EPA Human Studies Review Board (HSRB)

July 21 and 22, 2020 Meeting Minutes

Committee Members: (See EPA HSRB Members List – Attachment A)

Date and Time: Tuesday, July 21, 2019, and Wednesday, July 22, 2019, both 1:00 to 5:30 pm EST.

Locations: Via teleconference and webinar

Purpose: The HSRB provides advice, information and recommendations on issues related to scientific and ethical aspects of human subjects research.

July 21 meeting:

Meeting was called to order at 1:00 p.m.by Tom O'Farrell, designated federal official (DFO) for the HSRB. Roll was taken and the following members and observers were present:

HSRB members	EPA staff members
Jennifer Cavallari, Sc.D. (Chair) Thomas Lewandowski, Ph.D. Mark Aulisio, Ph.D. Janice Britt, Ph.D. AJ Allen, Ph.D., M.D. Ann Um, Ed.D. Lisa Corey, Ph.D. George Milliken, Ph.D. Julia Sharp, Ph.D. Kendra Lawrence, Ph.D. (consultant)	Michelle Arling (EPA, OPP) Clara Fuentes, Ph.D. (EPA, OPP) Helen Hull-Sanders, Ph.D. (EPA, OPP) Virna Stillwaugh, Ph.D. (EPA, OPP) Jenn Saunders, Ph.D. (EPA, OPP) Shannon Borges (EPA, OPP) Menyon Adams (EPA, OPP) Tom Tracy (OSAPE) Tom O'Farrell (OSAPE)
Members of the public, representatives of research sponsor and research team Genevieve Faherty (Citrefine) Alicia Werner (Citrefine) Bill Robel (ARCTEC) Sarah Dewhirst (ARCTEC) Robert Jones (ARTEC) Julie Chao (USDA)	

Dr. Tom O'Farrell provided an introduction to the meeting and outlined the Federal Advisory Committee Act (FACA) procedures and took role of the meeting participants. Dr. O'Farrell introduced new Board member Dr. Thomas Lewandowski.

Ms. Michelle Arling gave an update on a study from the Agricultural Handler Exposure Task Force where they looked at potential occupational exposure from handlers who were

mixing, loading, and transferring pesticides using a closed system reviewed by the HSRB. The Board had some recommendations for conducting different statistical analyses. EPA has acted on the Board's review by analyzing the differences in container type via regression (log exposure vs. log amount of active ingredient handled). The additional analysis support the original conclusion presented by EPA using mixed model ANOVA. Because this analysis found that there was no difference in the container type, meaning returnable or non-returnable containers, the data from both will be combined. EPA is planning to finalize its review and after coordinating with our regulatory stakeholders, may begin using the data in the late fall or early winter of 2020. Finally, the EPA review will include a synopsis of the HSRB's review and our response to that review. The finalized review can be shared with the Board.

The Board reviewed one study during the session on July 21, 2020, **"**A Single Group Trial to Determine the Complete Protection Time of an Insect Repellent Formulation Containing 30% Citriodiol ® (Oil of Lemon Eucalyptus) against three species of ticks."

The Agency's scientific review of this study was presented by Dr. Clara Fuentes of EPA's Office of Pesticide Programs (OPP). The purpose of the study was to determine the complete protection time for Citriodiol ®, a skin-applied repellent containing 30%, by weight, of the active ingredient oil of lemon eucalyptus, against ticks. The repellency testing was conducted with 25 subjects per species and involved three tick species that have been identified as representative public health risks. The study was conducted in compliance with GLP requirements and according to OCSPP 810.3700 Guidelines. The protocol was IRB-approved with revisions of the protocol version 1.0 as amended. Protocol Revision 1 was created in July of 2017 and was reviewed by EPA and HSRB and the final protocol version 3.4 became effective on October 10th, 2019. There were 10 deviations from the approved protocol that were determined not likely to compromise the validity of the data submitted. Protocol deviations included when excessive time points were missed with more than one individual due to a lack of questing behavior observed with *Dermacentor variabilis.* The protocol was modified, and testing was repeated with *Rhipicephalus* ticks and found acceptable. A miscalculation occurred and the dose was calculated across 24 subjects instead of 25. The higher dose of 0.801 microliters per square centimeter was calculated by mistake and used during testing with some subjects until the error was identified. The difference from the standard consumer dose calculated across 25 subjects was 0.008 microliters per square centimeter, which is within the margin of error. Therefore, the data for those individuals that received the slightly higher dose was included in the determination of complete protection time. Subsequently, testing continued with the correct dose of 0.793 microliters per square centimeter. The secondary objective was to determine the typical consumer dose that people apply to themselves. Repellency was tested using the standard consumer dose measured in milliliters per square centimeters of the skin surface area. The average consumer dose was determined to be 0.793 milliliters per square centimeter. The sponsor chose this over the EPA standard dose because they expected the calculated dose to be significantly higher, since the EPA standard dose is derived from calculated doses from applications to lower legs from mosquito studies. The average consumer dose used for testing repellency was adjusted to the surface area of subject forearms by multiplying the sum of three measurements of arm circumference by one third of the forearm length. Skin repellency questing

tests were conducted and the data were statistically analyzed to calculate a median complete protection time with 95% confidence interval. The tick species used were *Amblyomma americanum, Ixodes scapularis, and Rhipicephalus sanguineus*. For *Amblyomma americanum*, the median complete protection time could not be calculated because 15 subjects out of 25 were right censored (more than 50% of subjects ended the test without complete protection time). The calculated median complete protection time for *Ixodes scapularis* was 290 minutes. The calculated median complete protection time for *Rhipicephalus sanguineus* was 512 minutes, approximately eight hours. The complete protection time is measured for each individual testing a specific species of tick. Once all testing is completed with that species of tick, the median complete protection time for the specific tick species is calculated by evaluating all of the individuals' complete protection times. This process is repeated to measure the complete protection times and to calculate the median complete protection times for each species of tick tested. Based on EPA guidelines, the efficacy claim on the label should be based on the most conservative median complete protection time of three species. In conclusion, the study was conducted in conformity with EPA Guidelines 810.3700 for testing repellents applied to human skin and with revised study protocol and the GLP requirements. The data supports the label efficacy claim of four hours complete protection time based on the most conservative median complete protection time of the three species.

The Board asked questions about the science presentation. Dr. Tom Lewandowski asked the conclusions of weighing the spray bottle before and after application. Dr. Helen Hull-Sanders said EPA would include that in the final report. Dr. Lewandowski asked about one subject who said they did not know how to use the applicator and whether that data should be included and the observation that the application amount of the product was different than the standard amount. Dr. Fuentes said that the data were not analyzed for outliers and that data from that subject was included. Dr. Lewandowski had a concern that up to 80% of the product was lost into the gloves and asked EPA if there was a comment on that. Dr. Fuentes said that the measurement for glove absorption was not very accurate and that there was no correlation between the amount of product lost in the gloves and CPT and she agreed that this should be explained in EPA's report. Dr. Kendra Lawrence had a question about why the *Dermacentor t*ick species was replaced with *Rhipicephalus*. Dr. Hull-Sanders said *Rhipicephalus* has better questing behavior and that would be clarified in EPA's report. Dr. George Milliken asked if there was any insight on why the CPT values on the last seven days of testing were all small. Dr. Hull-Sanders said there was really no explanation for that.

Ms. Arling of EPA OPP reviewed the ethical aspects of the study protocol. In the first phase, 25 subjects were enrolled and completed the dosimetry study. In total, 65 subjects consented and participated in at least one test day. Of those, 33 were female and 32 were male. EPA concluded that this testing was in substantial compliance with the protocol. The study report noted a total of eight adverse events. Six were related to bites by ticks or mosquitoes and none of these had lasting effects on the subjects. All subjects were compensated in accordance with the proposed amounts in the protocol. The protocol was amended five times. This included adding another species of tick to replace *Dermacentor* and to clarify the stopping rules and handling of data where there were missed time points due to a lack of tick questing behavior. All

of the amendments were approved by both overseeing institutional review boards before they were implemented and did not impact the subjects overall welfare or safety. One deviation of the protocol was the miscalculation of consumer dose. Upon discovery, the study team put in place additional quality assurance checks to ensure that all data collected were included in tables before performing any calculations or analysis. There were also two instances of applications made to the incorrect arms. Another deviation occurred when a subject who was engaged in a test requested to end his potential station before CPT was achieved. None of the deviations had a negative impact on the health or welfare of the subjects. EPA reviewed the protocol and presented it to the HSRB in April of 2018. The HSRB's review noted that, with modifications recommended by EPA and the HSRB, the study would likely meet the applicable requirements of the Human Studies Rule. Following this review of the protocol, the study director addressed all comments and resubmitted the protocol to two overseeing IRB's. After approval from both overseeing IRBs, the research was initiated. EPA determined that the Western IRB review complied with the requirements of 40 CFR 26 subparts K through L, which is EPA Human Studies Rule. The research was overseen by two IRBs: the Western Institutional Review Board, and the London School of Hygiene and Tropical Medicine's Interventions Research Ethics Committee. All subjects were at least 18 years old and no pregnant or nursing women were enrolled based on pregnancy testing conducted on each day of testing. The study was conducted in substantial accordance with the protocol as approved and amended and conducted in accordance with practices that EPA concluded were at least as protective as those at 40 CFR 26 subparts K through L. Based on all available information reviewed, EPA concluded that the research was conducted in substantial compliance with procedures as protective as those in EPA Human Studies Rule.

The Board then asked questions regarding ethics review of the study. There were no questions regarding the ethics review of the study.

A public comment was given by Genevieve Faherty of Citrefine.

The HSRB's scientific review was presented by Board members Drs. Corey and Lewandowski and consultant Dr. Lawrence. Dr. Corey noted that the study protocol was reviewed by the HSRB in April 2018, and there were several recommendations by EPA and the HSRB at that time. Dr. Corey commented on the mistake in the calculation of the average consumer dose across 24 individuals other than 25 individuals but that the difference was within the standard error of the mean application rate and it would have minimal impact on the conclusions of the study. However, Dr. Corey noted that it was concerning that the study proceeded to that point. Dr. Lewandowski stated that the study does generate reliable data for both the consumer dose and the CPT. Dr. Lawrence said that overall the study was robust and provides a good measure of a product that is a public health product and intended to be used in that way.

The Board's statistical review was given by Dr. Julia Sharp. Dr. Sharp stated that appropriate descriptive statistics were used for establishing the CPT. Dr. Sharp recommended that the EPA report be more clear about the tick species that a CPT could not be established for, and why the report says it can be estimated but not calculated. Dr. Sharp stated that the Kaplan-

Meier analysis is appropriate to establish the median CPT and the median CPT is listed for all three species of ticks, even though more than half of the subjects tested with the *A. americanum* were right censored. Dr. Sharp recommended that the EPA clarify the justification for that in the report. Dr. Sharp also questioned whether the EPA report should say that among the three species tested, *I. scapularis* was recorded with a lowest median CPT of approximately four hours, instead of lowest CPT. Dr. Sharp concluded the research summarized in the report generated scientifically reliable data useful for deriving a typical consumer dose and estimating the median complete protection time of the product. Dr. George Milliken had a concern that using the median CPT of 4 hours means that it works for 50% of the people but not the other half. Dr. Lewandowski questioned why the median CPT is rounded down from 4.9 hours to 4 hours. Dr. Milliken suggested the CPT might be stated as approximately 4 hours. Dr. Lawrence said that this is EPA's policy to round down and that should be applied consistently to all product labelling. Dr. Hull-Sanders acknowledged rounding down is part of EPA's guidance. Dr. Cavallari said that there was some concern about the fact that the original calculation excluded one of the participants' data. Dr. Lewandowski suggested that the product label state all the ingredients in it. Dr. Lewandowski said it was helpful that EPA looked into whether there was any relationship between the amount of material still present on the glove and the measured CPT. The Board voted unanimously on the following answer to the science charge question: "The HSRB concludes that the research summarize in single group trials to determine the complete protection time of an insect repellent formulation containing 30% Citriodiol®, oil of lemon eucalyptus, against three species of ticks, provide scientifically reliable data useful for deriving a typical consumer dose and estimating the amount of time the product tested repels ticks."

Dr. AJ Allen presented the HSRB's ethics review of the study. Dr. Allen stated that out of 188 potential subjects identified by recruiting, there were 70 people who gave consent to participate in one or both phases of the study, and 65 individuals who actually participated in at least one testing event. Dr. Allen noted that oil of lemon eucalyptus has been registered by the EPA, and was found to present little or no risk when used as directed. Other hazards were addressed via precautions outlined in the protocol and were followed during this study. A draft protocol was reviewed by Western IRB and then sent for review by EPA. The protocol was then reviewed and discussed with HSRB on the 24th of April 2018. The HSRB report that was dated in July 2018, concluded that with modifications recommended by EPA and HSRB, the study's likely to meet the applicable requirements of 40 CFR Part 26, Subparts K-L. Dr. Allen said the protocol on related materials was subsequently revised to address the concerns that had been raised by EPA and the HSRB. The inclusion and exclusion criteria, listed in the study report in the EPA Ethics Review, were appropriate to meet the needs of the study and to minimize risk to study participants. One subject experienced swelling on the arm from after study participation, and that was diagnosed as a toxic effect of venom of other arthropods. That individual recovered without any lasting effects. There also was one subject who experienced a suspected tick bite and had a red area surrounding the site and itching. That itching was treated with an anti-itch cream and resolved. Two subjects experienced a general ill feeling and one of these people experienced fatigue, a headache and fever, and noted that her participation coincided with an exam period and that the symptoms might be related to stress. The medical monitor that evaluated this incident

determined that it was not related to study participation. There was a second subject with general ill feelings, who reported dizziness and was seen by a medical professional. The medical professional felt the dizziness was due to possible dehydration or a drop in blood pressure related to temperatures in the laboratory. That adverse event was also determined to not be study related. Both of these individuals recovered without any lasting effects. Dr. Allen stated that the protocol was amended five times and all amendments were reviewed and approved by both Western IRB and the LSHTM Ethics Committee, following the regulations and policies of those IRBs. Dr. Allen agreed with EPA's assessment that none of the amendments directly impacted the health, safety, or welfare of the subjects in the study. After reviewing the materials provided by EPA to the HSRB, Dr. Allen concluded that this study was conducted in substantial compliance with procedures that are at least as protective of subjects as all the applicable provisions of the Common Rule, as codified by the EPA and other federal agencies. Dr. Allen concluded that the available information supports that the study, a single group, to determine the complete protection time of an insect repellent formulation containing 30% Citriodiol ® oil of lemon eucalyptus against three species of ticks, was conducted in substantial compliance with the procedures at least as protective as those in the applicable requirements of 40 CFR Part 26, Subparts K-L. The Board voted unanimously in the affirmative to the charge question: Does the available information support a determination that the research was conducted in substantial compliance with procedures at least as protective as those in the applicable requirements of 40 CFR Part 26, Subparts K-L?

This concluded the Board's session for July 21, 2020 and the meeting was adjourned.

July 22 meeting:

Meeting was called to order at 1:00 p.m.by Tom O'Farrell, designated federal official (DFO) for the HSRB. Roll was taken and the following members and observers were present:

HSRB members Jennifer Cavallari, Sc.D. (Chair) Mark Aulisio, Ph.D. Janice Britt, Ph.D. AJ Allen, Ph.D., M.D. Ann Um, Ed.D. Lisa Corey, Ph.D. George Milliken, Ph.D. Julia Sharp, Ph.D.	EPA staff members Michelle Arling (EPA, OPP) Timothy Leighton (EPA, OPP) Timothy Dole (EPA, OPP) Alicia Denning (EPA, OPP) Tom O'Farrell (OSAPE)
Members of the public, representatives of research sponsor and research team Brian Lange (Lange Research and Consulting) Cameron Lange (Lange Research and Consulting) Jonathan Cohen (ICF, contractor to EPA)	

Leah Rosenheck (LR Risk Consulting) Michael Bartels (Dow Chemical) Renee Daniels (Perspective Consultants) Kate Sande (EcoLab) Julie Chao (USDA) Has Shah (ACC) Tom McDonald	

Dr. O'Farrell provided an introduction to the meeting and outlined the Federal Advisory Committee Act (FACA) procedures and took role of the meeting participants.

The Board reviewed one protocol on July 22, 2020 "A Study for Measurement of Potential Dermal and Inhalation Exposure During Pressurized Hand-Wand Spraying of Antimicrobial Products along with Study Addendum: Addition of Electrostatic Sprayers (AEA14)" by the AEATF.

The Agency's scientific review of this study was presented by Mr. Timothy Leighton of EPA OPP. The protocol examines dermal and inhalation exposure to antimicrobial products during use of pressurized wand equipment. This protocol has been in development by the AEATF for many years and was developed pre-COVID. The AEATF submitted an addendum to the original protocol to add monitoring of applicators using electrostatic sprayers. Use of this application method has increased significantly recently as a way to disinfect surfaces indoors in light of COVID-19. The study is meant generate comprehensive exposure data, unlike existing studies that monitor exposures separately and analyze "incomplete body parts." The study analyzes indoor vs. outdoor use of the equipment, dry environment vs. wet environment, and scenarios in which residential consumers and professionals typically use the equipment. There are three test groups in the proposed study, each with two units of exposure: 1A, 1B, 2A, 2B, 3A, and 3B. Scenario 1A and 1B will use outdoor spraying. Scenario 1A will have 18 monitoring events with volunteers that are consumers (general population) who are going to be using manually powered handheld tanks and hose and sprayers. With those 18 monitoring events, they will have a dermal set of exposure numbers and an inhalation set of exposure numbers. Also, for outdoor monitoring (Scenario 1B) the study will have 18 different professional applicators using mechanically powered, handheld, portable spray tanks. The 18 individual participants will also be monitored for dermal and inhalation exposures. Scenarios 2A and 2B examine manual, handheld, or electrostatic sprayers used in an indoor environment. Scenario 2A represents a situation in which a professional might use a hand-held tank and backpack sprayer indoors on hard surfaces typically for mold after a flooding event or disinfectants. Scenario 2B will collect a separate set of exposure data specifically for applicators using electrostatic sprayers indoors. Scenario 3 consists of wet environments and the subjects are professionals. The scenario for exposure being examined includes usage of a sprayer at food processing plants. The difference between 3A and 3B is the amount of PPE worn by the subjects; Scenario 3A includes subjects wearing the labeling-required PPE, and Scenario 3B includes subjects wearing additional PPE (e.g., raincoats, waterproof pants) reflective of the typical pre-application activity of spraying

down the area to be treated with hoses. The objective of the study is to develop more accurate information on exposures to antimicrobials, to support EPA's exposure assessments, which eventually go into EPA risk assessments and get put onto the labels to communicate to the users on how to, in this instance, use to spray and treat hard surfaces. One of the test mixtures (prior to dilution) will contain 5.5 % QAC, that is it contains 5.5% ADBAC and DDAC total, and the other one is 7.5% total QAC. There is a 90-day dermal rat study using ADBAC giving a LOAEL at about 1%, at 80 µg per cm^2. Based on the low concentration of ADBAC in the study, "…the highest concentration of total Quats that will be sprayed is 1160 ppm (1160 ppm total Quats of which ADBAC accounts for 40%), equivalent to 0.0464%" for dermal contact. In the rat study for DDAC, there were no observed effects at a concentration higher than that used by participants of this study. Unit exposures for indoors versus outdoors were separated. Product labeling information will be based on the scenario that generates the most exposure. The proposed lowest amount of test chemical used was reduced from 215 parts per million to 100 parts per million, to be able to get a bigger range to detect proportionality and get a better estimate on the power. Air temperature, humidity, the spray volumes, and the exposure durations will be collected. All participants will wear safety goggles or glasses and will be assigned a specific spray volume. The study will use the OVS tubes for measuring inhaled residues and the PPI samplers for respirable residues. In conclusion, EPA thinks that the study is going to fill an important data gap and cannot be done except for research with human subjects. The study has a clear scientific objective and as designed it should produce data adequate to achieve that objective.

The Board asked questions about the science presentation. Dr. Corey asked if participants will be working as part of a crew. Mr. Leighton said that crews will not be included in the study. Dr. Britt asked about whether the safety data sheet recommended gloves for prolonged use and if the products that people are going to be using in the field are going to be higher concentrations or lower concentrations, or a set concentration. Mr. Leighton responded that the labeling is based on the specific chemical or chemicals and will not change unless new exposure data is generated. Mr. Tim Dole added that the requirement for protective equipment is based on examination of all the individual ingredients in a product mixture. Dr. Sharp asked how the adequacy of the sample sizes of the completed studies will be revisited after the studies have been completed. Mr. Leighton said the AEATF may go back and do another companion study to increase the monitoring events. Dr. Cavallari commented that the analysis will not be stratified by group unless useful patterns are found and asked what those patterns would look like in order for them to stratify by group. Mr. Leighton said this is a good question; however, variables that might effect exposure such as humidity are not effective to be used as a regulatory mitigation measure if they cannot be communicated on the product label.

Ms. Arling of EPA OPP reviewed the ethical aspects of the study protocol. Candidates for the study will be recruited through newspaper advertisements and radio advertisements run in both English and Spanish. After the screening is completed and a candidate is still interested, the researchers will invite him or her in for a consent meeting. The protocol does not call for

targeting recruitment to any vulnerable populations and contains precautions to minimize any potential for coercion or undue influence. Criteria that apply to all scenarios include being at least 18 years old and good health relative to the task to be performed in each scenario, having adequate experience performing the task to be monitored, speaking and reading English or Spanish, not smoking or being willing to refrain during the test, and willing to wear all PPE specified in the protocol. Females will be screened for pregnancy and pregnant or nursing women as well as children will be excluded from participation. After the candidates have finished reading the consent form, a member of the study staff will review the consent materials orally. After a subject decides to participate, they must answer some questions about the study to demonstrate their comprehension of the consent materials. At this point, they can sign the consent form and complete the subject qualification worksheet. Subjects who would face increased risks from participation due to health conditions, allergies, and other factors will be excluded. To further minimize risks associated with performing the tasks, only those subjects with experience doing the type of work involved in the study would be eligible to participate. A medical professional will be onsite during each monitoring event. All subjects will be required to wear eye protection to participate, and all PPE will meet or exceed the minimum labeling requirements. Subjects in Scenarios 1B, 2B, 3A, and 3B will be required to use a NIOSH-approved respirator and will have a valid fit-test certification prior to participation. With EPA recommendations incorporated, the risk to subjects will be minimized in the design of the research and are reasonable in light of the likely benefits to society from the new data. The proposed compensation for subjects is adequate considering the inconvenience, missed employment opportunities, and travel to and from the test location. The protocol informed consent form, subject qualification form, and recruitment materials were reviewed and approved by Advarra IRB on February 20th, 2020. EPA recommends that the protocol and consent materials be revised to reflect any risks associated with COVID-19 and the precautions that will be taken to ensure the safety of subjects in research. EPA also recommends that the protocol consent and recruit materials be revised to include the electrostatic sprayer scenario, that as part of the screening, the researchers provide information about the types of equipment that will be available, and that the researchers consider enrolling or prioritizing enrollment of subjects who are familiar with using the available equipment in order to minimize the risks to subjects from using unfamiliar electrostatic sprayers. EPA recommends that the protocol and consent materials are revised as necessary to update the test substance and rate information, and then that the protocol and consent forms for scenarios 1A and 2A be revised to note that while respiratory protection is not required by the label, its use is optional for participating in the study, and then revising the protocol for scenario 1B to indicate that respiratory protection is required for all subjects to ensure their safety and because the sprayer pressure will not be known until the monitoring is occurring. EPA also recommends revising the telephone screening scripts to reflect the updated respirator requirements for each scenario and to ask subjects about their occupational practices and what equipment they use, and also clarifying in the protocol how Spanish-speaking subjects will complete the online medical questionnaire for respirator use. EPA concludes that if the Agency's comments are addressed and the amended protocol is approved by the overseeing IRB, this research is likely to meet the relevant ethical standards.

The Board then asked questions regarding ethics review of the study. Dr, Cavallari asked if it is a recommendation that symptoms of COVID-19 be considered an exclusion criteria. Ms. Arling said that it would be prudent to specifically exclude anyone who has symptoms of COVID, but the protocol has eligibility criteria that requires the participant being in good general health. Dr. Cavallari also asked if EPA has thought about the recommendation of whether or not someone is COVID-19 positive, but remains without symptoms? Would that be something to consider as an exclusion criteria? Ms. Arling replied that she would welcome the Board's recommendation on this. Dr. Britt asked about allergies and sensitivities to chemical products are part of the inclusion criteria. Ms. Arling said it is a great suggestion to expand the exclusion criteria to specifically call out any respiratory allergies or sensitivities, if that is an area of concern. Dr. Milliken asked if subjects would be supplying their own respirators. Ms. Arling said that they can bring their own respirator if they can bring all the necessary documentation to show they are eligible, such as the fit-test certification documentation, otherwise the task force will provide the respirators and perform all the steps necessary to ensure that it can be worn safely.

There was a call for public comments but there were none.

The HSRB's scientific review was presented by Board members Drs. Corey and Britt. Dr. Britt said that they basically agree with the EPA science review, and would like to encourage continued collaboration with EPA to ensure sufficient study power. Dr. Britt said they agree that the updated hand wand sprayer data needed to be more reflective of the use of modern studies compared to the data that EPA already has for agricultural chemicals. Dr. Britt also said the inclusion of the measurements from the electrostatic sprayers is going to be useful for future and current applications for COVID-19. They also agree that the planned diversity is going to bias toward higher-exposure elements and that's good. They commented that subjects might also be instructed to avoid eating during their activities in the study. If they do eat, it is suggested that the protocol specify as to how the chemicals are lost due to this activity, for example, similar to the description of the restroom use by participants. Dr. Britt asked if it was possible that the use of consumer products containing the test compound, or compounds in general, like shampoos, or wipes, or deodorants might present an additional source of target analytics that might overestimate exposure. Dr. Corey said that rinsing the residues from hands could cause some aerosolization that could spread to other parts of the body, or splashing, or something that might also unexpectedly increase for certain parts of the body and asked whether that was anything that needed to be addressed or whether that should be fine with the assumptions that EPA has addressed. Dr. Cavallari said she would be in agreement that the cleaning of the hands would likely result in a big decrease in dermal exposure from the hands and that, by not including it, they may be missing some of that aerosolization or other exposure areas, but that the protocol should proceed as planned. Dr. Cavallari suggested that the recommendation might just be to recognize that, while it is likely protective and capturing the exposure, it may not be capturing the exposure to other parts of the body.

The Board's statistical review was given by Dr. Ann Um. Dr. Um said that if all the assumptions are met, the researchers can do ANOVA and linear regression analysis. Overall, the EPA recommendations are reasonable, and the statistical analyses are appropriate. Dr. Julia

Sharp said it might be useful to perform sub-analysis of the scenarios to identify patterns, and then the sample sizes, and the post hoc sample size calculations that will be used to inform future studies. The Board voted unanimously in favor to the following response to the science charge question: “The research presented in the protocol, a study for a measurement of potential dermal and inhalation exposure during pressurized hand wand spraying of antimicrobial products and the study addendum, addition of electrostatic sprayers, is likely to generate scientifically reliable data useful for the assessment of exposures of those who apply products containing antimicrobial pesticides using hand wand or electrostatic sprayers, given the comments and recommendations provided by the EPA and HSRB are adequately addressed.”

Dr. Mark Aulisio presented the HSRB’s ethics review of the study. Dr. Aulisio concurred with the EPA ethics review that the study, if it is done with each item and the EPA ethics recommendations having been addressed adequately, will be in substantial compliance with 40 CFR, sub-part K, and sub-part L. Dr. Cavallari asked if there is a recommended experience level for the electrostatic sprayer participants of the study. Ms. Leah Rosenheck said for this type of a study with this type of equipment, that probably even a month's worth of experience would be sufficient. Dr. Aulisio suggested that training with electrostatic spraying should be sufficient. Dr. Allen said that it would be appropriate to exclude someone from the study who has symptoms of COVID. Dr. Allen also recommended that phone screening for COVID should be followed up with additional screening. The Board voted unanimously in favor of the following response to the ethics charge question: "The research proposed in the protocol, a study for measurement of potential dermal and inhalation setting during pressurized hand wand spraying of antimicrobial products, the study addendum, addition of electrostatic sprayers, and the related documents are likely to meet the applicable requirements of 40 CFR Part 26, Subparts K and L, given he recommendations of the EPA and HSRB are adequately considered."

This concluded the Board’s session for July 22, 2020 and the meeting was adjourned.

Respectfully submitted:

Thomas O’Farrell, Ph.D. Thomas J. O'Farrell 10/21/20
Designated Federal Officer
Human Studies Review Board
United States Environmental Protection Agency

Certified to be true by:

Jennifer Cavallari, Sc.D.
Chair
Human Studies Review Board
United States Environmental Protection Agency

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by Board members during the course of deliberations within the meeting. Such ideas, suggestions and deliberations do not necessarily reflect definitive consensus advice from the Board members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final report prepared and transmitted to the EPA Science Advisor following the public meeting.

Attachment A
EPA HUMAN STUDIES REVIEW BOARD MEMBERS

Chair

Jennifer Cavallari, Sc.D., CIH
Associate Professor
Department of Public Health Science
University of Connecticut School of Medicine
Farmington, CT

Vice Chair

Alesia Ferguson, Ph.D.
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Members

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Consultants to the Board

Kendra L. Lawrence, Ph.D., BCE, PMP
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Attachment B
Federal Registers Notice Announcing Meetings

ENVIRONMENTAL PROTECTION AGENCY

[FRL-10010-72-ORD]

Human Studies Review Board; Notification of Public Meetings

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The Environmental Protection Agency (EPA), Office of Research and Development announces two separate public meetings of the Human Studies Review Board (HSRB) to advise the Agency on the ethical and scientific review of research involving human subjects.

DATES: A two-day virtual public meeting will be held on Tuesday, July 21, 2020 and Wednesday, July 22, 2020, both from 1:00 p.m. to approximately 5:30 p.m. Eastern Time. A separate, subsequent teleconference meeting is planned for Thursday, September 17, 2020, from 2:00 p.m. to approximately 3:30 p.m. Eastern Time for the HSRB to finalize its Report of the July 21 and 22, 2020 meeting.

ADDRESSES: All of these meetings will be conducted entirely virtually and by telephone. For detailed access information visit the HSRB Website: https://www.epa.gov/osa/human-studies-review-board.

FOR FURTHER INFORMATION CONTACT: Any member of the public who wishes to receive further information should contact the HSRB Designated Federal Official (DFO), Thomas O'Farrell at the following telephone number: (202) 564-8451 or by email address at: ofarrell.thomas@epa.gov.

SUPPLEMENTARY INFORMATION:

Meeting access: These meetings will be open to the public. The full agenda with access information and meeting materials will be available at the HSRB Website: https://www.epa.gov/osa/human-studies-review-board. For questions on document availability, or if you do not have access to the Internet, consult with the DFO, Thomas O'Farrell, listed under FOR FURTHER INFORMATION CONTACT**.**

Special accommodations. For information on access or services for individuals with disabilities, or to request accommodation of a disability, please contact the DFO listed under FOR FURTHER INFORMATION CONTACT at least 10 days prior to the meeting to give EPA as much time as possible to process your request.

How May I Participate in this Meeting?

The HSRB encourages the public's input. You may participate in these meetings by following the instructions in this section.

1. Oral comments. To pre-register to make oral comments, please contact the DFO, Thomas O'Farrell, listed under FOR FURTHER INFORMATION CONTACT. Requests to present oral comments during the meeting will be accepted up to Noon Eastern Time on Tuesday, July 14, 2020, for the July 21 and 22, 2020 meeting and up to Noon Eastern Time on Thursday, September 10, 2020 for the September 17, 2020 meeting. To the extent that time permits, interested persons who have not pre-registered may be permitted by the HSRB Chair to present oral comments during either meeting at the designated time on the agenda. Oral comments before the HSRB are generally limited to five minutes per individual or organization. If additional time is available, further public comments may be possible.

2. Written comments. Submit your written comments prior to the meetings. For the Board to have the best opportunity to review and consider your comments as it deliberates, you should submit your comments via email by Noon Eastern Time on Tuesday, July 14, 2020, for the July 21 and 22, 2020 meeting and by Noon Eastern Time on Thursday, September 10, 2020 for the September 17, 2020 meeting. If you submit comments after these dates, those comments will be provided to the HSRB members, but you should recognize that the HSRB members may not have adequate time to consider your comments prior to their discussion. You should submit your comments to the DFO, Thomas O'Farrell listed under FOR FURTHER INFORMATION CONTACT. There is no limit on the length of written comments for consideration by the HSRB.

Background

The HSRB is a Federal advisory committee operating in accordance with the Federal Advisory Committee Act 5 U.S.C. App.2 § 9. The HSRB provides advice, information, and recommendations on issues related to scientific and ethical aspects of third-party human subjects research that are submitted to the Office of Pesticide Programs (OPP) to be used for regulatory purposes.

Topic for discussion. On July 21, 2020, the HSRB will review a completed study from Citrefine International Limited titled "A single group trial to determine the complete protection time of an insect repellent formulation containing 30% Citriodiol ® (Oil of Lemon Eucalyptus) against three species of ticks". On July 22, 2020, the HSRB will review a protocol from the Antimicrobial Exposure Assessment Task Force II titled "A Study for Measurement of Potential Dermal and Inhalation Exposure During Pressurized Hand-Wand Spraying of Antimicrobial Products".

The agenda and meeting materials for this topic will be seven calendar days available in advance of the meeting at https://www.epa.gov/osa/human-studies-review-board.

On September 17, 2020, the HSRB will review and finalize their draft Final Report from the July 21 and 22, 2020 meeting. The agenda and the draft report will be available seven calendar days prior to the meeting at https://www.epa.gov/osa/human-studies-review-board.

Meeting minutes and final reports. Minutes of these meetings, summarizing the topics discussed and recommendations made by the HSRB, will be released within 90 calendar days of each meeting. These minutes will be available at https://www.epa.gov/osa/human-studies-review-board. In addition, information regarding the HSRB's Final Report, will be found at https://www.epa.gov/osa/human-studies-review-board or can be requested from Thomas O'Farrell listed under FOR FURTHER INFORMATION CONTACT.

Dated:

Jennifer Orme-Zavaleta
EPA Science Advisor