Agricultural Handlers Exposure Task Force (AHETF)

VOLUME I

General Information

and Scenario Sampling Plan

April 7, 2008

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AGRICULTURAL HANDLER EXPOSURE TASK FORCE

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Volume I, Part A: Transmittal Letter

April 7, 2008

Mr. John Carley
Office of Pesticide Programs
U.S. Environmental Protection
Agency One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Dear Mr. Carley:

The Agricultural Handlers Exposure Task Force, LLC (AHETF) is pleased to provide the enclosed documents for review by the EPA and the Human Studies Review Board (HSRB) at their June 24-27, 2008 meeting. This submission consists of a scenario sampling plan for the closed cab airblast applicator scenario, plus protocols and supporting documents for two of the five studies that will contribute to the data set for this scenario. A revised Governing Document for the entire AHETF program is also included.

This submission consists of the following nine volumes:

Volume I	AHETF Transmittal letter, 40 CFR 26.1125 check lists for both studies, and the scenario sampling plan document for the closed cab airblast applicator scenario (52 pages)
Volume II	Protocol and supporting documents for Study AHE55 for applications to citrus in Florida (107 pages)
Volume III	Protocol and supporting documents for Study AHE56 for applications to pecans in Georgia (108 pages)
Volume IV	AHETF revised Governing Document (153 pages)

Volume V	AHETF original Governing Document submitted in May of 2007 with revisions tracked (198 pages)
Volume VI	All Standard Operating Procedures (SOPs) that are referenced in the documents in this submission (154 pages) Part A of this volume is a listing of all AHETF SOPs, including those that are not specifically cited. Copies of these other SOPs are available upon request.
Volume VII	Copies of all references cited in the documents that are not readily available to the general public (54 pages)
Volume VIII	All documents and correspondence transmitted between the AHETF and the Independent Investigational Review Board, Inc. (IIRB) for Study AHE55 (674 pages)
Volume IX	All documents and correspondence transmitted between the AHETF and the Independent Investigational Review Board, Inc. (IIRB) for Study AHE56 (551 pages)

The documents in this submission incorporate the general and specific suggestions made by the EPA through numerous communications over the past two years and comments from the HSRB at its June 2007 meeting. The AHETF appreciates the time and efforts of the EPA and HSRB to review and comment on the AHETF testing program. We will be pleased to respond to any questions or requests for additional information or clarifications.

Sincerely,

Richard H. Collier by [illegible]

Richard H. Collier, Ph.D.
AHETF Administrative Committee Chair

cc: William Jordan, EPA/OPP

Volume I, Part B: 40 CFR 26.1125 Check List

40 CFR 26.1125 Prior submission of proposed human research for EPA review

AHETF Closed Cab Airblast Applicator Protocol for Study AHE55 on Citrus in Florida
April 7, 2008

Any person or institution who intends to conduct or sponsor human research covered by §26.1101(a) shall, after receiving approval from all appropriate IRBs, submit to EPA prior to initiating such research all information relevant to the proposed research specified by §26.1115(a), and the following additional information, to the extent not already included:

	Requirement	Y/N	Comments/ Page References
	(1) Copies of • all research proposals reviewed by the IRB, • scientific evaluations, if any, that accompanied the proposals reviewed by the IRB, • approved sample consent documents, • progress reports submitted by investigators, and reports of injuries	Y n/a Y n/a	Volume VIII, Part A: 10; Part B: 230, 274; Part C: 469, 540. Volume VIII, Part B: 379, 406; Part D: 605, 614.
	(2) Minutes of IRB meetings . . . 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	Volume VIII, Part B: 377; Part D: 646.
	(3) Records of continuing review activities.	n/a	
	(4) Copies of all correspondence between the IRB and the investigators.	Y	Volume VIII, Part A: 4-8, 11-12, 14, 230, 274, 372, 373; Part B: 375, 403, 443, 444; Part C: 470, 540; and Part D: 589, 646, 651.
	(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, for example, full-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.	Y Y	IIRB roster and credentials on file with EPA.
	(6) Written procedures for the IRB in the same detail as described in §26.1108(a) and §26.1108(b).	Y	Separately submitted to EPA under confidentiality claim
	(7) Statements of significant new findings provided to subjects, as required by §26.11 16(b)(5).	n/a	

		(1) The potential risks to human subjects	Y	Volume II, Part A, Section 2.3: 11; Volume II, Part B: 51.
		(2) The measures proposed to minimize risks to the human subjects;	Y	Volume II, Part A, Section 2.3: 11-19.
		(3) The nature and magnitude of all expected benefits of such research, and to whom they would accrue	Y	Volume II, Part A, Section 2.4: 19 and Part B: 53. No discussion of magnitude of benefits
		(4) Alternative means of obtaining information comparable to what would be collected through the proposed research; and	Y	Volume IV, Section 3.2: 17, 18 Volume I, Part D, Section 3.0: 16, 17
		(5) The balance of risks and benefits of the proposed research.	Y	Volume II, Part A, Section 2.5: 20.
	§1125(b): All information for subjects and written informed consent agreements as originally provided to the IRB, and as approved by the IRB.		Y	Original – Volume VIII, Part A: 18, 68, 87. Approved – Volume II, Part B: 47; Part C: 57; Part D: 72 Volume VIII, Part B: 402; Part D: 591-628.
	§1125(c): Information about how subjects will be recruited, including any advertisements proposed to be used.		Y	Volume I, Part D, Section 5.2.3: 40, 41; Volume II, Part A, Sections 2.6: 20; 2.7: 22; 6.1: 28; 6.2: 28; 6.3: 29. Volume II, Part D: 72.
	§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	Volume II, Part A, Section 2.6-2.9: 22.
	§1125(e): All correspondence between the IRB and the investigators or sponsors.		Y	Volume VIII, Part A: 4-8, 11-12, 14, 230, 274, 372, 373; Part B: 375, 403, 443, 444; Part C: 470, 540; and Part D: 589, 646, 651.
	§1125(f): Official notification to the sponsor or investigator . . . that research involving human subjects has been reviewed and approved by an IRB.		Y	Volume VIII, Part B: 375; Part D: 589; Part E: 652

Volume I, Part C: 40 CFR 26.1125 Check List

40 CFR 26.1125 Prior submission of proposed human research for EPA review

AHETF Closed Cab Airblast Applicator Protocol for Study AHE56 on Pecans in Georgia

April 7, 2008

Any person or institution who intends to conduct or sponsor human research covered by §26.1101(a) shall, after receiving approval from all appropriate IRBs, submit to EPA prior to initiating such research all information relevant to the proposed research specified by §26.1115(a), and the following additional information, to the extent not already included:

Requirement	Y/N	Comments/ Page References
(1) Copies of • all research proposals reviewed by the IRB, • scientific evaluations, if any, that accompanied the proposals reviewed by the IRB, • approved sample consent documents, • progress reports submitted by investigators, and reports of injuries	Y n/a Y n/a	Volume IX, Part A: 5; Part C: 317, 389. Volume IX, Part B: 231; Part D: 441.
(2) Minutes of IRB meetings . . . 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	Volume IX, Part B: 289; Part D: 496.
(3) Records of continuing review activities.	n/a	
(4) Copies of all correspondence between the IRB and the investigators.	Y	Volume IX, Part A: 5; Part B: 228,292; Part C: 317, 389; Part D: 439, 501; Part E: 529.
(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, for example, full-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.	Y Y	IIRB roster and credentials on file with EPA.
(6) Written procedures for the IRB in the same detail as described in §26.1108(a) and §26.1108(b).	Y	Separately submitted to EPA under confidentiality claim
(7) Statements of significant new findings provided to subjects, as required by §26.11 16(b)(5).	n/a	

		(1) The potential risks to human subjects	Y	Volume III, Part A, Section 2.3: 11; Volume III, Part B: 52.
		(2) The measures proposed to minimize risks to the human subjects;	Y	Volume III, Part A, Section 2.3: 11-19.
		(3) The nature and magnitude of all expected benefits of such research, and to whom they would accrue	Y	Volume III, Part A, Section 2.4: 19 and Part B: 54. No discussion of magnitude of benefits
		(4) Alternative means of obtaining information comparable to what would be collected through the proposed research; and	Y	Volume IV, Section 3.2: 17, 18 Volume I, Part D, Section 3.0: 16, 17
		(5) The balance of risks and benefits of the proposed research.	Y	Volume III, Part A, Section 2.5: 20.
	§1125(b): All information for subjects and written informed consent agreements as originally provided to the IRB, and as approved by the IRB.		Y	Original – Volume IX, Part A: 13. 65, 84. Approved – Volume III, Part B: 49; Part C: 56; Part D: 72 Volume IX, Part B: 231, 251, 254; Part D: 441-495.
	§1125(c): Information about how subjects will be recruited, including any advertisements proposed to be used.		Y	Volume I, Part D, Section 5.2.3: 40, 41; Volume III, Part A, Sections 2.6: 20; 2.7: 22; 6.1: 29; 6.2: 29; 6.3: 30. Volume III, Part D: 117
	§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	Volume III, Part A, Section 2.6-2.9: 21.
	§1125(e): All correspondence between the IRB and the investigators or sponsors.		Y	Volume IX, Part A: 5; Part B: 228,292; Part C: 317, 389; Part D: 439, 501; Part E: 529.
	§1125(f): Official notification to the sponsor or investigator . . . that research involving human subjects has been reviewed and approved by an IRB.		Y	Volume IX, Part B: 228; Part D: 439.

Volume I, Part D:

Closed Cab Airblast Applicator Scenario Sampling Plan

AGRICULTURAL HANDLERS EXPOSURE TASK FORCE (AHETF)

Monitoring Unit Selection and Construction Plan for Scenario:

Airblast Application of Liquid Sprays to Crops Using Closed Cab Equipment

April 1, 2008

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1 INTRODUCTION AND OVERVIEW

This document describes the plan and rationale for selecting and constructing monitoring units (MUs) to represent future exposures to an arbitrary active ingredient under the closed cab airblast application scenario. It provides a characterization of the scenario, the basis for the number of monitoring sites (i.e., studies or clusters of MUs) and MUs per site, and methodology for diversification of important study conditions. Since no data exist for this scenario, the data collected from these studies will constitute the exposure data set in AHED® (Agricultural Handlers Exposure Database) for this scenario.

For this scenario, AHETF discussed plans to monitor airblast applicators with agricultural experts in a variety of states. These discussions were used to help the worker exposure experts from AHETF member companies to: define the scenario; identify airblast conditions that might have an impact on exposure; and guide the selection of geographic locations and crop types for this scenario. In addition, input from external experts will help guide selection of specific monitoring sites for each MU cluster as described in the individual study protocols for this scenario. The References section of the submission that accompanies this scenario plan includes a report that identifies the agricultural experts consulted and presents the information they provided (Bruce, 2008). Throughout this MU selection plan, expert input is briefly summarized to provide a rationale for various decisions related to the plan. The agricultural experts consulted for this scenario included:

- USDA Agricultural Extension Agents: in CA, FL, GA, MI, NY, OH, OK, PA, TX, VA
- Pest control advisors: in CA.
- Commercial pesticide applicators: in FL.
- Growers or Grower Associations: in CA (grapes, prunes), FL (citrus), GA (pecans), NY (apple and grape), WA (orchard and trellis fruit).
- Pesticide safety trainers: in PA, NY.
- Contract agricultural researchers: in, CA, FL, GA, ID, NM, NY, OH, OR, WA.

This scenario includes application of liquid sprays to actively growing, foliated crops using conventional airblast equipment and closed cab tractors.

Since this scenario contains no existing exposure data suitable for a generic database, the scenario design involves a first-stage selection of five monitoring sites followed by a second-stage selection of five MUs at each site. This yields 25 monitoring units representing the scenario. The basis for this standard configuration for a scenario with no data is described in Appendix C of the Governing Document (AHETF, 2008).

As discussed in the Governing Document, both stages of selection will formally induce sample diversity of conditions expected to influence exposure. At the first stage this is done by defining crop type and geographic strata (i.e., agronomic regions of the US) from which the monitoring sites will ultimately be selected. At the second stage of selection, diversity among MUs is based on stratification of the amount of active ingredient handled (AaiH) and the use of different workers for each MU. Many other incidental factors that might influence exposure, such as specific equipment set-up, will be indirectly diversified within the scenario as a result of the diversity selection of locations, AaiH, and workers. Table 1 summarizes the major steps in this two-stage diversity selection process.

The following five crop type/state combinations are proposed for this scenario that will provide the desired diversity in crop and geography:

- Citrus crops in Florida (e.g., oranges)
- Nut crops in Georgia (e.g., pecans)
- Pome fruit in Washington (e.g., apples)
- Stone fruit in Michigan (e.g., cherries)
- Trellis crops in California (e.g., grapes)

Workers will perform their tasks in their normal manner, that is, they will not be instructed to conduct their work in a specified manner. However, workers will be required to apply at least three loads and work for at least four hours. Conventional airblast equipment will be utilized and some variation in equipment (e.g., size, number of nozzles, spray volume per acre, etc.) will likely occur based on the grower's and/or worker's needs and/or preferences across the various crop types and geographical locations involved. Applications will be made only to trees or vines with foliage.

Closed Cab Airblast Application MU Selection Plan

Table 1. Summary of the Selection and Construction Plan for Closed Cab Airblast Application Monitoring Units

Selection Stage	Steps Involved	Program Level
Select Monitoring Site	Stratify orchard and trellis crops by crop type.	Scenario
	Determine which states are predominant growing areas for each crop type.	
	Stratify predominant growing areas (i.e., states) by EPA Growing Region.	
	Select one state from each of 5 crop type strata with no more than one state per geographic stratum.	
	Select one local area (i.e., site) within each of the selected states likely to support an efficient study (i.e., ample supply of growers, limited in area and test duration, near Local Site Coordinator). Timing of applications (i.e., study dates) determined by when airblast applications are made in the local area.	Study
Select and Construct Monitoring Units at each Site	Stratify the practical range of amount of active ingredient handled (AaiH) into 5 levels.	Scenario
	Construct a list of growers based on information from a variety of local resources.	Study
	In random order, screen the growers for eligibility, willingness to participate, availability of workers and airblast application conditions. Terminate screening when an adequate pool of growers is obtained.	
	Recruit workers from the randomly selected grower pool that will cost effectively provide the necessary airblast application conditions for the cluster of MUs.	
	Construct a cluster of 5 MUs by assigning one worker to each AaiH stratum. If multiple workers are available for a given AaiH, then they may be randomly selected.	

2 SCENARIO DEFINITION

This is an application scenario defined entirely by the application equipment, i.e., airblast sprayers with closed cabs. Airblast sprayers are used to apply chemicals to orchard trees and trellis crops (e.g., grapes, caneberries, etc.) by delivering pesticides as a liquid carried in a large volume of air. Other crop types, such as row and field crops, are not treated by airblast equipment and are therefore not relevant for this scenario. The air stream functions to move spray into the trees or vines to enhance the uniformity of deposition onto foliage, fruit, and wood. The air stream physically displaces the air space surrounding the foliage and deposits the chemicals on all surfaces of the leaves and branches. Nearly all airblast sprayers are fundamentally the same, although a variety of sprayer sizes and configurations exist.

One of the most important variables affecting worker exposure is the presence of a cab. Airblast sprayers can be pulled or hauled by open or closed cab vehicles and AHETF will address these two situations as separate scenarios. The scenario described in this document addresses only the closed cab configuration that is expected to result in lower dermal and inhalation exposures since the closed cab is an engineering control that reduces exposure potential during spraying.

Airblast applications are sometimes made to dormant crops (e.g., to control scale), but agricultural experts for orchard and trellis crops indicate that foliar applications (e.g., to control diseases and insects on foliage) are much more common. Overall, dormant applications are estimated to account for 15% or less of all airblast applications (Bruce, 2008). Nationwide, the following consensus from experts was clear:

- In trellis crops, several experts indicated dormant applications are rarely made; others indicated just one was made per season. By contrast, several foliar applications are typically made throughout the season depending on disease or insect pressure.
- In citrus crops, dormant applications are not made at all since this crop is non-deciduous.
- In other orchards (e.g., stone and pome fruits), generally one dormant spray is made versus several to many foliar applications (e.g., 5 to 15), again depending on disease and insect pressure.

Therefore, because foliar sprays are much more common than dormant sprays, AHETF intends to collect MUs for foliar applications only; dormant applications will be excluded from the target population of conditions for this scenario.

3 JUSTIFICATION FOR ADDITIONAL DATA

AHETF has identified the closed cab airblast application scenario as being within the scope of the task force goals and one for which data are lacking. A number of AHETF member products are labeled for this use pattern. This application scenario is applicable to a wide variety of commercially important crops (e.g., fruit trees, nut trees, and trellis crops). Therefore, it is necessary to have data in AHED for the application technique described by this scenario.

As discussed in detail in the Governing Document, most current pesticide handler exposure assessments are based on the Pesticide Handler Exposure Database (PHED), but that database has several technical limitations since the studies included in PHED were not designed to meet the needs of a generic database. In addition, it is now somewhat dated and many agricultural practices have changed. In January of 2007, the EPA [in conjunction with the California Department of Pesticide Regulation (CDPR) and the Canadian Pest Management Regulatory Agency (PMRA)] presented a summary of current pesticide handler exposure assessment procedures and existing data available for such assessments to a scientific advisory panel (SAP). The written summary of that SAP meeting concluded the PHED database has serious limitations and agreed with the regulatory agencies that new and improved exposure data are needed to meet regulatory requirements (SAP, 2007). However, each handler scenario needs to be examined individually to determine the extent that new data might be warranted. This conclusion was also reached by the Human Studies Review Board (HSRB) in response to their review of the 2007 draft of the AHETF Governing Document (Brimijoin, 2007).

Multiple sources of studies must be reviewed to determine whether data exist that might be useful for inclusion in this scenario. These sources include studies conducted by AHETF member companies, individual studies in PHED that may have utility for a generic database, and studies that have been submitted to the EPA that do not fit into the first two groups.

AHETF (in conjunction with EPA, PMRA, and CDPR, collectively the Joint Regulatory Committee (JRC)) reviewed handler exposure measurements in existing studies (mostly not included in PHED) to identify those that satisfy current acceptability criteria and qualify for inclusion in a generic database. For this particular scenario, the JRC reviewed two closed cab airblast application studies and did not identify any data from existing studies that were deemed useful for a generic database.

AHETF also conducted a detailed review of the data in PHED for this scenario to determine if any of the data were suitable for a modern generic database. Data for closed cab airblast application of liquid sprays comprise PHED Scenario 12 –Airblast Application, Closed Cab (APPL). Data within that scenario were graded by EPA as "Low Confidence" for the "No Clothes" and "Single Layer, No Gloves" clothing scenarios. The inhalation exposure data are also graded as "Low Confidence". The "Single Layer, Gloves" clothing scenario in PHED was graded as "High Confidence" but it was noted that there are a large number of non-quantifiable residues for this clothing scenario. In the AHETF detailed review of these PHED data, one MU from one study was found that possibly met the acceptance criteria established by AHETF. However, several issues associated with this MU make it of dubious quality and the logistical problems of obtaining a single MU from a single study provides sufficient rationale for not further pursuing these data (Exponent, 2007). Thus, there are no data currently in PHED for this scenario that are useful for a modern generic database.

Finally, EPA examined data from 13 existing airblast exposure studies or exposure assessments (for open and/or closed cabs) that were not available to the AHETF and concluded that none of the exposure data should be included in the AHETF database (correspondence from EPA on July 3 as a follow-up to a June 27, 2007 meeting with AHETF). This MU selection plan therefore proposes to collect a full set of new data for this closed cab airblast application scenario to meet the scientific objectives outlined in the Governing Document.

4 DESIGN OBJECTIVES AND SAMPLE SIZE DETERMINATION

The closed cab airblast scenario program will monitor instances of worker exposure resulting from the airblast application of pesticides. Each instance is termed a monitoring unit (MU). Each MU consists of a set of airblast application conditions (including the particular worker) that are intended to represent the scenario activities for a single workday. In many cases monitoring units will be selected from 'naturally occurring' airblast applicator-days. However, the selected application conditions are sometimes modified or scripted slightly to ensure that the sample of MUs reflects the expected diversity in the entire population of future airblast application-days. Thus, MUs are technically not 'sampled' from a population. More correctly, they should be viewed as synthetic closed cab airblast application-days derived from both selected and constructed conditions.

In the discussion below, N_C is used to denote the number of sites or clusters and N_M is used to denote the number of MUs per cluster.

4.1 Two-Stage Selection of Monitoring Units

Airblast applications can occur over a wide geographic area and at different times. Locating a potential worker and handling-day condition from which to construct an MU is a complicated process. No convenient national list of upcoming airblast application locations and dates is available. As a result, potential application conditions have to be selected in stages.

This selection process can be envisioned as occurring in two successive stages. The first stage consists of selecting specific geographic locations and a range of possible dates for monitoring at each location. Each such local area and range of potential monitoring dates is termed a 'site'. For example, a site might consist of one or more counties in Florida and a particular one-week period in August. The second stage of this process consists of selecting one or more airblast applicators and application conditions within each site and constructing up to five monitoring units.

N_C sites are selected at the first stage and N_M monitoring units will be obtained within each site at the second stage. When N_M is greater than one, the set of MUs at the same site is termed a 'cluster'. In general, MUs in the same cluster are expected to be more similar than those in different clusters. This correlation usually means that the smallest total sample sizes (i.e. number of MUs) are attainable when there is only a single MU per site. On the other hand, there are often substantial overhead costs per site that make multi-MU sites more efficient.

4.2 Diversity Selection

For this scenario the objective is not a representative sample of sites or a representative selection of handler-days within sites. Rather it is to obtain, as much as is practical for small sample sizes, a diversity of conditions that are expected to influence exposure, either directly or indirectly. Representative selection attempts to have the sample reproduce the actual frequencies of conditions in the population. In contrast, diversity selection attempts to create a sample that contains as many of the different conditions as possible that exist in the population. If the diversifying conditions are associated with exposure, then a diversity sample will tend to be more variable with respect to exposure than would a same-sized representative sample. As a result, a diversity selection sample will tend to have more extreme exposures (both higher and lower) and fewer exposures 'in the middle'. Thus, a diversity selection sample will tend to estimate central tendencies of the exposure distribution better than it will either upper or lower percentiles. To the extent that the diversifying conditions are associated with exposure, diversity selection will tend to under-predict lower percentiles and over-predict upper percentiles. This effect is illustrated by envisioning a normal, or even lognormal, distribution compared with its most extreme 'diversity selection' counterpart, a uniform distribution covering the same range.

In small samples it is more difficult to ensure that the population conditions occur in the correct frequencies than it would be to capture as many different conditions as possible. For regulatory purposes the important aspects of the distribution of exposures are the central tendencies and the upper percentiles. In addition, overestimation of these characteristics is less of a problem than underestimation since it is protective of workers. Therefore, a diversity selection goal is seen as more useful than one for representative selection.

Diversity selection can be based on either random or purposive choices of conditions. In the closed cab airblast scenario both types of selection are used and both utilize stratification as the diversifying mechanism. At each stage of selection, the potential sampling units are partitioned into groups, called strata. The strata are non-overlapping and, when taken together, comprise all the available sampling units. In diversity sampling, no more than a single unit is selected from each stratum. This contrasts with proportional stratified sampling, a form of representative sampling in which units are selected from larger strata more often than from smaller strata.

Random diversity selection means that a unit is chosen from each stratum randomly. Purposive diversity selection means than units are selected intentionally, usually for practical reasons. When the number of strata exceeds the desired sample size, then the strata used can either be selected randomly or purposively. When this occurs a purposive selection of strata can sometimes yield a more diverse sample than a purely random set of strata.

Random diversity selection avoids the appearance of intentional bias that can result when researchers choose some conditions and exclude others. When choices are equivalent and easily listed, this is a natural approach. On the other hand, purposive selection can be more efficient and cost effective whenever the possible choices are non-equivalent. Neither form of sampling provides justification for the use of statistical sampling theory. For this to be the case, all stages in the sampling would need to be random, representative, and conform to a rigorous statistical sampling protocol. In addition, all MUs would need to be completely observational. That is, MUs with synthetic (e.g., scripted) components would not be an element of an existing application-day population.

Diversity selection as it applies generally to the entire AHETF Monitoring Program is described more fully in the AHETF Governing Document (Section 9 and Appendix B). Details of the MU diversity selection and MU construction procedures for the closed cab airblast application scenario are described in Section 5 below.

4.3 Reference Distribution

As noted above, sample sizes can only be determined using statistical theory alone when either

1. There is assumed random, representative sampling from a population and the goal is to estimate some characteristic of that population; or

2. There is assumed randomization of experimental units to treatments and the goal is only to compare or to contrast treatments in some manner.

Only in these two situations can statistical theory predict how increasing sample size decreases estimation error. In other experimental situations, sample size must be determined using one of the two 'random' situations above as a reference model. The random reference model is constructed so that it reflects the actual situation (i.e., a mixture of random and non-random selection) as closely as possible. The sample size that is appropriate for the reference model is then used for the actual study design. In a real sense, then, the reference two-stage random sampling model is used to establish benchmark sample sizes that satisfy benchmark objectives. The use of benchmarks is not, however, a claim that true probability sampling occurs.

The closed cab airblast application scenario uses both natural and synthetic MUs that predict elements of the target population of future daily exposures. The goal is to use these data to characterize some 'population' aspect of the future exposure when applying agricultural pesticides by airblast. Hence, this scenario is more closely aligned with the random sampling situation (1) above.

For this airblast application scenario, random nested (or cluster) sampling is used as the reference model for the combination of purposive and random two-stage diversity selection actually used. This reference model assumes that:

- Exposure normalized by the amount of active ingredient handled is lognormally distributed with geometric standard deviation GSD. Equivalently, the logarithm of normalized exposure is normally distributed with standard deviation Log(GSD).
- There are N_C clusters (i.e. sites) and N_M MUs per cluster. The total number of MUs in this scenario is, therefore, $N_C \times N_M$.
- The within cluster (i.e., within-site) correlation of log normalized exposure is equal to ICC (intra-cluster correlation).

4.4 Benchmark Objectives

The primary benchmark objective for this scenario is that a sample from the hypothetical reference sampling distribution above be of adequate size to describe selected measures of the (normalized) exposure distribution with a pre-determined level of accuracy. EPA provides guidance to AHETF on the minimum degree of accuracy needed for regulatory use in particular scenarios. The current consensus is that estimates of the geometric mean, the arithmetic mean, and the 95^{th} percentile generally need to be accurate to within approximately 3-fold of the actual population value. AHETF and the Joint Regulatory Committee (EPA, California Dept. of Pesticide Registration, Pest Management Regulatory Agency [Canada], and the U.S. Department of Agriculture) agreed 3-fold accuracy is an appropriate benchmark for this scenario (meeting with AHETF, June 27, 2007).

It should always be kept in mind, however, that this objective is specified in terms of the reference random sampling distribution. This reference sampling model does have the same two-stage nesting structure as the actual sampling approach. The lognormal distribution assumption is also reasonable, robust, and consistent with existing data. However, the reference distribution assumes simple random sampling at each stage. It does not, and cannot, incorporate the combination of purposive and random diversity sampling actually used.

As noted above, the consequence of diversity sampling is expected to be a tendency for the sampling variation of normalized exposure to be overestimated. The sample should over-represent extremes and under-represent the more common values. Such diversity-oriented data collected for this scenario, but analyzed with respect to the two-stage reference distribution, is expected to have minimal bias for central tendency. In contrast, upper percentiles of exposure are expected to be, on the average, too large. There is no way to determine the actual magnitude of such overestimation. In this case, overestimation of upper percentiles is of minimal concern: for practical exposure assessments, overestimation of exposures is a conservative practice utilized by regulatory agencies. A tendency to both consider and even overestimate upper percentiles is consistent with this practice.

A minor (secondary) benchmark objective of this scenario is that the data, coupled with the reference sampling model, provide adequate power for a limited examination of the relationship between exposure and AaiH, the normalization factor. This objective is considered less important than the primary objective and will be accommodated only when it does not negatively impact the primary objective.

4.5 Sample Sizes

Appendix C of the Governing Document describes the methodology to calculate sample sizes when the reference model used is cluster sampling from a lognormal distribution. For the purposes of determining sample sizes, the default variation structure for normalized dermal exposure derived in Appendix C is also assumed applicable to the closed cab airblast application scenario. AHETF and the Joint Regulatory Committee agreed there is no evidence to suggest otherwise and no strong opinion to the contrary (meeting with AHETF, June 27, 2007). It is therefore appropriate to use the default relative variation structure consisting of a geometric standard deviation (GSD) of 4.0 and intra-cluster correlation (ICC) of 0.3. Appendix C shows that under these conditions (and where no suitable MUs exist) a sample of 5 clusters (N_C=5) with 5 MUs per cluster (N_M=5) is the most cost effective design configuration that meets the 3-fold accuracy requirement. This accuracy is possible with a variable number of MUs/cluster as long as the total number of MUs is at least 25 and no cluster has more than 5 MUs. Each cluster (i.e. monitoring site) will be addressed by a separate study protocol.

Appendix C of the Governing Document also shows that when the benchmark accuracy requirement above is met there may also be sufficient power to permit users of the database to perform a limited examination of the relationship between the normalizing factor (e.g., AaiH) and exposure. This is true provided: (1) the practical range of the normalizing factor is at least an order of magnitude and (2) there is adequate within-cluster variation in the normalizing factor. When these conditions occur, the MU sample will be of sufficient size and diversity to provide at least 80% statistical power to distinguish complete proportionality from complete independence between exposure and the normalizing factor used in the primary benchmark. Since these conditions can be satisfied for the reference sampling design, then the purposive diversity design for the closed cab airblast scenario should provide adequate power for the minor (i.e., secondary) objective: the ability to conduct limited examinations of the relationship between AaiH and exposure.

5 DIVERSITY SELECTION AND CONSTRUCTION OF AIRBLAST APPLICATION MONITORING UNITS

As described in Sections 4.1 and 4.2 above, the basic conditions necessary to construct MUs for the closed cab airblast application scenario are obtained by a two-stage diversity selection process. These two stages are:

1. Selection of a set of five monitoring sites that is diverse with respect to crop type and geography.
2. Selection and construction of five monitoring units per site that exhibit diversity in the amount of active ingredient handled without using the same worker repeatedly.

At both stages, diversity among selection units is induced by partitioning the available units into strata and then selecting no more than a single unit from each stratum. For practical reasons, selection of units will usually be purposive. However, whenever feasible, random selection of units will be used to reduce the possibility of intentional or unintentional selection bias.

5.1 First Stage Diversity Selection of Monitoring Sites

A monitoring site is defined as a particular local geographic area and range of dates associated with monitoring. Five sites need to be selected at the first stage. This process requires several steps:

1. Stratification of the crops associated with airblast application into a diverse set of important crop types
2. Identification of states associated with the predominant growing areas for each crop type
3. Partitioning the predominant growing areas into geographic strata

4. Selection of one state from each crop type stratum with no more than one state per geographic stratum. These selections are described in this document and are supported by discussions with various agricultural experts and crop acreage information.
5. Selection of a specific monitoring site within each selected state that will provide closed cab airblast application-days associated with the crop type. This selection will be made in individual study protocols (one for each site).

Specific timing of pesticide applications (i.e., dates) is generally chosen by the grower and is dependent on weather conditions, crop stages, as well as disease and insect pressure. Monitoring activities at each site could be conducted at any time the airblast applications are made. However efficiency and cost concerns create the desire to collect all MUs for a particular site (i.e., study) over a short period, such as within a week or two. This may involve choosing growers who intend to make pesticide applications at approximately the same time. The grower and worker selection process is described in Section 5.2.2 below. It will be documented in greater detail in the protocol and the raw data for each study.

5.1.1 Establishing Crop Type Strata

As indicated in Section 2 above, airblast application is made almost exclusively to trellis and orchard crops. Based on discussions with a variety of agricultural experts and the substantial expertise available within AHETF, crop type has been identified as an important parameter that might impact exposure potential and that should be diversified. This is primarily because factors such as crop size, crop height, row spacing, and foliage density impact equipment set-up and levels of suspended aerosol (e.g., spray direction, number of nozzles, etc.) and these factors could in turn impact exposure potential. In particular, AHETF experts suggest that applications to orchards might have a higher exposure potential due to greater levels of overhead exposure when compared to low trellis crops. However, AHETF and external experts agree the use of closed cab equipment will significantly reduce exposure potential and some experts feel the reduction will be large enough to make any difference in exposure potential attributable to crop conditions difficult or impossible to detect.

Closed Cab Airblast Application MU Selection Plan

During discussions with agricultural experts, the following items were mentioned as "parameters related to airblast spraying that might impact exposure potential for an applicator using an open cab tractor" (21 respondents):

- Wind (strength or direction, 15 responses)
- Use of PPE (respirator and/or gloves, 8 responses)
- Gallons Per Acre (GPA, 5 responses)
- Drift, general (3 responses)
- Crop height (3 responses)
- Canopy density (2 responses)
- Nozzle type (2 responses)
- Spray pressure (2 responses)
- Multiple rigs in field (2 responses)
- Turning into spray (2 responses)
- Repairs/contact (2 responses)
- Temp/RH (2 responses)
- Nozzle/spray trajectory (2 responses)
- Tractor speed (1 responses)

The most common response, wind, was a concern because wind can cause spray mixture to blow onto the worker and his equipment. Many of the other responses were also mentioned because they might impact the amount of suspended aerosols including: GPA; crop height and canopy, nozzle type and direction; spray pressure; multiple rigs in the field; turning into spray; and tractor speed.

When asked if the parameters they mentioned would be important when closed cab tractors are used, experts indicated:

- No or Probably Not (7 responses)
- No or Probably Not, unless the air filtration system is not functioning properly (7 responses)
- Yes, but to a lesser degree (6 responses)

When experts indicated the parameters they mentioned would probably not be important when closed cabs are used, some were asked what parameters might then be most important to exposure potential. Responses included:

- Contact with contaminated surfaces (e.g., exiting the cab or making repairs, 7 responses)

- Mixing and loading (4 responses)
- Use of PPE (1 response)

AHETF experts agree that exposure potential will be considerably less for closed cab situations than for open cab situations and believe that overhead spraying, exiting the cab, and contacting surfaces (e.g., while making adjustments or repairs) may be the most important parameters influencing exposure in closed cab situations. Since closed cabs do not provide complete protection, parameters that influence the amount of airborne spray reaching the worker during open cab situations can also influence exposure during closed cab situations. In particular, surface contamination (that leads to exposure during cab exiting and during performing adjustments or repairs) can result from suspended aerosols landing on the closed cab equipment. AHETF believes the best way to get diversity in these various parameters is to vary the crop type, especially for crop height and foliage density. This will ensure the collection of MUs includes some overhead exposure and a variety of equipment configurations and settings (see Section 6 for more details).

Crop conditions are therefore considered an important parameter that should be formally diversified. Consequently, any stratification should distinguish orchard and trellis crops, both commonly treated with closed cab airblast sprayers. In addition, the following specific crop types would provide diversity in crop profile or canopy:

- Grapes and caneberries – a few types of grapes (e.g., table/raisin, juice, and wine) and a wide variety of cultural and trellis systems. Grapes and caneberries do not generally involve overhead spraying since they are pruned to grow about 5 to 8 feet tall. Airblast rigs generally utilize fewer nozzles for grapes than for orchards and spray predominantly horizontally.
- Pome and stone fruits – these are similarly sized trees that are larger than grapes. Apples are generally maintained at 10 to 15 feet tall and pears at 12 to 20 feet. Stone fruits (e.g., cherries, peaches, plums) are generally maintained at 14 to 20 feet tall. Some pome and stone fruit orchards tend to have relatively narrow rows and canopies that are low and closed. Foliage density is moderate and there is significant space between the lowest branches/foliage and the ground.
- Citrus – a non-deciduous orchard crop (i.e., full foliage year round) with a very dense canopy that grows close to the ground

with small or no spaces between trees. Citrus groves are generally grown with larger tree and row spacing than pome/stone fruits. Standard citrus trees are 18 to 22 feet tall and dwarf varieties grow 8 to 12 feet tall.

- Nuts – the tallest orchard type (mature pistachios are typically pruned to 15 – 20 feet, almonds to 25 – 30 feet, walnuts to 30 – 40 feet, and pecans to 40 – 70 feet tall) with relatively low foliage density and large spaces below the lowest leaves and branches. These tall trees sometimes require special equipment set-up. In particular, airblast sprayers used in pecans may be truck-mounted and often involve spraying on only one side of the sprayer with air deflectors (or hoods) that focus the spray higher than for other orchard crops.

Figure 1 summarizes U.S. acreage statistics for these important groups of orchard and trellis crops. This chart indicates that five crop categories encompass approximately 97% of all the acreage that might be treated by airblast applications. This suggests the possibility of stratifying the crops treated by airblast into these five crop types:

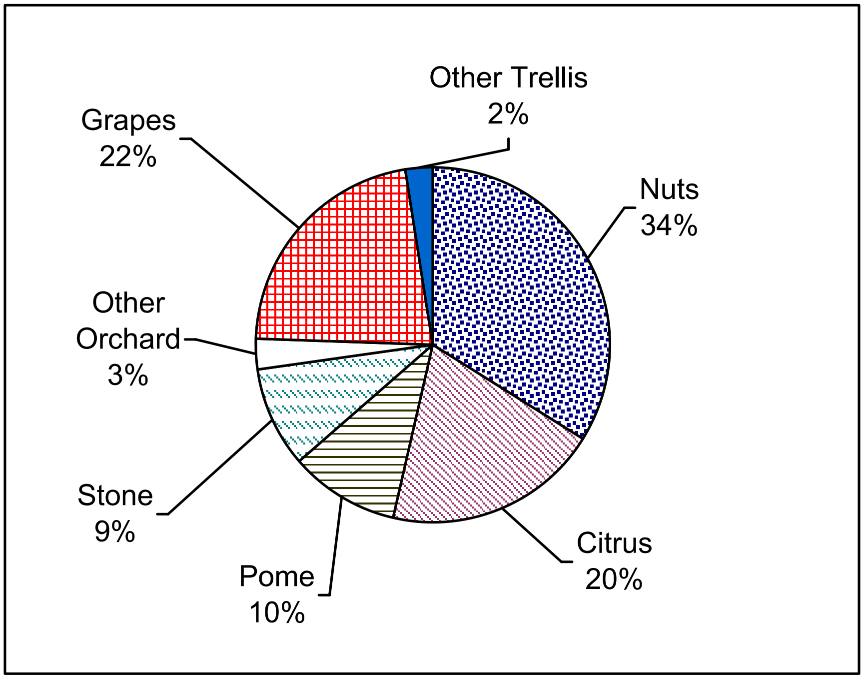
- Nut crops
- Citrus
- Pome fruit
- Stone fruit
- Trellis crops

The "other orchard" category will be restricted from the target population because overall acreage is relatively low and agricultural experts did not indicate there were fundamental differences in how these crops are treated by airblast. These orchard crops include avocados, dates, figs, guavas, olives, and papayas.

Trellis crops will be considered as a group with one exception – tall hops. Hops are treated with conventional airblast equipment like other trellis crops, but unlike grapes and caneberries they can grow very tall and involve overhead exposure similar to orchard situations. Since trellis crops are purposively included in the sampling plan because they are shorter than orchard crops and don't involve overhead exposure, this plan will restrict MUs involving trellis crops to situations that do not involve overhead exposure (i.e., tall hops will not be included).

However, exposure potential for workers who use airblast sprayers in tall hops will still be covered within AHED by data from orchard applications.

Figure 1. Percentages of Total 2006 Bearing Acres for Major Trellis and Orchard Crop Types (NASS, 2006 and NASS, 2007)



5.1.2 Crop Type Growing Areas

Acreage by state for each of the five crop types is readily available from USDA (National Agricultural Statistics Service, NASS 2006 and 2007) and provides a convenient way to identify where important crop types are commonly grown. Table 2 lists those states associated with the largest acreages for each crop type and the percent of total acres for the crop type that are found in that state. A 'predominant growing area' for each of the five crop types can be defined in terms of states that account for 5% or more of the total crop type acreage. These growing areas are listed in Table 3.

Table 2. Acreages for the Five Crop Types by State (NASS)

Crop Type	State	Bearing Acres, 2006	Percent of Total US Acres for Crop Type
Nut Crops	CA	797,667	53 %
	TX	180,719	12 %
	GA	128,550	9 %
	OK	85,740	6 %
	NM	37,763	3 %
	OR	28,300	2 %
	HI	17,800	1 %
	35 Others	109,905	7 %
Citrus	FL	576,400	66 %
	CA	250,500	29 %
	TX	27,300	3 %
	AZ	23,500	3 %
Pome Fruits	WA	180,000	40 %
	NY	46,400	10 %
	CA	42,000	9 %
	MI	41,300	9 %
	PA	22,900	5 %
	OR	21,600	5 %
	VA	15,000	3 %
	28 Others	76,100	17 %
Stone Fruits	CA	217,000	53 %
	MI	41,100	10 %
	WA	36,350	9 %
	OR	14,250	3 %
	SC	14,000	3 %
	GA	11,500	3 %
	TX	5,800	1 %
	PA	5,000	1 %
	22 Others	66,800	16 %
Trellis Crops	CA	806,920	77 %
	WA	90,032	9 %
	OR	32,596	3 %
	NY	31,700	3 %
	MI	30,900	3 %
	PA	12,100	1 %
	NJ	7,600	1 %
	CA	7,000	1 %
	10 Others	28,317	2 %

Table 3. Predominant Crop Type Growing Areas Defined by States with at Least 5% of the Total Crop Type Acreage

Crop Type	Predominant States in Growing Area (% of Total Crop Type Bearing Acres)
Nut crops	CA(53), TX(12), GA(9), OK(6)
Citrus	FL(66), CA(29)
Pome fruit	WA(40), NY(10), CA(9), MI(9), PA(5), OR(5)
Stone fruit	CA(53), MI(10), WA(9)
Trellis crops	CA(77), WA(9)

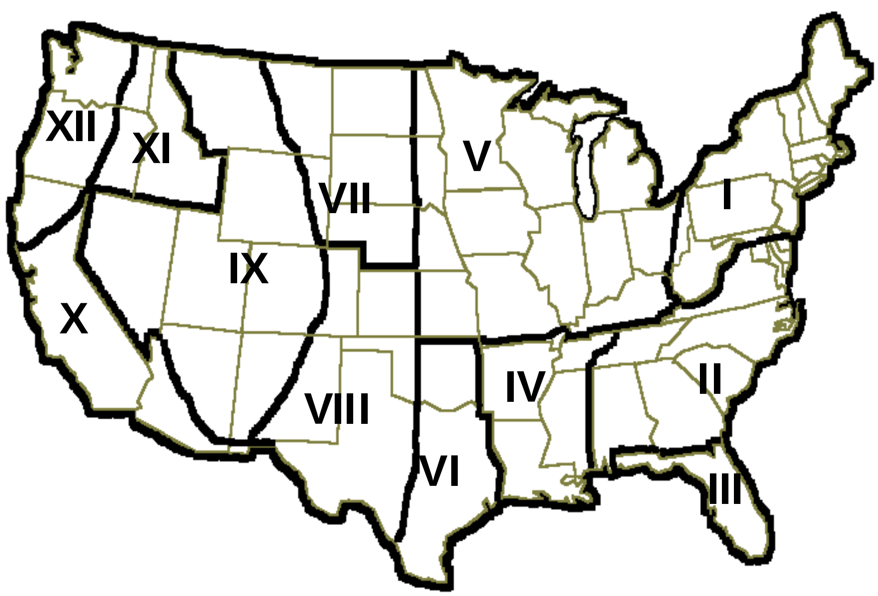
One state will ultimately be selected from each of these five crop type strata. It should be emphasized, however, that relative crop acreage was used only to delineate states associated with where most of the crops are grown. Acreages cannot be used to guide a "representative" sample of airblast application conditions. This is because information on the number of sprays performed per year by airblast with enclosed cabs in particular areas and for particular crops would be needed. This information is not readily available and it varies from year to year based on the amount and type of pest pressure in each crop in each area. Therefore, acreage data are used only as a guide to indentifying locations where enclosed cab airblast applications are probably common. Discussions with local agricultural experts are then used to verify that the scenario of interest is common and then specific study sites can be chosen.

5.1.3 Geographic Stratification

As discussed above, closed-cab airblast applications are made almost exclusively to orchard and trellis crops and these crops are grown in many regions of the country. This was confirmed by discussions with agricultural experts across the country and examination of crop acreage statistics. For this reason, geographic diversity between sites is also desired. Geographic diversity between clusters of monitoring units is expected to provide some variability in agronomic conditions and of other factors, such as equipment type, work practices, weather, etc. That is, it is viewed as a meta-factor that is associated with both known and unknown effects usually classified as simply 'study effects'. Some of these factors are discussed in Section 6 below. However, these factors will not be specifically analyzed for their effects on worker exposure. The objective is merely to capture diversity of different study conditions across the five clusters.

The 13 U.S. Growing Regions established by EPA (Figure 2) provide a convenient basis for geographic stratification. These regions have been used when planning and conducting pesticide residue trials for various crop types. The regions were based on natural geography and climatic boundaries (ACPA, 1992) and are therefore useful for indicating when locations selected for exposure monitoring are geographically diverse.

Figure 2. EPA Growing Regions
(EPA Region XIII includes Hawaii and Puerto Rico)



Not all EPA growing regions contain states belonging to the predominant growing areas for the crop types of interest. Those regions that do contain predominant states are listed in Table 4. The goal in diversity selection is to obtain no more than a single state from each EPA growing region.

Table 4. Stratification of Trellis and Orchard Crop Growing Area States by EPA Region

EPA Growing Region	States in Growing Region (all crop types combined)
I	NY, PA
II	GA
III	FL
V	MI
VI/VIII	TX, OK
X	CA
XI/XII	WA, OR

5.1.4 Selecting States from Crop Type and Geographic Strata

Table 5 lists the predominant growing states grouped jointly by crop type and geographic strata. There are 14 different combinations of crop type and EPA growing region. There are also 7 growing regions with at least one state indicated. Given the small number of sites (5) required for this scenario, it is not possible to select one state from each non-empty stratum. Consequently, the diversity selection goal is to choose one state for each crop type with the proviso that no two states are in the same EPA growing region. Guided by this rule and the information in Table 5, the following five combinations listed after the table were purposively selected.

Table 5. Predominant Growing Area States Stratified by Both Crop Type and EPA Growing Region

EPA Growing Region	Nut Crops	Citrus	Pome Fruit	Stone Fruit	Trellis Crops
I (Northeast)			NY, PA		
II (Southeast)	GA				
III (Peninsular Southeast)		FL			
V (Upper Midwest)			MI	MI	
VI or VIII (South central)	TX, OK				
X (West)	CA	CA	CA	CA	CA
XI or XII (Pacific Northwest)			WA, OR	WA	WA

1. Citrus / Florida

This citrus combination was chosen because of the dominant acreage for citrus crops in Florida (66%) and because it is the only combination in Region III. Florida was selected over California (the only other combination involving citrus) since California will be chosen for another crop type (see below). Florida reflects a hot and humid climate in the peninsular southeastern US (EPA Region III).

2. Trellis Crops / California

This trellis crop combination was chosen because of the dominant acreage for trellis crops in California (77%). California was selected over Washington (the number two acreage state) so that Washington could be selected for pome fruits due to its dominance in that crop type (see below). California reflects a hot and dry climate in the western US (EPA Region X).

3. Nut Crops / Georgia

This nut crop combination was chosen because California (the highest nut crop acreage) is already selected and because AHETF has a qualified Local Site Coordinator in Georgia that will likely result in a localized and efficient study. This state reflects a hot and humid climate in the southeastern US (EPA Region II).

4. Pome Fruit / Washington

This pome fruit combination was chosen because of the dominant acreage available for pome fruits (84%) and because it provides good geographic diversity. This state reflects a cool climate in the Pacific Northwestern US (EPA Region XI or XII).

5. Stone Fruit / Michigan

This stone fruit combination was chosen because Michigan has the highest acreage for a stone fruit after California. This combination also provides geographic diversity because it reflects a cool climate in the upper Midwestern US (EPA Region V).

Collectively, these crop type/state combinations cover five different EPA growing regions including the West, Northwest, Southeast, and upper Midwest portions of the US. They also cover all five of the crop types that are desired for diversity. AHETF also has acceptable Local Site Coordinators in each of these states. Finally, local agricultural experts have been contacted from each of these states to confirm airblast applications are common to the crop indicated.

5.1.5 Selection of Specific Monitoring Sites for Each Study

The final step for selecting sites is to choose a specific area within each selected state identified above where growers and workers can be recruited to conduct a study in a reasonable amount of time. This involves staging the study (i.e., site) in a reasonably limited geographic area so that MU identification and selection operations can be conducted efficiently in one local area within the state. This is necessary primarily to keep the costs of study conduct reasonable so an adequate number MUs can be obtained in the AHETF monitoring program.

Choosing a cost-effective configuration of MUs is necessary since costs escalate rapidly when a research team makes several visits to a location in order to monitor the desired five MUs. Cost-effectiveness is obviously maximized when all MUs are collected during the same visit so researcher salary, travel, food, lodging, and field fortification expenses are minimized. The table below provides relative total costs for the items listed above associated with collecting 5 MUs in the field for various degrees of efficiency. These efficiency ratios highlight the importance of selecting growers in a defined area that plan to handle product at approximately the same time.

Most Efficient ………….………………… Least Efficient				
1 Trip	2 Trips	3 Trips	4 Trips	5 Trips
1.0	1.3	1.7	2.1	2.5

Furthermore, stretching the study out over time may extend it beyond when pest pressure is sufficient to warrant pesticide treatment and will result in an incomplete cluster. Finally, scheduling for the contract research organizations (CRO) must be taken into account. There are only a limited number of qualified companies and they contract many studies each year. Studies must be scheduled within a finite window of time in order to fit everything into the limited agricultural growing season. For scheduling purposes then, it is important to identify a narrow time period during which each study can take place to ensure researchers can complete their monitoring as efficiently as possible. If studies cannot be scheduled into short periods of time, the number of studies that can be performed within each growing season will be limited and the total AHETF program will take longer and be more expensive.

Therefore, for each study (i.e., site), a particular area of each state will be selected and identified in the study protocol. This will be determined by discussions with local resources to indicate areas that are most likely to have sufficient growers, equipment, and workers to allow an efficient study. It may also be restricted based on the availability of a Local Site Coordinator who is responsible for providing logistical support to the CROs.

5.2 Second Stage Diversity Selection and Construction of Monitoring Units

Once the monitoring sites have been identified, a set of five MUs is constructed based on a second-stage diversity selection of closed cab airblast application conditions. This selection and construction process consists of several steps for each site:

1. Stratification of amount of active ingredient to be handled (AaiH) based on the practical range for the scenario.
2. Identification of a sufficient pool of eligible growers and workers willing to participate.
3. Selection of application conditions and construction of an efficient set of five monitoring units.

5.2.1 Stratification of Amount of Active Ingredient Handled (AaiH)

Since the number of pounds of active ingredient handled is the normalizing factor and indirectly influences many other handling conditions, efforts will be taken to generate data in as wide a range of AaiH as practical within each cluster of MUs. AaiH is selected since EPA currently normalizes closed cab airblast exposure by AaiH during pesticide product exposure assessments and there is no other factor identified as being more appropriate.

In addition to its potential direct relationship to exposure, the amount of active ingredient handled is also viewed as a meta-factor affecting parameters such as tank size, number of loads applied, etc. Thus, diversification of AaiH induces diversification of such associated factors as well.

AHETF has calculated a practical range in AaiH for this scenario taking into account such factors as the typical use rates of products, types of products available on the market, types of crops on which the products are used, number of acres that can be treated in a day, etc. AHETF has calculated a maximum amount of active ingredient handled per day as 200 pounds for this scenario. This is based on a high application rate of 4.0 lb. ai/A and a maximum of 50 acres treated per day for a commercial applicator using a relatively low spray volume per acre (Haskell, 1998). However, AHETF has established a practical upper limit of AaiH per day of 100 pounds. The practical limit is set lower than the maximum amount handled primarily to reduce the burden of workers handling extremely large amounts of product. This also avoids very long monitoring periods that may be unusual for the workers. In particular, AHETF discussions with growers and extension agents indicate that 30 acres of orchards or grapes is often a much more reasonable limit for acreage treated in a day by airblast application. AHETF has also set the lower practical limit for AaiH per day at 5 pounds of active ingredient. The lower end of the practical range is set to avoid an inordinate number of non-quantifiable residue levels in the exposure matrices.

The MUs for this scenario will span the practical AaiH range of 5 to 100 pounds, just over 1 order-of-magnitude. As noted in Section 4.5 above, it is also important that the AaiH levels be well-diversified within each cluster. This allows the data for this scenario to be used to discriminate a completely proportional relationship from a completely independent relationship between exposure and AaiH (if one of those two relationships were true). Within-cluster diversification of AaiH will be accomplished by following the standard approach of partitioning the practical AaiH range into five strata. These strata are:

- 5 to 9 pounds ai handled
- 10 to 17 pounds ai handled
- 18 to 30 pounds ai handled
- 31 to 55 pounds ai handled
- 56 to 100 pounds ai handled

All five strata are of equal width on the log AaiH scale. Within each cluster an attempt will be made to obtain a single MU from each of the five strata. As noted in Section 4.4 above and detailed in Appendix C of the Governing Document, this type of within-cluster diversification of AaiH satisfies the secondary benchmark objective for the scenario. That is, it provides adequate power to distinguish a proportional overall relationship between exposure and AaiH from a purely independent one.

5.2.2 Selecting a Grower Pool

As discussed in the Governing Document, AHETF must obtain grower cooperation before it can recruit workers since the grower must be willing to have his crop treated and often must also volunteer his equipment to make the applications and allow AHETF to recruit his/her workers. Because specific crop acreage must be identified, selecting growers is an important first step toward selecting all MUs.

AHETF has determined that a method of randomly choosing a working pool of growers is practical for this scenario. This pool of growers will provide the workers and application conditions needed to construct MUs for the study. Random selection of growers is preferable, when feasible, to reduce the possibility of selection bias that might arise from the Local Site Coordinator (LSC; i.e., a local agricultural researcher) purposively choosing which growers to contact. Therefore, a procedure for generating a list of available growers for each study (i.e., associated with each local monitoring site), and randomly selecting a pool of growers from that list, will be established in the protocol for that study. The general procedure to be followed is described in the following steps:

1. Contact local resources from each of the following groups and ask for a list of growers for the crop type of interest at the identified location (generally about one to three counties):
    - Local Site Coordinators
    - Commercial Applicator Firms
    - University / County Extension Agents
    - Crop Consultants (e.g., pest control advisors or commercial applicators)
    - Agricultural Researchers (including LSC)
    - Chemical Dealers or Sales Representatives
    - Grower Associations

2. Assemble a list of growers from all of the resources contacted and eliminate any duplicates.

3. Put the list of growers into random order.

4. Contact growers, one at a time, following the random order, and determine whether the grower is 'eligible' to participate. Eligibility generally means all of the following are true:
    - The grower is willing to cooperate with AHETF, including the ethical aspects of the research
    - The grower still grows the crop(s) of interest
    - The grower sprays his crop(s) with conventional airblast equipment with closed cabs
    - The grower has at least one worker with experience making closed cab airblast applications
    - The grower is willing to allow AHETF to recruit his/her worker(s)
    - The grower has sufficient acreage that the minimum AaiH can reasonably be handled by a worker in one day
    - The grower is willing to use at least one of the surrogate active ingredients listed in the study protocol

    Growers who indicate they use commercial applicators to make airblast applications to their crop will also be considered. Those growers will be asked to identify their preferred commercial applicator(s) and AHETF will contact them to screen them for willingness to cooperate by providing suitable equipment and workers to spray that specific grower's crop. The important consideration with this step is that first the crop acreage is identified and then equipment and workers associated with that acreage are identified. The actual workers involved could be the grower himself, a grower's employee, or an employee of a commercial applicator.

5. Each grower identified as eligible (sometimes along with an associated commercial applicator) is placed into a working pool along with information on:

    - Crop(s) available, with acreage that might be treated
    - Specific location of crop(s) that might be treated

- Description of equipment available (e.g., number, type, and size)
- Surrogate chemical(s) that might be utilized
- Approximate timing of surrogate applications
- Number of workers available
- AaiH those workers might be able to handle in a day

Screening of the grower list (in random order) continues until a pool of eligible growers (and/or commercial applicators) that is sufficiently large is obtained. This pool should include more growers and more workers than are ultimately needed since growers might change their mind about cooperating, workers might not volunteer to participate, expected applications might not be made due to lack of pest pressure, various growers have different application timing, etc. In addition, several restrictions on application and worker conditions that will be used when constructing MUs (see 5.2.3 below) will be considered when determining sufficiency of the grower pool. Generally, there will be a greater number of workers available for the low levels of AaiH and fewer workers available for the highest levels (due to acreage and/or equipment size limitations).

This process results in a random sample of eligible growers and, by association, a random pool of potential workers associated with eligible growers. These grower (and/or commercial applicator) contacts will generally be made by the Local Site Coordinator, but this will be specified in each study protocol. All discussions and decisions made during this eligibility screening will be documented (e.g., as phone logs) and retained as raw data for the study.

5.2.3 Selection and Construction of MUs

After the randomly-selected pool of eligible growers is assembled, researchers (e.g., Local Site Coordinator and Study Director) will examine the details of potential MUs and identify a configuration of MUs (i.e., growers, chemicals, workers, AaiH, timing) that will result in an efficient study. An efficient configuration will generally involve a group of growers that are in the same geographical area, that can provide separate workers for all the strata of AaiH, that involve some diversity in equipment, and that are expected to make applications within a narrow time frame. This configuration should still include excess workers for the reasons listed above.

The growers and/or commercial applicators in the chosen configuration provide the pool of workers from which study participants will be recruited. When constructing MUs, three restrictions will be enforced to ensure diversity within the cluster of MUs:

- No worker may be used for more than one MU in the cluster. Worker-related behaviors are also viewed as a meta-factor since individual practices might be associated with exposure potential.
- No airblast sprayer may be utilized more than once (so a grower with 2 workers, but just one sprayer, can contribute only 1 MU to the cluster)
- No more than 2 MUs may be obtained from any grower or grower/commercial applicator combination (so a grower with several workers and several sprayers can contribute only a maximum of 2 MUs)

From the cost-effective configuration chosen, workers will be recruited as described in the Governing Document and specific study protocols. In general, this might begin with sending a flyer to growers in the eligible pool, followed by site visits where the Local Site Coordinator and/or Study Director meets the growers and confirms the suitability of their crops, equipment, and willingness to cooperate (including discussions about non-coercion of workers). Then the workers associated with the chosen growers and/or commercial applicators may be contacted directly (e.g., by Study Director) to begin recruitment.

As the scheduling time approaches, growers and/or workers may decide they are no longer interested in participating. If necessary, additional growers and workers can be recruited from workers already characterized in the pool. If there are insufficient workers available in the pool to obtain a new efficient configuration, the random working pool can be expanded by continuing to contact additional growers from the original randomized list.

6 EXPECTED DIVERSITY OF OTHER FACTORS IN THE SAMPLE OF MONITORING UNITS

As described above, the diversity in handling conditions in the sample of MUs for this scenario is driven by the formal use of distinct selection units (i.e., distinct sites and distinct workers) and by the additional stratification imposed on these units (i.e., crop type, geography, and AaiH). Many of the conditions varied should be considered meta-factors with respect to their impacts on exposure. That is, they might not themselves cause differences in exposure but are associated with factors (both known and unknown) that impact exposure. Some of this indirect diversity is described below. With the possible exception of AaiH and the effect of 'cluster', the AHETF does not claim that the resulting data will be sufficient to assess the impact of any of these factors on exposure. Such diversity will usually be treated as 'natural variation' in any analysis (e.g. see Section 8 below). The impact of using diversity selection as a surrogate for random representative sampling is discussed in the Governing Document and in Section 4.2 above.

6.1 Work Activity and Duration

The workers will be allowed to follow their normal procedures as long as they fit the scenario definition and do not conflict with EPA's Worker Protection Standard (WPS) regulations. The duration of the work activity will be partially determined by the amount of AaiH but will involve the application of at least three loads and a minimum duration of four hours.

For this particular scenario the applicator will be in a closed cab while the actual spraying takes place. The cab enclosure should reduce dermal and inhalation exposure from airborne spray that would otherwise reach the operator. This protection is due to the physical barrier between the pesticide spray and the worker. When doors or windows are opened, however, this barrier is no longer effective and the potential for worker exposure is increased. Opening windows during actual spraying would be contrary to the WPS and a violation of the label. This will, therefore, not be allowed.

AHETF suspects that exposure potential, especially dermal exposure, may be impacted by how often the applicator gets out of the closed cab, where that exiting occurs, and what the worker does while outside the cab. Exiting the cab might occur to make sprayer adjustments, perform repairs, or prepare a new load. Therefore, exiting might occur within or outside of the treated area. By exiting the cab, the worker might be subjected to lingering airborne sprays and/or surfaces that may have been sprayed with pesticide including the crop itself, the ground, various parts of the sprayer, and the outside of the cab. Exiting the cab is not, however, something that can be predicted or controlled in advance since it depends on factors such as worker preference, number of loads performed, and whether repairs or adjustments are necessary. The agricultural experts consulted by AHETF indicated that exiting the cab is rare. Number of exits, therefore is not amenable to formal diversification, but will likely vary as a result of purposive diversity in AaiH, and other factors such as crop type, equipment, etc. The number of times the applicator exits the cab and a description of each event will be recorded in the field raw data.

Another parameter that might impact exposure is the number of loads applied since the applicator typically gets out of the closed cab between loads, even if someone else prepares the next load. AHETF has a standard practice that each MU will apply a minimum of three tank loads. This ensures the generic database will contain exposure data generated from work periods that represent a full day (i.e., generally four hours or more) and from repeated mixing/loading or application cycles that increases the chances of exposure (and therefore won't underestimate exposure potential). Some diversity in the number of loads will naturally occur since AaiH and equipment size will vary.

Duration of monitoring is another parameter that could vary between MUs, especially since the AaiH will be varied by more than an order of magnitude. Airblast applicators often spend several hours making applications, so all MUs for this scenario must meet the general rule of being at least 4 hours long. This is designed to overcome the criticism of early exposure studies where many of the sampling regimes monitored workers for only a few minutes. Avoiding very short monitoring intervals will ensure that daily exposure estimates are not biased by unusual conditions during that short interval. If necessary, some minor scripting of worker activities will be done to ensure the lowest levels of AaiH are handled and/or a minimum of four hours are monitored. For example, a worker might be asked to use a smaller tank, make smaller loads, or increase the spray volume slightly in order to apply 3 loads in four hours for the lowest AaiH.

6.2 Equipment

Study participants will use equipment that is typical for this scenario and that the workers have recently operated (within the last year). Recent experience is required in order to minimize the risk of injury to the workers and to ensure that the activity performed by the worker is one that they typically perform. In addition, any particular piece of airblast equipment cannot be used more than once (e.g., by two different workers at one grower site). This will ensure diversity in equipment within each cluster.

Standard airblast sprayers used in agriculture include the following components (adapted from Cromwell, 1975):

- spray tank with agitation system (to contain diluted pesticide mixtures)
- pump system (to pressurize the liquid)
- pressure regulator and gauge (to adjust and monitor liquid pressure)
- control valves (to turn on/off all or part of the spray), a fan, and sometimes air director vanes (to move air upward and outward)
- spray nozzles (one or more manifolds)

Sprayers are commonly drawn by a tractor or vehicle to move the sprayer through the orchard or vineyard, but can also be mounted on a tractor or other vehicle. Agricultural experts indicated that nearly all airblast sprayers are fundamentally the same, although a variety of sprayer sizes and configurations exist. In addition, a myriad of adjustments can be made to the liquid and air delivery systems to fit a wide range of crop conditions (e.g., crop type, size, and degree of foliage).

Airblast sprayers can involve open or closed cab vehicles. This scenario will address only closed cab configurations. For this closed cab scenario, the Worker Protection Standard (WPS) provides a definition of closed cab as including a non-porous barrier that totally surrounds the occupants and prevents contact with pesticides outside of the cab. Another important component is an air filtration system; some are designed to remove only dust/mist and others are designed to remove organic vapors as well. AHETF proposes that any filtration system is appropriate for inclusion in the sampling program as long as the cab enclosure is intact and appears to be in good condition. The WPS also has provisions for eliminating the need for respiratory protection (required for some products) if the closed cab has been "certified" by the manufacturer or a governmental agency that it provides similar protection against dust, mist, or vapors. However, these certifications are exceedingly rare and AHETF has adopted the policy that respiratory protection required by the label will always be worn by applicators when inside the closed cab in its studies. Further, AHETF will not attempt to locate and include in its monitoring program cabs with certified respiratory protection. Each closed cab spray rig will however be inspected by the Study Director or designee prior to use in a monitoring study to ensure its integrity and proper operation, including the air conditioning system. During study conduct, researchers will record a full description of the filtration attributes of the cab used by each MU.

Other application equipment types can sometimes be used as an alternative to conventional airblast sprayers. Agricultural experts indicated the following are sometimes alternatives in orchard or trellis crops: aerial application, directed-spray rigs, wrap-around sprayers, covered boom sprayers (e.g., tunnel or curtain), electrostatic sprayers, and mist blowers. Mist blowers produce droplets that are finer than most other sprayers and are used for low volume applications. The other sprayer types are more similar to groundboom sprayers in that there is no air "blast" that helps force the spray into the foliage. However, they may include small fans or directed airstreams that assist with carrying spray droplets toward the target crop. Discussions with a variety of agricultural experts in several areas of the country indicate these alternative systems are not nearly as common as conventional airblast sprayers for either trellis or orchard crops. AHETF will therefore limit its MU collection to include exposure to workers operating conventional airblast sprayers.

Setup of an airblast sprayer can be very complex involving the following factors and others: nozzle type, nozzle size, nozzle placement, number of nozzles, orientation of air director vanes, liquid pressure setting, spray volume per acre (GPA), engine speed, ground speed, etc. These factors often act interactively, rather than independently, to affect sprayer performance, generally by impacting droplet size, force of spray, or amount of spray per acre. These factors are generally chosen by the grower depending on crop conditions, the pest being treated, and the particular products being used. Collectively, these factors might also have an impact on exposure potential for airblast applicators, for example by influencing the amount of spray that remains airborne long enough to reach the operator or that contaminates surfaces the operator may later contact. However, the protection offered by the closed cab is expected to reduce the magnitude of exposure to such a degree that none of these factors will have a direct measurable impact on exposure.

Because of the diversity that will be obtained for AaiH and the variability in the crops that will be used in this study, the overall type, size, and configuration of equipment will vary indirectly because of their natural correlation with AaiH or crop type. Examples include smaller equipment for trellis crops, deflector vanes for very tall orchard crops, higher volumes for dense foliage, and larger equipment for high AaiH.

7 ACTIVE INGREDIENTS

The AHETF has developed several pesticide active ingredient compounds for use as surrogates. These include herbicides, insecticides and fungicides with a wide range of label uses. These surrogates were developed specifically because they only require minimal Personal Protective Equipment (PPE), have low toxicity, and are commonly used on a wide variety of crops and areas of the country. Since the AHETF is developing a generic database that will be applicable to nearly all pesticide products and uses, any of the AHETF surrogates can be used for generating exposure data for this scenario. The choice of surrogate at each location will depend largely upon the preference of the grower and pest pressure on his crop at that time.

Whenever possible, surrogate products that require minimal PPE are utilized. AHETF has designed the AHED database to allow estimation of exposure to workers who wear additional PPE or clothing. For this scenario, pesticide products are available which allow a single layer of clothing plus chemical-resistant gloves (and sometimes protective eyewear). Consistent with the Worker Protection Standard (WPS), workers must remove gloves that were worn in the treated area before entering the closed cab and AHETF will enforce this requirement. Therefore, the desired PPE and clothing situation for this scenario is:

- Long pants and long-sleeved shirt
- Chemical-resistant gloves (new, provided by AHETF) only when contacting treated surfaces outside the closed cab
- Any footwear that are required by the label or that the workers choose to wear (as long as they are consistent with the WPS)
- Any eyewear required by the label or desired by the worker (except full face shields that would prevent face exposure)
- Any respiratory protection required by the label or desired by the worker (except full face respirators which would prevent face exposure)

The following active ingredients are approved for use on orchards and trellis crops, meet the minimum PPE requirements listed above, and will be considered for use in this closed cab airblast application scenario. The commercial products of these active ingredients that might be used in particular studies will be listed in study-specific protocols.

- Carbaryl (insecticide; orchards or trellis)
- Malathion (insecticide; orchards or trellis)

These surrogate active ingredients also typically have high use rates for the potential crops of interest that enables measurements at the high end of AaiH per day. Additionally, cooperating growers who will use these products are likely to be available. Finally, these active ingredients have been used as surrogates in other studies and are known to have the required stability under field study conditions.

Since this scenario involves only applications of liquid sprays, any product with the proper registration that can be added to water and applied as a liquid spray is suitable. The actual product and packaging type has no influence on the potential exposures to these applicators and is, therefore, not an important consideration for this scenario.

To quantify the risk to study participants of handling these active ingredients during the studies for this scenario, margins of exposure (MOE) for workers wearing two layers of clothing have been calculated for each of them. Data from PHED (Keigwin, 1998, Scenario 12. Airblast Application, Enclosed Cab (APPL)) were used in the calculations since they are the best data currently available. Other data such as toxicology study No-Observeable-Effect-Levels (NOEL) and the required MOE (or level of concern) for each active ingredient were obtained from the recent Re-registration Eligibility Documents (RED) authored by the EPA (Carbaryl, 2007 and Malathion, 2006). Table 6 summarizes the data for these MOE calculations. For each of the active ingredients that may be used in this scenario, the calculated MOEs greatly exceeded the minimum required MOE for the individual dermal and inhalation routes of exposure, as well as for the combined exposure, and their use is acceptable for this scenario.

It should be noted that the MOE calculations are for the highest AaiH for this scenario. Workers handling lesser amounts will have even higher MOE values. These calculated MOE values will also be presented in each study protocol for this scenario.

Table 6. MOE Calculations for Active Ingredients in the Closed Cab Airblast Application Scenario

Parameter	Carbaryl	Malathion
Maximum AI handled/day (lbs) [a]	100	100
PHED Unit Exposure - Dermal (mg/lb AI) [b]	0.019	0.019
Adjusted PHED Unit Exposure - Dermal (mg/lb AI) [c]	0.018	0.018
PHED Unit Exposure - Inhalation (mg/lb AI) [d]	0.00045	0.00045
Daily Dermal Exposure (mg/kg) [e]	0.026	0.026
Daily Inhalation Exposure (mg/kg) [f]	0.00064	0.00064
Short-term Dermal NOEL (mg/kg/day) [g]	86	127
Short-term Inhalation NOEL (mg/kg/day) [g]	1.1	25.8
Dermal Margin of Exposure (MOE) [h]	3,308	4,885
Inhalation Margin of Exposure (MOE) [i]	1,719	40,313
Combined MOE (dermal + inhalation)	**1,131**	**4,348**
Minimum Required MOE for Dermal Endpoint [g]	100	100
Minimum Required MOE for Inhalation Endpoint [g]	100	1,000
Minimum Required MOE for Dermal + Inhalation [g]	100	100

[a] Highest AaiH set for this scenario.
[b] PHED (Scenario 12) data are best available data; for single layer of clothing with gloves (no available data without gloves).
[c] PHED exposure value for “Upper and Lower Arm, Chest, Back, Thigh, and Lower Leg” decreased by 50% due to additional layer of clothing (long underwear inner dosimeter) then added back to “Head and Neck” and “Hand” values to derive the Adjusted total dermal exposure.
[d] PHED data are best available data.
[e] (AI handled x Adjusted PHED Unit Exposure) / 70 kg BW.
[f] (AI handled x PHED Unit Exposure) / 70 kg BW.
[g] Values from recent Re-registration Eligibility Document (RED).
[h] Short Term Dermal NOEL / Daily Dermal Exposure.
[i] Short Term Inhalation NOEL / Daily Inhalation Exposure.
[j] Combined Dermal & Inhalation MOE = 1/[(1/Dermal MOE) + (1/Inhalation MOE)]. MOE value must be > Minimum Required MOE for that endpoint.

8 DATA ANALYSIS

The goal of conducting closed cab airblast applicator studies is to develop a set of generic dermal and inhalation exposure data which regulators and other potential users of the generic database can utilize to characterize a predicted distribution of future exposures, and perform exposure assessments for this scenario. As detailed in the Governing Document, the data collected from the studies for this scenario will only be statistically evaluated with respect to the benchmark measures of adequacy. These two categories of data adequacy are:

1. The relative accuracy of selected statistics characterizing the distribution of exposure normalized by amount of active ingredient handled (AaiH).

2. How well the data can be expected to describe a relationship between exposure and AaiH, if one existed.

As emphasized both in the Governing Document and in Section 4 above, it important to keep in mind that, like the sample size determination, both of the above statistical adequacy benchmarks are relevant only within the context of the reference random sampling distribution defined in Section 4.3. In particular, the monitoring data will be treated as if it were collected as a two-stage random sample from an infinite population. Technically, there is no statistical theory that can be applied to non-random samples (or even to random samples for which the probability structure is unspecified). Nearly all monitoring data used for regulatory purposes is of this type. As has always been the case, any statistical conclusions based on such data imply the qualification: "to the extent that the data can be viewed as deriving from a true random sample." As pointed out in Section 4.2 above, diversity selection is expected to yield MUs that tend to overestimate the true variation among future exposures. This suggests that the estimates of upper percentiles will tend to be overestimated (and lower percentiles underestimated) in the resulting monitoring data. With the small sample sizes used in this scenario, however, such estimation bias is probably trivial relative to ordinary uncertainties due to sampling, whether random or purposive.

8.1 Relative Accuracy of the Normalized Exposure Distribution

The primary benchmark objective is that selected lognormal-based estimates of normalized dermal exposure distribution be accurate to within 3-fold, at least 95% of the time. The benchmark estimates specified are those for the geometric mean, arithmetic mean, and the 95th percentile.

To evaluate how well the collected data conform to this benchmark, the 95 percent bound on relative accuracy will be calculated from the confidence interval for each of the three parameters given above. Details of these calculations are provided in Appendix C of the Governing Document.

This primary benchmark objective strictly applies to only dermal exposure. However, for uniformity, the 95 percent bounds on the three parameters will also be computed for inhalation exposure.

8.2 Adequacy of the Data for Distinguishing a Proportional from an Independent Relationship between Exposure and AaiH

This secondary benchmark objective applies to the closed cab airblast scenario because the practical range in the amount of active ingredient handled (AaiH) exceeds an order of magnitude. In this case it is reasonable to consider the linear regression of log dermal exposure on log AaiH. Such a regression would use a mixed model formulation in order to incorporate random cluster effects. As described in the Governing Document, in such a model the true slope, β, would be equal to one if dermal exposure were directly proportional to AaiH. If exposure were independent of AaiH, then $\beta=0$. This benchmark objective requires that the number of clusters and the allocation of AaiH levels to MUs should be adequate to ensure that the regression analysis has at least 80% power to reject the hypothesis that $\beta=0$ when β is actually equal to one. By symmetry, the mixed model linear regression would also have the same power to reject the hypothesis that $\beta=1$ when $\beta=0$. This is the precise meaning of being able to 'discriminate between proportionality and independence'.

To evaluate this benchmark, a mixed model regression of log dermal exposure on log AaiH will be performed and a confidence interval obtained for β. With this information, power analyses are irrelevant. Even a post-hoc power analysis is less informative than the confidence interval itself. Calibration of the confidence interval for β with the pre-data power analysis is relatively simple. If the adequacy benchmark were satisfied, the mean width of a 95% confidence interval for β would be approximately 1.4. Therefore, if the width of the confidence interval obtained from regression on the actual data is 1.4 or less, then the data will be judged adequate with respect to the secondary benchmark. Note that in this case the adequacy of the data depends only on the width of the confidence interval, not on the endpoints of the interval or on the estimated slope, b. Details of this analysis are described in Appendix C of the Governing Document.

As was the case for the primary objective, the secondary object only applies to dermal exposure. However, for uniformity, the same regression analysis and assessment of the confidence interval will be conducted for inhalation exposure.

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