

US EPA ARCHIVE DOCUMENT



AHETF Scenario Design and Field Study Protocols:

***Closed System Loading of Liquids (CSLL)
in Non-Returnable Containers
and
CSLL in Returnable Containers***

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Overview

- The proposed research will measure exposure of workers loading liquids using closed systems into pre-mix tanks or application tanks
- Closed systems are designed to enclose the pesticide to prevent it from contacting handlers
- Closed systems are defined in EPA's Worker Protection Standard as those that "enclose the pesticide to prevent it from contacting handlers or other persons"



Overview

- Two scenarios:
 - Loading from non-returnable containers
 - Loading from returnable containers
- Exposure will be monitored while subjects are mixing and loading (and rinsing, if applicable)
- Subjects will not be applying; exposure from application will be covered by other AHETF scenarios



What's Familiar about this Proposal?

- Design objectives and rationale are similar to several previous AHETF scenarios reviewed by the HSRB
- Protocol procedures related to ethical conduct are similar



***AHETF Scenario Designs: Closed
System Loading Liquids (CSLL)
in Non-Returnable Containers
and
CSLL in Returnable Containers***

Science Assessment

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Scenario Definition(s)

- Exposure of individuals involved in Closed System Liquid Loading (CSLL) as defined by container type: non-returnable (NR) and returnable (R)
- The two scenarios do not involve applying. Application is covered by other AHETF scenarios
- Based on the use of CSLL systems that are consistent with the intent of the Worker Protection Standard (WPS):
 - "...designed by the manufacturer to enclose the pesticide to prevent it from contacting handlers or other people while it is being handled. Such systems must function properly and be used and maintained in accordance with the manufacturer's written operating instructions."
 - The term "manufacturer" also applies to custom systems developed by individual growers, custom applicators etc.



Scenario Definition(s) clothing

- The attire to be worn by participants for both scenarios will consist of long-sleeved shirt, long pants, shoes plus socks; **and PPE shall consist of chemical resistant gloves.**
 - Participants will wear their own clothing provided it is WPS compliant
- Additional Personal Protective Equipment (PPE) that may be required for closed loading systems:
 - Protective eyewear for systems under pressure (can be worn by participants)
 - Aprons – required if the end-use product is in acute toxicity category I or II for acute dermal or skin irritation or if EPA required closed systems based risk assessments
 - However, aprons are not part of the scenario design, individuals who use them will be excluded from consideration



Potential Scenario Differences

	Non Returnable	Returnable
Container Size	Small	Generally > 55 gallons
Loading Events	Likely to be more events	Fewer loading events
Rinsing Containers	Yes	No
Equipment types	Suction/Extraction, Gravity Feed, Container Breach	Mostly Suction/Extraction
Available Data	No	Two pre-rule studies



Suction Extraction - Probe





Suction Extraction





Suction Extraction





Gravity





Container Breach





Dry Coupling Systems





Non-Returnable Study Design Details

- Seven clusters with 3 MUs per cluster
 - A cluster/monitoring area is an entire state
 - Arizona, Florida, Michigan, Mississippi, Nebraska, Texas and Washington
 - AaiH Strata
 - From 12 to 30 lbs
 - From 31 to 310 lbs
 - From 311 to 800 lbs



Returnable Study Design Details

- Consists of two existing studies for a total of 22 MUs
 - Purchased study conducted in CA
 - AHETF pre-rule study conducted in TX
- Plan on collecting and additional 15 MUs for a total of 37 MUs



Returnable Study Design Details

MU	Amount AaiH (lbs)			
ID	Day 1		Day 2	
A	1,531	1,569	1,569	
E	1,531	1,430	682	1,196

- Purchased study conducted in CA
- 7 MUs utilizing 2 participants
- One participant 4x the other 3x.
- Same worker, same day correlations



Returnable Study Design Details

- AHETF pre-rule study conducted in TX
- 15 MUs utilizing 7 participants
- Four participants 3x the others 1x.
- Same worker correlations



Existing and Current Designs

Existing Studies:

Emphasis on logistics

- Could have repeated measures of same workers on the same farm/operation

● **New Studies:**

- No repeated measures
- Different employers in each monitoring area
- Different farms
- AaiH strata



Returnable Study Design Details

- AHETF also found that, although limited, the data are not inconsistent with the assumption of $GSD=4$ and $ICC=0.3$ (p value=0.61, likelihood ratio test.)
- Therefore using the reference model, AHETF propose 15 additional MUs with a 5x3 design as an adequate sample size which will then be added to the existing 22 MUs



Returnable Study Design Details

- AHETF propose 5 new clusters with 3 MUs per cluster
 - A cluster/monitoring area is an entire state
 - Arizona, Florida, Michigan, Nebraska and Washington
 - AaiH Strata
 - From 60 to 119 lbs
 - From 120 to 1,200 lbs
 - From 1,201 to 2,400 lbs
- This configuration, when added to the existing data, is likely to result in achieving the primary and secondary objectives



Available Surrogate Pesticides

Surrogate Pesticide	NR Containers	R Containers
Carbaryl	Yes	No
Chlorothalonil	Yes	Possible
Dacthal (DCPA)	Yes	No
Fosamine	Yes	Yes
Glyphosate	Yes	Yes
Imazapyr	Yes	Yes
Imidacloprid	Yes	Limited
Malathion	Yes	Yes
Simazine	Yes	Possible
Sulfur	Yes	Unknown
Thiophanate-methyl	Yes	Unknown
2,4-D	Yes	Yes
2,4-DB	Yes	Yes



Available Surrogate Pesticides

- Surrogate pesticides have low toxicity and do not require aprons
- Wide range of application rates to help fill AaiH strata
- Can be used safely under the conditions of the proposed studies
- Acceptable analytical methods for all dosimetry
 - Whole body (upper and lower sections) hand rinse, face neck wipes and OVS tubes



Anticipated Challenges

- Diversifying Equipment Types
 - Wide variety of manufactured systems (Suction extraction, container breach, gravity feed, glove box)
 - Limited manufacturing base with some firms now out of business
 - Many custom made systems
- Recruitment
 - Limited use: many CSLL users have to do so because they are using highly toxic pesticides and thus may typically wear aprons – will not be recruited
 - Not all systems are entirely closed (e.g., the Handler®)
 - Recruitment is expected to be difficult (finding 3 or more participants at the same time for a given monitoring area)



Solutions

- The monitoring area (cluster) is the entire state (states selected are those with high use of closed systems)
- More states with less MUs per state
- Consider all systems, including custom made systems, provided they meet WPS definition
- Where possible, diversify CSLL types as best as possible
- Monitor participants as soon as they are available



Introducing Random Elements in a Purposive Design

- **Recruitment**: The AHETF process for identifying handler subjects recruited from growers or commercial pesticide application firms includes:
 - Contacting resources such as Farm Market ID and Meister Media Worldwide to identify growers using closed mixing/loading systems
 - Assembling a list of growers from all resources contacted and eliminating duplicates
 - Assembling a list of commercial applicators in each state from sources such as pesticide applicator licensing authorities and the National Agricultural Aviation Association.



Introducing Random Elements in a Purposive Design

- Contact a random subsample from the combined grower and commercial applicator list (i.e., employer list), one at a time, in the sequence of the randomized list, to determine whether the grower is 'eligible' to participate
- Placing eligible employers into a “working pool”
- If the original randomized list is exhausted without finding enough interested handlers to complete the field study design, another list will be generated. Alternatively, the AHETF may consider monitoring as soon as there is an eligible participant if recruitment proves to be too difficult.



Conclusions of Science Assessment

- We agree with the AHETF study design approach to have more clusters and less MUs per cluster
- We agree with AHETFs proposed number of samples per scenario (21 MUs for non returnable containers and 15 new MUs for the returnable container)
- We expect diversity will be achieved—randomly or purposively—in the course of assigning mixer/loaders to Amount active ingredient Handled (AaiH) strata within each cluster
- We accept the potential for recruitment difficulties and agree with having the option available to monitoring individual volunteers before others are identified



Additional Recommendation

- Given the importance in this study of capturing information about observed worker behavior, the AHETF should provide study observers with a list of specific types of behaviors that should be noted in the field log. This guidance could complement the general information provided in SOP 10.C.5.
- An example: visible residue/liquid on the system linkages/couplings



Conclusions of Science Assessment

- The Scenarios are well defined and the study is likely to produce reliable mixer/loader data to assess the potential exposure of handlers using CSLL with non-returnable and returnable containers



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Ethics Assessment

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Value to Society

- Additional data needed to support EPA risk assessments:
 - Returnable: Data collected through this research will be combined with some pre-existing data to populate the scenario in AHED®
 - Non-returnable: Pre-existing data not adequate; new data will completely populate the scenario in AHED®
- Data will be used to estimate dermal and inhalation exposure for a wide range of pesticides



Subject Selection

- Eligible commercial growers identified; to participate, growers must sign non-coercion statement
- Subjects will be recruited among employees who mix and load liquid pesticides using closed systems
- Subjects will be recruited who:
 - Have experience within the last year using the piece of closed equipment that will be used in the study
 - Meet the other subject eligibility criteria



Recruitment Process

- Permission sought to approach employees of eligible growers, or to post recruitment flyer in common work area
- Recruitment meetings held with interested employees, without employers/supervisors
- Program, study, procedures, risks and benefits explained to prospective subjects



Consent Process

- Private consent interviews
- Equivalent processes for Spanish and English speakers, relying on bilingual investigators
- Consent form contains all elements required by 40 CFR 26.1116
- Organization and presentation of risk information in consent forms is acceptable
 - Risk information thoroughly presented in consent forms
 - Surrogate product-specific risk information from the label and MSDS will be provided to each worker prior to monitoring



Risks

Five categories of risk; protocol provides appropriate measures to minimize each

1. Heat-related illness
2. Exposure to surrogates
3. Exposure to surfactants
4. Scripting of field activities
5. Psychological risks



Benefits

- No direct benefits to subjects
- Sponsors will benefit from improved risk assessments more accurately reflecting actual exposure
- Likely societal benefit is higher quality exposure and risk assessments for liquid pesticides that are mixed and loaded using closed systems



Risk-Benefit Balance

- Risks have been fully identified and effectively minimized
- Residual risks to subjects will be low
- Risks to subjects are reasonable in light of potential societal benefits



Respect for Subjects

- Payments to subjects reasonable
- Subjects free to withdraw at any time, for any reason
- Medical care for research-related injuries will be provided at no cost to the subjects
- Procedures to protect subject privacy



Independent Ethics Review

- The Independent Investigational Review Board (IIRB) of Plantation FL:
 - Reviewed and approved the protocol and informed consent materials
 - IIRB is independent of the sponsors and investigators, registered with OHRP, and accredited by AAHRPP
- IIRB's "Human Research Protection Program Plan" and Current Membership Roster is on file with EPA and has been provided to the HSRB



Applicable Ethical Standards

- Proposal for third-party research involving intentional exposure of human subjects to a pesticide, with the intention of submitting the resulting data to EPA under the pesticide laws
- The primary ethical standards applicable to the conduct of this research are 40 CFR 26, Subparts K and L and FIFRA 12(a)(2)(P)



Revisions Requested by EPA in Future Protocols

- Develop criteria for the on-site medical professional to use to decide whether a subject is too sick to refuse medical treatment, and document the criteria in an SOP
- Incorporate the forthcoming guidance from the HSRB about how to provide personal exposure results to subjects



Conclusion

- Protocol meets the applicable ethical requirements of 40 CFR 26, subparts K and L



Charge Questions

If the proposed research is revised as suggested in EPA's review and if the research is performed as described:

1. Is the research likely to generate scientifically reliable data, useful for assessing the exposure of workers using closed systems to load liquid pesticide products from returnable and non-returnable containers?
2. Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?