UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

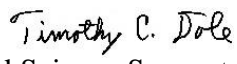**MEMORANDUM**   September 20, 2021

SUBJECT: Science Review of the AEATF II Immersion/Dip/Soak (IDS) Human Exposure Monitoring Study (AEATF II Project ID AEA12; MRID 51588901).

PC Code(s): Not Applicable (NA)	DP Barcode(s)/No(s): NA
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Petition No(s).: NA	Regulatory Action: Human Health
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This memorandum presents the EPA/Office of Pesticide Program (OPP) Antimicrobials Division (AD) science review of the human exposure immersion/dip/soak (IDS) 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) immersion/dip/soak (IDS) study. The AEATF II designed the study to develop unit exposures for people who immerse, dip, and/or soak (restaurant-type) equipment and utensils, or use a rag/sponge in a bucket to wipe surfaces, with a treatment solution of an antimicrobial product. The results of the study are reported herein. 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 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 reviews are to be presented to the HSRB at the planned October 21, 2021 meeting.

The study investigators monitored inhalation and dermal exposures to a total of 54 different test subjects. The 54 subjects were separated into three distinct "sub" scenarios within this overarching study called immersion/dip/soak (IDS). The three "sub" scenarios for which the distinct inhalation and dermal exposures have been developed are (1) Bucket and rag/sponge, (2) 3-compartment sink, and (3) Clean-out-of-place (COP). Each of the three "sub" scenarios comprised 18 of the subjects, and none of the subjects participated in more than one of the scenarios. Both the C14 analog of alkyl dimethyl benzyl ammonium chloride (ADBAC) (dermal) and didecyl dimethyl ammonium chloride (DDAC) (inhalation) were used as the active ingredients (a.i.) as the surrogate test compound by all test subjects. ADBAC inhalation exposures were also measured but were not used in this science review because of issues with background contamination in the controls, instead DDAC was used for inhalation sampling. These two Quats were selected as surrogate compounds because of their stability, low vapor pressure, low detection limits, and registered uses. All test subjects were recruited from the food service, janitorial, hotel, etc. industries. All cleaning (sanitizing) activities were performed indoors. The term "cleaning" is used colloquially within this review as the test substance as well as the tasks being performed are meant to be used to "sanitize", which is a specific pesticidal claim to control a specific microorganism. Each subject was randomly assigned within each of the three scenarios to perform the specific cleaning (i.e., sanitizing) tasks for a given concentration of a.i. and time. Subjects were instructed to work as they normally would. EPA confirms that the data are considered the best available data for assessing handler exposures from antimicrobial treatment solutions for immersing, dipping, and soaking equipment and utensils, as well as cleaning surfaces with a bucket and rag/sponge. The reader is referred to Section 3.0 for a discussion on the data limitations and use of the data as a surrogate for other a.i.s.

EPA intends to use these AEATF II immersion/dip/soak unit exposures for hard surface sanitizing and disinfectant uses in food service areas as well as for wiping when product labels allow for bucket and rag/sponge. These scenarios do not cover the pouring of an antimicrobial product into the containers to make up the treatment solutions. Those mixer/loader scenarios are monitored in separate AEATF II studies (the mixer/loader portion was conducted separately

because many different formulations can be used such as liquids, powders, flakes, metering systems, etc).

Select summary statistics for the "unit exposures" (i.e., exposures normalized to the concentration of a.i. in the treatment solution (ppm a.i.) and to the duration of exposure (hours)) are presented in Table 1 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, forearm wipe or lower arm, upper arm, etc.).

Table 1. Unit Exposures (UE) for the AEATF II Immersion/Dip/Soak (IDS) Scenarios.			
Exposure Route	**Clothing and/or Inhalation[a] (Normalization Units)**	**AEATF II[b, c] (n= 18)**	
		Arithmetic Mean[d]	**95th Percentile[e]**
Bucket Rag & Sponge			
Dermal	Long pants/short-sleeves, no gloves (mg/(ppm a.i. x hours))	0.096	0.211
Inhalation	Dose (mg/(ppm a.i. x hours))[f]	1.98E-6	5.61E-6
	8-hr TWA ((mg/m^3)/(ppm a.i. x hours))[g]	2.47E-7	7.01E-7
3-Compartment Sink			
Dermal	Long pants/short-sleeves, no gloves (mg/(ppm a.i. x hours))	0.0371	0.0072
Inhalation	Dose (mg/(ppm a.i. x hours))[f]	3.88E-6	1.48E-5
	8-hr TWA ((mg/m^3)/(ppm a.i. x hours))[g]	4.85E-7	1.85E-6
Clean-Out-of-Place (COP)			
Dermal	Long pants/long-sleeves, gloves (mg/(ppm a.i. x hours))	0.000734	0.00258
Inhalation	Dose (mg/(ppm a.i. x hours))[f]	5.73E-5	2.10E-4
	8-hr TWA ((mg/m^3)/(ppm a.i. x hours))[g]	7.16E-6	2.63E-5

[a] Unit Exposures (UEs) reported in Table 1 have been converted to represent "hours" rather than the "minutes" which are the duration units reported throughout this review and Appendix A.

[b] Dermal and inhalation UEs are corrected for laboratory recoveries (field recoveries >100%).

[c] Statistics are estimated using a lognormal simple random sampling model. Non detected (ND) values are estimated using substitution by ½ the limit of quantification (LOQ). Details are described in Appendix A.

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

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

[f] Inhalation (mg/(ppm a.i. x hours) = air conc ((mg/m^3) / (ppm ai * duration)) * breathing rate (1 m^3/hour) * exposure duration (hours/day)

8-Hour Time Weighted Average (TWA) ((mg/m^3)/(ppm a.i. x hours)) = air conc (mg/m^3) / (ppm a.i. x hours) * study exposure duration (hours/day) / 8 (hours)

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

- The unit exposures reported in Table 1 have had their units converted from the review herein and Appendix A from "ppm x minutes" to "ppm x hours" for ease of use by exposure assessors as worker exposure durations are reported in "hours" rather than "minutes". The unit exposure conversion was calculated by multiplying the unit exposures reported herein by "60" to convert the minutes to hours.
- The dermal unit exposures recommended in Table 1 are based on the short-sleeved shirt, long pants, no gloves for the bucket and sink scenarios and the long pants, long-sleeved shirt, gloves for the COP scenario. The hand exposure for all three scenarios represents nearly 100% of the exposure (i.e., the other body parts round-out for the bucket and sink scenarios and nearly round-out for the COP scenario).
- Estimates of the dermal unit exposures for the geometric mean (GM), arithmetic mean (AM), and 95th percentile (P95) were shown to be accurate within 3-fold with 95% confidence for all but the P95 for the COP scenario for the empirical simple random sampling model (see Table 7 below). The inhalation unit exposures meet the 3-fold relative accuracy objective for all but the P95 for all three of the IDS scenarios for the empirical simple random sampling model. At this time, no additional monitoring for the three IDS scenarios is required.
- The statistical analysis (Section 2.4) provides evidence consistent with log-log-linearity with a slope of 1[1] between dermal exposure and the treatment solution concentration and exposure duration for the bucket and sink scenarios, but not the COP scenario. 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 ppm x duration (a slope of zero) is rejected and that log-log-linearity with a slope of 1 is not rejected. The results reported in Section 2.4, Table 8 of this analysis indicate the following:
  - For the bucket scenario, the confidence intervals for the slope exclude 0 and include 1 for both dermal and the inhalation 8-hr TWA. Thus, the "unit exposure" approach for both the dermal and inhalation for the 8-hr TWA is a reasonable approximation.
  - For the sink scenario, the confidence intervals for the slope exclude 0 and include 1 for dermal. Thus, the "unit exposure" approach for the dermal is a reasonable approximation. However, for inhalation 8-hr TWA exposure, the slope is negative and the confidence intervals include 0 but not 1, thus the assumption of

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[1] The statistical analysis of log-log-linearity tests whether the slope of log exposure against log a.i., or for this IDS study, the log ppm a.i. x duration, 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 amount of a.i. handled (AaiH), or in the IDS study, ppm x duration, but instead assume that the logarithm of the exposure is linear in the logarithm of a.i. (or in the IDS study, ppm a.i. x duration) 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."

independence was supported and the assumption of log-log-linearity with slope 1 was rejected. The results for inhalation exposure seem to be counterintuitive.
- o For the COP scenario for both the dermal and inhalation 8-hr TWA exposure, the confidence intervals include 0 but not 1, thus the assumption of independence was supported and the assumption of log-log-linearity with slope 1 was rejected. This suggests that the exposure does not depend on the normalizing factor.

- A secondary study objective for EPA is to meet 80% power for detecting log-log-linearity with a slope of 1. This objective is met if the widths of the confidence intervals for the slopes are ≤ 1.4. This secondary objective was met for all scenarios; therefore, the statistical (post-hoc) power is greater than 80%.
- The statistical analyses reported here and in Appendix A are for exposure normalized by the product of ppm and duration, which is a reasonable way to account for the effects of both concentration and duration on exposure. In the Supplement to Appendix A, we explored and report results where exposure is either normalized by ppm alone, which does not account for the effects of duration, or where exposure is not normalized at all.

To assess the risks resulting from cleaning restaurant equipment/utensils and cleaning with a bucket and rag/sponge, 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 (e.g., hours worked) in the standard pesticide handler exposure algorithm: Potential exposure = UE (mg/ppm ai/hour) x absorption (%) if applicable x maximum label rate (ppm a.i. weight) x hours worked conducting the task.

1.0 Background

The AEATF II is developing a database representing inhalation and dermal exposure during many 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., paint brush/roller, airless paint sprayer, ready-to-use wipes, bucket and rag/sponge, trigger pump sprayer, mopping, pressure treatment of wood, 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 shirt). Hand exposure as well as inhalation exposures are also being monitored. Prior to conducting intentional exposure studies in humans, the protocols are reviewed by the HSRB. The HSRB reviewed this IDS exposure study protocol on October 23, 2018.

1.1 Immersion/Dip/Soak (IDS) Scenario Defined

The three IDS "sub" scenarios in this study are defined as subjects, recruited from the food service and janitorial industries, cleaning restaurant equipment/utensils and surfaces using techniques as they normally would do. The study conditions were simulated/designed to mimic actual work conditions and the subject's own routines that cause them to interact/be exposed to the a.i. were based on their own experiences.

Each of the three "sub" scenarios are described in detail as follows (the mixing/loading of the concentrate was not performed by the subjects, the mixing/loading exposure data are available in prior AEATF II studies):

(1) **Bucket and rag/sponge**: Subjects from the janitorial industry dipped a rag or sponge into a diluted sanitizing solution in a bucket, wrung out the rag/sponge, and wiped vertical and horizontal surfaces.

(2) **3-compartment sink**: Subjects from the food service industry manually washed, rinsed, and sanitized cookware/bakeware that do not fit in dishwashers. This scenario is typical in restaurants/bars/schools/etc. *"The first sink is used to wash the items, the second sink is to rinse the items, and the third sink is to sanitize the items as described in the Food and Drug Administration (FDA) 2017 Food Code. The sanitization step requires that articles are placed into a sanitizing solution following the time and temperature requirements of the sanitizer being used. After the articles have been dipped and/or soaked in the sanitizer, they are removed from the sink and place on a clean dry surface to air dry. Although the focus of this study is on exposure during the immersion of equipment and/or utensils into an antimicrobial solution, in the case of the food service industry, workers must follow a strict three-step process to clean, rinse, and sanitize. Since this is a sequential activity, the entire process of using a three-compartment sink was monitored in the study."* (AEATF 2021, page 21)

(3) **Clean-Out-of-Place (COP)**: Subjects from the food processing industry used a stainless-steel COP tank to clean and sanitize industrial equipment parts. *"Equipment that [is] cleaned using COP include removable articles such as fittings, clamps, product handling utensils, tank vents, pump rotors, impellers, blades, knives, casings, and hoses. ... Once the equipment has been disassembled, manual dry cleaning may take place to remove debris from the equipment parts followed by placement into the COP tank. ... After the cleaning step, the tank is drained... Once the tank is drained... the parts may be rinsed by spraying them with a hose, and then the tank is refilled, and a sanitizing solution is added, and the jets are turned back on. After the specified circulation time, the sanitizing solution is drained, and the cleaned and sanitized articles are removed and placed on racks to air dry.*

The entire cleaning and the sanitization processes in COP tanks were monitored in this study. It was not necessary to use dirty equipment parts because ...all the parts are placed into a single tank, and they remain in the same tank throughout the cleaning, rinsing, and sanitizing steps. Once the parts are in the tank, there is no manual contact with the parts until they are removed from the tank after the sanitizing step. ...Most of the time workers conduct one cycle of equipment cleaning in a COP tank during a work shift, with the majority of their time spent on taking apart equipment for cleaning, running CIP cleaning systems, and manual cleaning/scrubbing of equipment.

The monitored activity for this use scenario included placing various pieces of equipment into an empty COP tank, adding water and turning on the circulation to simulate the cleaning cycle, draining the wash water, rinsing of the items in the tank by spraying with a hose, filling the tank with water for the sanitizing step, allowing the items to soak in the circulating sanitizing solution for at least 15 minutes, draining the tank, and finally removing the items and placing them on racks to air dry. ... once the water has reached the correct level and the detergent, acid, or sanitizer has been added, the worker turns off the water supply, turns on the jets, and walks away to do other tasks such as disassembling equipment, cleaning floors, and running clean-in-place systems in certain equipment. This was simulated in the study by having the subjects move away from the COP tank for a minimum of 30 minutes during the simulated cleaning cycle and 15 minutes during the sanitizing cycle. Once the 15 minutes was up following the sanitizing cycle, the subject drained the COP tank and removed the sanitized articles from the tank, placing them on a wire rack to air dry." (AEATF 2021, pages 22-23)*

Subjects wore whole body dosimeters (WBD) underneath short-sleeved shirts, and long pants, and no gloves plus one personal air sampler in the bucket & rag/sponge and 3-compartment sink scenarios. The subjects participating in the COP scenario wore similar clothing configurations except they wore long-sleeved shirts and 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 sanitizing/disinfecting surfaces and equipment by IDS cleaning methods. Dermal and inhalation exposure monitoring was conducted while study participants sanitized various surfaces and equipment by various methods (i.e., the three exposure scenarios discussed above). These exposures will be used in pesticide exposure assessments as "unit exposures".

"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. Unit exposures are typically expressed as the amount of active ingredient (a.i.) handled by participants in scenario-specific exposure studies (e.g., mg a.i. exposure/lb a.i. handled). In these IDS scenarios, the logical normalization variable, based on the job function/task of dipping one's hand in a solution over time, is the treatment concentration times the duration of exposure (e.g., ppm a.i. x hour). 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). As outlined in the AEATF II Governing Document (ACC 2011), the criteria are 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 "professional/commercial" employed subjects cleaning/sanitizing hard surfaces and restaurant-type of equipment.

A secondary objective for EPA is to meet 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 ≤1.4.

1.3 Protocol Modifications, Amendments, and Deviations

1.3.1 Protocol Modifications Based on EPA and HSRB Reviews

EPA and the HSRB provided science-based changes to the IDS protocol during the review (EPA 2018 and HSRB 2019). The review comments and AEATF II responses are summarized in Table 2a for the EPA comments and Table 2b for the HSRB comments.

Table 2a. EPA Science Review and AEATF II Responses.		
EPA Issue Raised	**AEATF Response**	**EPA Comments**
1. Increase the range of quat concentrations used in the bucket & rag/sponge and the 3-compartment sink scenarios in order to increase the statistical power; two options were proposed. If AEATF chooses Option 1, this is above the rate for no-rinsing of food contact surfaces, so the articles used in the study must be rinsed prior to them being used for food contact.	Agreed to incorporate Option 1 (increase levels to 1000, 600, and 100 ppm quat). Agreed to rinse all the test articles (bakeware/cookware and equipment parts) when all the monitoring is done. These will be items AEATF has purchased and/or borrowed for the study and will not be used for food contact until after the monitoring is complete. These changes will be added to the protocol.	According to AEATF (2021) page 38 of the study report, for the sink scenario, *"After the subject completed the work activity and was escorted out of the kitchen, a researcher rinsed all the sanitized cookware to remove quat residues. The rinsed items were placed on clean metal wire racks and allowed to air dry. Soiled cookware that had not been cleaned by the subject was washed and rinsed by the researcher and allowed to air dry on the wire racks. The sinks and areas around the sinks were rinsed with water and wiped dry to remove any quat residues. The sponge/scrub pad(s) used by the test subject was thrown away."* Similar rinsing and wiping were performed by the researchers after the bucket scenario (see AEATF 2021, page 42) and COP scenario (see AEATF 2021, page 46).

Table 2a. EPA Science Review and AEATF II Responses.

EPA Issue Raised	AEATF Response	EPA Comments
2. Make every effort to record the volume of dilute test solution used by each ME	Agreed, but noted that in some cases these will be estimates; this is already noted in the protocol.	The following volumes were estimated: Bucket and Rag/Sponge: 4.75 gal of water prepared for multiple MEs (AEATF 2021, Table 17) Sink: 9.8 to 22.4 gallons (AEATF 2021, Table 8) COP: 50 to 201 gal water per tank, half the MEs used two tanks per monitoring period (AEATF 2021, Table 26)
3. Allowing some subjects to participate in multiple scenarios will result in a statistical correlation which is not desirable. Either have all or almost all of the subjects participate in both the bucket & rag and 3-compartment sink scenarios or have no one participate in more than one scenario.	Agreed to change the protocol to specify that no one can participate in more than one scenario.	There were no repeat measurements of test subjects (i.e., each ME was a different individual).
4. Various editorial changes to the protocol	These will be incorporated	No further comments.

Table 2b. HSRB Review and AEATF II Responses.

HSRB Recommendation	AEATF Responses	EPA Comments
1. Measure the water temperature	The water temperature of the sanitizing solution used by each ME will be measured; additionally, the temperature of the wash and rinse water in the sinks will be measured as well as the wash and rinse water used in the COP tank scenario. This will be added to the protocol.	Water temperatures are reported in the study report.
2. Add willingness to conduct the work (for bucket & rag and 3-comparetment sink) without wearing gloves as part of the inclusion criteria	This will be added to the inclusion criteria in the protocol, ICF, and recruiting materials	No further comments in the science review.
3. Make sure that the test sites have a range of tables and chairs and surfaces for the subjects to wipe during the bucket & rag scenario	This is the plan; this detail will be added to the protocol	Appendix C of the study report shows pictures of the short and long rectangle tables, round tables, and various types of chairs.

Table 2b. HSRB Review and AEATF II Responses.		
HSRB Recommendation	**AEATF Responses**	**EPA Comments**
4. Remove the statement that having Spanish speakers adds diversity to the study	This statement was not found in the protocol	No further comments in the science review.
5. Measure the height of the subjects or the height of the sampler to the sink; measure the size of hands of subjects	The protocol already states that the height of the subjects will be recorded. Because subjects will be moving around while they work, it would not be practical to measure the height of the air-sampler above the sink; however, the height of the sinks and COP tanks will be recorded. Work habits including whether a subject gets unusually close to the sink or tank will be documented. Measuring hand size is not practical nor would it provide useful information regarding exposure potential and will not be done.	The water depths in the sinks were measured (6 to 9 inches) as well as the depths of the wash and rinse sinks (AEATF 2021, Table 7 page 99). The subject's heights were also measured. Detailed observational notes are not included in the study report for all MEs, rather a few observational notes are added such as "*nothing in the observation notes to explain…high-end residues*". For ME16 bucket scenario it is noted that the subject's face was 1 to 2 inches from surfaces he was wiping and air sampling tube touched surface. Hand exposure was monitored using hand washes, although relative hand size among subjects might have given some insight into the magnitude of exposure among MEs, it would not have been definitive to change how the unit exposures are being estimated or used in risk assessments.

Table 2b. HSRB Review and AEATF II Responses.		
HSRB Recommendation	**AEATF Responses**	**EPA Comments**
6. Address what will be done if the subject wants to drink/eat/take a break with respect to sample collection and making sure that residues are not lost; what will be done if the subject wants to wipe their face with their hand or forearm? How will this affect exposure?	As requested by EPA, the AEATF will clarify that the subjects will be allowed to handle and hold a beverage container. It will be made clear that if the subject needs to stop to eat during the monitoring event, a hand wash and face/neck wipe will be conducted first; however due to the relatively short monitoring periods it is unlikely this will occur. Subjects will be allowed to take breaks if they want to (this will be added to the [Informed Consent Form] ICFs). A chair covered with plastic will be provided as well as water and Gatorade/sports drink. Wiping sweat from one's forehead or scratching/rubbing one's face or other body parts are normal activities that occur while working and therefore such activities will not be prohibited; however, this type of activity will be noted in the observation records so that any unusually high residues might be explained.	For the bucket scenario, "Most subjects worked continuously for the monitoring period; a few took breaks at their discretion." MEs 4, 8, and 12 took breaks. For the sink scenario, *"Ten of the 18 subjects worked continuously for the monitoring period, while the other eight took one or more breaks at their discretion. As kitchen workers are normally allowed to drink from containers with lids, subjects were allowed to drink the provided bottles of Gatorade or water while they worked and/or during their breaks, and most did."* (AEATF 2021, page 66) For the COP scenario, "Subjects were allowed to drink the provided bottles of Gatorade or water while they sat at the table during the wash and sanitizing cycles." (AEATF 2021, page 72) No observations of noteworthy activities during breaks were reported.

1.3.2 Protocol Amendments

AEATF (2021) (page 86) lists 4 protocol amendments. The amendments included (1) increased the compensation to the subjects in 2 of the 3 scenarios (approved by institutional review board (IRB)); (2) made changes to heat index cutoff for stop work to be consistent with SOP AEATF II-11B.1 (approved by IRB); (3) increased the compensation to the 3rd (and final) scenario (approved by IRB); and (4) *"corrected the reporting procedures for sending protocol deviations to the IRB to harmonize with the IRB requirements"* (AEATF 2021, page 86) (approved by IRB).

1.3.3 Protocol, Method, and SOP Deviations

Two laboratory, 17 protocol, and four standard operating procedure (SOP) deviations were noted in the study (study report pages 86 and 88). Examples of the reported deviations include different size buckets for the wipe scenarios were used (i.e., 6 and 10 qt buckets instead of 3 and 6 qt buckets); direction of airflow in relationship to subjects wiping was not recorded because subjects were constantly changing directions; airflow measurements for the COP scenario were not taken since there was no HVAC system and vents to outside were shut; anti foam agent was needed for COP; LOQ for face/neck wipes and forearms was increased because of recovery issues and background interferences in blank samples during method development; inhalation samples were analyzed for both C14-ADBAC (as planned) and DDAC because of background levels found in blank OSHA Versatile Sampler (OVS) tubes; the 3-compartment sink sites ended up with one less subject at one site and one extra subject at another; etc. For a detailed description of each of the 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. Although switching the active ingredient appears to be a major deviation, the active ingredient included (i.e., DDAC) was already part of the pesticide formulation being monitored and was assessed during the protocol review by EPA and the HSRB (and has existing analytical methods as it has been used by the HSRB in previous studies).

1.4 Material & Methods

The following is a summary of the key field aspects of the study.

- *Study Location:* The IDS study was conducted indoors at three sites in Orlando, FL for the bucket & rag/sponge and 3-compartment sink scenarios. Each of the two scenarios were monitored in the kitchens/banquet halls of two churches and an Elks Lodge to increase the variability in the sink sizes and variety of the room layouts. For the COP scenario, the demonstration room in a COP tank manufacturing facility in Madison, WI was used for the monitoring. Test site schematics and photos of the site/rooms are in Appendix C starting on page 330 of the study report.
- *Substance Tested:* The product applied and monitored in the study was the Oasis® 146 Multi-Quat Sanitizer, EPA Reg. No. 1677-198. The two test substances in Oasis® 146, used in the study, were alkyl (C14, 50%; C12, 40%; C16, 10%) dimethyl benzyl ammonium chloride (known as ADBAC) and didecyl dimethyl ammonium chloride (known as DDAC). *"The specific quaternary ammonium analog that was analyzed in all matrices is the C14-ADBAC (CAS Number 139-08-2) which makes up 50% of total ADBAC in Oasis 146. In addition, because high levels of background C14- ADBAC were found in new air-sampling tubes during the analysis of the study samples, DDAC residues, along with C14-ADBAC residues, were quantified in the OVS air-sampling tubes generated during the field phase."* (AEATF 2021, page 24)
- *Test System:* The study was designed to monitor exposures to subjects cleaning (i.e., sanitizing) equipment and surfaces within the three IDS scenarios while varying concentrations of the a.i.(s) and volumes of treatment solutions applied. Thus, the total amount of active ingredient handled (AaiH) was also varied. The test systems for each of the three IDS scenarios were setup as follows:

- o **Bucket & rag/sponge**: Subjects wiped horizontal and vertical surfaces (e.g., countertops, refrigerators, tables, etc) in the kitchens and banquet halls at the 3 sites discussed above. Specifics of the sites and equipment are as follows:
  - Site 1 - Kitchen ~16 ft x ~27 ft; banquet hall 64 ft x ~61 f with round and rectangular tables and plastic chairs to wipe
  - Site 2 - Kitchen 15 ft x 24 feet; banquet hall 69 ft x ~71 f with rectangular tables and plastic chairs to wipe
  - Site 3 - Kitchen ~69 ft x ~20 ft; banquet hall 50 ft x 93 ft; banquet hall with a serving buffet/salad bar and rectangular and round tables and plastic chairs to wipe
  - Subjects were also given their choices of cleaning implements to use from the following list of buckets and rag/sponges:
    - 6-quart red sanitizing Kleen-Pail (WebstaurantStore)
    - 10-quart red sanitizing Kleen-Pail (WebstaurantStore)
    - 3-gallon plastic blue pail with a spout (Home Depot)
    - 11-quart grey bucket made by Design (Target)
    - 16 x 19-inch 100% cotton bar towels (white and gold stripe)
    - 14 x 18-inch microfiber bar cleaning towels (white)
    - 11.5 x 24-inch Chix food service wipers (pink)
    - 3M C31 jumbo sponge (yellow)
    - 8.25 x 4.25-inch extra-large sponge (yellow)
    - Premiere pads, large cellulose commercial cleaning sponge (yellow)
- o **3-compartment sink**: Subjects washed (i.e., sanitized) kitchen ware at the same three sites used and described above for the bucket & rag/sponge scenario. Each of the three sinks had capacities of 22.4, 20.8, and 34.3 gallons at Sites 1, 2, and 3, respectively. Subjects filled each sink to the level they would normally fill it to. "*A variety of used and new cookware and bakeware was purchased for this study from a commercial kitchen supply store. A total of 128 items such as mixing bowls, cookie sheets, round cake pans, cupcake pans, frying pans, spatulas, ladles, gravy boats, loaf pans, pizza rounds, pots and pans were purchased.*" (page 35) "*On each day of monitoring and prior to each ME, items were soiled by smearing hot oatmeal over the surfaces with gloved hands to mimic soiled cookware that would be washed in a restaurant or other food service establishment. This was done by researchers prior to the start of the ME by boiling water, adding oatmeal (Quaker Oats, Quick 1 Minute), and letting the mixture thicken for about 3 to 4 minutes before applying it to the items.*" (AEATF 2021, page 35)

  Subjects were provided the following sponges/scouring pads to choose from:
    - 3M 74CC Scotch Brite medium duty scrub sponge (yellow and green, 6.125 x 3.625 inches)
    - Scotch Brite non-scratch scrub sponge (blue, 4.4 x 2.5 inches)
    - Scotch Brite #96 general purpose scouring pad (green, cut in half to 6 x 4.5 inches)

o **COP:** Subjects were provided various food processing-type equipment to clean (i.e., sanitize) in stainless steel COP tanks that were setup in the demonstration room discussed at the site location above. The room was 26 ft x 44 ft and included floor drains to drain the tanks. The HVAC system was not operating and the doors were closed, thus there was no air flow during the monitoring. The COP tank volumes were 95, 185, and 275 gallons and each tank included jets. The tanks were roughly 2 ft deep, roughly 2 ft wide, and their lengths varied from roughly 4, 6, and 10 ft and roughly 4 ft off the ground. (AEATF 2021, pages 42 and 43)

Figures 1 - 4 below illustrate the test systems, including equipment types and cleaning (sanitizing procedures).

Figure 1. Selection of bucket & rag/sponges.

Figure 2. Wringing out a rag/sponge.

Figure 3. Researcher adding sanitizing product to 3-compartment sink.

Figure 4. Subject sanitizing kitchen equipment/utensils.

Figure 5. Subject removing sanitized equipment/parts from COP tank.

- *Sample Size:* The study consisted of 18 monitoring events (ME) in each of the three IDS scenarios. Each ME is a different subject (i.e., different person/individual, no repeat subjects between IDS scenarios). The 54 MEs in this study generated a total of ~1,700 samples of individual dosimeters and QA/QC samples.

- *Duration:* The sampling times for the bucket & rag/sponge scenario included half of the subjects being monitored for 20 minutes and half for 60 minutes (AEATF 2021, Table 15 page 107). The duration of the monitoring for the 3-compartment sink scenario was evenly split between 1 hour and 2 hours (AEATF 2021, Table 6 page 98). The COP monitoring duration was also evenly split between 1 and 2 hours (since the COP tank was either run once or run twice) but the times were more varied (i.e., 66 to 75 minutes and 126 to 153 minutes as reported in AEATF (2021) Table 24, page 116). A summary of the individual ME start/stop sampling times is also reported in the study report alongside the durations.

- *Concentration of Active Ingredient (ppm):* Typically, the amount of active ingredient (AaiH) is used to normalize the inhalation and dermal exposures to calculate unit exposure normalized by the pounds of a.i. handled. The protocol for this IDS study had planned to

normalize the exposures by the concentration (ppm ai) because workers are exposed while immersing their hands into buckets, sinks, and tanks rather than using a define amount of treatment solution. The concentrations of the two a.i.s used for the three IDS scenarios are reported below.

IDS Scenario	Average Measured C14-ADBAC Concentration (ppm)	Average Measured DDAC Concentration (ppm)
Bucket & Rag/Sponge	88.7	92.3
	171	185
	331	420
3-Compartment Sink	20	22.7
	124	146
	198	231
COP Tank	19.4	26.7
	123	143
	192	228

- **Surface Area Wiped and Equipment Cleaned/Handled:** For the bucket scenario, the subjects wiped surfaces *"...such ... as countertops, backsplashes, refrigerators, ice makers, stoves, tables, and chairs. Each surface to be wiped in the bucket and rag/sponge scenario was identified and measured beforehand."* (AEATF 2021, page 39). The surfaces wiped for the MEs in the 20 minute duration group ranged from 107 to 846 ft^2. In the 60 minute duration group, the surface area wiped ranged from 569 to 1,635 ft^2 (AEATF 2021, page 107). For the sink scenario, *"...a total of 128 items such as mixing bowls, cookie sheets, round cake pans, cupcake pans, frying pans, spatulas, ladles, gravy boats, loaf pans, pizza rounds, pots and pans were purchased."* (AEATF 2021, page 35). The MEs in this scenario were grouped in either the 1- or 2-hour monitoring timeframes. The 9 MEs in the 1-hour group cleaned 31, 40, 40, 46, 47, 58, 60, 66, and 77 items while the 9 MEs in the 2-hour group cleaned "not reported", 32, 38, 78, 114, 115, 122, 128, and 218 items. *"Because subjects cleaned at different rates and to ensure that subjects met a minimum time period for this work activity, the ME ended when the target monitoring duration was reached, rather than basing it on cleaning a set number of items. In two cases, subjects cleaned at a faster than expected rate and were told to reclean their items so that they worked for the target time. The actual number of items cleaned was recorded for each ME to give an idea of the work efficiency."* (AEATF 2021, page 35). For the COP scenario, the food processing-type of equipment cleaned (equipment was placed in a choice of 5 different size wire baskets by the subjects for cleaning in the COP tanks) included: 4 valves, 14 miscellaneous fittings, 22 miscellaneous clamps, 3 end caps (2 inches diameter), 28 gaskets (rubber, 2-3 inches diameter), 5 pipes (14-24 inches long), 1 long pipe (3 feet long), and 3 hoses (2 to 4 feet long).

- **Cleaning (Sanitizing) Procedures**: For all three of the IDS scenarios, researchers added the a.i. to the treatment solution, not the subjects (mixer/loader exposure was monitored in previous AEATF II studies).

For the bucket scenario, the subjects were *"...shown the selection of buckets, rags, and sponges and asked to pick the one(s) he/she wanted to use. It was explained to the subject that he/she could use more than one rag or sponge and that if the water in the bucket got too dirty, they could get a fresh bucket of sanitizing solution. ... Most subjects worked continuously for the monitoring period; a few took breaks at their discretion. Most subjects placed their bucket either on the floor and bent over to immerse the rag/sponge into the bucket and wring it out or they placed the bucket on a table or chair where they could access it without bending over. They would pick up and move the bucket as they moved from table to table in the banquet hall and to various places in the kitchen. ... If the subject finished wiping all the designated surfaces in both rooms, but had not met the target activity duration (either 20 or 60 minutes), the subject was brought back to the first room and told to re-wipe the same surfaces. ... The last activities done by the subjects was to wring out the rag/sponge and pour the used solution down the sink drain."* (AEATF 2021, page 41-42).

For the sink scenario, the subjects were *"...shown the sink, drying racks, and soiled cookware and then shown the selection of sponges/souring pads and asked to pick the one(s) he/she wanted to use. It was explained to the subject that he/she needed to fill each sink with water to a typical depth (at a minimum half full) and add detergent to the first sink as they normally would. ... Subjects filled the sinks with water to the desired depths, adding as much detergent as they wanted to the wash sink, then stepped aside so that the observer could measure the depth and temperature of each sink. ... Workers placed the dirty items into the wash sink and then moved them to the rinse sink, and then to the sanitizing sink after which the items were placed on a drying rack or surface to air dry. This process was repeated until the target work time was reached. Splashing onto the subjects, especially in the torso area, was noted with most subjects. The last activity done by the subjects was to drain the sinks by removing the stoppers by inserting their hand into each sink to pull out the plug; subjects were allowed to do this in any order they wanted."* (AEATF 2021, pages 37-38).

For the COP scenario, the subjects placed *"...the various pieces of equipment into the empty COP tank, placing the smaller parts into one or more wire baskets. Next the subject turned on the tank water valve and filled the tank for the simulated wash cycle. Once the water reached the desired level, the subject turned off the water and turned on the circulation which operated the jet agitation. At this point, the subject removed his safety glasses and gloves, placed them on the wire rack, and sat at a table placed on the far side of the test room. After allowing the water to circulate for approximately 30 minutes for the simulated wash cycle, the subject put his safety gear back on and drained the tank by flipping a lever on the bottom of the tank which released water out of the bottom of the tank onto the floor and down the floor drain. Once the water had drained, the subject conducted a simulated rinse cycle by spraying the items in the tank with water from a hose. Next the subject filled the tank with water for the sanitization step. When the water level reached the desired height, the subject turned off the water valve and stepped aside so that a researcher could add the defoamer and Oasis 146 to the tank. Once this was complete, the subject turned on the circulation for a few minutes to allow the solution to mix thoroughly before turning it off and stepping back again so that*

researchers could collect the aliquots. Once this was done, the subject turned the circulation back on, checked to see if everything was working correctly, and then removed his/her PPE, and sat down at the table again. The subject was required to put his/her PPE back on and to walk to the tank to check it one time during the approximately 15-minute sanitizing cycle. Once the time was up, the subject put the PPE back on and drained the sanitizing solution from the tank by opening the valve at the bottom of the tank which released the solution onto the floor and down the drain. Once the tank had been drained, the subject picked up the parts from the tank and placed them on the wire racks to air dry. This included removing all the small parts from the wire baskets. Since the parts were wet, it was not uncommon to see diluted sanitizing solution drip from the parts as they were being moved. Once all the parts had been placed on the rack, the work activity was completed. For subjects doing one cleaning/sanitizing cycle, at this point the monitoring event was complete; for those who had to conduct two cleaning/sanitizing cycles, the entire process was repeated with a second set of clean, dry equipment parts. Subjects doing a second cycle rinsed the COP tank with a hose after removing the first set of parts or they added water to the empty tank using the valve at the bottom on the tank and then drained it. The method used to rinse the tank between cycles was up to the subject." (AEATF 2021, pages 45-46).

- ***Environmental Conditions*:** Environmental conditions (humidity and indoor temperatures) are reported for each individual ME on page 78 of the study report. Indoor temperatures for the bucket scenario ranged from 65.4 to 79.6 F and the humidity indoors ranged from 24.1 to 77.8% (AEATF 2021, page 42); for the sink scenario indoor temperatures ranged from 64.1 to 85 ° F and the humidity indoors ranged from 30.9 to 80.2% (AEATF 2021, page 38); and for the COP scenario indoor temperatures ranged from 69.7 to 76.8 F and the humidity indoors ranged from 28.9 to 59.7%. The sites for the bucket and sink scenarios had air flow measurements taken which showed in the kitchens 12.7, 11.7, and 15.2 air changes per hour (ACH), at sites 1, 2, and 3 respectively. For the bucket scenario, the banquet halls had air flows of 3.6, 7.8, and 10.4 ACH, at sites 1, 2, and 3, respectively. The air flow direction relative to the subjects at the sinks indicated no significant sustained air flow based on anemometers and visual observations. The air flow direction relative to the subjects for the bucket scenario was not meaningful as the subjects moved around the room as they wiped/cleaned. For the COP scenario, there was no air flow as there was no vents/open doors.

2.0 Results

2.1 QA/QC

Controls. The non-fortified method validation control samples (blanks) indicated contamination in the OVS tubes. The study report's Table 30 (AEATF 2021, page 122) shows for C14-ADBAC that all 8 of the OVS tube controls had detectable residues ranging from 10.3 to 47.4 ng/tube. Because of the background contamination, and the need for low LOQ for the IDS scenario that would potentially lead to low inhalation exposures, the AEATF II decided to include OVS sampling of DDAC residues (and only the inhalation results for DDAC are reported herein). For DDAC, 6 of the 8 controls for the OVS tubes also had detectable residues, but at

much lower levels, ranging from 0.08 to 3.4 ng/tube. Finally, the outer dosimeters also showed background interference with C14-ADBAC and the AEATF II chose to increase the LOQ for this matrix from 3 to 10 µg/sample.

The results of the non-fortified field and laboratory control samples (blanks) were as follows: All the C14-ADBAC and DDAC field control matrix samples were less than the limit of quantification (LOQ) (AEATF 2021, page 75); the C14-ADBAC laboratory control matrix samples were also all less than the LOQ (AEATF 2021, page 74). One OVS tube DDAC non-fortified laboratory control sample had detectable residues of DDAC (12.8 ng compared to the LOQ of 12 ng).

The C14-ADBAC LOQs (LODs) for the various matrices were: air sampling OVS tubes 100 (30) ng/sample, neck/face wipe 0.25 (0.075) µg/sample, forearm wipe 1 (0.3) µg/sample, outer WBD sections 10 (3) µg/section, inner WBD sections 3 (0.9) µg/section, and hand wash 1 (0.3) µg/sample. The DDAC OVS LOQ (LOD) was 12 (3.6) ng/tube (page 58).

Method Validation. In this IDS study, the AEATF II noted that since the analytical methods for C14-ADBAC in the same sampling matrices have been previously developed and used in many other AEATF II exposure studies, that the method validation was conducted under non-GLP (good laboratory practices) (AEATF 2021, pages 73-74). Each of the sampling matrices were fortified using triplicate samples at a low-, mid- and high-levels (as opposed to the typical 7 samples per fortification level) (AEATF 2021, page 58). The results of the method validation for C14-ADBAC ranged from 83.0±2.4% (mean ± standard deviation) for the low-level fortification of the inner dosimeters to 105±6.7% for the high-level fortification of the outer dosimeters (AEATF 2021, Table 29 page 121).

As discussed above, the OVS tubes showed background levels of C14-ADBAC that would potentially interfere with the expected low inhalation exposures in the IDS scenarios, and therefore, the AEATF II also included the monitoring of DDAC specifically for the OVS tubes. The results of the method validation for DDAC in the OVS tubes at the fortifications of 10, 500, and 4,000 ng/tube were 73.7%, 91.4%, and 88.4%, respectively (AEATF 2021, Table 30 page 122).

Laboratory Recoveries. The concurrent laboratory recovery samples for C14-ADBAC and DDAC were fortified at levels expected in the exposure study. Typically, the field recoveries are used to correct the actual field monitoring samples, however, the field recoveries in this study were all greater than 100% and therefore the laboratory recoveries were used to correct the field samples (if the laboratory recoveries <100%). *"The number of replicates per fortification level within a matrix ranged from 1 to 20. The overall average recoveries across fortification levels for each matrix ranged from 90.8% (face/neck wipes) to 105% (OVS tubes, C14-ADBAC) … the concurrent fortification recoveries within each analytical set were averaged; if that average was less than 100%, the subject samples (and field fortified samples if included in the analytical set) within that set were adjusted by that average recovery."* (AEATF 2021, page 75) The results of the laboratory recoveries are provided in AEATF (2021) Tables 31 to 37, pages 123-129.

Field Recoveries. The field recovery samples were transported, stored, and analyzed with the corresponding field (dosimeter) samples. Results of the field recoveries for C14-ADBAC are summarized in AEATF (2021) on pages 75-76, Tables 38-41. Since the field recoveries were >100%, they were not used to correct the actual field exposure samples. The field recoveries for C14-ADBAC averaged 105±7.66% (n=18) for the hand wash, 103±4.81% (n=18) for the face/neck wipes, 101±9.56% (n=18) for the inner dosimeters, and 116±14.7% (n=9) for the OVS tubes.

"*Unlike the solutions used to fortify other matrices, the field fortification solutions prepared by the analytical lab to fortify the OVS tubes were made using C14-ADBAC reference standard, not Oasis 146. For this reason, the field fortified OVS tubes could not be used to determine DDAC recovery. However, DDAC has been used as the test substance in several AEATF II studies including AEA02 (Spray and Wipe Study, MRID No. 48375601), AEA03 (Mop Study, MRID No. 48210201), and AEA05 (Pour Liquid Study, MRID No. 48917401). The stability of DDAC in OVS tubes under field and frozen conditions is well documented.*" EPA notes the average field recoveries in the AEATF II's liquid pour study for all matrices for both C14 ADBAC and DDAC were roughly 90 to 100%. "*To support the longer time that the OVS tubes were in frozen storage during this study, a new DDAC freezer storage stability study in OVS tubes was conducted…Tubes were spiked at 123 ng DDAC/tube and 4,930 ng DDAC/tube with Oasis 146 and analyzed on day 0 and at 8 months after fortification. The study showed no loss of DDAC through 8 months in frozen storage (recoveries ranging from 94.3 to 117%)…*" (AEATF 2021, page 76-77).

2.2   Calculating Unit Exposures

Dermal Unit Exposure. As discussed in the protocol, dermal exposure was 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 for the COP scenario and short-sleeved shirt and long pants for the other two IDS scenarios as the subject's arms were dipped into the buckets and sinks). The normal work clothing worn over the inner WBDs were also analyzed and reported as outer dosimeters. Dermal exposures monitoring techniques also included hand washes, face/neck wipes, and forearm wipes for the bucket and sink scenarios (since those techniques included dipping subject's arms into the treatment solution). The inner and outer WBDs were sectioned and analyzed by body part (i.e., upper and lower arms, front and rear torso, and upper and lower legs). Samples were adjusted, as appropriate, according to recovery results from laboratory fortification samples (i.e., all field recovery results were >100% so laboratory recovery results were used to correct the actual exposure/field samples where laboratory recoveries were <100%).

Hand wash removal efficiency studies were previously conducted by the AEATF II and reviewed by EPA and used in other AEATF II scenarios (e.g., USEPA 2010, USEPA 2012). These same two studies were used in this study to correct hand and face/neck samples. "*A study to measure the removal efficiency of DDAC (CAS 7173-51-5) from skin using a washing technique showed an average recovery of 90.3% DDAC (Boatwright 2007). A similar study was conducted with the structurally related compound alkyl dimethyl benzyl ammonium as the saccharinate salt (ADBAS; CAS 39387-42-3) using a wipe technique rather than a wash*

technique resulting in an average recovery of 89% (Boatwright, 2008). Based on these studies, a 90% dermal removal efficiency correction factor is used to adjust the C14-ADBAC hand-wash residues while a 89% correction factor is used to adjust the face/neck wipe residues." (AEATF 2021, pages 62-63)

One final adjustment factor was used for the face/neck samples to correct for the area of the face covered by the safety glasses. A correction factor of 1.1 (as per AEATF SOP 9K.0, Section 2.2.1) was used to correct the face/neck residue values (AEATF 2021, page 62). Dermal samples were not adjusted for background levels of C14-ADBAC.

The analyses of residues on the dosimeters worn by each individual subject allow for the estimation of exposure for various clothing configurations from long- to short-sleeved shirts (long-sleeved shirts not available for bucket and sink scenarios because the subjects lower arms were monitored by forearm wipes rather than the WBD) and long- to short-pants. The results of these various clothing configurations are available in Appendix A. For brevity and usefulness (i.e., the majority of the dermal exposure is to the hands while the other body parts round-out when values are reported to 3-significant figures) only the following clothing configurations are reported in the main body of this review:

> (1) "Long-Short Dermal" = long pants, short-sleeved shirt, and no gloves for bucket & rag/sponge and 3-compartment sink scenarios; and
> (2) "Long-Long Dermal" = long pants, long-sleeved shirt, and gloves for the COP scenario.

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, short-sleeved shirts (Long-Short) plus face/neck wash, forearm wipes, and hand wash for the bucket and sink scenarios:

- 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, long-sleeved shirts (Long-Long) plus face/neck wash and hand wash for the COP scenario:
- inner lower arms,
- inner upper arms,
- inner front and inner rear torso, and
- inner lower and inner upper legs.

Dermal unit exposures (mg a.i.) are normalized by the product of the concentration of the treatment solution (ppm a.i.) and the duration of exposure (hour) to yield units of mg/(ppm * hr). The dermal unit exposure (mg/(ppm*hr)) is calculated by dividing the summed total exposure by the measured ppm a.i. concentration*measured exposure duration.

Inhalation Exposure. Inhalation exposure was measured using a single personal air sampling pump. The inhalation sampling consisted of *"...a low-volume, SKC personal air-sampling pump was attached to the subject's belt or waistband. This was connected to an OSHA Versatile Sampler (OVS) air-sampling tube containing a glass filter and XAD-2 sorbent (SKC catalog number 226-30-16). The OVS tube is designed to capture both particulates or aerosols and vapor to provide total inhalable residue. The tube was attached to the subject's collar in the subjects' breathing zone... The tube intake was positioned downward to simulate the nasal passage of the subject. The airflow of each pump was calibrated to a target airflow of approximately 2.0 liters per minute prior to use and documented."* (AEATF 2021, page 48). Background levels of DDAC in the OVS tubes were low and thus the background levels were not used to adjust any of the samples (AEATF 2021, page 74). Based on the high background levels for C14-ADBAC in the OVS sampling tubes described above, only the DDAC sampling for inhalation exposures are reported herein.

Inhalation unit exposures for the DDAC OVS sampling tubes (measuring total inhaled residues) are provided using the two following methods:

(1) Air concentration expressed as an 8-hour time weighted average (TWA) and normalized by ppm and duration (i.e., $(mg/m^3)/(ppm \times minutes)$) is calculated as the air concentration $((mg/m^3) / (ppm\ a.i. \times minutes)) *$ sampling duration (hours/day) / 8 (hours / day).

(2) Inhalation exposure (mg/ppm a.i. x minutes) or dose is calculated as the air concentration $((mg/m^3) / (ppm\ a.i. \times minutes) *$ breathing rate (1 m³/hour) * sampling duration (hours/day).

2.3   Dermal and Inhalation Exposure Results

Results. A summary of the individual and mean dermal and inhalation results from the three IDS scenarios are presented in Table 4. 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 Table 1. The various clothing configurations for the three IDS scenarios are provided. 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 subject along with empirical and lognormal simple random sampling method statistical summaries.

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

- Empirical simple random sampling model; and
- Lognormal simple random sampling model.

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 Table 1 above). The estimates using substitution of half the LOQ for non-detected values below the LOQ or below the LOD are recommended. For a detailed discussion of the lognormal simple random sampling model calculations and results the reader is referred to

Appendix A, which includes quantile plots to compare normal and log-normal distributions for the unit exposures.

Appendix A also provides various alternative statistical models for estimating the exposure from the ppm x duration instead of simply using the unit exposures multiplied by the ppm x duration. The main model is a linear regression model for log exposure against the log of the ppm x duration. Also included is the HSRB-recommended quadratic regression model regressing log exposure against log (ppm x duration) and log (ppm x duration) squared. Quantile and regression plots are used to evaluate the linear regression model. Additional models considered in Appendix A are log-log-logistic, three-parameter logistic, and gamma regression models recommended by the HSRB. Of these alternative regression models, the best-fitting models for most exposure routes are either the linear or gamma models, based on the AIC statistical criterion. Since the gamma model's AIC scores were not very different from the linear models and the linear models are much easier to implement, the linear models were selected.

Impact of Non-detects. All the hand sampling results for the three IDS scenarios had detectable residues. All the forearm sampling results for the bucket and sink scenarios had detectable residues. The outer lower arm for the WBD sampling had detectable residues for 16 of the 18 MEs for the COP scenario. The neck/face was detectable for most of the MEs (44 of 54 MEs). The rest of the individual WBD for inner sectioned body parts were mostly below the limit of quantification (LOQ), while most of the outer dosimeters had detectable residues. Most of the OVS tubes had detectable residues where only 6, 4, and 0 of the samples were below the LOQ for the bucket, sink, and COP, respectively. Both dermal and inhalation exposure results were estimated using various methods of handling non-detects, including ½ the LOQ, substituting of the non-detects with the midpoint of lowest and highest value, maximum value, minimum value, and the maximum likelihood method for censored data. Because the dermal exposures are dominated by the hand exposures, the non-detects had no impact on the dermal unit exposures for the bucket and sink scenarios and a very minimal impact on the COP scenario. Most inhalation exposures had detectable residues and the handling of the non-detects had only slight impact on the results, except in some cases using the maximum or minimum substitution method. The alternative estimates for handling non-detects (i.e., substituting the maximum and minimum LOQ values and censored data maximum likelihood (MLE)) are provided in Appendix A (bucket scenario Table AB10 page 14; sink scenario Table AS10 page 56; COP scenario Table AC10 page 92).

Table 4a. Bucket & Rag/Sponge: Summary of Dermal and Inhalation Unit Exposure Estimates.						
Monitoring Event (ME)	ADBAC Conc (ppm)	DDAC Conc (ppm)	Duration (Min)	Dermal Unit exposure (mg/(ppm ADBAC * min))		Inhalation 8 Hour TWA Unit Exposure $((mg/m^3)/(ppm\ DDAC * min))$
				Long-Short	Hands	
1	87.28	92.16	22	0.00538	0.00537	3.11E-09
2	87.28	92.16	60	0.00124	0.00123	1.17E-09
3	87.28	92.16	20	0.00116	0.00114	7.61E-09
4	88.45	92.49	60	0.00180	0.00179	4.86E-09
5	89.23	92.03	21	0.00248	0.00248	3.21E-09
6	89.23	92.03	61	0.00050	0.00049	3.35E-09
7	175.06	187.32	21	0.00143	0.00143	1.64E-09
8	175.06	187.32	61	0.00281	0.00281	3.46E-09
9	173.40	187.06	22	0.00156	0.00153	3.24E-08
10	175.06	187.32	60	0.00101	0.00101	2.54E-09
11	164.11	181.61	20	0.00120	0.00120	1.71E-09
12	164.11	181.61	61	0.00124	0.00124	1.78E-09
13	331.05	435.46	20	0.00221	0.00220	1.92E-09
14	331.05	435.46	61	0.00076	0.00076	9.25E-10
15	340.97	436.55	20	0.00134	0.00133	4.57E-09
16	340.97	436.55	61	0.00131	0.00129	5.18E-09
17	320.94	388.95	20	0.00050	0.00049	8.00E-10
18	320.94	388.95	61	0.00095	0.00094	2.23E-09
Empirical Mean	196.75	232.62	40.67	0.00161	0.00160	4.58E-09
Empirical SD	103.87	142.69	20.59	0.00113	0.00113	7.15E-09
Lognormal Simple Random Sample Mean	199.45	236.41	41.29	0.00160	0.00159	4.12E-09
Lognormal Simple Random Sample SD	120.12	167.67	24.81	0.00101	0.00102	4.29E-09

Let X_i be the ith 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 $= S_X = \sqrt{\sum_{i=1}^{18} (X_i - \overline{X})^2 / 17}$. 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 $S_Y = \sqrt{\sum_{i=1}^{18} (Y_i - \overline{Y})^2 / 17}$.

Lognormal Simple Random Sample SD = Estimated population standard deviation of X = Estimate of

$\exp(\mu + \frac{1}{2}\sigma^2) \sqrt{\exp(\sigma^2) - 1} = \exp(\overline{Y} + \frac{1}{2} S_Y^2) \sqrt{\exp(S_Y^2) - 1}$.

Monitoring Event (ME)	ADBAC Conc (ppm)	DDAC Conc (ppm)	Duration (min)	Dermal Unit exposure (mg/(ppm ADBAC * min))		Inhalation 8 Hour TWA Unit Exposure ((mg/m^3)/(ppm DDAC * min))
				Long-Short	Hands	
1	19.75	24.15	64	0.000562	0.000488	1.09E-08
2	19.78	21.69	120	0.000308	0.000202	1.37E-08
3	20.69	24.75	60	0.000645	0.000622	2.88E-08
4	20.82	23.67	121	0.000395	0.000370	2.09E-08
5	19.14	20.24	61	0.000638	0.000538	1.53E-08
6	19.88	21.95	121	0.000969	0.000910	1.48E-08
7	125.26	148.61	60	0.000557	0.000544	7.07E-10
8	126.13	140.99	120	0.000237	0.000157	3.76E-10
9	125.15	144.13	62	0.001437	0.001339	8.06E-09
10	129.72	151.68	120	0.000428	0.000423	2.13E-09
11	121.10	141.50	60	0.000950	0.000933	7.35E-10
12	115.01	148.80	120	0.000506	0.000407	1.13E-09
13	202.72	237.72	62	0.000756	0.000725	1.56E-09
14	200.88	246.79	120	0.000238	0.000228	7.07E-10
15	205.47	244.22	60	0.000453	0.000411	1.41E-09
16	183.28	202.49	123	0.000579	0.000520	1.14E-09
17	196.25	229.63	62	0.000720	0.000680	4.40E-10
18	200.55	222.65	121	0.000668	0.000641	1.02E-09
Empirical Mean	113.98	133.09	90.94	0.000614	0.000563	6.88E-09
Empirical SD	75.36	88.30	30.61	0.000293	0.000290	8.59E-09
Lognormal Simple Random Sample Mean	132.34	155.68	91.35	0.000619	0.000574	8.09E-09
Lognormal Simple Random Sample SD	178.46	214.95	32.94	0.000308	0.000337	2.27E-08

Table 4b. 3-Compartment Sink: Summary of Dermal and Inhalation Unit Exposure Estimates.

Let X_i be the ith 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 $= S_X = \sqrt{\sum_{i=1}^{18} (X_i - \overline{X})^2 / 17}$. 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 $S_Y = \sqrt{\sum_{i=1}^{18} (Y_i - \overline{Y})^2 / 17}$.

Lognormal Simple Random Sample SD = Estimated population standard deviation of X = Estimate of

$\exp(\mu + \frac{1}{2} \sigma^2) \sqrt{\exp(\sigma^2) - 1} = \exp(\overline{Y} + \frac{1}{2} S_Y^2) \sqrt{\exp(S_Y^2) - 1}$.

Monitoring Event (ME)	ADBAC Conc (ppm)	DDAC Conc (ppm)	Duration (Min)	Dermal Unit exposure (mg/(ppm ADBAC * min))		Inhalation 8 Hour TWA Unit Exposure ((mg/m^3)/(ppm DDAC * min))
				Long-Long	Hands (gloves)	
1	18.13	23.55	71	5.58E-05	5.22E-05	2.05E-07
2	19.76	26.95	133	2.92E-05	2.58E-05	5.98E-08
3	19.31	26.40	67	1.28E-05	9.23E-06	7.82E-08
4	20.17	27.85	139	1.14E-05	9.24E-06	6.94E-08
5	19.65	30.40	72	2.36E-05	1.01E-05	9.67E-07
6	19.15	25.35	151	2.64E-05	2.19E-05	6.54E-07
7	119.69	145.76	66	5.31E-06	4.03E-06	1.39E-08
8	121.28	144.12	136	1.46E-06	6.16E-07	1.83E-08
9	127.49	135.61	69	1.14E-05	9.73E-06	3.89E-08
10	115.78	136.22	126	4.90E-06	2.21E-06	1.92E-08
11	129.49	148.26	75	4.22E-06	6.18E-07	7.00E-08
12	126.56	147.84	152	6.37E-06	5.08E-06	1.07E-07
13	191.43	229.78	68	1.57E-06	8.71E-07	2.02E-08
14	191.14	228.45	131	8.83E-07	5.52E-07	1.63E-08
15	190.96	228.05	73	1.53E-06	1.51E-06	8.88E-09
16	191.05	227.30	139	2.10E-06	1.80E-06	1.06E-08
17	193.18	230.64	73	4.88E-06	2.90E-06	5.14E-08
18	194.93	228.24	153	2.06E-06	2.98E-07	4.10E-08
Empirical Mean	111.62	132.82	105.22	1.14E-05	8.82E-06	1.36E-07
Empirical SD	73.14	85.24	36.48	1.42E-05	1.31E-05	2.56E-07
Lognormal Simple Random Sample Mean	130.16	150.07	105.69	1.22E-05	1.05E-05	1.19E-07
Lognormal Simple Random Sample SD	177.06	181.86	38.99	2.22E-05	2.99E-05	2.58E-07

Table 4c. Clean-out-of Place (COP): Summary of Dermal and Inhalation Unit Exposure Estimates.

Let X_i be the ith 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 $= S_X = \sqrt{\sum_{i=1}^{18} (X_i - \overline{X})^2 / 17}$. 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 $S_Y = \sqrt{\sum_{i=1}^{18} (Y_i - \overline{Y})^2 / 17}$.

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 IDS scenario meets 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 (starting page 15) 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"), normal and lognormal quantile plots of dermal and inhalation UEs are provided in Appendix A (bucket scenario Figures AB1 to AB14 for empirical quantile plots and Figures AB15 to AB21 for quantile plots for residuals starting on pages 19 and 30; sink scenario Figures AS1 to AS14 for empirical quantile plots and Figures AS15 to AS28 for quantile plots for residuals starting on pages 60 and 69; and COP scenario Figures AC1 to AC14 for empirical quantile plots and Figures AC15 to AC28 for quantile plots for residuals starting on pages 96 and 105) to illustrate that the lognormal distribution is a better fit than the normal distribution for the normalized exposure (albeit in some cases the difference between the normal and log-normal fit is small). Overall, 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 95th percentile of the maximum of the two ratios of the sample statistic to the parameter, after the parameter is replaced by its estimated value. The results of the long pants, short sleeved shirts, no gloves (Long-Short) for the Bucket and Sink scenarios and the long pants, long sleeved shirts, gloves (Long-Long) for the COP scenario, as well as the inhalation exposures for the OVS 8-hr TWA are presented below in Table 5 for the bucket scenario (Appendix A pages 16 to 18); Table 6 for the sink scenario (Appendix A pages 57 to 60); and Table 7 for the COP scenario (Appendix A pages 94 to 96). Appendix A also presents fRA values calculated using a non-parametric bootstrap approach, with generally similar results. The results indicate that for the dermal unit exposures under consideration, the IDS study meets the 3-fold relative accuracy objective for all but the 95% confidence limit for the COP scenario for the empirical simple random sampling model (i.e., P95s in Table 7 below). The inhalation unit exposures meet the 3-fold relative accuracy objective for all but the 95% confidence limit for all three of the IDS scenarios for the empirical simple random sampling model (i.e., P95s in Tables 5, 6, and 7).

Table 5: Results of Primary Benchmark Analysis for the Bucket & Rag/Sponge Scenario.

Statistic	Dermal Exposure (Long Short)			Inhalation Exposure (8-hr TWA)		
	Unit Exposure Estimate (mg/ppm x mins)	95% CI	fRA	Unit Exposure Estimate ((mg/m^3)/ (ppm x min))	95% CI	fRA
GM$_S$	0.0014	0.001 to 0.0018	1.3	2.85E-9	1.93E-9 to 4.28E-9	1.5
GSD$_S$	1.788	1.47 to 2.18	1.2	2.358	1.772 to 3.155	1.3

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"

Statistic	Unit Exposure Estimate (mg/ppm x mins)	95% CI	fRA	Unit Exposure Estimate ((mg/m^3)/ (ppm x min))	95% CI	fRA
AM$_S$	0.0016	0.0012 to 0.0021	1.3	4.578E-9	2.55E-9 to 6.583E-9	1.7
AM$_U$	0.0016	0.0012 to 0.0022	1.3	4.117E-9	2.617E-9 to 6.707E-9	1.6

AM$_S$ = average of 18 unit exposures
AM$_U$ = arithmetic mean based on GM$_S$ = GM$_S$*exp{0.5*(ln(GSD$_S$)^2}

Statistic	Unit Exposure Estimate (mg/ppm x mins)	95% CI	fRA	Unit Exposure Estimate ((mg/m^3)/ (ppm x min))	95% CI	fRA
P95$_S$	0.0054	0.0023 to 0.0077	2.2	3.235E-8	6.233E-9 to 3.691E-8	4.7
P95$_U$	0.0035	0.0023 to 0.0053	1.5	1.168E-8	6.278E-9 to 2.158E-8	1.9

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 3-Compartment Sink Scenario.

Statistic	Dermal Exposure (Long Short)			Inhalation Exposure (8-hr TWA)		
	Unit Exposure Estimate (mg/ppm x mins)	95% CI	fRA	Unit Exposure Estimate ((mg/m^3)/ (ppm x min))	95% CI	fRA
GM$_S$	0.00055	0.00045 to 0.00069	1.2	2.709E-9	1.383E-9 to 5.469E-9	2.0
GSD$_S$	1.60	1.37 to 1.88	1.2	4.388	2.683 to 7.249	1.6

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"

Statistic	Unit Exposure Estimate (mg/ppm x mins)	95% CI	fRA	Unit Exposure Estimate ((mg/m^3)/ (ppm x min))	95% CI	fRA
AM$_S$	0.00061	0.00049 to 0.00078	1.3	6.882E-9	2.836E-9 to 2.097E-8	2.7
AM$_U$	0.00062	0.00049 to 0.00078	1.3	8.086E-9	3.149E-9 to 2.401E-8	2.7

AM$_S$ = average of 18 unit exposures
AM$_U$ = arithmetic mean based on GM$_S$ = GM$_S$*exp{0.5*(ln(GSD$_S$)^2}

Statistic	Unit Exposure Estimate (mg/ppm x mins)	95% CI	fRA	Unit Exposure Estimate ((mg/m^3)/ (ppm x min))	95% CI	fRA
P95$_S$	0.00144	0.00085 to 0.00226	1.7	2.877E-8	1.044E-8 to 2.241E-7	5.8
P95$_U$	0.00120	0.00085 to 0.00168	1.4	3.085E-8	1.057E-8 to 8.886E-8	2.9

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 Clean-out-of-place (COP) Scenario.						
	Dermal Exposure (Long Short)			**Inhalation Exposure (8-hr TWA)**		
Statistic	**Unit Exposure Estimate (mg/ppm x mins)**	**95% CI**	**fRA**	**Unit Exposure Estimate ((mg/m^3)/ (ppm x min))**	**95% CI**	**fRA**
GM_S	5.91E-6	3.4E-6 to 1.05E-5	1.8	5.01E-8	2.75E-8 to 9.37E-8	1.9
GSD_S	3.342	2.24 to 5.03	1.5	3.737	2.41 to 5.85	1.6
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	1.14E-5	5.68E-6 to 2.54E-5	2.1	1.361E-7	4.97E-8 to 2.71E-7	2.5
AM_U	1.22E-5	6.06E-6 to 2.70E-5	2.1	1.194E-7	5.37E-8 to 2.94E-7	2.3
AM_S = average of 18 unit exposures AM_U = arithmetic mean based on GM_S = GM_S*exp{0.5*(ln(GSD_S)^2}						
$P95_S$	5.58E-5	1.78E-5 to 2.17E-4	3.5	9.672E-7	1.67E-7 to 2.57E-6	5.2
$P95_U$	4.30E-5	1.80E-5 to 1.02E-4	2.4	4.379E-7	1.69E-7 to 1.124E-6	2.6
$P95_S$ = 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 (more precisely, the expected value of the exposure) is a multiple of the concentration of the treatment solution x the exposure duration (ppm x minutes). 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 either the amount of active ingredient handled or in the case of the IDS scenarios the ppm x minutes. If the log-log-linear model has a slope of 1, then the arithmetic mean exposure will be a multiple of the ppm x minutes. The statistical test compares the slope of 1 with a slope of 0, where 0 corresponds to complete independence between exposure and the ppm x minutes.

To evaluate the relationship for this scenario EPA performed regression analysis of log(exposure) against log(ppm x minutes) 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 ppm x minutes but not proportionally, so that, for example, doubling the ppm x minutes 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 ppm x minutes but not proportionally. Note: the slope for the dermal (or inhalation) exposure measures the change in log mg dermal (or inhalation) exposure for each unit change in log ppm x minutes. A slope of 1 implies that the log of the unit exposure (mg/(ppm x minutes)) is equal to a constant plus a random error, so that the unit exposure has the same mean for any ppm x minutes, and thus the mg dermal (or inhalation) exposure is proportional to the ppm x minutes.

The resulting regression slopes and confidence intervals for the clothing scenarios and 8-hr TWA inhalation exposures to be used by EPA in our assessments are summarized in Table 8. A more detailed discussion and table of the slopes along with the other clothing scenarios is presented in Appendix A (for the Bucket scenario pages 27-29 and Table AB18, for the Sink scenario pages 68-69 and Table AS18, for the COP scenario pages 104-105 and Table AC18).

For the bucket scenario, the confidence intervals for the slope exclude 0 and include 1 for both dermal and the inhalation 8-hr TWA. Thus, the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was supported (more precisely, did not reject proportionality (a slope of one)). Therefore, the "unit exposure" approach for both the dermal and inhalation for the 8-hr TWA is a reasonable approximation.

For the sink scenario, the confidence intervals for the slope exclude 0 and include 1 for dermal. Thus, the assumption of independence was rejected and the assumption of log-log-linearity with slope 1 was supported (more precisely, did not reject proportionality (a slope of one)). Therefore, the "unit exposure" approach for the dermal is a reasonable approximation. However, for inhalation 8-hr TWA exposure the slope is negative and the confidence intervals include 0 but not 1, thus the assumption of independence was supported and the assumption of log-log-linearity with slope 1 was rejected. The results for inhalation exposure seem to be counterintuitive.

For the COP scenario, for both the dermal and inhalation 8-hr TWA exposure the confidence intervals include 0 but not 1, thus the assumption of independence was supported and the assumption of log-log-linearity with slope 1 was rejected. This suggests that the exposure does not depend on the normalizing factor.

A secondary objective for EPA is for meeting 80% power for detecting log-log-linearity with a slope of 1. This objective is met if the widths of the confidence intervals for the slopes are at most 1.4. This secondary objective was met for all scenarios and so the statistical (post-hoc) power is greater than 80%.

Table 8. 95 Percent Confidence Intervals for the Slope of Log Exposure (mg) versus Log ppm x minutes for Dermal and Inhalation Exposures.				
Scenario/Clothing	Slope	Confidence Interval	Confidence Interval Width	Appendix A
Bucket (Long-Short, no gloves)	0.711	0.348 – 1.074	0.726	Table AB18 Long Short Sub mid value
Sink (Long-Short, no gloves)	0.923	0.694 – 1.152	0.458	Table AS18 Long Short Sub mid value
COP (Long-Long, gloves)	0.038	-0.257 to 0.334	0.591	Table AC18 Long Sub mid value
Bucket Inhalation (8-hr TWA)	0.712	0.193 – 1.231	1.038	Table AB18 TWA Sub mid value
Sink Inhalation (8-hr TWA)	-0.174	-0.541 to 0.194	0.735	Table AS18 TWA Sub mid value

COP Inhalation (8-hr TWA)	0.102	-0.394 to 0.598	0.992	Table AC18 TWA Sub mid value

Figures 7 to 9 show the data and corresponding fitted regression models for the dermal exposure routes. The data points marked with the symbols "A" are the shorter durations with lower C14 ADBAC concentrations (i.e., 20-minutes for the bucket scenario and 1-hour for both the sink and COP scenarios) and "B" are the longer durations and higher C14 ADBAC concentrations (i.e., 1-hour for the bucket scenario and 2-hours for both the sink and COP scenarios). Appendix A also presents probability plots of the residuals from these fitted regression models (figures for specific quantile plots and page numbers in Appendix A are referenced above); these probability plots show that this simple log-log-linear regression model fits reasonably well except for the inhalation exposure for the COP scenario (Appendix A pages 107-108). Appendix A also includes the fitted regression models for the inhalation exposure routes (Appendix A pages 34 to 41 for the bucket scenario, pages 73 to 79 for the sink scenario, and pages 109 to 115 for the COP scenario).
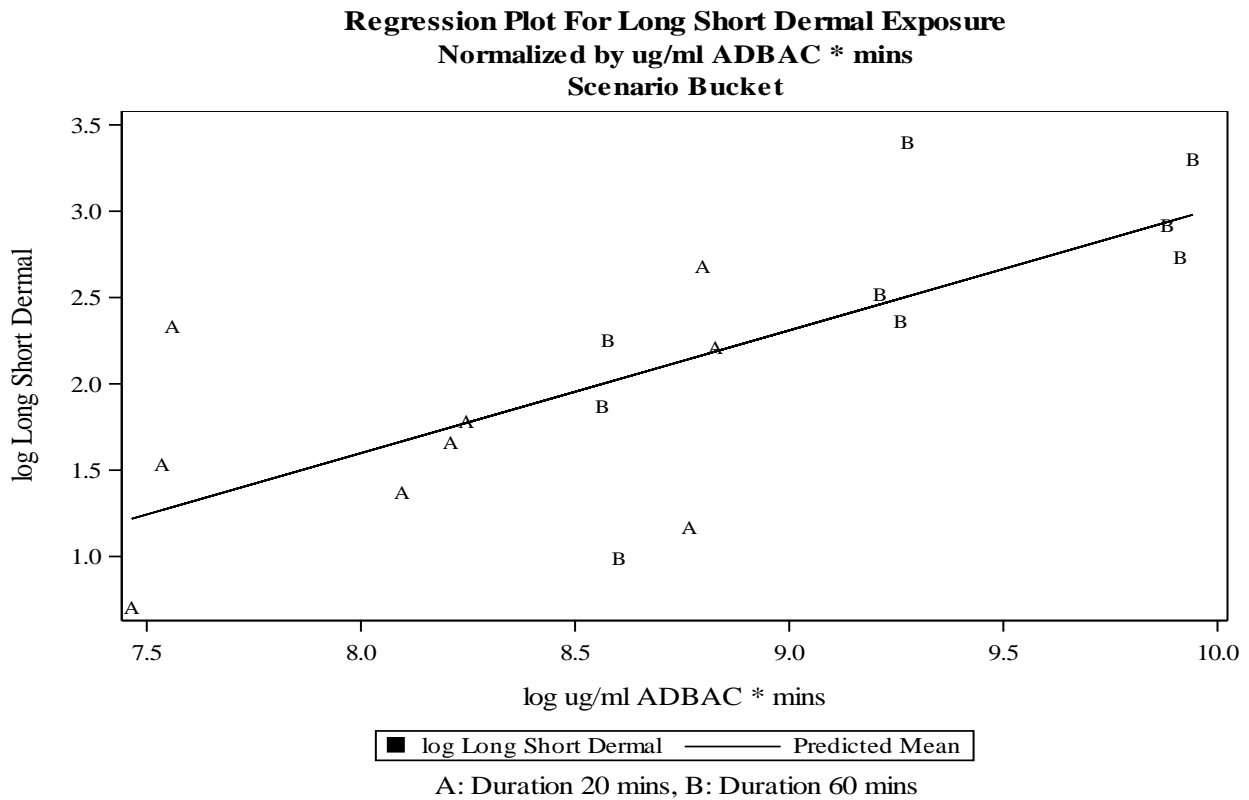

Regression Plot For Long Short Dermal Exposure
Normalized by ug/ml ADBAC * mins
Scenario Bucket

A: Duration 20 mins, B: Duration 60 mins

Figure 7. Bucket Scenario: Regression plot for Long Short Dermal (mg/(ppm x mins))

Regression Plot For Long Short Dermal Exposure
Normalized by ug/ml ADBAC * mins
Scenario Sink

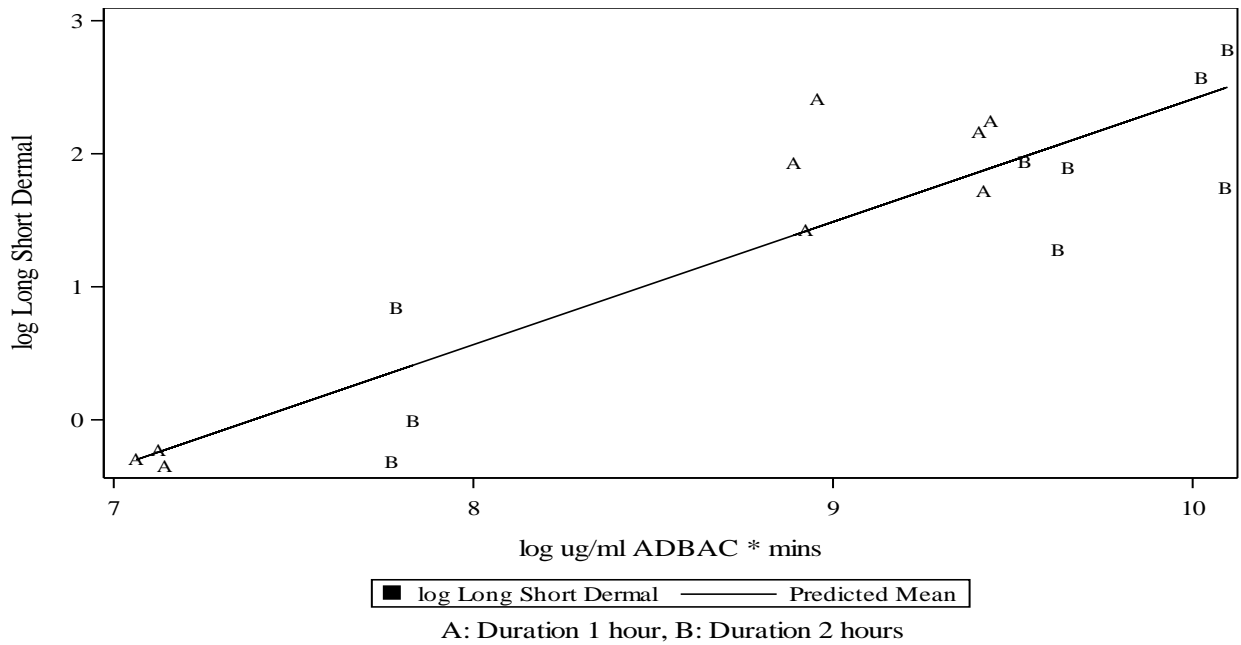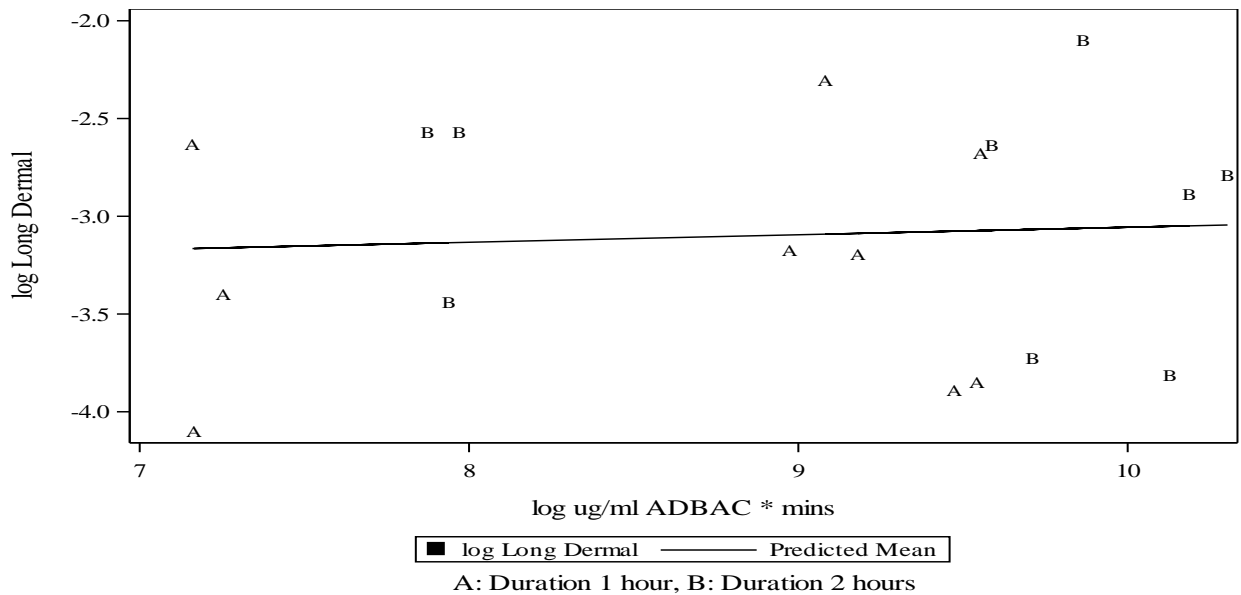A: Duration 1 hour, B: Duration 2 hours

Figure 8. Sink Scenario: Regression plot for Long Short Dermal (mg/(ppm x mins))

Regression Plot For Long Dermal Exposure
Normalized by ug/ml ADBAC * mins
Scenario COP

A: Duration 1 hour, B: Duration 2 hours

Figure 9. COP Scenario: Regression plot for Long Long Dermal (mg/(ppm x mins))

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 the three IDS scenarios 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 sites in Orlando, FL, and Madison, WI, as the study locations. 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 using sanitizers in locations other than Orlando, FL, and Madison, WI, and it is not possible to use these data to estimate the potential bias or 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 Joint Regulatory Committee (JRC). It is reasonable to assume that the cleaning routines to wipe hard surfaces and clean (sanitize) restaurant-type equipment in sinks and tanks in Orlando and Madison are not substantially different than cleaning the same types of surfaces and equipment throughout the country. Given a limited set of resources for the overall AEATF II monitoring program, the assumption that cleaning/sanitizing does not vary geographically was sufficiently reasonable to forgo the random site selection (of all buildings throughout the country) in favor of spending the limited resources to monitor additional distinctly different scenarios (e.g., pressure treatment of wood, trigger pump spray & wipe, painting, hand held spray wands, 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 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 (meeting better than the 3-fold relative accuracy goal, except in a few instances as discuss above).

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 experienced restaurant/food processing workers (i.e., dishwashers, banquet servers, hotel/housekeeping, busboys, janitors, caterers, bartenders, creamery/dairy/food processing plant workers) living in Florida and Wisconsin (e.g., those that had experience sanitizing surfaces with bucket & rag/sponge, 3-compartment sink setups, or COP tanks but did not volunteer), buildings (e.g., churches, Elk Lodge, and manufacturer of COP tanks were selected for this study), and time periods (e.g., summer versus winter, day versus night, 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).

(4) In this study/scenario/review we evaluated the presumption of "proportionality" that the mean exposure is a positive multiple of the concentration of a.i. and duration of exposure (i.e., the mean exposure is proportional to the ppm a.i. times hours and the exposure tends to increase with increasing ppm and duration of exposure). Proportionality is evaluated by testing if the log-log-linear model has a slope of 1. The analyses of log-log-linearity then shows that dermal and inhalation exposure tends to increase proportionally with ppm a.i. times hours exposed. Although this proportionality holds true for nearly all of the exposure scenarios developed throughout the AEATF II's monitoring program, a few scenarios have not, including the COP scenario within this study. For the long-long dermal exposure in the COP scenario, the slope was 0.038 and the confidence interval was from −0.257 to 0.334, which does not include a slope of 1. Several theories may help explain this lack of exposure trending proportionally with increasing treatment solution concentration and exposure duration, such as the fact that the subjects wore long-sleeve shirts and additional personal protective equipment (PPE) in the form of gloves, which may be more relevant to this task/job. The clothing scenario of long pants and short-sleeved shirts (with gloves, because all subjects were monitored wearing gloves) showed higher forearm exposures and resulted in a slope of 0.416 and a confidence interval from -0.066 to 0.898. Although the long pants short-sleeved shirt clothing scenario fit the unit exposure modeling approach better, EPA did not choose to use this estimate because workers operating COP tanks typically wear the long-sleeved shirts and gloves. Another theory is that the duration the equipment soaked in the tanks was irrelevant to exposure and the normalization factor of concentration is more relevant. The Supplement to Appendix A provides alternative normalization evaluations (i.e., by ppm, page 74, or by "1" to represent unnormalized, page 144). Normalizing by the treatment solution concentration only for the long-long clothing scenario did not improve the outcome (when normalized by ppm the slope is -0.019 and the confidence interval is from -0.333 to 0.295 (Supplement to Appendix A, Table BC18, page 91)). Another explanation is that exposure is inherently highly variable and the sample size was not large enough to accurately model the trend in exposure to the normalization variables. EPA did consider using the data for the COP scenario to estimate the exposure using the fitted log-log-linear model with the estimated intercept and slope rather than using unit exposures that correspond to a slope of one. However, EPA has decided to continue using the unit exposure approach corresponding to a slope of one for the COP scenario as the conservative estimate of exposure and to be consistent with the surrogate unit exposure approach developed through the SAP (2007) and the AEATF Governing Document (ACC 2011).

(5) The subjects monitored in this study were professional workers employed in the restaurant/hotel/food processing plant occupations for a duration from 1 to 30 years for the bucket scenario, 1 to 40 years for the sink scenario, and 4 months to 30 years for the COP scenario. The rationales for selecting professionals instead of consumers as test subjects were discussed in the protocol review (e.g., the 3-compartment sink and COP tank are less common for consumers). The use of occupational workers as test subjects is representative of the use pattern based on the equipment (e.g., 3-compartment sink and COP); but somewhat less known for the bucket & rag/sponge scenario. There is a potential for the unit exposures for the bucket & rag/sponge to be different than if consumers were selected due to

the subject's greater experience with the task. EPA's regulatory approval process for sanitizers in the past has been based on the trigger pump spray and wipe; now EPA has the availability to compare the trigger pump spray and wipe to the results of the bucket and rag/sponge scenario which will allow for better risk characterization. The duration of exposure by the worker compared to the consumer will tend to drive the higher daily exposure towards the worker's but it is unknown if the differences in the unit exposure (and if the consumer even has a higher unit exposure) outweighs the duration of exposure.

 (6) The planned use of C14 ADBAC for the inhalation OVS tubes was interrupted by background residues of C14 ADBAC. Although the researchers could have increased the LOQ to above background levels, the anticipated inhalation exposures for the IDS study were for low air concentrations and a low LOQ would be needed. Therefore, the AEATF II researchers switched to using DDAC as the surrogate compound for the OVS monitoring. The switch from C14 ADBAC to DDAC for the OVS tubes because of the background levels was a sound choice. Unfortunately, the OVS tubes had been fortified with the C14 ADBAC reference standard instead of the formulated product Oasis 146, which contains both DDAC and C14 ADBAC. This resulted in no OVS field recovery samples for the inhalation monitors. Although the lack of field recoveries for the OVS tubes results in an uncertainty in the inhalation monitoring, DDAC has been previously shown to be stable in OVS tubes in the field and during transport in several other AEATF II monitoring studies. Furthermore, a new storage stability study was conducted specifically for this study to account for any losses during sample storage. EPA believes the inhalation results for DDAC are sufficiently sound to be used in risk assessments but the high background contamination in the ADBAC OVS tubes were such that they are unusable.

4.0   Conclusions

EPA has reviewed the AEATF II IDS study and concludes that the AEATF II made the appropriate changes to the protocol proposed by the EPA and HSRB and has properly executed the study. The protocol deviations that occurred and were properly reported have not adversely impacted the reliability of these data. The EPA recommends that the inhalation and dermal UEs generated in this IDS 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 sanitizing of hard surfaces and restaurant-type equipment with bucket & rag/sponge, 3-compartment sinks, and COP tanks. The AEATF II unit exposures summarized in Table 1 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 (except in only a few instances). At this time, no additional monitoring for the IDS scenarios is required.

5.0   References

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Appendix A

Statistical Review of the AEATF II Immersion/Dip/Soak (IDS) Study

And

Supplement to Appendix A

(To be included as a separate electronic file)