0.003953	0.0000195
7	28.690	0.088	0.281	2.226	0.042002	0.0002605
8	31.920	0.073	0.271	3.448	0.060177	0.0003354
9	38.380	0.227	0.383	6.959	0.085879	0.0008230
10	42.940	0.012	0.106	0.860	0.011093	0.0000634
11	34.200	0.129	0.329	3.773	0.011819	0.0001840
12	23.560	0.141	0.210	1.093	0.024074	0.0002243
13	71.820	0.045	0.263	2.926	0.020789	0.0001109
14	50.540	0.007	0.067	0.383	0.004850	0.0000214
15	57.760	0.059	0.316	3.606	0.049328	0.0007804
16	61.180	0.007	0.047	0.625	0.006223	0.0000640
17	66.310	0.064	0.221	2.628	0.021559	0.0002088
18	70.870	0.005	0.044	0.142	0.002591	0.0000322
Empirical Mean	37.092	0.064	0.207	2.291	0.025565	0.0002080
Empirical SD	21.551	0.063	0.124	1.907	0.022485	0.0002339
Lognormal Simple Random Sample Mean	39.355	0.078	0.226	2.748	0.028040	0.0002221
Lognormal Simple Random Sample SD	33.141	0.155	0.228	4.402	0.037128	0.0003323

Let X_i be the i^{th} AaiH or unit exposure value and let $Y_i = \ln(X_i)$.

Empirical Mean = $\overline{X} = \sum_{i=1}^{18} X_i / 18$

Empirical SD = $S_X = \sqrt{\sum_{i=1}^{18} \left(X_i - \overline{X}\right)^2 / 17}$. Suppose X is lognormally distributed, so that Y = ln(X) is normally distributed with a population mean μ and a population variance σ^2.

Lognormal Simple Random Sample Mean = Estimated population mean of X = Estimate of $\exp(\mu + \frac{1}{2}\sigma^2) = \exp(\overline{Y} + \frac{1}{2} S_Y^2)$ where $\overline{Y} = \sum_{i=1}^{18} Y_i / 18$ and $S_Y = \sqrt{\sum_{i=1}^{18} \left(Y_i - \overline{Y}\right)^2 / 17}$.

Lognormal Simple Random Sample SD = Estimated population standard deviation of X = Estimate of $\exp(\mu + \frac{1}{2}\sigma^2) \sqrt{\exp(\sigma^2) - 1} = \exp(\overline{Y} + \frac{1}{2} S_Y^2) \sqrt{\exp(S_Y^2) - 1}$.

2.4 Evaluation of Scenario Benchmark Objective

Benchmark Objective. The data from the study has been analyzed to see if the four solid pour scenarios meet the AEATF II objective of a relative 3-fold accuracy (i.e., K = 3). These analyses used the SAS code originally developed by the Agricultural Handler Exposure Task Force (AHETF) and independently confirmed by the Health Effects Division (HED) (and now modified by the Antimicrobial Division (AD)). Appendix A (pages 29 to 36) provides the detailed benchmark analysis which is summarized as follows:

Benchmark Objective: fold Relative Accuracy (fRA)

The benchmark objective for AEATF II 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" also expressed as "K-factor"). EPA has analyzed the data using various statistical techniques to evaluate this benchmark. First, to characterize the unit exposures (also referred to as "normalized exposure"), lognormal probability plots of dermal and inhalation UEs are provided in Appendix A (pages 37 to 53, Figures 1 to 32) to illustrate that the lognormal distribution is a better fit than the normal distribution for the normalized exposure. These plots support the assumed lognormal distributions for the normalized exposure. Note: all logarithms defined in this review are natural logarithms.

Next, EPA calculated estimates of the GM, AM and P95 based on two different calculation methods:

- Empirical estimates; and
- Assuming a lognormal distribution and a simple random sample (SRS).

The 95% confidence limits for each of these estimates were obtained by generating 10,000 parametric bootstrap samples from the fitted lognormal distribution. 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. With the exception of the empirical 95th percentile, EPA has determined that the solid pour study results meet the 3-fold relative accuracy objective for three of the dermal and all four of the inhalation exposure scenarios (see Tables 5 to 8). The one dermal exposure scenario that does not meet the 3-fold accuracy goal is for the consumer granules. The results of the consumer granules dermal exposure scenario assuming a lognormal distribution are slightly above the targeted 3-fold relative accuracy; for this scenario, K = 3.6 for the arithmetic mean and K = 3.3 for the 95th percentile. When excluding ME 9 from this scenario, the 3-fold relative accuracy is met (Note: EPA is not suggesting to exclude ME 9 as an outlier). The individual results of the benchmark analysis for several other clothing configurations and inhalation exposures are reported in Appendix A (pages 30 to 36, Tables 21 to 36). The complete set of benchmark analysis results for all configurations and scenarios can be provided as Excel files upon request. Appendix A also presents fRA values calculated using a non-parametric bootstrap approach, with generally similar results.

Table 5: Results of Primary Benchmark Analysis for the Consumer Granules (Short pants, Short-sleeved Shirt and Inhalation (Inhalable TWA)).						
	Dermal Exposure			**Inhalation Exposure**		
Statistic	**Unit Exposure Estimate (mg/lb ai)**	**95% CI**	**fRA**	**Unit Exposure Estimate (8-hr TWA mg/m^3/lb ai)**	**95% CI**	**fRA**
GM_S	0.490	0.235 – 1.058	2.2	0.000197	0.000121 – 0.000328	1.7
GSD_S	5.143	2.965 – 8.939	1.7	2.964	2.057 – 4.277	1.4
GM_S = geometric mean assuming SRS = "exp(average of 18 ln(UE)) values" GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 18 ln(UE)) values"						
AM_S	2.937	0.549 – 5.484	5.4	0.000359	0.000184 – 0.000661	2.0
AM_U	1.874	0.624 – 6.668	3.6	0.000355	0.000191 – 0.000690	1.9
AM_S = average of 18 unit exposures AM_U = arithmetic mean based on $GM_S = GM_S * \exp\{0.5*(\ln(GSD_S)^2\}$						
$P95_S$	26.788	2.159 – 64.758	12.4	0.002221	0.000527 – 0.005029	4.2
$P95_U$	7.748	2.196 – 23.179	3.3	0.001176	0.000533 – 0.002543	2.2
$P95_S$ = 95th percentile (i.e., estimated as the maximum unit exposure from the 18 unit exposures) $P95_U$ = 95th percentile based on $GM_S = GM_S * GSD_S^{1.645}$						

Table 6: Results of Primary Benchmark Analysis for the Consumer Powder (Short pants, Short-sleeved Shirt and Inhalation (Inhalable TWA)).						
	Dermal Exposure			**Inhalation Exposure**		
Statistic	**Unit Exposure Estimate (mg/lb ai)**	**95% CI**	**fRA**	**Unit Exposure Estimate (8-hr TWA mg/m^3/lb ai)**	**95% CI**	**fRA**
GM_S	4.299	2.410 – 7.726	1.8	0.003113	0.001921 – 0.005078	1.6
GSD_S	3.551	2.331 – 5.438	1.5	2.879	2.027 – 4.110	1.4
GM_S = geometric mean assuming SRS = "exp(average of 18 ln(UE)) values" GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 18 ln(UE)) values"						
AM_S	10.494	4.155 – 20.683	2.5	0.005510	0.002854 – 0.009935	1.9
AM_U	9.595	4.414 – 22.537	2.3	0.005446	0.002975 – 0.010385	1.9
AM_S = average of 18 unit exposures AM_U = arithmetic mean based on $GM_S = GM_S * \exp\{0.5*(\ln(GSD_S)^2\}$						
$P95_S$	80.527	13.055– 189.913	6.2	0.023192	0.007868 – 0.073510	3.2
$P95_U$	34.557	13,733 – 85.849	2.5	0.017730	0.008207 – 0.037892	2.2
$P95_S$ = 95th percentile (i.e., estimated as the maximum unit exposure from the 18 unit exposures) $P95_U$ = 95th percentile based on $GM_S = GM_S * GSD_S^{1.645}$						

Table 7: Results of Primary Benchmark Analysis for the Occupational Granules (Long pants, Long-sleeved Shirt and Inhalation (Inhalable TWA)).						
	Dermal Exposure			**Inhalation Exposure**		
Statistic	**Unit Exposure Estimate (mg/lb ai)**	**95% CI**	**fRA**	**Unit Exposure Estimate (8-hr TWA mg/m^3/lb ai)**	**95% CI**	**fRA**
GM_S	0.039	0.029 – 0.054	1.4	0.005617	0.003449 – 0.009186	1.6
GSD_S	1.946	1.562 – 2.425	1.2	2.873	2.028 – 4.073	1.4
GM_S = geometric mean assuming SRS = "exp(average of 18 ln(UE)) values" GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 18 ln(UE)) values"						
AM_S	0.048	0.035 – 0.069	1.4	0.008761	0.005239 – 0.017867	2.0
AM_U	0.049	0.035 – 0.069	1.4	0.009803	0.005447 – 0.018519	1.9
AM_S = average of 18 unit exposures AM_U = arithmetic mean based on $GM_S = GM_S * \exp\{0.5*(\ln(GSD_S)^2\}$						
$P95_S$	0.128	0.072 – 0.286	2.2	0.035618	0.014525 – 0.130844	3.7
$P95_U$	0.118	0.073 – 0.188	1.6	0.031875	0.014918 – 0.066932	2.1
$P95_S$ = 95th percentile (i.e., estimated as the maximum unit exposure from the 18 unit exposures) $P95_U$ = 95th percentile based on $GM_S = GM_S * GSD_S^{1.645}$						

Table 8: Results of Primary Benchmark Analysis for the Occupational Powder (Long pants, Long-sleeved Shirt and Inhalation (Inhalable TWA)).						
	Dermal Exposure			**Inhalation Exposure**		
Statistic	**Unit Exposure Estimate (mg/lb ai)**	**95% CI**	**fRA**	**Unit Exposure Estimate (8-hr TWA mg/m^3/lb ai)**	**95% CI**	**fRA**
GM_S	0.159	0.109 – 0.235	1.5	0.016899	0.010710 – 0.026919	1.6
GSD_S	2.310	1.750 – 3.061	1.3	2.736	1.960 – 3.837	1.4
GM_S = geometric mean assuming SRS = "exp(average of 18 ln(UE)) values" GSD_S = geometric standard deviation assuming SRS = "exp(standard deviation of 18 ln(UE)) values"						
AM_S	0.207	0.142 – 0.352	1.7	0.025565	0.015552 – 0.049300	1.9
AM_U	0.226	0.145 – 0.363	1.6	0.028040	0.016037 – 0.051630	1.8
AM_S = average of 18 unit exposures AM_U = arithmetic mean based on $GM_S = GM_S * \exp\{0.5*(\ln(GSD_S)^2\}$						
$P95_S$	0.409	0.336 – 1.979	4.8	0.085879	0.041531 – 0.349403	4.1
$P95_U$	0.631	0.342 – 1.157	1.8	0.088463	0.042403 – 0.183340	2.1
$P95_S$ = 95th percentile (i.e., estimated as the maximum unit exposure from the 18 unit exposures) $P95_U$ = 95th percentile based on $GM_S = GM_S * GSD_S^{1.645}$						

Presumption of Log-log-linearity With Slope 1. EPA evaluated the presumption that the mean exposure is a multiple of the amount of active ingredient handled (AaiH or ai). In the Governing Document and in statistical reviews of some previous AEATF II studies, this presumption has been referred to as "proportionality" but we are now referring to this analysis as a "log-log-linearity" analysis to clarify that the statistical models do not assume that the exposure is directly proportional to the amount of active ingredient handled. If the log-log-linear model has a slope of 1, then the arithmetic mean exposure will be a multiple of the amount of active ingredient handled. The statistical test compares the slope of 1 with a slope of 0, where 0 corresponds to complete independence between exposure and amount of active ingredient handled.

To evaluate the relationship for this scenario EPA performed **regression analysis of log(exposure) against log(AaiH)** to determine if the slope of this log-log-linear model is not significantly different than 1 – providing support for a "proportional" (an abbreviation for " log-log-linear with slope 1") relationship – or if the slope is not significantly different than 0 – providing support for an independent relationship. If the slope is positive, not zero and not 1, then the arithmetic mean exposure tends to increase with the AaiH but not proportionally, so that, for example, doubling the AaiH will not tend to double the exposure. If the slope confidence interval excludes both 1 and 0 but the slope is positive, then the statistical evidence rejects both proportionality and independence and shows that the exposure tends to increase with the AaiH but not proportionally. **Note: the slope for the dermal exposure measures the change in log mg dermal exposure for each unit change in log lb ai. A slope of 1 implies that the log of the unit exposure (mg/lb ai) is equal to a constant plus a random error, so that**

the unit exposure has the same mean for any amount of ai, and thus the mg dermal exposure is proportional to the lb ai.

The resulting regression slopes and confidence intervals are summarized in Tables 9 and 10. Table 9 gives the slopes for the short pants, short-sleeved shirt dermal exposure in the consumer granules and powder scenarios and for the long pants, long-sleeved shirt dermal exposure in the occupational granules and powder scenarios. Table 10 gives the slopes for the inhalation time-weighted exposures in all four scenarios. More detailed tables of the slopes for these and other exposure scenarios (including calculations for alternative treatments of potential outliers and/or non-detects) are presented in Appendix A (pages 56 to 61, Tables 37 to 40).

For dermal exposures in the consumer granules scenario, the slopes ranged from about 0.3 to 0.5 and the confidence intervals for the slope included zero but in most cases did not include one. Thus the analyses supported (more precisely, did not reject) independence (a slope of zero) and rejected proportionality (a slope of one). For inhalation exposures in the consumer granules scenario, the slopes were about 0.8 and in most cases the confidence intervals for the slope included one but not zero. Thus the analyses of inhalation exposures supported proportionality and rejected independence.

For dermal and inhalation exposures in the consumer powder scenario, the slopes ranged from about 0.3 to 0.8 and the confidence intervals for the slope did not include zero, and included one in about half of the cases. Thus the analyses rejected independence and sometimes rejected proportionality.

For dermal and inhalation exposures in the occupational granules scenario, the slopes ranged from about 0.9 to 1.7 and the confidence intervals for the slope included one and did not include zero. Thus the analyses rejected independence and supported proportionality.

For dermal and inhalation exposures in the occupational powder scenario, the slopes ranged from about 0.4 to 1.1 and the confidence intervals for the slope mostly included one and did not include zero. Thus the analyses rejected independence and supported proportionality.

A secondary objective for EPA is for meeting 80% power for detecting log-log-linearity with a slope of 1. This objective is approximately met if the widths of the confidence intervals for the slopes are at most 1.4. For both consumer scenarios, this secondary objective was met. For the occupational scenarios, this objective was not met for about half of the cases, as illustrated in Table 10.

Figures 2 to 9 show the data and corresponding fitted regression models for the same selected scenarios. Additional regression plots are presented in Appendix A (pages 72 to 87, Figures 49 to 64). The data points marked with the symbol “E” are the experienced consumers or occupational workers (all the occupational workers were experienced). The data points marked with the symbol “O” are the two potential consumer outliers (ME 9 for consumer granules and ME 17 for consumer powder). The data points marked with the symbol “I” are the other two inexperienced consumers. Appendix A (pages 63 to 71, Figures 33 to 48) also presents probability plots of the residuals from these fitted regression models; these probability plots show that this simple log-log-linear regression model fits reasonably well but a more complicated model might give an improved fit.

Table 9. 95 Percent Confidence Intervals for the Slope of Log Exposure (mg) versus Log Pounds of Active Ingredient for Dermal Exposures.

Clothing	Scenario	Slope	Confidence Interval	Confidence Interval Width
Short pants, short sleeved-shirt	Consumer granules	0.41	−0.18 – 1.00	1.19
	Consumer powder	0.59	0.22 – 0.96	0.74
Long pants, long sleeved-shirt	Occupational granules	1.39	0.88 – 1.89	1.01
	Occupational powder	0.69	0.10 – 1.27	1.17

Table 10. 95 Percent Confidence Intervals for the Slope of Log Exposure (mg/m^3) versus Log Pounds of Active Ingredient for Inhalation 8-hr TWA Exposures.

Scenario	Slope	Confidence Interval	Confidence Interval Width
Consumer granules	0.77	0.34 – 1.20	0.85
Consumer powder	0.75	0.42 – 1.09	0.67
Occupational granules	1.51	0.69 – 2.33	1.64
Occupational powder	0.82	0.09 – 1.54	1.44

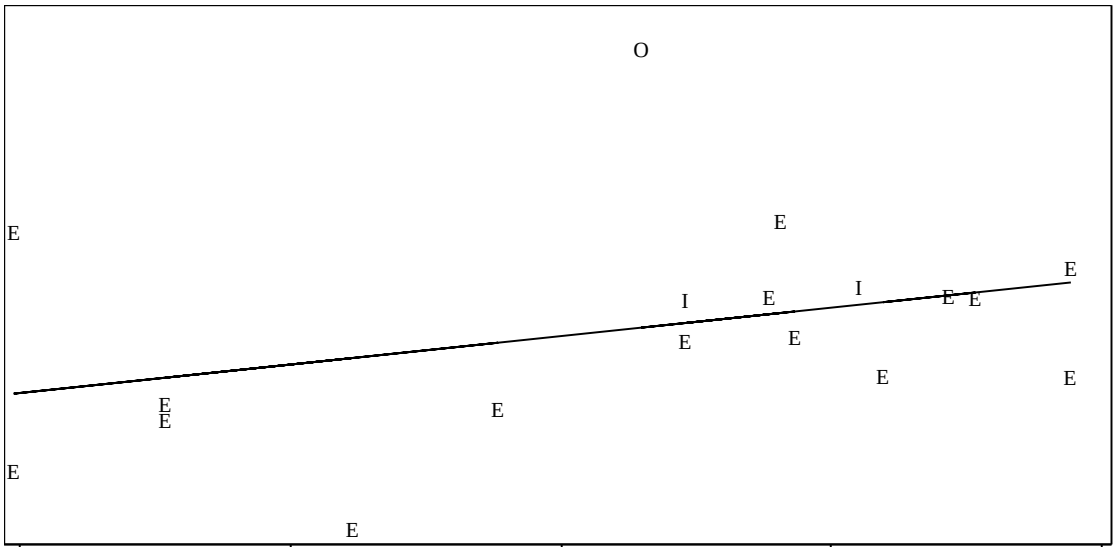

Figure 2. Regression plot for Consumer Granules, Short Dermal

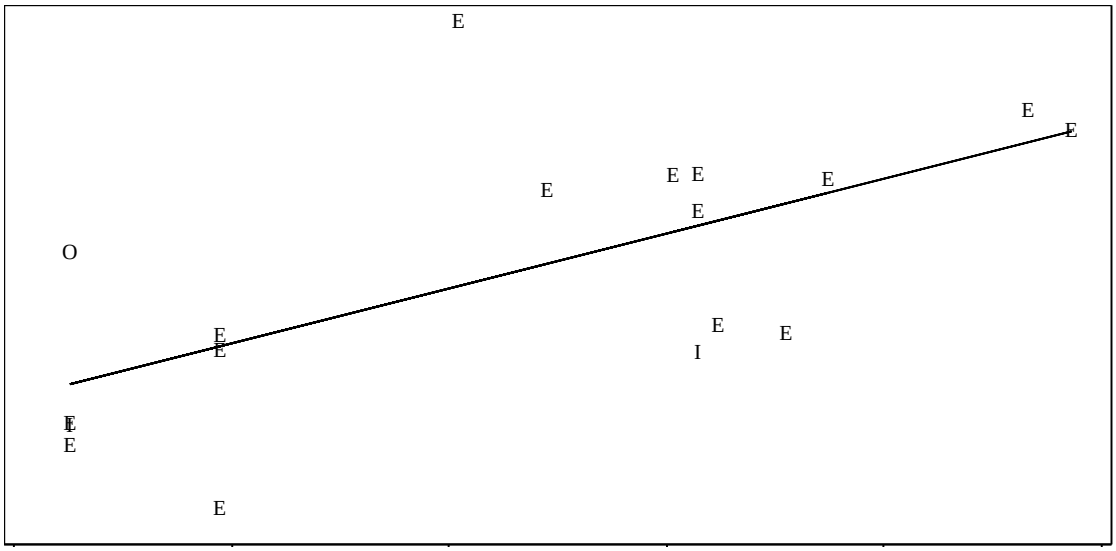

Figure 3. Regression plot for Consumer Powder, Short Dermal

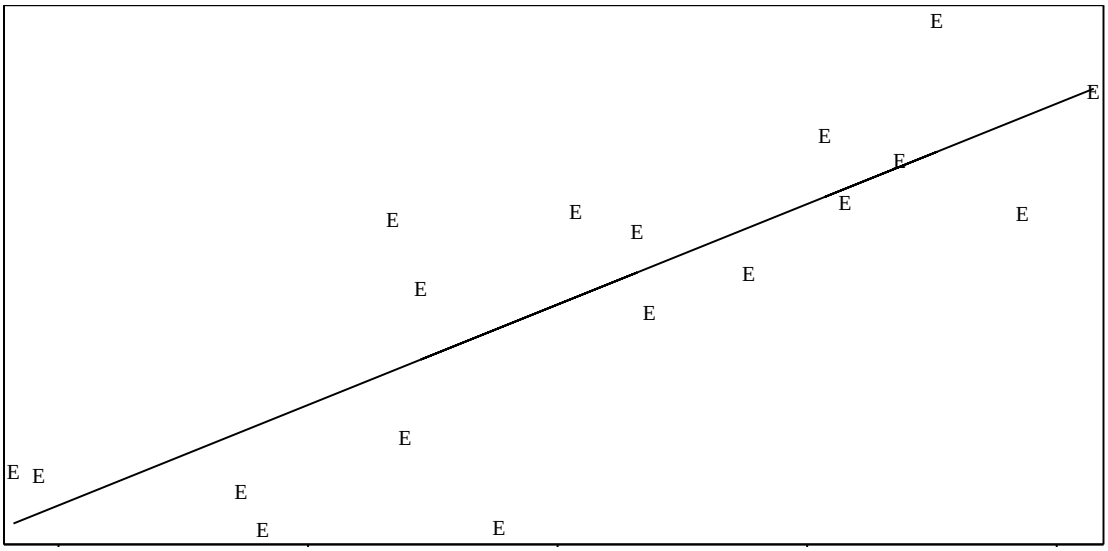

Figure 4. Regression plot for Occupational Granules, Long Dermal

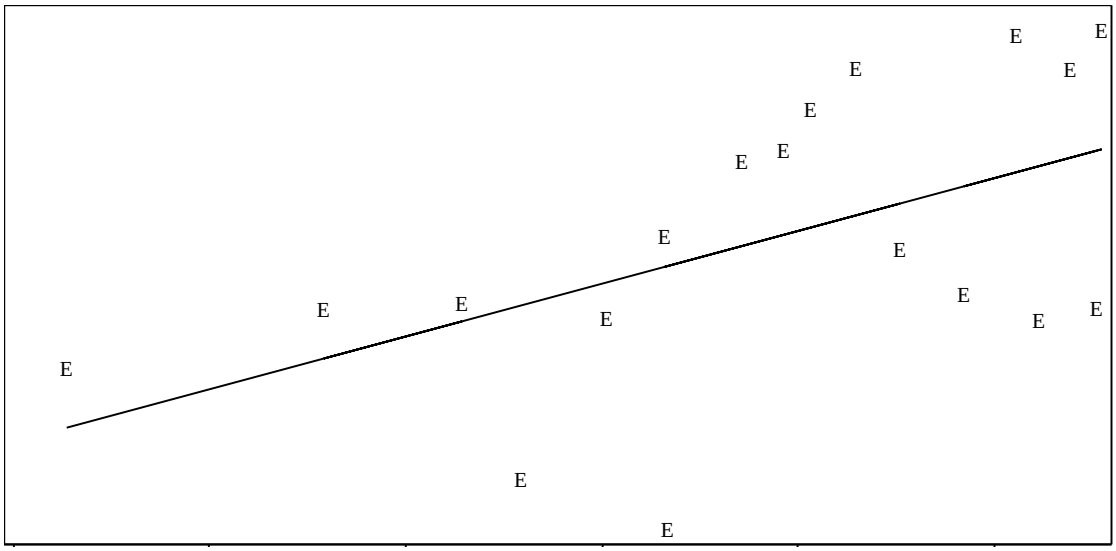

Figure 5. Regression plot for Occupational Powder, Long Dermal

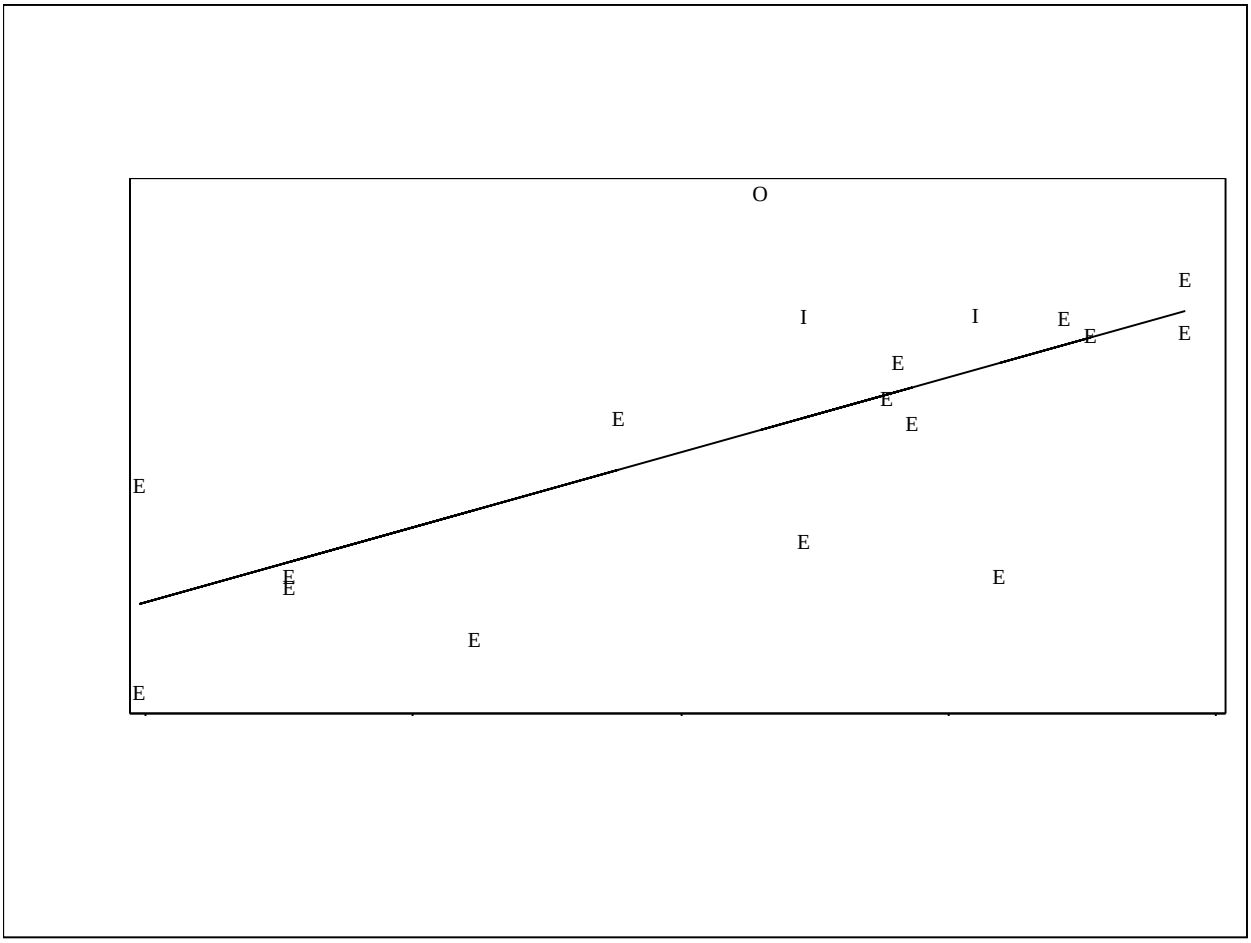

Figure 6. Regression plot for Consumer Granules, Inhalation Time-weighted Average

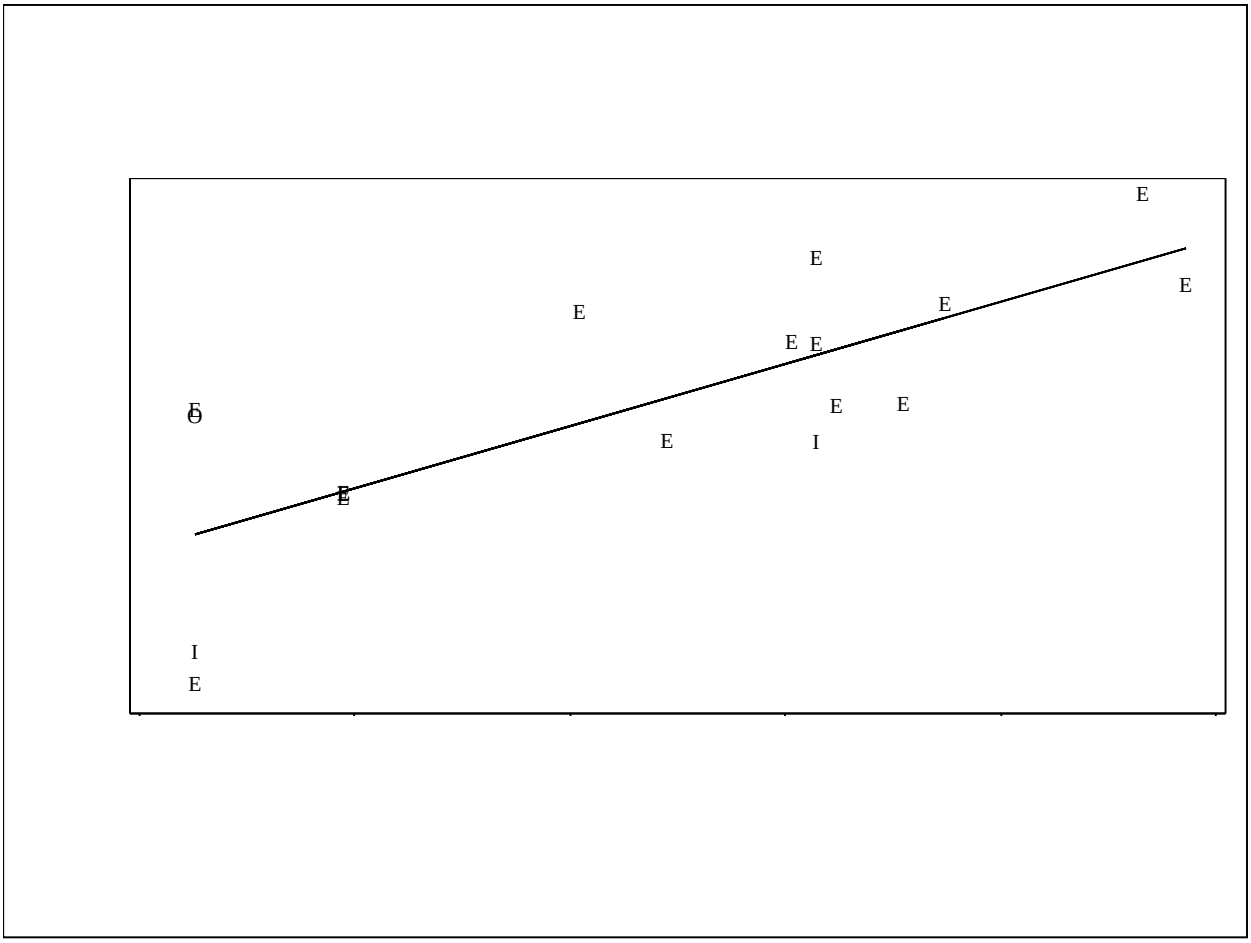

Figure 7. Regression plot for Consumer Powder, Inhalation Time-weighted Average

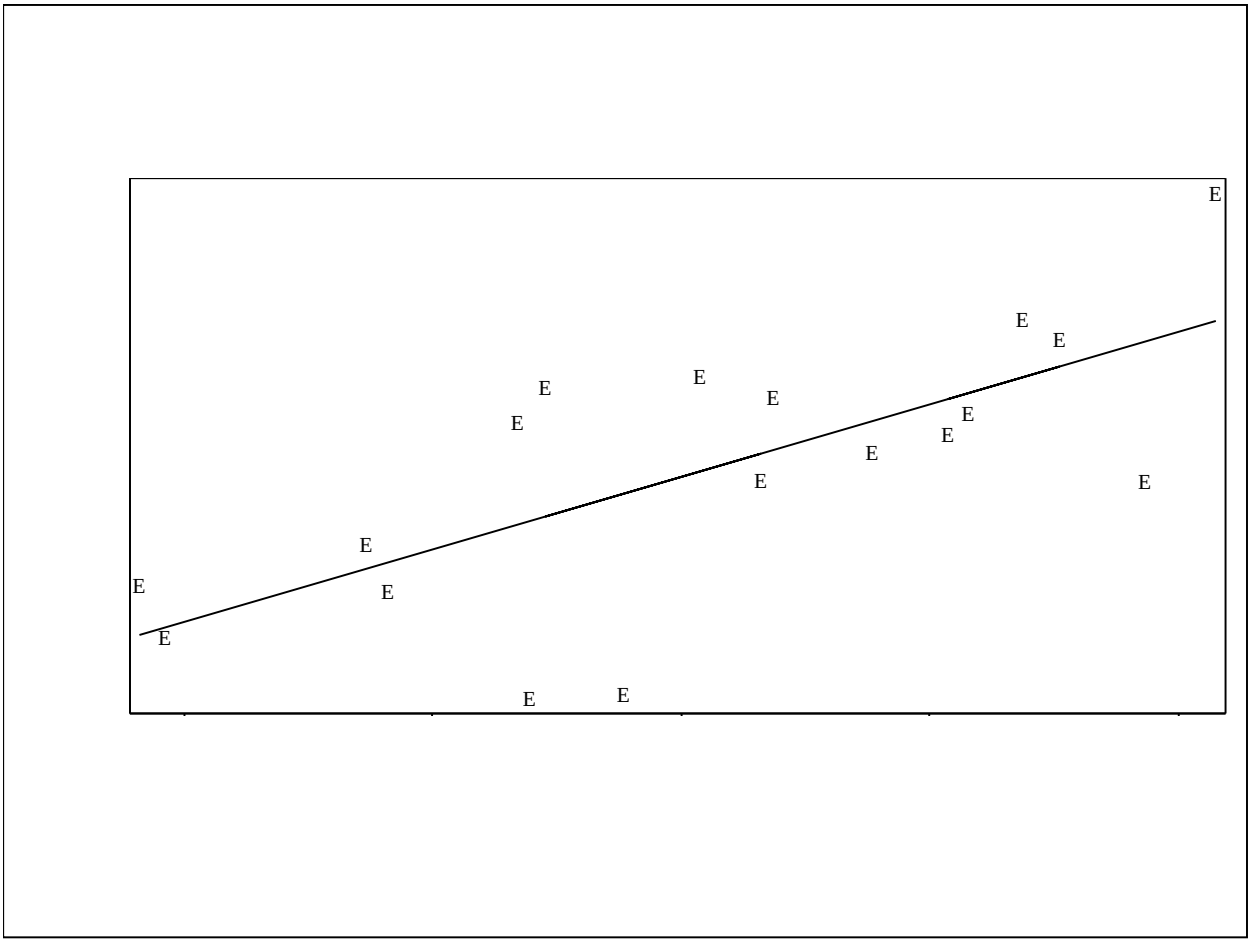

Figure 8. Regression plot for Occupational Granules, Inhalation Time-weighted Average

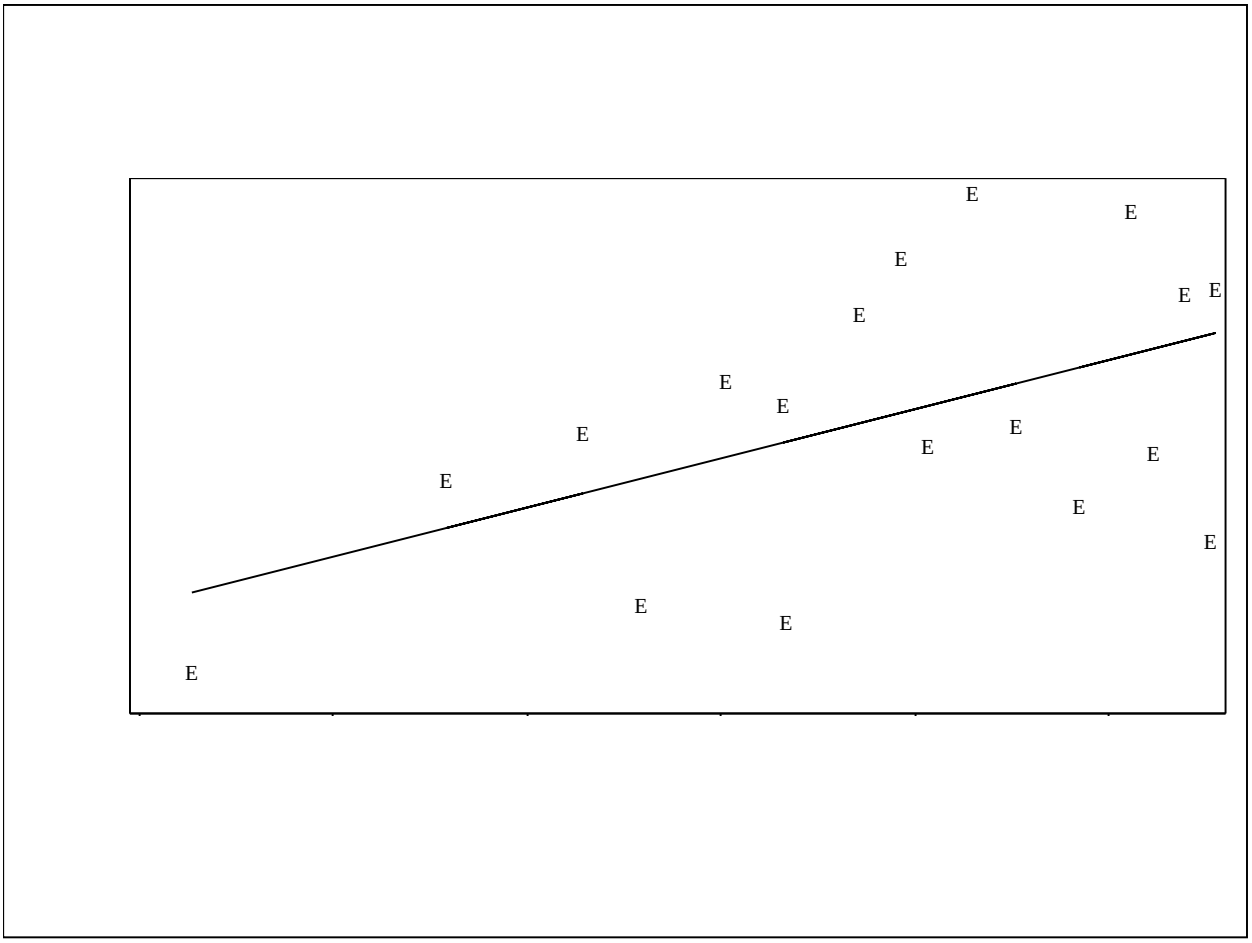

Figure 9. Regression plot for Occupational Powder, Inhalation Time-weighted Average

Threshold of AaiH for Over- or Under-Predicting Exposure – The log-log-linear regression model regresses the log exposure against the log lb ai. The normalized (unit) exposure model is the log-log-linear regression model where the slope of log exposure against log lb ai is assumed to be equal to 1. The analysis is based on comparing the two model predictions of the conditional means, i.e., the estimated arithmetic means for a given amount of active ingredient. It is shown in Appendix A (pages 89 to 90) that if the regression formulation is correct and the estimated regression slope is less than one, then the conditional arithmetic mean exposure for a given amount of ai will be over-predicted if the normalized exposure model is extrapolated to high levels of the amount of active ingredient and the conditional arithmetic mean exposure will be under-predicted at low levels of the amount of active ingredient. This applies to all the cases for consumer granules and consumer powder, a few of the cases for occupational granules, and most of the cases for occupational powder.

For the rest of the cases for occupational granules and occupational powder, the slope was higher than one, and in this case the conditional arithmetic mean exposure for a given amount of ai will be under-predicted if the normalized exposure model is extrapolated to high levels of the amount of active ingredient and the conditional arithmetic mean exposure will be over-predicted at low levels of the amount of active ingredient.

For selected cases, Tables 11 and 12 give the threshold amounts of active ingredient handled which are the minimum amounts of active ingredient handled for which the normalized

exposure mixed model will over-estimate the expected exposure (under-estimate if the slope is greater than 1). Also tabulated are the corresponding exposure values at the threshold levels of active ingredient. Results for all cases are given in Appendix A (pages 56 to 61, Tables 37 to 40).

Table 13 illustrates these threshold implications for the Long Dermal exposure for the occupational granules and powder scenarios. For occupational granules, the slope is greater than 1 and so the exposure estimates using the UE method are lower than the regression estimates for levels of ai above the threshold (36.7 lb ai). For occupational powder, the slope is less than 1 and so the exposure estimates using the UE method are higher than the regression estimates for levels of ai above the threshold (29.5 lb ai).

Table 11. Threshold values for the minimum amount of active ingredient handled for which the normalized exposure model will over- or under-estimate dermal exposure.

Clothing	Scenario	Slope (log mg / log lb ai)	Threshold (lb ai)	Exposure at threshold (mg)
Short pants, short sleeved-shirt	Consumer granules	0.41	6.5	12.3
	Consumer powder	0.59	2.4	22.6
Long pants, long sleeved-shirt	Occupational granules	1.39*	36.7*	1.8*
	Occupational powder	0.69	29.5	6.7

*For this case, slope > 1 and so the normalized exposure model under-predicts exposure for pounds of active ingredient above the threshold

Table 12. Threshold values for the minimum amount of active ingredient handled for which the normalized exposure model will over- or under-estimate inhalation TWA.

Scenario	Slope (log (mg/m^3) / log lb ai)	Threshold (lb ai)	Exposure at threshold (mg/m^3)
Consumer granules	0.77	9.2	0.003
Consumer powder	0.75	3.0	0.016
Occupational granules	1.51*	36.5*	0.358*
Occupational powder	0.82	34.0	0.952

*For this case, slope > 1 and so the normalized exposure model under-predicts exposure for pounds of active ingredient above the threshold

Table 13. Predicted Exposures for Long Dermal Occupational Granules and Powder.

Scenario	Dermal UE (mg/lb AaiH)	AaiH (lb)	Exposure (mg) using UE method (UE * AaiH)	Exposure (mg) using regression equation	Difference in Exposure Estimates	
					mg[c]	The UE approach is x% over- under-predicting the regression equation at the AaiH value[d]
Occupational Granule[a] (atypical slope > 1)	0.049	10	0.491	0.297	0.194	40% over-predicting
		20	0.981	0.776	0.206	21% over-predicting
		30	1.472	1.361	0.111	8% over-predicting
		40	1.962	2.028	−0.066	3% under-predicting
		60	2.944	3.559	−0.615	21% under-predicting
Occupational Powder[b] (typical slope < 1)	0.226	10	2.261	3.178	−0.917	41% under-predicting
		20	4.521	5.110	−0.589	13% under-predicting
		30	6.782	6.747	0.035	1% over-predicting
		40	9.043	8.217	0.825	9% over-predicting
		60	13.564	10.850	2.714	20% over-predicting

[a]This example (Occupational Granule) shows exposure implications (under- or over-predict) at the threshold AaiH value (Figure 12) when the slope > 1 as shown in Table 12. Table 9 provides the slope (slope = 1.39 for this scenario) and 95% confidence intervals for the slope.

[b]This example (Occupational Powder) shows exposure implications (under- or over-predict) at the threshold AaiH value (Figure 13) when the slope < 1 as shown in Table 12. Table 9 provides the slope (slope = 0.69 for this scenario) and 95% confidence intervals for the slope.

[c]Difference in exposure (mg) = Exposure (mg) using UE method – Exposure (mg) regression eq.

Where: A negative difference in mg of exposure means that we are under-predicting exposure (mg) at a given AaiH by the reported amount of mg of exposure and a positive difference in mg of exposure means that we are over-predicting exposure (mg) at a given AaiH

[d]The UE approach is x% over- under-predicting the regression equation at the AaiH value,

$$x = [|\text{Exposure Regression} - \text{Exposure UE}|/\text{Exposure UE}] \times 100$$

Where: When using the UE method, the over- or under-prediction of the exposure from the regression (mg) is x% of the UE estimate.

Figures 10 through 17 show the statistical models and thresholds for the same set of selected cases; additional cases are shown in Appendix A (pages 92 to 107, Figures 65 to 80). These figures display the measured values together with the predicted conditional arithmetic mean exposure calculated using the normalized exposure model (where the slope of log exposure against log ai is assumed to be one) and using the more general regression model (where the slope of log exposure against log ai is estimated). The threshold is the amount of ai for which the two predicted conditional means are the same. The plotted points are labeled for experienced subjects (E), inexperienced subjects (I), and potential outliers (O), as in the regression plots. The normalized exposure model calculation is plotted as a green line; this calculation uses unit exposures to estimate the conditional mean exposure for a given amount of active ingredient. The log-log-linear regression model calculation is plotted as a brown curve, since both axes are linear; this calculation uses the log-log-linear regression model to estimate the conditional mean exposure for a given amount of active ingredient.

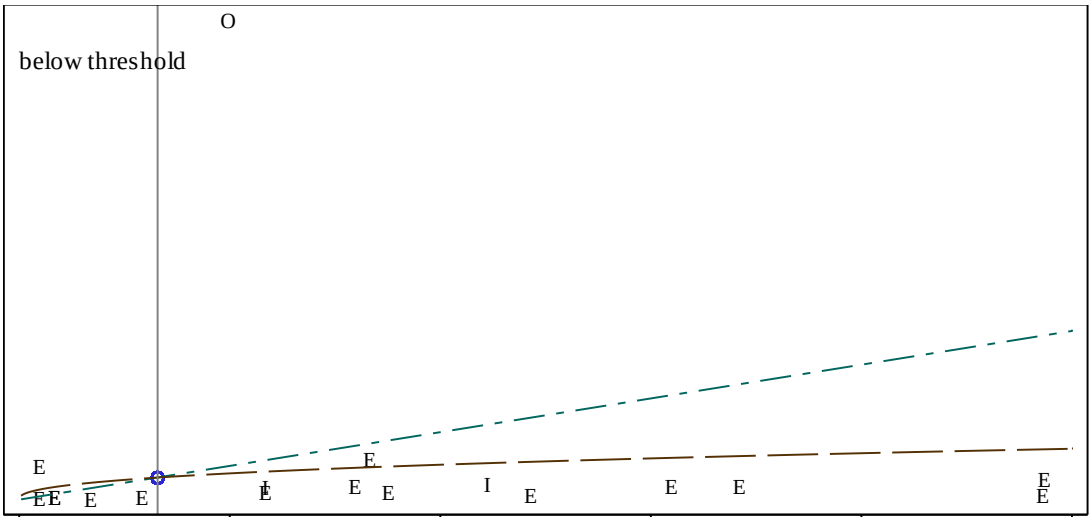

Figure 10. Conditional means for short dermal exposure from consumers pouring granules predicted using the normalized exposure model and the general log-log-linear model; threshold value.

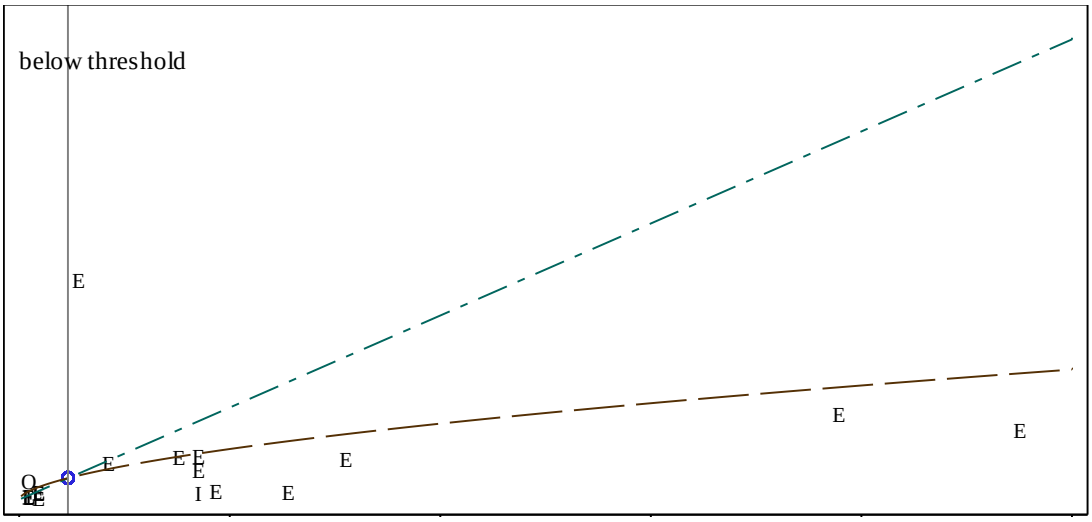

Figure 11. Conditional means for short dermal exposure from consumers pouring powder predicted using the normalized exposure model and the general log-log-linear model; threshold value.

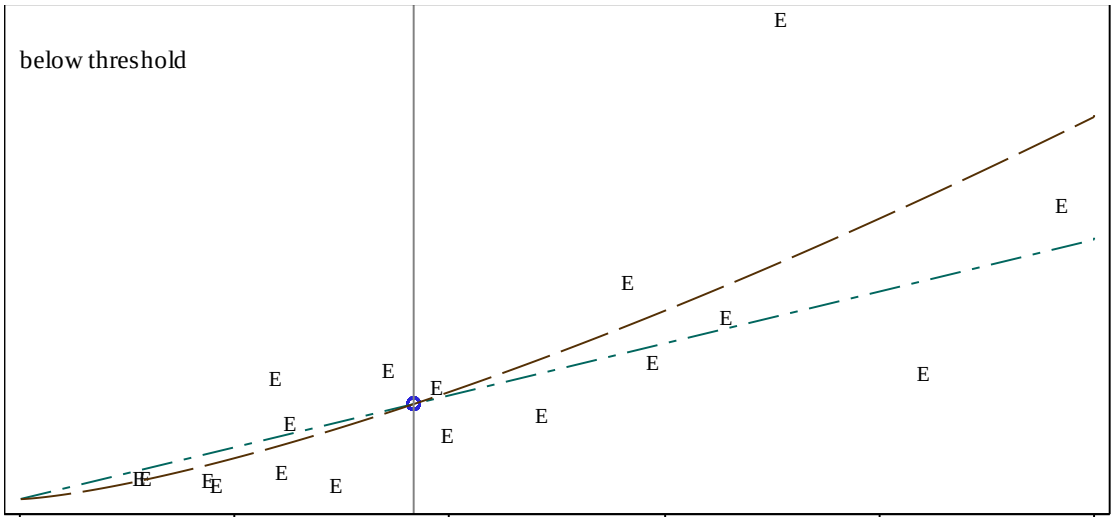

Figure 12. Conditional means for long dermal exposure from occupational workers pouring granules predicted using the normalized exposure model and the general log-log-linear model; threshold value.

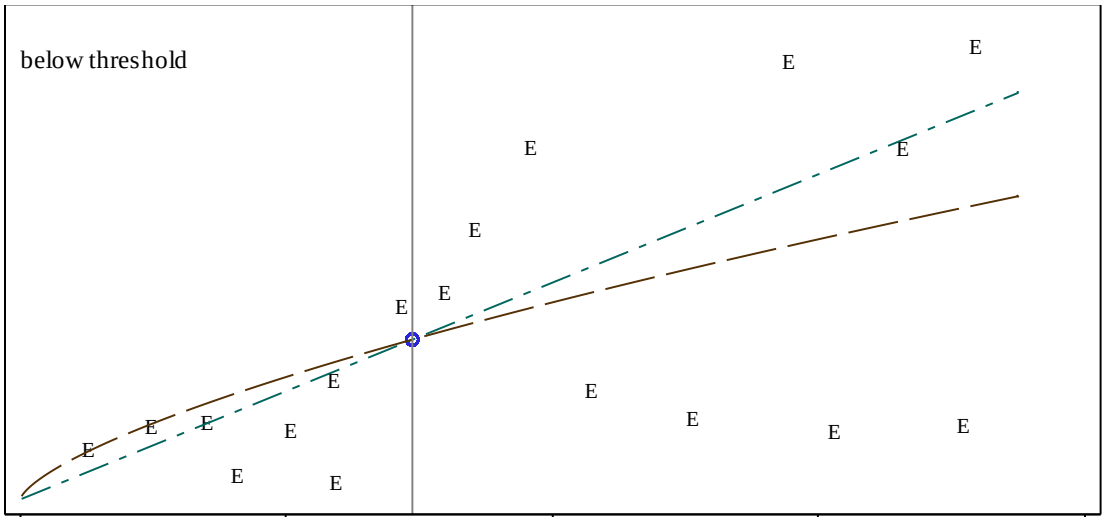

Figure 13. Conditional means for long dermal exposure from occupational workers pouring powder predicted using the normalized exposure model and the general log-log-linear model; threshold value.

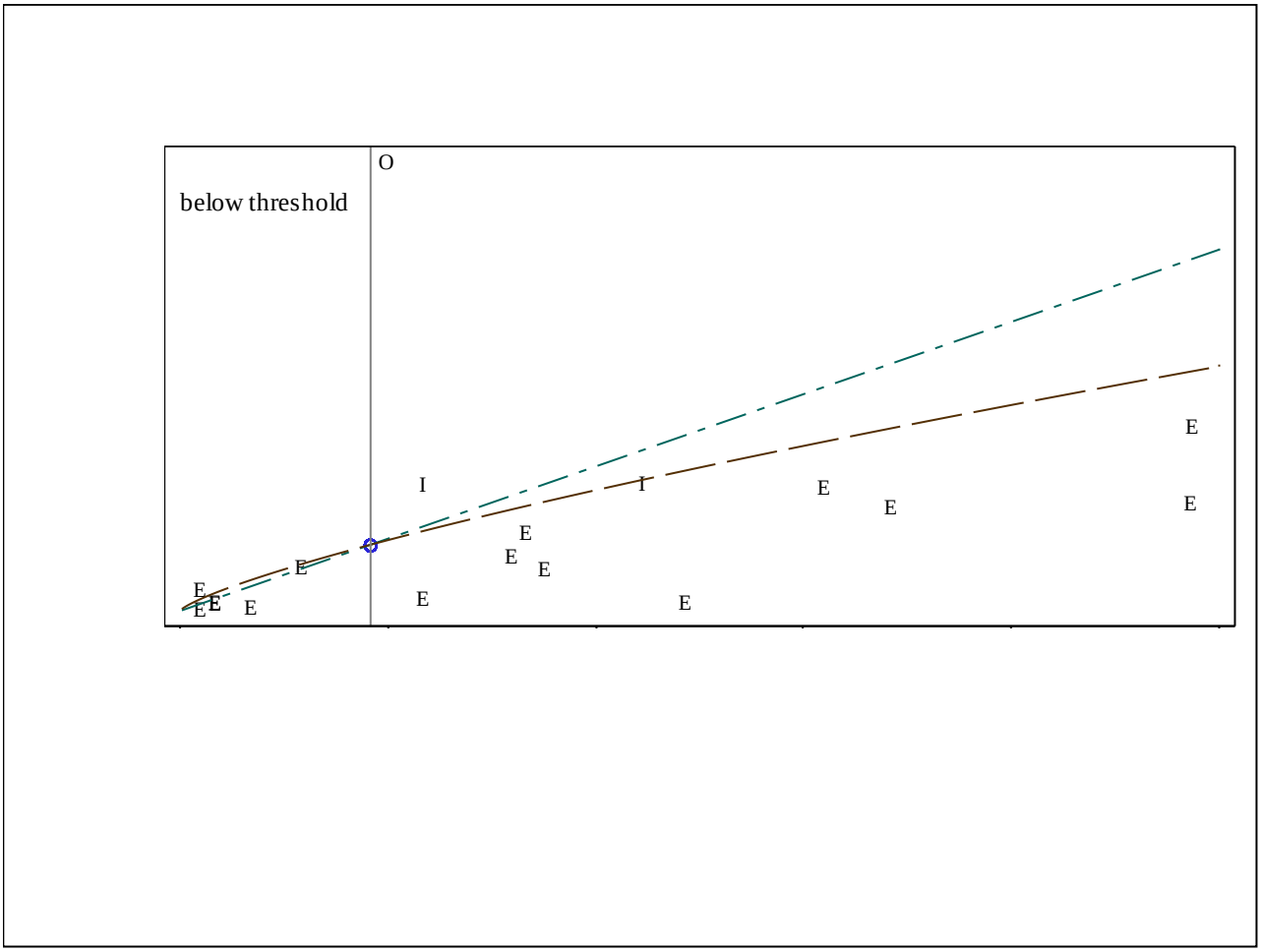

Figure 14. Conditional means for inhalation time-weighted average exposure from consumers pouring granules predicted using the normalized exposure model and the general log-log-linear model; threshold value.

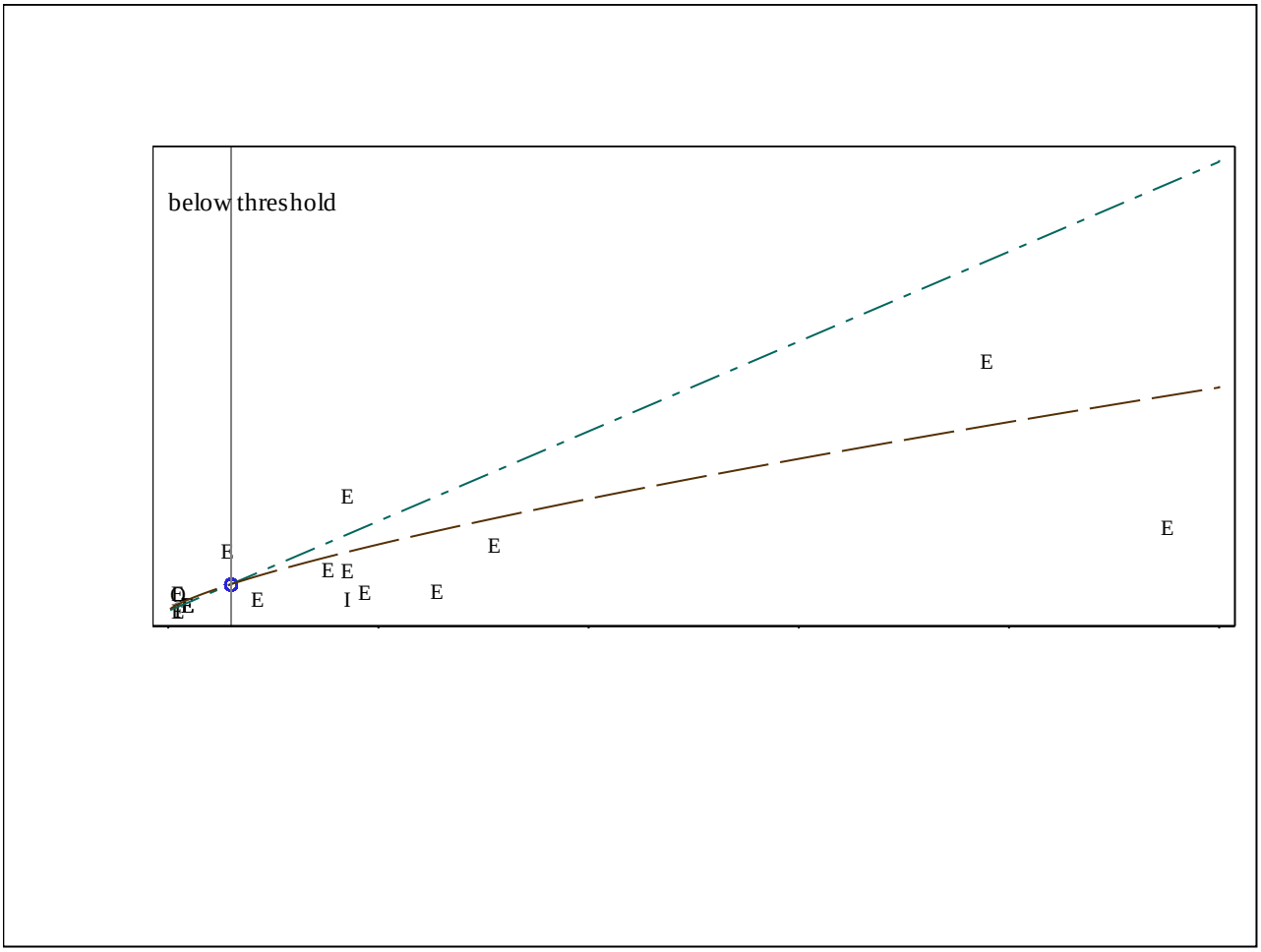

Figure 15. Conditional means for inhalation time-weighted average exposure from consumers pouring powder predicted using the normalized exposure model and the general log-log-linear model; threshold value.

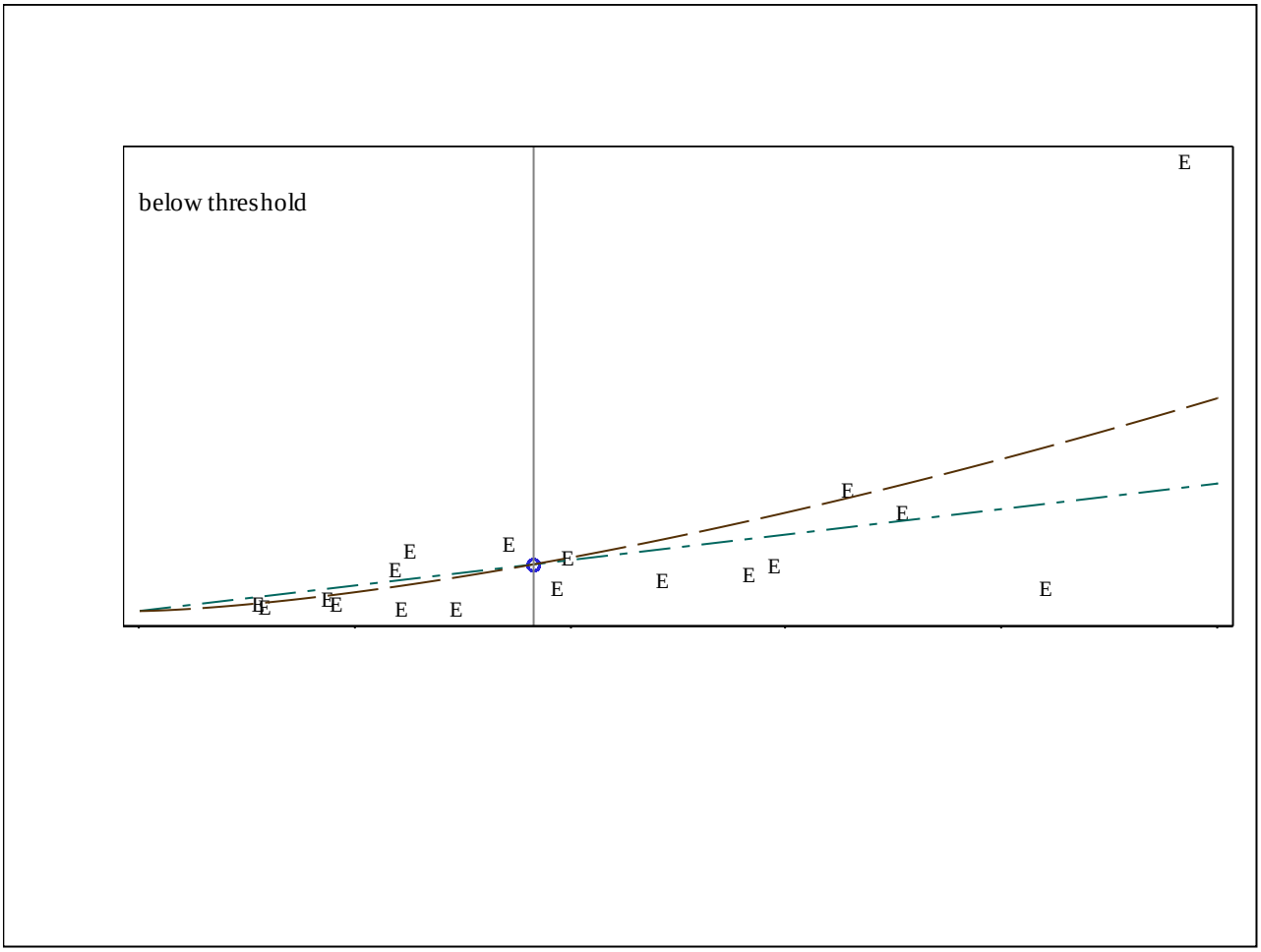

Figure 16. Conditional means for inhalation time-weighted average exposure from occupational workers pouring granules predicted using the normalized exposure model and the general log-log-linear model; threshold value.

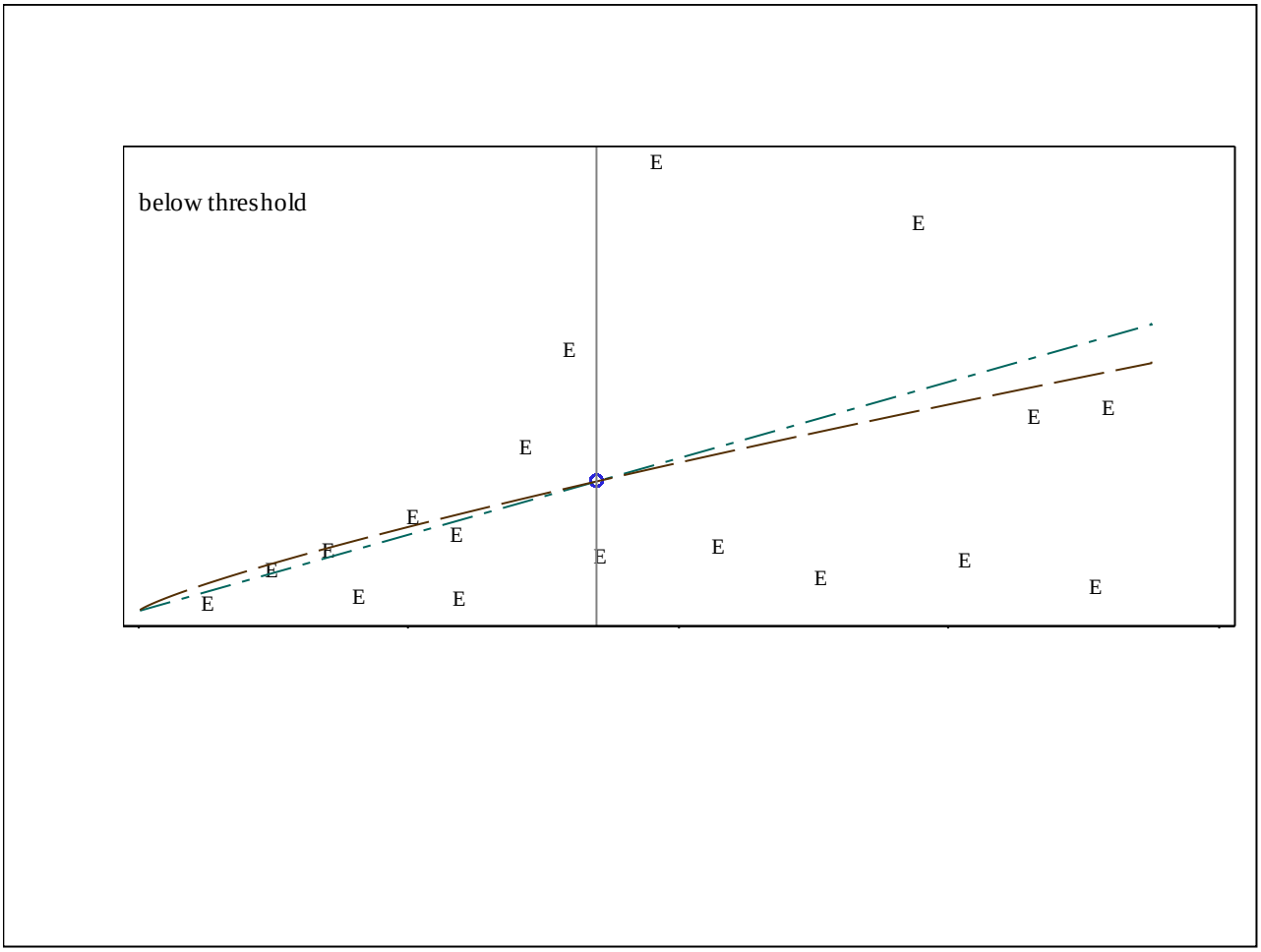

Figure 17. Conditional means for inhalation time-weighted average exposure from occupational workers pouring powder predicted using the normalized exposure model and the general log-log-linear model; threshold value.

3.0 Discussion of Data Generalizations and Limitations

The regulatory need for a generic data base of pesticide handlers for antimicrobial pesticide products has been discussed previously (SAP 2007). The study design for this solid pour study incorporated random diversity selection where feasible. Such a study design requires a discussion of how the data can be generalized and the limitations of the results. The following items are provided to potential users of these data to characterize the results of this sampling effort:

(1) The study purposively selected Concord, Ohio, as the study location. This selection criterion, rather than a random selection of sites across the country, limits to some degree the statistical generalizations of the data. Thus we cannot determine whether these results provide unbiased estimates of exposure distributions from pouring solid antimicrobial products in locations other than Concord, Ohio, and it is not possible to use these data to estimate the potential bias or the geographic variability. To generalize these results to the whole country requires an assumption that the exposure distribution for these scenarios is independent of the geographic location. The statistical limitations of the purposive site selection are deemed acceptable by the JRC. It is reasonable to assume that the mechanics

of pouring a solid product indoors and/or outdoors in a swimming pool located in Ohio are not substantially different than pouring a solid inside other buildings and/or outdoor swimming pools throughout the country. The outdoor swimming pool site is also deemed a worse-case scenario compared too indoors. Given a limited set of resources for the overall AEATF II monitoring program, the assumption that pouring solids does not vary geographically was sufficiently reasonable to forgo the random site selection (of all buildings and/or swimming pools throughout the country) in favor of spending the limited resources to monitor additional distinctly different scenarios (e.g., painting, metal working fluids, pressure treatment of wood, etc).

(2) The data generated in this study are acceptable to use as surrogate for assessing other chemicals considered to have low volatility (i.e., vapor pressures less than ~1E-4 mmHg @ 20ºC). This "rule-of–thumb" for the vapor pressure threshold is reviewed by EPA on a case-by-case basis, particularly for those antimicrobial pesticides with vapor pressures that are near to this threshold. For example, for those chemicals with vapor pressures of ~1E-4 mmHg, EPA reviews the available inhalation toxicity data to see if the toxicity studies were performed as a gas or with an aerosol.

(3) The data generated in this study are acceptable to use as surrogate to assess pesticide labeled uses that require the open pouring of powders and granules; except for (a) large 25 lb buckets of powders for residential uses as noted in the above review, and (b) occupational use of large supersacks containers (see discussion in Section 4 below).

(4) The particle size of the powders and granules are provided above in Table 3 above. When using these exposure data, especially the respirable portion of the inhalation exposure, assessors need to review the particle size of the products being assessed and determine the representativeness of these surrogate data in comparison to their situation.

(5) The small sample size by itself does not create statistical limitations since the confidence intervals for the summary statistics based on the primary statistical model were reasonably narrow (in most cases meeting 3-fold relative accuracy goal or better).

More important is the fact that the original sets of subject participants, locations, and dates from which the subjects, and sampling dates were chosen were limited and hence might not be representative of all Ohio users that pour solids (e.g., those that use solid products but did not volunteer), buildings (e.g., a warehouse was selected for this study), and time periods (e.g., winter versus summer, night versus day, etc.). In other words, the most significant limitation is that these data were not derived from a fully stratified random sample of MEs even though the statistical analyses made that assumption. At a minimum this increases the uncertainty of the estimates (so the calculated confidence intervals are too narrow) and there may also be some bias (e.g., study participants not in the volunteer pool might be more or less prone to exposure than the selected group).

(6) EPA will continue using exposures normalized by AaiH as a default condition. In this review we evaluated the presumption of "proportionality" that the mean exposure is a positive multiple of the AaiH (i.e., the mean exposure is proportional to the AaiH and the exposure tends to increase with increasing AaiH). Proportionality is evaluated by testing if the log-log-linear model has a slope of 1. The analyses of log-log-linearity show that dermal and inhalation exposure tend to increase with pounds of active ingredient handled (AaiH) for all the scenarios. The analyses of the two occupational scenarios (powder and granules)

for both dermal and inhalation exposures, in most cases rejected independence and supported proportionality. For the consumer powder scenario, the results rejected independence in every case and supported proportionality in about half of the cases. For the consumer granules, the analyses rejected independence and supported proportionality for the inhalation exposure in most cases, but for the dermal exposure the analyses did not reject independence and supported proportionality. Data will continue to be collected by the AEATF II to add to the knowledge base of normalized exposures.

4.0 Conclusions

EPA has reviewed the AEATF II solid pour study and concludes that the AEATF II made the appropriate changes to the protocol proposed by the EPA and HSRB and has executed the study successfully. The protocol deviations that occurred and were reported and those identified by EPA have not adversely impacted the reliability of these data. The EPA recommends that the inhalation and dermal UEs generated in this solid pour study be used provided the data are used within the boundaries set forth in this review. The following is a summary of our conclusions:

- The AEATF II data for inhalation and dermal exposures represent reliable data for assessing the pouring of powder and granule products. The AEATF II unit exposures summarized in Tables 1a and 1b are recommended to be used for regulatory purposes.

- Estimates of the GM, AM, and P95 were shown to be accurate within 3-fold with 95% confidence for all scenarios except for the consumer granules scenario for dermal exposure where the accuracy goal is 2.2 for GM, 3.6 for AM, and 3.3 for P95. At this time, no additional monitoring for the solid pour scenarios is required.

- Additionally, Tables 11 (dermal exposures) and 12 (inhalation exposures) provide a threshold that is the minimum AaiH value where exposure will be over-estimated when extrapolating the normalized exposure (mg dermal/lb ai or mg/m^3 inhalation/lb ai) to other chemical assessments (i.e., using these unit exposures as surrogates to assess other chemicals that handle more active ingredient than the threshold). Because the slope > 1 for the occupational granules for both dermal and inhalation exposure, the exposures are under-predicted for AaiH values above the threshold of 36.7 lb ai. As shown in Table 13 the under-prediction is not substantial but will be noted when characterizing the use of this scenario. As acknowledged in the study design document, these unit exposures are not recommended for assessing exposures to workers using bulk flexible containers (e.g., 1000 lbs), sometimes called supersacks ("Super Sack®" is a registered trademark of B.A.G. Corp). Additionally, the consumer powder scenario's unit exposures are not representative of large (25 lb) packaging containers as the use of these size containers were discontinued during the study.

5.0 References

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Appendix A

Statistical Review of the AEATF II Solid Pour Study

(To be included as a separate electronic file)