UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

September 16, 2021

MEMORANDUM

SUBJECT: Ethics Review of Completed AEATF II IDS Study (AEA12)

FROM: Michelle Arling, Human Research Ethics Review Officer
Office of Pesticide Programs (OPP)

TO: Anita Pease, Director
Office of Pesticide Programs
Antimicrobials Division (7510P)

REF: Rosenheck, L. (2021) A Study for Measurement of Potential Dermal and Inhalation Exposure During Antimicrobial Applications Involving Immersion, Dip, and Soak. Sponsored by the Antimicrobial Exposure Assessment Task Force II. Study Number AEA12, 1133 pages. May 5, 2021. (MRID 51588901)

I have reviewed the available information concerning the ethical conduct of the research reported by the Antimicrobial Exposure Assessment Task Force II (AEATF II) in the referenced document. The study report describes the implementation and results of a study whose objective was to evaluate potential dermal and inhalation exposure of workers making antimicrobial pesticide applications through immersion, dipping, and soaking. The submission also includes correspondence with and submissions to the overseeing institutional review board (IRB).

After reviewing all available documentation, I have determined that the conduct of study AEA12 met applicable ethical standards for the protection of human subjects of research, and that it the submission satisfied requirements for documentation of ethical conduct of the research. Therefore, if study AEA12 is determined to be scientifically acceptable, I find no barrier in regulation to the EPA's reliance on the results in actions under FIFRA or §408 of FFDCA.

In addition, under 40 CFR 26.1604, the EPA is required to consult with the Human Studies Review Board (HSRB) before relying on intentional exposure human studies covered by the EPA's Human Studies rule that are initiated after April 7, 2006. The EPA will share study AEA12, the associated support documents, and the EPA's science and ethics reviews of the study with the HSRB for their review. This memorandum and its attachments constitute the EPA's ethics review.

Summary Characteristics of the Research

This study was sponsored by the AEATF II "to determine the potential dermal and inhalation exposure to consumers and/or professional workers who conduct manual immersion/dipping/soaking (IDS) of articles, equipment, and/or utensils into solutions containing an antimicrobial and the immersion/dip/soak of a rag or sponge into a bucket containing an antimicrobial to sanitize hard surfaces" (p. 13). Within this study, there were three distinct scenarios: bucket and rag/sponge, 3-compartment sink, and clean-out-of-place (COP) tank. Subjects in the bucket and rag/sponge scenario dipped a rag or sponge into a container with sanitizing solution, wrung it out, and wiped hard surfaces (e.g., countertops, backsplashes, refrigerators, ice makers, stoves, tables, and chairs). Subjects in the 3-compartment sink scenario conducted manual washing, rinsing, and sanitizing of cookware and bakeware in commercial 3-compartment sinks. Subjects in the COP scenario used a stainless-steel COP tank to clean and sanitize industrial equipment parts in the food processing industry (p. 13).

Subject monitoring for the bucket and rag/sponge scenario and the 3-compartment sink scenario occurred at three different facilities rented in Orlando, Florida between March 4, and March 31, 2019. Each of the facilities had a commercial 3-compartment sink and various surfaces that could be wiped. The facilities varied in size and layout. For the COP scenario, monitoring occurred between April 26 and May 4, 2019 at a single location in Madison, Wisconsin.

Subjects wore inner and outer dosimeters and an air sampling pump to measure exposure. For the bucket and rag/sponge and 3-compartment sink scenarios, the inner and outer dosimeter tops were short sleeved because the tasks involved immersing the hands and forearms into liquid. For the COP scenario, the dosimeter tops were long sleeved. All subjects wore long pants and their own footwear. Dermal exposure to the face and neck was measured by hand washes and face/neck wipes. Researchers also performed forearm washes to measure dermal exposure to subjects in the bucket and rag/sponge and 3-compartment sink scenarios. The study uses the term "monitoring event" (ME) to refer to a single subject's one-day participation in the study. A total of 18 MEs per scenario, or 54 MEs total, were conducted under this study.

Required Reviews of Protocol & Ethics-Related Chronology

The protocol for this study was conditionally approved by Advarra Institutional Review Board (IRB) on July 18, 2018. The IRB-approved protocol, consent form, and related materials were submitted to the EPA for review. The protocol and the EPA's ethics review[1], dated September 27, 2018, were discussed by the HSRB on October 23, 2018. With regard to ethics, the HSRB's final meeting report concluded that "EPA staff have made a number of ethics and privacy comments and recommendations. The Board has reviewed these and agrees with recommendations EPA staff have made. With the changes recommended by EPA staff the Board believes this study complies with the applicable ethical standards [40 CFR 26, subparts K and L, as well as FIFRA 12(a)(2)(P)]."[2] Attachment 1 contains the EPA's summary of the ethics-related recommendations from the EPA's review of the protocol and the HSRB's final report, and how the AEATF II addressed them.

[1] Leighton, Arling, & Cohen. Science and Ethics Review of AEATF II Immersion/Dip/Soak Scenario Design and Protocol for Exposure Monitoring. September 27, 2018. https://www.epa.gov/sites/default/files/2018-10/documents/1._epa_science_and_ethics_review_of_aeatf_ids_protocol_aea12_sept_27_2018.pdf.
[2] Dawson, Liza. October 23rd, 2018 EPA Human Studies Review Board Meeting Report. EPA-HSRB-19-1. https://www.epa.gov/sites/default/files/2019-02/documents/hsrb_final_report_science_aea12_protocol.pdf

Advarra IRB approved the protocol and consent forms (English) (p. 843) and the worksheets and phone script (English) (p. 877) on January 28, 2019. Advarra IRB provided certified Spanish translations of all relevant documents related to AEA12 following approval of the English versions of documents and radio ads. Protocol and AEATF II Standard Operating Procedures (SOP) amendments and deviations are included on pages 277-97 of the study report. The IRB-approved consent form is included starting on page 299 of the study report. The IRB-approved protocol, amendments, and deviations, as well as a complete record of correspondence with the IRB are included in the study report beginning on page 698.

Advarra IRB holds a Federal-Wide Assurance from the Office of Human Research Protection (OHRP) and is accredited by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP).

Completeness of Submission

The submission by the AEATF II and additional materials provided by Advarra IRB satisfy the requirements of §26.1303. A checklist indicating how each requirement has been satisfied is provided in Attachment 2.

Recruiting

Recruitment was conducted according to the approved protocol and Amendments 1 and 3. The protocol called for advertising via newspapers, radio spots, and Craigslist. The advertisements all provided a brief description of the study, overview of subject qualifications, that compensation would be provided, and a toll-free number to call for more information. Advertising was conducted in English and Spanish, and interested individuals could contact either the Study Director or a bilingual researcher to learn more.

For the bucket and rag/sponge and 3-compartment sink scenarios, newspaper ads ran in the printed and online versions of the Orlando Sentinel (between February 9 and 20, 2019). The radio spots were 30 seconds long and ran on three stations (top 40, country music, Spanish music) between February 11 and 17, 2019; additional ads were aired on the English-language stations on February 19 and 20, and additional airtime was purchased on the Spanish music station during the originally scheduled run. Ads in English and Spanish were posted on Craigslist for the Orlando region and ran February 17 to 20, 2019.

For the COP scenario, newspaper ads in English ran in the printed and online versions of the Wisconsin State Journal and the Capitol Times, between April 10 and April 24, 2019. The Spanish language advertisement ran in the VozLatina on April 12, 2019. Additionally, radio spots were aired on three radio stations (classic rock, sports, Spanish-language).

Respondents to the advertisements spoke English and Spanish. Using the IRB-approved telephone screening scripts, study staff interviewed interested callers via telephone in their preferred language to determine if they met the inclusion criteria and to provide an overview of the study to potential subjects. During this phase, it became clear that due to the geographical range of the recruitment and the traffic in the Orlando area, and the distance that would need to be travelled for those who were qualified to participate in the COP scenario in Madison, the compensation for attending the consent meeting and participating in a monitoring day was not adequate. The protocol was amended to increase these amounts for each scenario. See “Protocol Amendments and

Deviations" below.

After subjects responded that they met the criteria outlined by the interviewer and confirmed their interest in learning more about the study, the interviewer asked them to attend a consent meeting. In the bucket and rag/sponge and 3-compartment sink scenarios, 22 people per scenario were scheduled to participate in a consent meeting, and additional respondents were put on a waitlist. Seven people from the waitlist were contacted to participate in consent meetings when those originally scheduled to participate did not show up. For the COP scenario, 24 individuals were invited to participate in a consent meeting, 23 showed up for their scheduled consent meeting, and 22 enrolled in the study.

Consent & Enrollment

Consent meetings were held in conference rooms at hotels located near the test sites in Orlando, FL and Madison, WI and were conducted by the Study Director, Study Monitor, and bilingual researcher (if necessary). Consent meetings for the bucket and rag/sponge and 3-compartment sink scenarios were held February 26 through March 3, 2019. Consent meetings for the COP scenario were held from April 20 to 25, 2019. On January 28, 2019, Advarra IRB approved the consent forms (p. 843). Amended consent forms reflecting the updated compensation amounts were approved on February 15, 2019 (p. 970) and March 26, 2019 (p. 1043), prior to the start of the consent processes in the respective locations. Advarra IRB provided certified translations from English to Spanish of the recruitment and consent materials.

As per the protocol, each person was offered the option to have the meeting conducted in English or Spanish. When Spanish was requested, the bilingual researcher was present at the consent meeting. In the bucket and rag/sponge scenario, four individuals requested the consent to be conducted in Spanish (W03, W07, W14, and W16). In the 3-compartment sink scenario, two subjects were Spanish speakers (W11 and W12). All candidates in the COP scenario requested the consent meetings be held in English. Candidates were asked to read the informed consent materials, and then the researcher conducting the meeting reviewed the consent form and answered any questions. During this review, the researcher encouraged candidates to ask questions throughout the consent process and during the study itself, and reminded candidates that they were free to withdraw from the study at any time. Candidates were invited to take the forms home to think about them and discuss with family and friends prior to enrolling.

Once a candidate decided to continue with enrollment, they were evaluated against the eligibility criteria listed in the protocol (pp. 176-7). If a person met the criteria, they were asked to meet privately with a member of the research team to continue the consent process. In this private setting, the candidate was asked again whether they had any questions. The researcher asked a standard set of questions to ensure comprehension of the consent materials (SOP AEATF II-11J), and after demonstrating and understanding of the consent materials the candidate was asked to sign and date the informed consent form.

Next, the subject answered questions from the Worker Qualification Worksheet (pp. 881-3) and researchers verified age by checking the government-issued photo identification. The worksheet asked individuals to confirm that they met the eligibility criteria, including whether the subject was pregnant or nursing, in good health, free of skin conditions, at least 18 years old, experienced in performing the tasks to be monitored, and free of allergies to cleaning and disinfecting products,

soaps, or latex gloves. Individuals also provided height, weight, age, gender, clothing size, and more specific information about their experience performing tasks to be monitored.

Upon completion of these steps and confirmation of eligibility, a person was considered enrolled in the study. At this point, the researcher conducting the meeting presented the schedule of monitoring events and subjects were invited to indicate which of the monitoring days would work best for their participation. All subjects received a copy of their signed consent form

A total of 22 individuals per scenario consented and were enrolled in the study.

Demographics

Summaries of subjects' demographics and experience are included in Tables 3-4 (3-compartment sink, pp. 95-6), 12-13 (bucket and rag/sponge, pp. 104-5), and 21-22 (COP, pp. 113-4).

3-Compartment Sink Scenario

Of the 18 subjects monitored, there were 9 females and 9 males. Subjects' ages ranged from 20 to 62 years old, and they had from 7 months to 40 years of experience performing the tasks being monitored. Ten of the subjects were currently employed in a position that involved this type of work, and the frequency with which they performed the cleaning tasks ranged from once a week to multiple times per day.

Bucket & Rag/Sponge

Of the 18 subjects monitored, there were 7 females and 11 males. Subjects' ages ranged from 20 to 52 years old, and they had from 2 years to 30 years of experience performing the tasks being monitored. All but one of the subjects were currently employed in a position that involved this type of work, and the frequency with which they performed the cleaning tasks ranged from twice a week to multiple times per day.

COP Scenario

Of the 18 subjects monitored, there were 2 females and 16 males. Subjects' ages ranged from 19 to 67 years old, and they had from 4 months to 30 years of experience performing COP-related tasks. All but two of the subjects were currently employed in a position that involved COP tasks. The frequency of their COP tasks ranged from once a month to multiple times per day.

Randomization

Subjects were randomly assigned according to the study protocol. In each scenario, subjects were randomly assigned a subject ID by drawing a piece of paper with a number (W01-W22) out of a container. Subjects W01-W18 were designated test subjects and subjects W19-W22 were designated alternates. Test subjects then chose a piece of paper from another container that indicated the ME to be performed (e.g., concentration of quat, test site/tank, length of task/number of items/number of cycles). The randomized assignments of subjects to monitoring events are presented in the Study Report in Tables 5 (p. 97), 14 (p.106), and 23 (p. 115).

Subject Monitoring

Subject monitoring generally followed the protocol. The night before the study, subjects were called to remind them about their scheduled monitoring day. Upon arrival at the test site and before starting any monitoring procedures, subjects were reminded about the study's purpose and conduct and asked whether they had any questions. At this point, they were also reminded about their freedom to withdraw at any time for any reason. The study's medical professionals checked the subject's skin for broken skin and open sores. Female subjects were required to take a pregnancy test as described in the protocol, and negative results were verified by a female member of the study team prior to exposure of female subjects. After these steps were completed, the subject was directed to begin preparing for the ME. First, the subject washed his or her hands and face with soap and towels. Then they moved to the private changing room to don the inner and outer dosimeters with the assistance of a same-gender researcher. The air sampler pump was attached to the subject's belt and the sampler was attached to the collar. Subjects in the COP scenario put on steel-toe protectors (facility requirement) if they were not wearing steel-toed boots.

After the subject was prepared for monitoring, the study staff reminded the subject about safety and administrative information related to the study. This included that subjects could withdraw at any time, a reminder to wear the required safety equipment (eyewear), and how to avoid heat stress. To ensure all information was covered before each ME, the researchers used a volunteer checklist. Subjects in the 3-compartment sink were shown the sponges and scouring pads and asked to choose which they would use. Subjects in the bucket and rag/sponge scenario were shown the available equipment (buckets, rags, sponges) and asked to choose which they would use. Subjects in the COP scenario also received information on how to use the specific COP tanks at the test site to ensure that subjects were not injured and that the tanks were not damaged. Finally, the subject put on the safety glasses (all scenarios) and chemical-resistant gloves (COP scenario only), and the air sampling pump was turned on and the monitoring began.

When the subject completed the activities being monitored or met the time requirement, the subjects' air sampling pump was turned off, they removed their glasses, and they returned to the changing area. In the changing area, researchers removed the subject's air pump. Then the subject submitted to the protocol-specified hand (all scenarios) and forearm (bucket and rag/sponge and 3-compartment sink only) washes and face/neck wipes. After completing those processes, researchers removed the subjects' outer dosimeter, then inner dosimeter. The subject re-dressed in his or her own clothing, and then washed hands and face with Ivory soap and water. The medical professional checked the subject's hands, face, and skin for signs of irritation or redness. The researcher provided the compensation for the ME and subjects were free to leave.

Safety Precautions

The protocol called for several precautions to ensure the safety of subjects, which were followed. Subjects were screened according to the eligibility criteria, which ensured that subjects had experience performing the tasks to be monitored, were physically capable of handling the equipment, and did not have skin conditions that would be exacerbated by participating.

The protocol required all subjects to wear eye protection during their MEs, and researchers offered safety glasses or safety goggles designed to be worn over eyeglasses. Just before the monitoring event, subjects were reminded to wear the safety glasses.

Researchers complied with AEATF II SOP 11-B.1 and the protocol language regarding heat stress. The heat and humidity at study site were monitored. The study was conducted between March and May in Florida and Wisconsin, when temperatures were relatively cool. The monitoring occurred indoors in facilities with air conditioning. Subjects were briefed on the signs of heat stress, and reminded to take breaks as needed and to alert the study staff if they felt overheated, sick, or experienced skin or eye irritation. The researchers provided subjects access to cold water and sports drinks for the duration of their participation in study.

The researchers complied with the protocol's process for having a medical professional on site during the monitoring events. The medical professional was responsible for checking each subject's skin prior to and following the monitoring events and providing assistance if needed. All subjects' skin was clear at the start and end of their test days.

Confidentiality

The study followed the measures outlined in the protocol regarding confidentiality. For example, as discussed on page 48 of the study report, each photographs and short videos were taken while subjects were performing the tasks being monitored, and of the hand wash procedures. The photographers took care not to include subjects' faces, or to either delete or edit photos where facial features were clear. Subjects had assigned ME numbers, which were used rather than the subject's name in the study to identify individuals. Females were provided with a private place to take the pregnancy test, and all subjects changed into and out of the study-provided dosimeters in a private location with a member of the research team of the same gender.

Freedom to Withdraw

Subjects were informed of their freedom to withdraw from the study at any time, for any reason, as indicated in the informed consent form and in many interactions between researchers and subjects. After the consent meeting for the COP scenario, a prospective subject took the form home to consider whether to enroll and decided not to return to continue the process (p. 32). Two subjects withdrew from the 3-compartment sink scenario; W4 did not show up on his scheduled test day, and W18 withdrew for personal reasons (pp. 64-5). One subject withdrew from the bucket and rag/sponge scenario because they were too busy (p. 67). No subjects withdrew from any of the scenarios once monitoring had begun.

Compensation

Subjects were compensated according to the amended protocol (see below). All eligible persons who attended a consent meeting for the bucket and rag/sponge scenario and the 3-compartment sink scenario received $50. All subjects in these two scenarios, whether they were monitored or served as an alternate, were compensated $150. All eligible persons who attended a consent meeting for the COP scenario received $75, and enrolled subjects (monitored or alternate) were compensated $250. The protocol was amended to increase compensation based on the travel time to visit the consent and test locations, which was longer than originally anticipated. Subjects received compensation for attending the consent meetings in cash at the end of the session. Subjects received compensation for participating in a monitoring event in cash at the end of the day. Alternates received compensation in cash by traveling to the test site on the last day of the scheduled monitoring events for each scenario.

Protocol Amendments & Deviations

The protocol was amended 4 times during the course of the study, and the amendment process was consistent with the protocol and the IRB's practices. Amendments 1 and 3 revised the compensation amounts for participation in the consent meetings and monitoring day based on the estimated time to participate was longer than originally anticipated. Amendment 1 related to the 3-compartment sink and the bucket and rag/sponge scenarios, and increased the compensation for attending a consent from $20 to $50, and for participating in monitoring (or serving as an alternate) from $100 to $150 (p. 277). This amendment was submitted to the IRB on February 14, 2019 (p. 963). The IRB approved the amendment and revised consent form in English on February 15, 2019 (p. 970) and subsequently translated the revised consent form into Spanish. Corresponding edits to the recruitment scripts were submitted to and approved by the IRB. The Study Director signed the amendment on February 15, 2019, prior to the start of the consent meetings. Amendment 3 related to the COP scenario, and raised the compensation for consent from $20 to $75, and for participating in monitoring (or serving as an alternate) from $200 to $250 (p. 279). This amendment was submitted to the IRB on March 26, 2019 (pp. 1041-2). The IRB approved the amendment and revised consent form on March 26, 2019 (p. 1044). The Study Director signed the amendment on March 27, 2019.

Amendment 2 corrected a typographical error related to the stop criteria to align the protocol with the AEATF II SOP on heat stress (AEATF II 11B.1) (p. 278). Amendment 4 changed the criteria for reporting deviations to Advarra IRB; only deviations that affect subject safety or the consent process are required to be reported to the IRB (pp. 280-1).

There were 17 reported deviations from the protocol (pp. 282-91). Many of the deviations were administrative or related to sample collection and/or analysis. Some were related to the conduct of the study and subject-facing actions. Deviations 1-4 discussed changes to the bucket and rag/sponge and 3-compartment sink scenarios (pp. 282-3). Subject-related deviations included that subjects' shoes were not removed by researchers prior to entering the changing area, and that the bucket sizes differed from those specified in the protocol. The protocol language about removal of shoes was carried over from a previous protocol where contamination was likely, which is not the case in these scenarios. Additionally, the floor of the changing room was covered with paper that was changed between subjects to minimize that potential. The bucket size was changed because the 3-quart bucket discussed in the protocol was smaller than expected and not appropriate for the proposed tasks to be monitored.

Deviations 5-11 discussed changes to the conduct of the COP scenario (pp. 284-5). Subject-related changes included not allowing subjects to choose the temperature of the water in the COP tank, not requiring researchers to remove subjects' shoes prior to entering the changing area, and not requiring subjects monitored for two cycles to split the equipment to be cleaned into two batches in set 2, but rather dividing the equipment equally between the two cycles. The water temperature could not be adjusted as the only opportunity for hot water was as steam during the washing cycle; to protect the subjects from the risk of injury from steam and because heated water is not used during the sanitizing phase, subjects choosing the water temperature was not necessary. Researchers did not have to remove boots as subjects wore waterproof shoe covers that could be removed instead. The change to how the equipment to be washed was divided made the monitoring events more consistent.

Deviation 16 occurred on March 28, 2019 (p. 290). It changed the requirements for the 3-compartment sink scenario from length of time it took to clean a certain number of soiled objects to the target monitoring duration. This change ensured that subjects did not rush through the cleaning

process and that the target exposure could be obtained. As this duration was discussed in the protocol and consent forms, the change in the metric from number of soiled items to length of time was not significant. The same deviation reported a change in the number of MEs held at each location for the 3-compartment sink scenario because the alternate called in to replace a subject who did not show up at the monitoring site was not available until after the study had moved to another location. The parameters for the ME remained the same and there was no impact on the subject's health or welfare, or on the data generated during this ME.

There were 3 deviations to the AEATF II SOPs and 3 analytical deviations. Of note, SOP deviation 2 related to subjects' comprehension of the consent materials (p. 293). The AEATF II SOP 11J.1 requires that all subjects be asked a standard set of questions to measure their comprehension of the study procedures and risks, and that a copy of the form with the questions and the subject's answers be included in the study file. SOP deviation 2 noted that for one subject in the 3-compartment sink scenario, the form was retained but had not been completed and for another subject in the same scenario, the form was not retained. Though these errors represent a deviation, they did not impact either subject's health or welfare.

From an ethics perspective, there is no indication that the deviations negatively impacted the study's conduct or subjects' health or welfare. The EPA's science review also discusses deviations related to the scientific conduct of the study and "accepts the study authors conclusions that these deviations did not adversely affect the outcome of the study" (p. 12).

Applicable Ethical Standards

The following provisions of 40 CFR 26 Subpart Q define the applicable ethical standards which read in pertinent part:

> **§26.1703**: Except as provided in §26.1706, the EPA shall not rely on data from any research subject to this subpart involving intentional exposure of any human subject who is a pregnant woman (and therefore her fetus), a nursing woman, or a child.
>
> **§26.1705**: Except as provided in §26.1706, the EPA must not rely on data from any research subject to this section unless the EPA determines that the research was conducted in substantial compliance with all applicable provisions of subparts A through L of this part.

In addition, §12(a)(2)(P) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) applies. This passage reads:

> In general, [i]t shall be unlawful for any person . . . to use any pesticide in tests on human beings unless such human beings (i) are fully informed of the nature and purposes of the test and of any physical and mental health consequences which are reasonably foreseeable therefrom, and (ii) freely volunteer to participate in the test.

Findings

Pregnancy testing of female subjects on the day of testing was conducted and no pregnant or lactating women were enrolled in the study. All subjects who participated in study AEA12 were at least 18 years old. Therefore, 40 CFR §26.1703 does not prohibit reliance on this research.

40 CFR §26.1705 requires that the EPA have "adequate information to determine that the research was conducted in substantial compliance with subparts A through L of this part." Within this range, only subparts K and L are directly applicable to the conduct of third-party research such as this. The AEA12 study was conducted in substantial compliance with subparts K and L.

As documented in Attachment 2 to this review, the central requirements of 40 CFR §26 subpart M, §26.1303 to document the ethical conduct of the research were addressed.

The requirement of FIFRA §12(a)(2)(P) that human subjects of research be "fully informed of the nature and purposes of the test and of any physical and mental health consequences reasonably foreseeable therefrom," and "freely volunteer to participate in the test," was met for this study.

Conclusion

This study reports research conducted in substantial compliance with the requirements of 40 CFR 26 subparts A through L. In its conduct, study AEA12 met applicable ethical standards for the protection of human subjects of research, and requirements for documentation of ethical conduct of the research were satisfied. From the EPA's perspective, if this study is determined to be scientifically valid and relevant, there is no regulatory barrier to the EPA's reliance on it in actions under FIFRA or §408 of FFDCA. This research will also undergo review by the HSRB.

cc: Ed Messina
Mike Goodis
Anna Lowit
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Melissa Panger
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Attachment 1: AEATF II actions in response to comments from the EPA and the HSRB on the protocol
Attachment 2: §26.1303 Completeness checklist for AEA12 Study

Attachment 1
Ethics Comments from October 2018 HSRB Meeting & AEATF II Actions

EPA Comments on AEA12 Protocol	AEATF II Actions to Address Comments
Revise the eligibility criteria to include: - Which apply to all three scenarios - Subjects must be non-smokers or willing to refrain for the duration of the testing - That subjects must have at least 2 months experience	The protocol was revised to reflect these recommendations.
Add to the protocol that confidentiality could be breached through photos or videos of the subjects	This information was added to the protocol; it was already included in the consent materials.
Explain the circumstances under which data from a subject withdrawing from the study could be retained and used, and when an alternate would be asked to perform a monitoring event.	The protocol was revised to include this information.
Specify that a subject withdrawing will be assisted in the removal of the dosimeters and instructed to wash their hands before leaving.	The protocol was revised to include this information.
Clarify that all subjects must pass a comprehension test prior to signing the consent form.	This information was clarified in the protocol.
Revise the consent forms to indicate that the test substance is a pesticide.	The documents were revised to include this language.

HSRB Comments on AEA12 Protocol	AEATF II Actions to Address Comments
Add willingness to conduct the work (for bucket & rag and 3-comparetment sink) without wearing gloves as part of the inclusion criteria	The eligibility criteria were amended to include this condition.
Explain what will be done if the subject wants to drink/eat/smoke with respect to sample collection and potential loss of residues. What will be done if the subject wants to wipe their face with their hand or forearm?	The protocol was revised to include this information.

Attachment 2
§ 26.1303 Checklist for Completeness of AEA12 Submitted for EPA Review

Any person who submits to the EPA data derived from human research covered by this subpart shall provide at the time of submission information concerning the ethical conduct of such research. To the extent available to the submitter and not previously provided to the EPA, such information should include:

Requirement			Y/N	Comments/Page References
(a) Copies of all of the records relevant to the research specified by § 26.1115(a) to be prepared and maintained by an IRB	§1115(a)(1): Copies of • all research proposals reviewed, • scientific evaluations, if any, that accompany the proposals, • approved sample consent documents, • progress reports submitted by investigators, and reports of injuries to subjects.		Y	Appendices A, B, E
	§1115(a)(2): Minutes of IRB meetings which shall be in sufficient detail to show • attendance at the meetings; • actions taken by the IRB; • the vote on these actions including the number of members voting for, against, and abstaining; • the basis for requiring changes in or disapproving research; • a written summary of the discussion of controverted issues and their resolution.		Y	Appendix E
	§1115(a)(3): Records of continuing review activities.		Y	Appendix E
	§1115(a)(4): Copies of all correspondence between the IRB and the investigators.		Y	Appendix E
	§1115(a)(5): • A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; • any employment or other relationship between each member and the institution		Y	Separate IRB roster file
	§1115(a)(6): Written procedures for the IRB in the same detail as described in § 26.1108(a) and § 26.1108(b).		Y	On file with the EPA
	§1115(a)(7): Statements of significant new findings provided to subjects, as required by § 26.1116(b)(5).		n/a	
(b) Copies of all of the records relevant to the information identified in § 26.1125(a)-(f)	§ 1125(a) A discussion of:	(1) The potential risks to human subjects;	Y	Appendices A & B
		(2) The measures proposed to minimize risks to the human subjects;	Y	Appendices A & B
		(3): The nature and magnitude of all expected benefits of such research, and to whom they would accrue;	Y	Appendices A & B
		(4) Alternative means of obtaining information comparable to what would be collected through the proposed research; and	Y	Appendices A & B
		(5) The balance of risks and benefits of the proposed research.	Y	Appendices A & B
	§1125(b): All information for subjects and written informed consent agreements as originally provided to the IRB, and as approved by the IRB.		Y	Appendices A, B, E
	§1125(c): Information about how subjects will be recruited, including any advertisements proposed to be used.		Y	Appendices A, B, G
	§1125(d): A description of the circumstances and methods proposed for presenting information to potential human subjects for the purpose of obtaining their informed consent.		Y	Appendices A & B
	§1125(e): All correspondence between the IRB and the investigators or sponsors.		Y	Appendix E
	§1125(f): Official notification to the sponsor or investigator, in accordance with the requirements of this subpart, that research involving human subjects has been reviewed and approved by an IRB.		Y	Appendix E
(c) Copies of sample records used to document informed consent as specified by §26.1117, but not identifying any subjects of the research			Y	Appendices B, E
(d) If any of the information listed in paragraphs (a) through (c) of this section is not provided, the person shall describe the efforts made to obtain the information.			n/a	