Agricultural Handlers Exposure Task Force (AHETF) Study No. AHE34 Protocol Review
Closed Mixing/Loading Of Liquids Protocol
Agency Reviewers: Jeff Evans & Jeff Dawson (Date of Review: 5/31/2006)

STUDY TYPE: Mixer/Loader/Applicator Passive Dosimetry Study Based On Whole-Body Dosimetry & Handwashing Techniques

TEST MATERIAL: Malathion 8EC or Gowan Malathion 8 (2 names for same product)
EPA Registration Numbers: 51036-214 or 10163-21
Lot & Container Descriptions: To be recorded at field site.
Common Chemical Name Of Active Ingredient: malathion
CAS Number of Active Ingredient: 121-75-5
Nominal concentration of active ingredient: 8lb ai/gallon

[In this study, the stability of the active ingredient in storage and a purity analysis of the formulated products will be conducted and tracking/storage conditions will also be documented. A sample will be retained as well for future needs.]

SYNONYMS: Malathion

CITATION: Closed System Mixing/Loading Of Liquids Protocol; Study No. AHE34; Determination of Dermal and Inhalation Exposure To Workers During Closed System Mixing/Loading A Liquid Pesticide Product

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EXECUTIVE SUMMARY:

This study is part of a series of studies that are to be conducted by the Agricultural Handlers Exposure Task Force (AHETF). The premise of the AHETF is that data from these studies can be used generically by various stakeholders (e.g., applicants, registrants, EPA, and others) for calculating exposures for the occupational handlers of pesticides. Given this context, this protocol defines only this particular AHETF study to quantify exposures for those who mix and load liquid pesticide products with examples of various closed loading systems. Field applicator exposure will also be monitored if the situation is feasible for such occurrences. [Note: Additional information concerning the overall scope of the AHETF is available that illustrates how this particular study will be integrated in the resulting database to be used for calculation of pesticide handler exposures.] The Agency believes these data are necessary because they will provide a means for considering current agricultural practices, equipment and techniques in its assessments allowing for more refined results. The monitoring techniques to be used for this study also have been standardized within the context of the AHETF which will provide a similar basis for analyzing trends in exposure compared to currently available data which can be confounded because of monitoring technique issues (i.e., disparity amongst studies). More refined data will allow the Agency to better establish the sensitivity of worker exposure levels to changes in various factors such as the amount of active ingredient handled, type of application equipment used, application rate used, volumes handled, and personal protective equipment used (i.e., data will allow for a better evaluation of exposures as a function of many variables to be measured during the conduct of this study).

The primary objective of this study is to collect up to 13 replicates of individuals mixing/loading a range of amounts of liquid pesticide formulations using small 'suction and rinse' type, closed mixing systems such as the Chemprobe® (i.e., 10 are anticipated) with the additional replicates occurring from monitoring application events (i.e., 3 are anticipated). Field investigators will monitor actual agricultural practices so the nature of the situations to be monitored will depend somewhat on the agricultural requirements for those situations thus necessitating flexibility in the design of this study. The events that investigators in this study are attempting to capture are that subjects mix/load enough pesticide to accommodate a range of tank loads (2 – 7) using a range of container sizes (2.5 – 55 gallons) with applications to follow based on each agronomic situation. An example scheme which illustrates the range of practices AHETF is attempting to capture in this study is presented below (based on their example from the protocol):

Replicate	Day	Container Size	Number of Containers	Pounds ai Mixed
M1	1	2.5	2	25
M2	1	2.5	7	125
M3	1	5	6	225
M4	2	30	2	325
M5	2	5	11	425
M6	2	55	2	525
M7	3	30	3	625
M8	3	55	2	725
M9	4	55	2	825
M10	4	55	3	925

Mixer/loaders will prepare a minimum of three loads for one or more spray rigs (aerial or ground equipment) for a duration of 4 hours. The application rate will range from 0.5 to 2 pounds per acre depending on field conditions at the time and location of the study. All mixer/loader replicates will be performed by a separate worker. However, some mixer/loaders may also perform the application, that is mix/load on day one and apply on day two. These logistical decisions will be made at the discretion of the study director. The applicator monitoring is discussed in AHE 36 and AHE 37.

The clothing to be worn by the volunteers will consist of long sleeved shirts and long pants, shoes plus socks, in accordance with the Worker Protection Standard (WPS). Volunteers may wear their own clothing provided they are freshly laundered (otherwise the AHETF will provide freshly laundered clothing). Any personal protective equipment (PPE) that may also be required by the WPS, such as chemical resistant gloves and protective eyewear, will be provided by the study director.

Dermal exposure measurements will employ long cotton underwear (a surrogate for skin) worn under the volunteers single layer of clothing (long sleeved shirt and long pants), hand rinses and face/neck wipes. The face and wipe solutions will consist of 0.01% Aerosol OT solution. OSHA Versatile Samplers (OVS) outfitted with glass filters, XAD-2 sorbent, and tygon tubes will be used to measure inhalation exposure. The pumps will be calibrated at a rate of 2L/minute. The tubes will be attached to the volunteer's collars with the openings positioned in their breathing zones.

After monitoring, the dosimetry will be collected in the following order: inhalation, hand rinses, face and neck wipes and finally the inner dosimeters (with outer clothing being removed by the individuals privately). The inner dosimeters for mixer/loaders and open cab applicators will be cut into six sections representing the upper and lower arms, the front and back torso and the upper lower legs. For closed cab/cockpit applicators, the inner dosimeters will be divided into two sections, upper and lower body.

Hand rinses will be collected using 0.01% Aerosol OT. Hands will be washed prior to monitoring. Rinses will be collected at the end of the monitoring period with additional rinses being collected if a volunteer stops to eat, smoke or use the toilet. Likewise, the face and neck wipes will also use 0.01% Aerosol OT and collected with s gauze sponges with additional wipes being performed in a volunteer stops to eat, smoke or use the toilet.

On at least two study days, each dosimetry matrix will be fortified in triplicate at the following levels (µg/sample). Decisions to conduct additional fortifications on additional days are left to the discretion of the study director.

Matrix	Level (µg/sample)
Inner Dosimeter	5, 100, 5000
Face and Neck Wipes	5. 100, 2500
Hand Rinses	5, 100, 5000
OVS	0.05, 1.0, 50

The fortified samples will be exposed to the field conditions at a nearby location upwind of the mixer/loader or application operations. The inner dosimeters will be covered with shirt material and be exposed to the same conditions as the measurement dosimeters. Fortified air samples will be operated in a similar manner as worn by the volunteers. The hand wash and face/neck wipes will be fortified and be placed directly into storage.

On each field fortification day, duplicate samples of the inner dosimeters fortified at the highest fortification level will be processed for immediate frozen storage and serve as travel spikes. Duplicate OVS tubes fortified at the highest fortification level will serve as a travel spike. In addition there will be two untreated controls for the inner dosimeter and OVS matrices. However, the controls will be handled in the manner of the field fortifications.

In addition to the results of the analysis of the dosimetry and field fortifications, the following records will also be provided in the study report:

- Test substance (reference and control number)
- Crop description and stage of growth
- Mixing/loading and or application details, observations and equipment type
- Application maintenance records
- Environmental conditions (portable weather station data or nearest NOAA recording site
- Personal details of the workers (including consent forms)
- Location and site map, dimensions of plots
- Pounds active ingredient handled per replicate
- Dermal exposure sample information
- Inhalation exposure sample information
- Field observations (including photographs)
- Sample information (including chain of custody).

The dosimetry and analytical details described above are the same for the remaining studies discussed in this memorandum. For the remaining studies, only study design specifics (e.g., mix/load or application details) will be discussed.

The Agency believes that this study, if appropriately conducted, will provide critical information related to the exposures that would be expected for individuals who mix/load liquid agricultural pesticides with closed loading systems of various types. It is also believed that the monitoring techniques proposed for this study represent the current state-of-the-art. However, the Agency also recognizes that use of the data resulting from this study will also take careful scrutiny and may require a number of adjustments depending upon the results. Finally, the overall design of this study should be considered in the context of the goals of the AHETF which are to develop a broad-based database that can be generically used as a predictive tool for estimating exposures to pesticide handlers and that the interpretation of the results of this study may or may not necessitate the need for additional monitoring data for closed system mixing/loading of liquids.

COMPLIANCE:

Study Conduct: This study will be conducted in compliance with the U.S. EPA FIFRA Good Laboratory Practice (GLP) Standards (40CFR160) and will adhere to applicable AHETF and/or field facility standard operating procedures (SOPs). Both the field and analytical phases of this study will be audited as well as the generation of the final report by the independent Quality Assurance Unit for the investigators as required by the GLPs with findings being available for review in the final study report. Any protocol amendments or deviations will be included in the final report as well as an assessment of their overall impact on the results of the study.

[See http://frwebgate1.access.gpo.gov/cgi-bin/waisgate.cgi?WAISdocID=794275183132+39+0+0&WAISaction=retrieve]

Ethics & Informed Consent: The Agency's review of the ethical components of this study is included in a separate document for consideration by the HSRB (i.e., see John Carley memo, 2006). This protocol was reviewed by the Western Institutional Review Board (WIRB), Olympia Washington. A series of documents produced by the either the AHETF or the WIRB pertaining to this study are included as Appendix A as background information for the HSRB to consider in its deliberations. These include: WIRB submission requirements and other administrative correspondence; a WIRB approved informed consent form (along with working drafts and WIRB required edits); an emergency hospitalization procedure for subjects; a WIRB *"Certificate of Approval"* for this study; and a list of the WIRB panel members. [See http://www.wirb.com/]

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GUIDELINE OR PROTOCOL FOLLOWED:

The protocol for this study is based on a design that was developed by the AHETF after joint discussions with the United States Environmental Protection Agency, Health Canada, and the California Department of Pesticide Regulation. This protocol was specifically developed in the context of the overall research plan for AHETF where the effect of different parameters on exposure levels will be evaluated based on these and other similar data that will be used to populate a database which will be used for analysis purposes.

The basic elements of the protocol are described in the following Agency guidance documents including:

- U.S. Environmental Protection Agency, Occupational and Residential Exposure Test Guidelines, Series 875.1000 through 875.1600. (1996) The guidelines are available at the following:

  http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/875_Occupational_and_Residential_Exposure_Test_Guidelines/Series/

- U.S. Environmental Protection Agency, Working Draft - Occupational and Residential Exposure Test Guidelines, Series 875 Group-B, Postapplication Exposure Monitoring Test Guidelines Version 5.4 (1998) The working draft guidelines are available at:

  http://www.epa.gov/scipoly/sap/1998/march/contents.htm

The initial protocol design for this study was developed based on the guideline documents referenced above. However, the design of this study has been considered in the context of the goals of the AHETF to compile information across many studies in order to evaluate how factors can impact exposures.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material: Malathion 8EC or Gowan Malathion 8 (2 names for same product)
EPA Registration Numbers: 51036-214 or 10163-21
Lot & Container Descriptions: To be recorded at field site.
Common Chemical Name Of Active Ingredient: malathion
CAS Number of Active Ingredient: 121-75-5

2. Relevance of Test Material to Proposed Formulation(s):

The use of a malathion 8 EC formulation for the purposes of this study is considered appropriate. The intent of the AHETF is to develop a series of data that can be used to generically predict handler exposure levels. In order to accomplish this in a systematic fashion and to alleviate the potential for confounding results that may be caused by analytical methodology issues the AHETF selected a limited number of chemical active ingredients for use in their research program. These ingredients, including malathion, tend to have broad use patterns across agriculture in order to allow for the evaluation of exposures in many different settings which are included in the research plan for AHETF (i.e., end-use product labels for these chemicals allowed use on many crops and using many types of equipment). These chemicals also have analytical methods for the monitors which are to be used in this study that provide for reproducible results in a reliable manner and that have appropriately low screening levels.

3. Packaging:

The product packaging which will be evaluated in this study will be of 2 general categories and include plastic jugs in the 2.5 to 5 gallon volume range and larger drums in the 30 to 55 gallon range. The size of the container often times will be dictated by the closed transfer system which is used because often times containers are mated to specific systems (e.g., Chemoprobe © or custom built systems with particular fittings).

B. STUDY DESIGN

The AHETF overall research plan is to evaluate exposures for occupational pesticide handlers in agricultural settings using a wide array of mixing/loading and application equipment and different types of personal protective clothing/equipment in order to develop an exposure database that can be generically used by stakeholders to predict exposures for occupational pesticide handlers.

The primary goal of this study is to address an element of the overall goal by quantifying exposures for those involved in mixing/loading liquid products with closed systems (e.g., Chemprobe©) in preparation for typical agricultural applications of pesticides. A secondary goal, should an appropriate field situation arise, is to also quantify the exposures of applicators using either airblast or aerial application equipment with the resulting solutions (see discussion of other AHETF protocols for further information, AHE 36 & AHE 37).

Critical elements of the proposed study are described below and include (1) the numbers and types of workers/sites to be monitored; (2) the level of personal and protective clothing/equipment to be used by the monitored subjects; (3) a description of the mixing/loading equipment and application equipment to be used; (4) a description of the application rate to be used; (5) a description of the exposure monitoring methods to be used; (6) a description of the analytical methodology; (7) a summary of the analytical quality control elements contained in the proposed study; and (8) the relevancy of the proposed monitoring to current agricultural practices and the available data that can currently be used to assess these uses.

1. Number and type of workers and sites:

In Section 5 (page 14 of 34) of the protocol, it is indicated that "ten different mixer/loader workers (or replicates) will be monitored for exposure" based on the following suggested scheme:

Replicate	Day	Container Size	Number of Containers	Pounds ai Mixed
M1	1	2.5	2	25
M2	1	2.5	7	125
M3	1	5	6	225
M4	2	30	2	325
M5	2	5	11	425
M6	2	55	2	525
M7	3	30	3	625
M8	3	55	2	725
M9	4	55	2	825
M10	4	55	3	925

As also indicated above, application events may also be monitored at the discretion of the Study Director (i.e., 3 are anticipated for total N = 13). It is optimal that each "replicate" be a unique individual. [Note: In Section 3 (page 7 of 34) the protocol indicates that the "number of workers monitored will be determined based on available resources in the field and will be detailed in the raw data. The anticipated number of total replicates is thirteen (13)." It is believed that this implies some of the anticipated monitoring events will be for applications and not just mixing/loading since only 10 mixer/loader events are cited above. It is also important to consider the number of monitored workers in the context of the overall AHETF database development goals.]

In Section 3 (page 7 of 34) it is indicated that "all monitored workers will be professional agricultural workers who will be required to give their informed consent to participate in the study. Section 5.3 (page 8 of 34) provides additional information pertaining to the workers to be monitored in this study. This section indicated:

> "Adult workers will be selected who are experienced in the work activities under study and who consider themselves to be in good health. In particular, the mixer/loader workers will have experience with the specific closed system being used. They should also have a willingness to cooperate in a study of this type and have no conflict of interest in the conduct or outcome of the study. The reproductive status of all potential female participants will be ascertained through the use of a supervised urine pregnancy test conducted within 24 hours prior to initiation of monitoring. Any pregnant subjects will be excluded from the study. The volunteers will be at least 18 years of age.
>
> A signed informed consent form will be obtained from each worker prior to their participation in the study. This protocol, as well as the informed consent form and worker selection process, will be reviewed and approved by an Institutional Review Board (IRB) prior to worker exposure monitoring. [Note: See Appendix A for further information.]
>
> Each worker will be provided with a full explanation of the study, its requirements, and any potential risks. Workers will be advised of their right to withdraw from the study at any time and for any reason without jeopardizing their normal position with their employers. In order to maintain confidentiality in their final report, only the unique worker identity number will identify each worker.
>
> Personal details including name, age, gender, previous experience in the work activity, and a general health statement will be provided by each worker. In addition, the body weight and height of each worker will be measured by researchers. All personal information will be maintained in the study file."

All study sites are to be located in California. Field maps and other data will be collected to document the site and equipment used for each monitoring event. In Section 5.9 (page 13 of 34) it was indicated " the exact configuration and size of equipment will be dictated by what is available in the field; however, the study director will make an attempt to utilize a variety of standard equipment throughout the study."

2. <u>Protective clothing & Equipment:</u>

The workers will wear normal work clothing with whole-body dosimeters underneath. Normal work clothing will be "WPS compliant" [i.e., Worker Protection Standard] according to the protocol and will consist of long-pants and long-sleeved shirts. These garments will be either "freshly laundered or new and free from pesticide residues" based on a worker self certification process. Shoes and socks will also be required. According to the malathion labels, chemical resistant gloves and protective eyewear are also required and shall be worn by each monitored subject.

All liquid handling systems for mixer/loaders will be closed systems. If airblast applications are monitored (i..e, a common application method on tree crops or grapes) either open or closed-cab tractors could be used (i.e., closed-cabs offer more protection and are considered an engineering control). If aerial applications are monitored, the aircraft will be of the closed cockpit variety which dominate the industry.

3. <u>Mixing/loading/application method:</u>

As indicated above, the primary purpose of this study is to monitor workers who mix/load spray solutions prepared with liquid products with a closed loading system. The target duration for each monitored interval will be 4 hours. According to the protocol (Section 5.7, page 11 of 34) "all mixing/loading activities will involve transferring the liquid product from commercial product packaging into a suitable tank and dilution with carrier. This transfer will involve closed system transfer using a small-volume suction and extraction system such as a Chemprobe© or similar system.." Section 5.9 (page 13 of 34) also indicated " mixing/loading will involve transfer using small volume, suction and rinse type, closed loading systems into appropriate mixing or application tanks. For example, a Chemprobe ® system could be used which secures to a container, suctions product out through a sealed connection to the

spray tank, and then rinses the test substance container into the tank. Custom systems with the same basic design may also be used. Test substance may be packaged in a range of container sizes (e.g., 2.5 or 5 gallon jugs and 30- or 55-gallon drums for closed system transfer)."

The accuracy of the equipment used will be verified prior to use in the study including equipment used to weigh, pump, or meter test substance and carrier (i.e., water).

If applications are monitored, it is suspected that a typical airblast sprayer with either an open- or closed-cab tractor will be used for tree fruit (e.g., http://johnbeansprayers.durand-wayland.com/series/redline/redline600c.html) or applications with a typical fixed wing aircraft (e.g., http://www.airtractor.com/models/502/) to a variety of crops will be used. However, it was also indicated in the protocol that applications could be made with any label approved method.

In most of the situations to be monitored, it appears that normal work practices are to be followed. Mixer/loaders may also prepare spray solution for more than 1 application rig. Mixer/loader activities may also include "routine preparation, clean-up, and container disposal activities … according to the workers' typical procedures for the equipment used during his mixing/loading task." For applicators, "spray equipment set-ups will be determined by the worker according to his/her usual practice." One possible exception to normal work practices is that "for all workers, the mixing/loading and/or application parameters will be adjusted to the target of at least four hours of exposure monitoring are met. For example, the workers who mix/load smaller amounts of product might use smaller tank sizes and prepare less concentrated spray mixtures so that multiple loads are necessary and the work time is extended. Similarly, the spray volume and/or application rate may be adjusted to that applicators reach the target of at least 4 hours of monitoring time."

4. Application Rate:

As indicated above in Section B.1 the intent is to monitor subjects for approximately 4 hours who handle in the range of 25 to 925 pounds of active ingredient during the monitoring event.

If applications are to be completed, the target application rate, according to the protocol in Section 5.7 (page 11 of 34), will depend "on target crop and field needs, but application rates will generally range from 0.5 to 2.0 lb active ingredient per acre. Actual application rates will be documented in the study raw data."

Application volumes will also "depend on target crops and field needs, but application volumes will generally range from 20 to 60 gallons/acre for groundboom applications and 5 to 10 gallons/acre for aerial applications."

5. Exposure monitoring methodology:

Pesticide exposure predominantly occurs to the skin with smaller amounts (e.g., typically 5 percent or less of the total) occurring as inhalation exposure. There are essentially two basic techniques for quantifying exposures to pesticide chemicals: these include biological monitoring or passive-dosimetry. Each technique has negative and positive attributes associated with it as described in the guideline documents referenced above. The AHETF has opted to use a passive dosimetry approach, which is the more common monitoring method. The passive dosimetry techniques which are to be utilized by AHETF in the completion of this study are the most commonly employed approaches for completing occupational monitoring studies.

Dermal exposure sampling typically includes defining the amount of residues that could potentially be deposited on the skin of a monitored individual. To adequately quantify dermal exposures for the entire body, three different monitoring approaches are to be used in this study including whole-body dosimetry which will cover skin areas from the neckline to wrists and feet. A wiping technique will be used to collect residues from the face and neck area and a washing technique will be used to collect residues from the hands. Full details of the processes and procedures to be used for dermal sampling are included in the standard operating procedures (AHETF SOPs 8.A; 8.B; 8.C; 8.D; 8.H; and 10.E) which are available for review. Separate procedures are also available that pertain to inhalation sampling (AHETF SOPs 8.D & 10.A).

A brief summary of the techniques to be used for both dermal (all types) and inhalation sampling is provided below.

Dermal Using Whole-Body Dosimeter: As indicated above in ***Section 2 – Protective Clothing*** and AHETF SOP 8.A, normal work clothing will be worn over top of the whole-body dosimeter. The intent of the whole-body dosimeter is to capture residues that could deposit on the surface of the skin which in turn could be available for absorption through the skin resulting in a dose. The dosimeter "will consist of 100 percent white cotton long underwear provided by the AHETF. The inner dosimeter is designed to represent the worker's skin and will act as a collection medium that will be analyzed. It will be worn throughout the period of monitoring and will be removed at the end of the work period. At the end of the monitoring period (and after the inhalation exposure equipment are removed), the worker will first remove his/her gloves and shoes, and then enter a clean, private area for collecting the remaining samples. Once inside the private area, the worker will remove his/her outer clothing and socks. The outer layer of clothing will not be collected or analyzed." Once removed, for the mixer/loaders or open cab applicators "each inner dosimeter will be sectioned into 6 sections: upper and lower arms; front and back torso; and upper and lower legs. For any closed cab or closed cockpit applicators, each dosimeter will be sectioned into two sections: upper and lower body." Samples will be wrapped in aluminium foil then stored frozen in pre-labelled containers.

Dermal Face and Neck: As indicated in AHETF SOP 8.C, a wipe technique will be used to quantify exposure levels to the face and neck area. This will be accomplished by "wiping the entire face and neck areas (front and back) with two gauze sponges, sequentially, that have been wetted with 0.01 percent Aerosol OT" which is a mild aqueous soap solution. If workers stop to eat during the monitoring period, wipe samples will be collected. Workers will be asked to wash their face or wipes will be used before the monitoring period begins to clean their faces so that only residues which are deposited during the monitoring period will be collected. Like the whole-body dosimeters, samples will be wrapped in aluminium foil then stored frozen in pre-labelled containers.

Dermal Hand: As indicated in AHETF SOP 8.B, a washing technique will be used to quantify exposure levels to the hands (i.e., the amount of residues deposited on the hands). This will be accomplished by "having the worker wash their hands in a 0.01 percent Aerosol OT solution according to a standardized washing procedure" as described in the SOP. Workers will be asked to wash their hands before the monitoring period begins to clean their faces so that only residues which are deposited during the monitoring period will be collected. Handwash samples will be collected from workers "whenever a worker would normally wash his/her hands (e.g., before using the toilet, before using tobacco, etc.). .)." Samples will also be collected at the end of the monitoring period. All handwash samples will be kept separate and individually labelled and will be stored frozen in pre-labelled containers.

Inhalation: As indicated in AHETF SOPs 8.D & 10.A, a personal air pump coupled with an OVS (OSHA Versatile Sampler) tube (e.g., http://www.msanorthamerica.com/catalog/product685.html & http://www.skcinc.com/prod/226-30-16.asp) will be used to monitor inhalation exposure levels. The OVS tube will contain a glass fiber filter and XAD-2 sorbent. Pumps will be calibrated to a flow rate of 2 Lpm before and after sampling. Pumps will be attached to the workers' belts and the OVS sample tube (attached via tubing to the pump) will be located on the workers' collars in their breathing zones to capture representative air samples of concern. Like with the other sampling devices described above, OVS samplers will be collected at the end of each monitoring period and stored frozen and individually labelled.

It should be noted that these monitoring techniques are very commonly used for the monitoring of occupational exposures to pesticides. The use of these techniques does not preclude adjustments to the resulting data based on a variety of possible factors that could account for such phenomena as losses during sampling of collected residues, possible incomplete residue collection (e.g., from hands) and other factors such as breakthrough or volatility losses from OVS samplers which could be determined in the analysis of these data.

6. Analytical Methodology:

For each of the sampling media in this study (i.e., whole-body dosimeters, handwash, face/neck wipes, and OVS tubes) there is a separate analytical method which has been developed in order to quantify the levels of malathion residues contained in that media. In addition to the sampling media, representative lots of the malathion 8 EC formulation and the spray solutions will be collected and analyzed to verify the levels of malathion in the materials handled/prepared by the monitored subjects.

The specific analytical methods to be used in this study are referenced below (and have been provided separately for review purposes):

- Analytical Method No. ARTF-AM-005: Determination Of Diazinon And Malathion In Inner Dermal Dosimeters;
- Analytical Method No. ARTF-AM-006: Determination Of Diazinon And Malathion In Handwash Solutions;
- Analytical Method No. ARTF-AM-009: Determination Of Diazinon And Malathion In OVS Air Sampling Tubes; and
- Analytical Method No. ARTF-AM-010: Determination Of Diazinon And Malathion In Facial/Neck Wipes.

The methods used for malathion on each of the sampling media used for this study have been evaluated and are applied generically within the scenarios to be evaluated by the AHETF where malathion may be used to estimate exposures for several occupational handler tasks. The screening limits established for these methods have been deemed appropriate for these types of studies. Substitutions of equivalent instrumentation, reagents, or other materiel are allowable. Procedural changes require study director approval. All data will be calculated against a standard curve with a limit of determination (r^2) $\geq$ 0.90 or regression coefficient (r) $\geq$ 0.94.

All manner of records will be maintained in accordance with FIFRA Good Laboratory Practice requirements and will include (but not necessarily be limited to) worksheets, notebooks, chain-of-custody records, chromatograms. Instrument log and maintenance books, substance use logs and archival samples of the analytical materials used will also be retained.

7. Quality Control:

The proposed study incorporates several quality control elements into its overall design. The first is that extensive records will be kept that pertain to the design, conduct of the study in the field, conduct of the study in the analytical laboratory, and the reporting phase. Additionally, independent quality assurance unit will audit each critical phase of the study and report to the sponsor organization any items of note as specified in the FIFRA Good Laboratory Practices.

Field records will document a variety of elements of the study including the chemicals used, the cultural practices in which the monitored subjects are involved, any equipment used by the subjects in the study, the exposure monitoring methods, and any data related to the nature of the site that is important (e.g., sample storage conditions). Photographic and video records will also be collected and maintained to aid in the interpretation of the results of this study (e.g., video records of subjects engaged in various monitored activities). Calibration of appropriate equipment will also occur and may include flow rates for personal sampling pumps, flow meters for adding water when preparing spray solutions, scales/balances for preparing analytical solutions and spray solutions, and spraying systems (e.g., airblast sprayer and tractor) if applications are monitored in this study. Logs that track chemical usage will also be maintained in order to ensure proper preparation of test solutions and to document the use of appropriate chemicals during the conduct of the study.

In addition to the procedures outlined above and elsewhere in the protocol, a number of control samples (both positive and negative) will be generated and analyzed in order to ensure the overall viability of the analytical phase of this study and also to allow for the derivation of appropriate residue adjustment factors which can be used to account for the loss of residues from field monitors during the monitoring periods themselves, during sample transport/storage, possible contamination of field monitors, and from analytical methods which do not quantitatively evaluate residues (i.e., are only capable of capturing a certain percentage of the available residues). These can be categorized in the following manner:

Prefield Testing & Method Performance Evaluations: These types of samples are intended to evaluate the overall ability of the analytical method to extract and quantify the residue of interest (in this case malathion) from the various media used for sampling (e.g., cotton whole-body dosimeter shirts). These evaluations are commonly referred to as method validation. Additionally, it is important to also ascertain how much possible residue loss from a sampler might occur under field conditions (e.g., OVS tube after air has been pulled though it) in order to anticipate the performance of the method while monitoring under actual field conditions. This work has already been completed and will be documented for each media in the analytical methods referenced above.

Laboratory Recovery: During the analysis of samples in the laboratory, it is important ensure that the analytical method is performing appropriately (e.g., instruments are working and processes are appropriately completed). In order to do this both positive and negative control samples are analyzed with each batch of field samples to ensure that no adverse levels of unwanted contamination are present (i.e., negative controls) and that the analytical method is functioning properly within given performance criteria (i.e., positive controls). A minimum of "two laboratory spikes must be included in each analytical set." For larger sets of samples, a positive control sample is to be included for every 10 field samples. Positive control samples will be fortified at levels expected to bracket the levels anticipated in the field samples.

Field Recovery: As with the laboratory recovery samples above, both negative and positive control samples will be generated. Negative control samples will be used to evaluate the possibility for sample contamination throughout the sample handling and storage process prior to analysis. The positive control samples are intended to evaluate "the stability of the active ingredient [in this case, malathion] under field, storage, and transit conditions in or on the sampling materials (inner dosimeters, handwash solutions, face/neck wipes, head patches, and air sampling matrices)." Field recovery procedures will be completed as described in AHETF SOP 8.E.

On at least two study days, each dosimetry matrix will be fortified in triplicate at the following levels (µg/sample). Decisions to conduct additional fortifications on additional days are left to the discretion of the study director.

Matrix	Level (µg/sample)
Inner Dosimeter	5, 100, 5000
Face and Neck Wipes	5. 100, 2500
Hand Rinses	5, 100, 5000
OVS	0.05, 1.0, 50

The fortified samples will be exposed to the field conditions at a nearby location upwind of the mixer/loader or application operations. The inner dosimeters will be covered with shirt material and be exposed to the same conditions as the measurement dosimeters. Fortified air samples will be operated in a similar manner as worn by the monitored subjects (i.e., air drawn through at 2 Lpm for the duration of the monitoring period). The hand wash and face/neck wipes will be fortified and be placed directly into storage which is what would occur during actual sampling since they would be done at the end of a monitoring period.

Positive control field recovery samples can evaluate sampling media residue losses from the point of field monitoring inception through field storage, shipment, and analysis. In many cases, the most significant losses occur from the sampling media during actual field monitoring because they can last for hours and typically occur under field conditions that are conducive to residue losses (i.e., hot and humid weather). To better characterize where potential losses may occur in the sample collection through analysis timelines, AHETF is also proposing the generation of "travel spikes" will occur to evaluate losses solely due to storage and shipment because they are not exposed to field conditions as they are packaged and freezer storage immediately after dosing. If analyzed, these will provide additional information to help characterize where in the lifetime of the collected samples where residue losses possibly occurred.

8. Relevancy of Study to Proposed Use:

One of the clearest trends in agricultural production and related engineering fields over the last 25 years or so is the movement toward more automation in machinery that is employed by growers and producers. This trend allows for much more efficient crop and commodity production. Notable changes have included the development of more sophisticated tractors with enhanced cabs and global positioning devices. Also, a number of devices have been developed with a goal of reducing occupational exposure to pesticide chemicals including devices such as induction bowls, bulk and mini-bulk transfer systems and all manner of closed loading systems.

In a majority of the occupational risk assessments completed by the Agency, the use of engineering controls for mixer/loaders is considered as a matter of course. This allows risk managers to evaluate the overall risk picture associated with a chemical at varying levels of personal protection, including engineering controls, which is important for the Agency's decision making process. The data which the Agency currently uses for assessing exposures to mixer/loaders using engineering controls was generated in the 1980s through the early 1990s. It represents the common devices used at that time. The majority of these data include results for a custom-made system and also a puncture-type device in which a container is placed and a large prong punctures and drains the container. More modern devices typically use a probe-type siphon pump and dry-couplers which are very reliable and also, it is anticipated, will more reliably reduce exposures for the user population as they become more prevalent.

Given this backdrop, the Agency believes that there is a need for updated monitoring data with which to predict exposures for occupational mixer/loaders using closed systems and liquid products. The Agency believes that the proposed data will provide information that is more relevant to the systems that are more typical in modern agriculture. Thus, it follows that the exposure values predicted using such data would also be more representative of modern agricultural practices.

The following summarizes some of the key issues related to the representativeness of the proposed study.

Element	Applicability/Comments
Active ingredient	A malalthion 8EC formulation is to be used in this study. Malathion and its associated use practices as representative of chemicals widely used in agriculture.
Formulation	An 8 EC liquid formulation (i.e., emulsifiable concentrate) is very typical of many of the liquid formulations widely used in agriculture.
Packaging	The packaging sizes proposed for this study are representative of the range of commonly
Max. application rate	The unit exposure estimates to be generated from this study are exposures normalized by the amount of active ingredient handled and these values are to be used generically. As such, achieving the maximum rate is not critical. It is important, however, that sufficient quantities of material be used to achieve measurable results. It does appear to be the case with this study given that analytical screening limits are very low.
Total ai handled	The range of proposed amounts of total active ingredient handled appear reasonable and the range represents a likely range to be anticipated in agricultural settings.
Mixing/loading method	The proposed systems appear appropriate given the state of current agricultural practices.
Application equipment	The proposed systems appear appropriate given the state of current agricultural practices.
Clean-up, repair, etc.	The proposed systems appear appropriate given the state of current agricultural practices.
Protective clothing	The proposed levels appear appropriate given the current malathion labels.

II. RESULTS AND CALCULATIONS:

The manner in which the results are summarized will depend upon the nature of the situations that are monitored (e.g., types of equipment, clothing & personal protective equipment used), the quality control results and the exposure values that are identified. The ultimate goal is to provide summary exposures for the types of scenarios that have been monitored. Pesticide handler exposures are typically presented on a unit basis and the most commonly used is amount of exposure per pound of active ingredient handled (i.e., µg/lb active ingredient handled). For example, if both mixing/loading and application are monitored in this study, then a different unit exposure for each activity would be calculated. As appropriate, different statistical values will also be defined (e.g., mean, median, percentiles of exposure).

III DISCUSSION

A. LIMITATIONS OF THE STUDY:

At this point, and given the context of how this study will be used in relation to the overall goals of the AHETF to create a generic database for generically predict pesticide handler exposures, the Agency does not believe that this protocol has serious technical limitations. Defining all possible limitations associated with the proposed monitoring of occupational pesticide mixer/loaders during the preparation (and possible application) of varying amounts of malathion spray solution is indeterminate at this time because the results and associated limitations of the study will greatly depend upon the situations which are identified and monitored by the field investigators. They will also depend on the performance of the analytical methods and how samples are collected and handled in the field. From a design perspective, this study represents the current state-of-the-art approach for conducting a passive-dosimetry based monitoring study.

It should be noted, however, that the use of the data generated in this study by the U.S. EPA and other stakeholders will depend upon the nature of the results. For example, the adequacy of the field or laboratory recovery data may dictate that correction factors are applied to adjust monitored exposure levels to account for losses from field samplers or low performing analytical methods. Additionally, other factors may be possibly employed related to the use of the data from this study. For example, the proposed handwash technique that is to be used to measure hand exposures is under scrutiny and a factor could be used by the Agency to adjust for incomplete collection of residues from the hands if this is deemed appropriate.

B. CONCLUSIONS:

The Agency believes that this study, if appropriately conducted, will provide critical information related to the exposures that would be expected for individuals who mix/load liquid agricultural pesticides with closed loading systems of various types. It is also believed that the monitoring techniques proposed for this study represent the current state-of-the-art. However, the Agency also recognizes that use of the data resulting from this study will also take careful scrutiny and may require a number of adjustments depending upon the results. Finally, the overall design of this study should be considered in the context of the goals of the AHETF which are to develop a broad-based database that can be generically used as a predictive tool for estimating exposures to pesticide handlers and that the interpretation of the results of this study may or may not necessitate the need for additional monitoring data for closed system mixing/loading of liquids.

Appendix A
AHE34 Protocol Review
WIRB Documents