UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

September 13, 2019

MEMORANDUM

SUBJECT: Ethics Review of Completed AEATF II Study AEA10 – Airless Sprayer (AEATF II Project ID AEA10; MRID 50879401)

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

TO: Melissa Panger, Ph,D., Acting Branch Chief
Risk Assessment and Science Support Branch (RASSB)
OPP/Antimicrobials Division (7510P)

REF: Rosenheck, L. and Lange, B. (2019) A Study for Measurement of Potential Dermal and Inhalation Exposure During the Application of Paint Containing an Antimicrobial using an Airless Sprayer. Study Number AEA10, 1372 p. June 10, 2019 (MRID 50879401)

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 using airless paint sprayer equipment to apply paints containing antimicrobial pesticides. The submission also includes a report titled "Analysis of Propiconazole Used as an In-Can Paint Preservative in Wall Wipe Samples Collected from Dried Paint During an Airless Paint Exposure Monitoring Study" and an appendix that 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 AEA10 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 AEA10 is determined to be scientifically acceptable, I find no barrier in regulation to EPA's reliance on the results in actions under FIFRA or §408 of FFDCA.

In addition, under 40 CFR 26.1604, EPA is required to seek input from the Human Studies Review Board (HSRB) for intentional exposure human studies covered by EPA's Human Studies rule that are initiated after April 7, 2006. EPA will share study AEA10, the associated support documents, and EPA's science and ethics reviews of the study with the HSRB for their review. This memorandum and its attachments constitute EPA's ethics review.

Summary Characteristics of the Research

This study was sponsored by the AEATF II "to provide information for evaluating potential dermal and inhalation exposures of occupational workers who apply paints and coatings containing antimicrobials with an airless sprayer." (p. 18 pf 1372) Subject monitoring was conducted from March 24, 2018 to April 15, 2019. For the study, warehouse space was leased in Orlando, Florida and 3 simulated buildings were constructed. The simulated buildings ranged from 2,600 square feet (s.f.) to 3,100 s.f., and ceilings were 8 or 10 feet. The simulated buildings did not have installed doors and windows; however, unhung doors were placed in the centers of rooms to be painted.

The study recruited subjects with experience using an airless sprayer occupationally to perform applications of one of three specific volumes of paint (up to 10, 15, or 30 gallons of paint) containing the antimicrobial active ingredient propiconazole at one of two concentrations (1,200 ppm or 12,000 ppm). To measure exposure, subjects wore inner and outer dosimeters, two air sampling pumps, and painter's hat. Dermal exposure to the face and neck was measured by hand washes and face/neck wipes. Subjects also were fit tested for and required to wear a respirator during the monitoring phase of the study. 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 were conducted under this study.

Required Reviews of Protocol & Ethics-Related Chronology

The protocol for this study was conditionally approved by Schulman IRB on August 8, 2017. The IRB-approved protocol, consent form, and related materials were submitted to EPA for review. The protocol and EPA's ethics review[1], dated September 29, 2017, were discussed by the HSRB on October 25, 2017. With regard to ethics, the HSRB's January 3, 2018 final meeting report concluded that "the research presented in the protocol 'A Study for Measurement of Potential Dermal and Inhalation Exposure During the Application of Paint Containing an Antimicrobial Using an Airless Sprayer' (AEA10) is likely to meet the applicable requirements of 40 CFR 26, Subparts K and L, if modified…" according to the HSRB's recommendations.[2] Attachment 1 contains EPA's summary of the ethics-related recommendations from EPA's review of the protocol and the HSRB's final report, and how the AEATF II addressed them.

The protocol and English consent form for AEA10 was reviewed and granted final approval by Schulman IRB on February 12, 2018. Schulman IRB provided certified Spanish translations of all relevant documents related to AEA10 following approval of the final protocol and English versions of recruitment and consent documents. Protocol and SOP amendments and deviations are included on pages 253-69 of the study report. The IRB-approved consent form is included starting on page 1191 of the study report. The IRB-approved protocol, amendments, and deviations, as well as a complete record of correspondence with the IRB, including and the minutes of IRB meetings where this research was discussed, are included in the study report beginning on page 779.

During the course of the study, oversight was transferred from Schulman IRB to Advarra

[1] Leighton, Arling, & Cohen. Science and Ethics Review of AEATF II Airless Sprayer Painting Scenario Design and Protocol for Exposure Monitoring. September 29, 2017. https://www.epa.gov/sites/production/files/2017-10/documents/epa_science_and_ethics_review_of_airless_paint_sprayer_protocol_-_sept_29_2017.pdf

[2] Dawson, Liza. October EPA Human Studies Review Board Meeting Report. January 3, 2018. https://www.epa.gov/sites/production/files/2018-01/documents/hsrb-finalreport-oct_2017meeting.pdf

IRB. Schulman IRB reviewed and approved the protocol and study-related materials and oversaw the study's conduct until July 2018. On July 27, 2018, the Study Director was informed that the study's oversight and documentation had been transferred from Schulman IRB to Advarra IRB. (pp. 1355-7 of 1372) Both IRBs hold Federal-Wide Assurances from OHRP and are accredited by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP).

Completeness of Submission

The submission by AEATF and additional materials provided by Schulman IRB and 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 Amendment 1. The protocol called for advertising via newspapers, radio spots, and printed flyers. The advertisements all provided a brief description of the study, overview of subject qualifications, and a toll-free number to call for more information. Advertising was conducted in English and Spanish. Newspaper ads ran in the printed and online versions of the Orlando Sentinel (daily, March 9-20, 2018) and El Sentinel (weekly on March 10, 17, and 24, 2018). With store management approval, flyers were posted in 14 paint stores in the area where the study was to be conducted beginning on March 9, 2019. The radio spots were 30 seconds long and ran on three stations (sports, country music, Spanish music) March 9-18, and 20-21, 2018. Due to low enrollment using the advertising methods listed in the protocol, the Study Director submitted an amendment to advertise using Craigslist. Schulman IRB approved the amendment and advertisement on March 16, 2018, (pp. 1291-2 of 1372) and it was posted for one day to the Orlando Region site on March 19, 2018.

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. The interviewer asked respondents who were both eligible for the study and interested in learning more to attend a consent meeting.

Consent & Enrollment

Consent meetings were held at the warehouse leased for the study, and conducted by the Study Director, Study Monitor, and bilingual researcher from March 18 to March 27, 2018. On February 12, 2018, Schulman IRB approved the consent form. The IRB-approved consent form is included on pages 270-282 of the study report. Schulman 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. Four potential candidates requested communications and materials presented in Spanish, and the bilingual researcher was present at all of these sessions. The remaining consent meetings (24) were 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. The researcher also noted the study requirement for subjects to wear a

properly-fitted respirator during the research and explained the medical evaluation and fit testing process.

Potential candidates were evaluated against the eligibility criteria listed in the protocol (pp. 147-8 of 1372). If a person met the criteria, he or she was 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 he or she 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 (p. 823 of 1372) and researchers verified age by checking the government-issued photo identification. Upon completion of these steps, a person was considered enrolled in the study. All subjects received a copy of their signed consent form

After enrolling in the study, subjects were asked to complete an online health questionnaire from Safety Links, the company hired to fit subjects for respirators for use during the study. This occurred in a private room. The questionnaire was available only in English. For the four Spanish-speaking subjects, the bilingual researcher was present in the room and available to translate as necessary as the subjects completed the form. Those who passed the health questionnaire were contacted by researchers and asked to return to the study site at a specific time for respirator fit test. After passing the fit test, subjects were invited to indicate which of the monitoring days would work best for them and were scheduled to participate in the study.

Demographics

A total of 35 respondents passed the phone screening and were invited to an informed consent meeting. Of these, 28 subjects participated in a consent meeting and consented to enroll in the study. Three of these individuals did not pass a subsequent medical screen and one did not pass a respirator fit test. Two subjects withdrew prior to being monitored in the study for personal reasons (scheduling, family emergency) and were replaced by alternates. Ultimately, 24 test subjects were enrolled in the study.

Of the 18 subjects who were monitored, 5 were female and 13 were male. Subjects' age ranged from 28 to 66 years old. These subjects had anywhere from 2 years to 28 years experience using an airless sprayer. One enrolled subject indicated a preference for Spanish, all others received materials and information in English.

Randomization

Subjects were randomly assigned according to the study protocol. Subject identification codes (AEA10-W01 through AEA10-W26) were written on paper, then the paper was folded and placed into a container. The subjects chose a slip of paper. Subjects with numbers AEA10-W01 through AEA10-W18 were selected for monitoring. The remaining subjects were held as alternates. Next, subjects who were selected for monitoring pulled a paper out of a second bowl. This bowl held numbers 1-18. Subjects were assigned to a specific target amount of paint to apply and concentration of propiconazole based on the number selected.

Table 1. Randomization of Subjects. From page 24 of 1372 of Study Report.

Spray Group	Target Amount of Paint Sprayed	Propiconazole Concentration	Target Amount of Propiconazole Handled	ME Numbers
Group 1	10 gallons	1,200 ppm	0.144 lb	1-3
		12,000 ppm	1.44 lb	4-6
Group 2	15 gallons	1,200 ppm	0.216 lb	7-9
		12,000 ppm	2.16 lb	10-12
Group 3	30 gallons	1,200 ppm	0.432 lb	13-15
		12,000 ppm	4.32 lb	16-18

Subject Monitoring

Subject monitoring followed the protocol, with a deviation related to the post-ME handwash, described below. 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. On the day of their MEs, females 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. The study's medical professionals (EMTs licensed by Florida) checked the subject's skin for broken skin and open sores. 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-sex researcher. The air sampler pumps were attached to the subject's belt and the samplers were attached to the collar. Last, the subject put on a painter's hat with a patch on the inside.

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 (respirator and goggles), and how to avoid heat stress. To ensure all information was covered before each ME, the researchers used a volunteer checklist. Next, the subject received an overview on how to use the spray equipment purchased for the study, shown the paint and available equipment (nozzles, wands, wrench, ladder, fan), shown the areas to be painted, and instructed to strain the paint before using it. Then the air sampling pumps were turned on and the monitoring began. During the ME, researchers replaced the OVS sampling tubes for inhalation exposure monitoring every 30 minutes, and the parallel particle impactor tubes every 60 minutes during the MEs. Three subjects requested a handwash during the study; two requested a hand wash before taking a break to smoke and one requested a hand wash after using his hands to squeeze the paint strainer bag.

When the subject completed the painting activities, they cleaned up the work area by performing the tasks detailed in the protocol. Each subject removed his or her own safety equipment (glasses, respirator) and the researchers turned off the air sampling pumps. The researcher put the respirator into a bag for the subject to take upon completion. The subject was taken back to the changing area, and a researcher removed the subject's shoes prior to entering the changing area. In the changing area, researchers removed the subject's hat and the air pumps. Then the subject submitted to the protocol-specified hand 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. Once the subject was dressed, the medical professional checked the subject's hands, face, and skin for signs of irritation or redness. The researcher gave the subject the respirator plus cartridges or new N95 filtering facepiece respirators, provided the compensation for the ME, and subjects were free to leave.

The study included a deviation for the hand wash procedure across all MEs. (p. 262 of 1372) The protocol called for using a specified amount of wash fluid (50 mL) drawn from a larger container and for the researchers to rub the subjects' hands with gauze pads. The initial amount of handwash dispensed varied based on the amount of paint on subjects' hands. Additionally, rather than having the researchers wipe with gauze, subjects used the gauze to wipe dried paint from their own hands. These changes did not affect the integrity of the study, and the study director noted that "this was a more efficient method to completely remove dried paint from the subjects' hands, fingers, and fingernails." (p. 262 of 1372)

Safety Precautions

The protocol called for several precautions to ensure the safety of subjects, which were followed except for two minor deviations.

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 heavy paint containers, did not have skin conditions that would be exacerbated by participating, and were willing to wear a respirator. AEATF contracted with an occupational safety training company to ensure that all subjects were medically cleared to wear a respirator and wore a respirator for which they had been fit tested. On pages 13-14, the study report details the process for complying with these study conditions:

> *Respirator Medical Evaluation Questionnaire*
> Immediately following the informed consent meeting, consented volunteers were asked to complete an on-line medical questionnaire to determine if they were medically eligible to wear a respirator. The questionnaire was part of the respirator fit testing program administered by Safety Links, an Orlando-based occupational safety training company in Longwood, Florida. Subjects completed the on-line questionnaire on a desktop computer in a separate and private office to ensure confidentiality of responses. Everyone who completed the medical questionnaire was given an additional $20 for their time.
>
> *Respirator Fit Test*
> Volunteers who passed the respirator medical evaluation were asked to return to the test site to be administered a respirator fit test. Out of all the subjects enrolled in the study, only one (W5, ME 11) was already fit tested to wear a respirator. Volunteers selected the style of respirator they wished to wear from those provided by the Study Director, either a disposable N95 filtering facepiece (3M or Aura Brand) or one of three models (all 3M Brand) of half-face respirator with vapor cartridges and prefilters or they were allowed to wear their own half-face respirator. Only the subject (W5, ME11) who already had a respirator fit test certificate wore his own respirator, all other subjects were fit tested for their selected respirator by a technician from Safety Links. Volunteers who passed the fit-test were issued a Respirator Fit Test Record, a copy of

which was retained in the study records. Once the subject completed his/her fit test, his/her respirator was placed into a plastic sealable bags and the subject's name was written on the bag. Respirators were kept in an office at the test site until the subject showed up to be monitored. Subjects were allowed to keep their respirators after participating in the study. Table 7 contains a description of the respirator worn by each enrolled subject. Everyone who returned to the test site for the respirator fit test was given $100 for their time and travel expense.

--- *end of excerpt* ---

The study was conducted in accordance with this section of the protocol except for one deviation. (Deviation 7, p. 265 of 1372) According to the protocol, one subject went through the fit test procedure prior to receiving an approved medical recommendation. The subject had completed the medical screen and was scheduled for the fit test at their convenience. However, the subject was not formally approved for unrestricted use of a respirator until the day after the respirator fit test was conducted. All elements of the medical clearance and fit test were completed prior to the subject's monitoring event. This is a minor deviation from the protocol and did not negatively affect the subject's welfare or safety.

The protocol required all subjects to wear eye protection during their MEs, and researchers informed subjects that they would clean the safety glasses as often as requested during the MEs. The researchers provided the necessary equipment, and all subjects started the study wearing it. One subject (ME10) removed her safety glasses when pouring paint, and paint splashed in her eye. The study team followed the protocol, responding immediately. The medical professional provided the subject with an eye wash bottle to flush her eye. The subject recovered and requested to continue her ME, which was permitted. The study report notes that "[a]fter that incident, the researchers made sure that every test subject wore their safety glasses whenever handling the paint, not just during the paint spraying." (p. 37 of 1372) This was reported as a deviation. (Deviation 2, p. 260 of 1372) This was an isolated incident and did not negatively affect the welfare and safety of the subject. For future studies, EPA recommends that AEATF consider revising the pre-monitoring discussion to note where equipment must be worn. For example, rather than "Please wear your respirator and safety glasses" (p. 32 of 1372), where use of equipment is mandatory the reminder should include stronger language such as "You must wear your respirator and safety glasses for the duration of your participation in the study."

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 in March and April in Florida, when temperatures were relatively cool. 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 protocol noted that subjects would be offered 2 types of hearing protection, but not required to use either. The study report notes that all subjects opted not to use hearing protection, as it was not part of their normal work practices.

The researchers complied with the protocol's process for having a medical professional check each subject's skin prior to and following the monitoring events. All subjects' skin was clear at the start of their test days. The skin of all but one of the subjects was clear at the post-monitoring

skin check. During the post-monitoring skin check of ME11 by the medical professional, dermal irritation was discovered on the forearms. According to the study report, ME 11 did not raise the irritation to the attention of the researchers prior to the skin check, attributed the irritation to sweat, and was not concerned (pp. 37-8 of 1372). The area was washed with soap and water. The subject followed up with the Study Director later on the same day as the monitoring and indicated that the irritation was gone. Nothing about this incident triggered the protocol's stop criteria. (pp. 173-5 of 1372)

Confidentiality

The study followed the measures outlined in the protocol regarding confidentiality. For example, as discussed on page 13 of the study report, each enrolled subject was given a private place to complete the medical evaluation necessary for respirator fit testing. Subjects were assigned ME numbers, which were used in the study as opposed to the subject's name. The study report includes representative pictures (Appendix D), but none of these images could be used to identify the subjects.

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. Two subjects withdrew from study prior to their test days, one for scheduling reasons and one for a family emergency. No subjects withdrew from the study during a monitoring event.

Compensation

Subjects were compensated according to the protocol. All eligible persons who attended a consent meeting received $20. All subjects completing the medical evaluation questionnaire received $20. All subjects who attended a respirator fit testing session received $100. Finally, all subjects, whether they were monitored or served as an alternate, were compensated $200. The study team confirmed that alternates were contacted by phone and invited to come to the test facility on the last day of monitoring to pick up their compensation.

Protocol Amendments & Deviations

The protocol was amended 5 times during the course of the study, and the amendment process was consistent with the protocol and the IRB's practices. Amendment 1 revised the recruitment section of the protocol to utilize Craigslist, billboards, and social media in addition to the methods initially approved by the IRB. This amendment was submitted to the IRB on March 16, 2018 (pp. 1281-1283 of 1372). The IRB approved the amendment on March 16, 2018 (p. 1288 of 1372) and the advertisement to be used on March 19, 2018 (p. 1292 of 1372). The Study Director signed the amendment on March 19, 2018 and the Craigslist ad was posted the same day.

Amendment 2 changed the collection time for air samples and allowed for different storage of the painters hats and inner dosimeters. (p. 254 of 1372) Amendments 3 and 4 corrected typographical errors in the protocol related to the heat index cut off and experimental start date. (pp. 255-6 of 1372) Amendment 5 revised the requirements for reporting deviations to align with the IRB's SOPs. This amendment occurred after subject monitoring was completed and did not affect the reporting of any protocol deviations.

There were 7 reported deviations from the protocol. Three were related to subjects' welfare and were discussed earlier in this memo. Deviation 2 reported a subject's failure to wear safety glasses for the duration of the study, deviation 4 reported a change in the handwash procedure for all subjects, and deviation 7 reported a subject being fit tested for a respirator before receiving formal medical approval to wear a respirator. The remaining 4 deviations were related to the timing of signatures on amendment 1, preparation and analysis of field fortification samples, an additional spray tip made available to subjects without a protocol amendment, and a change in the testing facility management representative. EPA agrees with the study director's assessment that none of the deviations negatively impacted the study's integrity.

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, 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, EPA must not rely on data from any research subject to this section unless 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 AEA10 were at least 18 years old. Therefore, 40 CFR §26.1703 does not prohibit reliance on this research.

40 CFR §26.1705 requires that 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 AEA10 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 AEA10 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 EPA's perspective, if this study is determined to be scientifically valid and relevant, there is no regulatory barrier to EPA's reliance on it in actions under FIFRA or §408 of FFDCA. This research will also undergo review by the HSRB.

cc: Richard Keigwin
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Attachment 1: AEATF II actions in response to EPA and HSRB comments on protocol
Attachment 2: §26.1303 Completeness checklist for AEA10 Study

Attachment 1
Ethics Comments from October 2017 HSRB Meeting & AEATF II Actions

EPA Comments on AEA10 Protocol	AEATF II Actions to Address Comments
Revise the protocol to require all study participants to use respiratory protection based on the OSHA PEL. Require that subjects have a valid fit test certification before participating in a monitoring event.	The protocol and consent materials were revised to note that all subjects must wear a properly fitted respirator. The screening and consent processes were revised to include a medical screening form and fit testing of qualified subjects by an OSHA-compliant group.
Clarify the time period that will elapse between monitoring events using the same rooms.	The protocol was revised so that during the study at least 36 hours elapsed between monitoring events in the same rooms.
Clarify when and how alternate subjects will receive their compensation.	The protocol and consent forms were revised to note that alternates not called in to replace an enrolled subject would be contacted by phone after all monitoring events were completed to set up a time and place for study staff to provide the compensation to the alternate subject.

HSRB Comments on AEA10 Protocol	AEATF II Actions to Address Comments
Remove the upper age limit of 65 or justify why there is an age limit	The upper age limit was removed
Revise recruitment ads to indicate that a government-issued ID is needed	The need to provide a government-issued ID was added to advertisement materials. See, e.g., p. 1219.
Provide at least 2 types of hearing protection	Two types of ear plugs were made available for test subjects to use. Over the head hearing protection or ear muffs were not be provided as these would have interfered with the hat dosimeter.

HSRB Comments on AEA10 Protocol	AEATF II Actions to Address Comments
Add the risk of climbing a small ladder to the protocol and ICF	Both documents were revised as follows. See p. 151 and p. 278. Protocol – "3. Physical Risks associated with painting activities and using a ladder: … *In addition, subjects will be asked to perform other activities associated with a commercial painting job, such as climbing a portable 6 foot ladder, if needed, to reach higher walls or ceilings and maneuvering of the airless paint sprayer, hose, and paint buckets into different rooms or areas of a building. There is a risk of falling from the ladder. Falling risks will be minimized by using a new ladder purchased specifically for this study; the ladder will be used on a stable and level surface; and ensuring that the maximum load rating of the ladder (300 lbs) is not exceeded.*" Consent form - "Physical stress: Because you may be lifting and handing up to six 5-gallon paint containers as well as using the airless paint sprayer, you may experience muscle fatigue or muscle strain. *You will also be able to use a portable 6 foot ladder if needed. There is a risk of falling from the ladder. Falling risks will be minimized by using it on a stable and level surface and ensuring that the maximum load rating (300 pounds) of the ladder is not exceeded.* You will be allowed to rest whenever you need which will help to make sure you do not overexert yourself."
Revise the protocol to provide more detail about videotaping. Give subjects the option to indicate that they do not wish to be videotaped.	Consent form was revised as follows. See p. 276. "We may also take pictures or video to show what happened in the study, but those pictures will not show your face. If you face is shown, it will be edited or deleted. Videotaping will be done using a hand-held camera and will be done only for a few minutes so that we can document how you paint. You will not be photographed or videotaped at any time while changing into or out of the dosimetry clothing. **If you do not want to have your picture taken or notes taken on what you are doing, you should not participate in this study**."

HSRB Comments on AEA10 Protocol	AEATF II Actions to Address Comments
Revise the study screening material to ask whether subjects have ever had an allergic response to paint instead of asking whether they are allergic to propiconazole.	Consent form was revised as follows. See p. 273. "You will also not be allowed to participate if you are pregnant or breastfeeding; if you've had allergic reactions to soap, latex-based products *particularly latex paint* or latex gloves, propiconazole, triazoles, or chemical-based products; if you have open sores or cuts on your hands and/or face; if you are not able to lift and move up to six 5-gallon buckets of paint; if you are unwilling or unable to conduct the paint spraying without gloves; or if you are not medically able to wear a respirator or cannot pass a respirator fit test."

Attachment 2
§ 26.1303 Checklist for Completeness of AEA10 Submitted for EPA Review

Any person who submits to 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 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, G
	§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	pp. 1254-1256 Separate IRB Minutes file
	§1115(a)(3): Records of continuing review activities.		Y	Appendix G
	§1115(a)(4): Copies of all correspondence between the IRB and the investigators.		Y	Appendix G
	§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 rosters 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 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
	§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 G
	§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 G
(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, G
(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	