AHETF Scenario Designs and Field Study Protocol for Two Rights of Way Application Exposure Techniques: ***Backpack and Handgun Sprayers***

Jeff Evans
Kelly Sherman
Office of Pesticide Programs

AHETF Status Recap

- 2008: Closed-cab and open-cab airblast scenarios favorably reviewed by HSRB
- 2008/2009: Closed-cab and open-cab airblast field studies conducted
- June 2009: Mixing-loading wettable powder in water soluble packaging scenario favorably reviewed by HSRB
  - This scenario has been revised and will be re-reviewed by the HSRB (October 2010)

What's Familiar about this Proposal?

- Design objectives, sample size and rationale are similar to previous AHETF scenarios reviewed
- Protocol procedures related to ethical conduct are similar

What's Different about this Proposal?

- The study is comprised of two scenarios
- Two new surrogates - fosamine and imazapyr
- Updated SOPs and Governing Document
- New cluster configuration (3x7, not 5x5)
- Allows for >1 MU per employer
- Does not include individual Product Risk Statements

Completeness; Ripeness for Review

- The protocol submission contained all elements of documentation required by 40 CFR 26.1125
- EPA believes these proposals are ripe for HSRB review

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Science Assessment

Jeff Evans
Health Effects Division
Office of Pesticide Programs

Scenario Definitions

- Two *Non-Agricultural* scenarios addressing exposure of individuals involved in vegetation control using hand held equipment in utility Rights-of-Way (ROW):
  - 1) Applying ROW sprays using backpack sprayers
  - 2) Applying ROW sprays using handgun sprayers

Scenario Definitions

- Minimum attire for participants will include *long sleeved shirts, long pants, shoes, socks and chemical resistant gloves*
- Also permitted: hardhats, baseball style caps, eyewear (prescription, safety or sunglasses) and safety vests
- Not permitted: leggings, chaps or chemical resistant headgear (surrogate pesticides do not require)

Scenario Definitions

- Backpack ROW sprayers
  - Worn on back of the applicator
  - Used in areas having difficult terrain or when making spot treatments in integrated vegetation management programs
  - No mixing will be performed by the participants; however, they typically fill their spray tanks with dilute sprays from truck mounted tanks or other containers

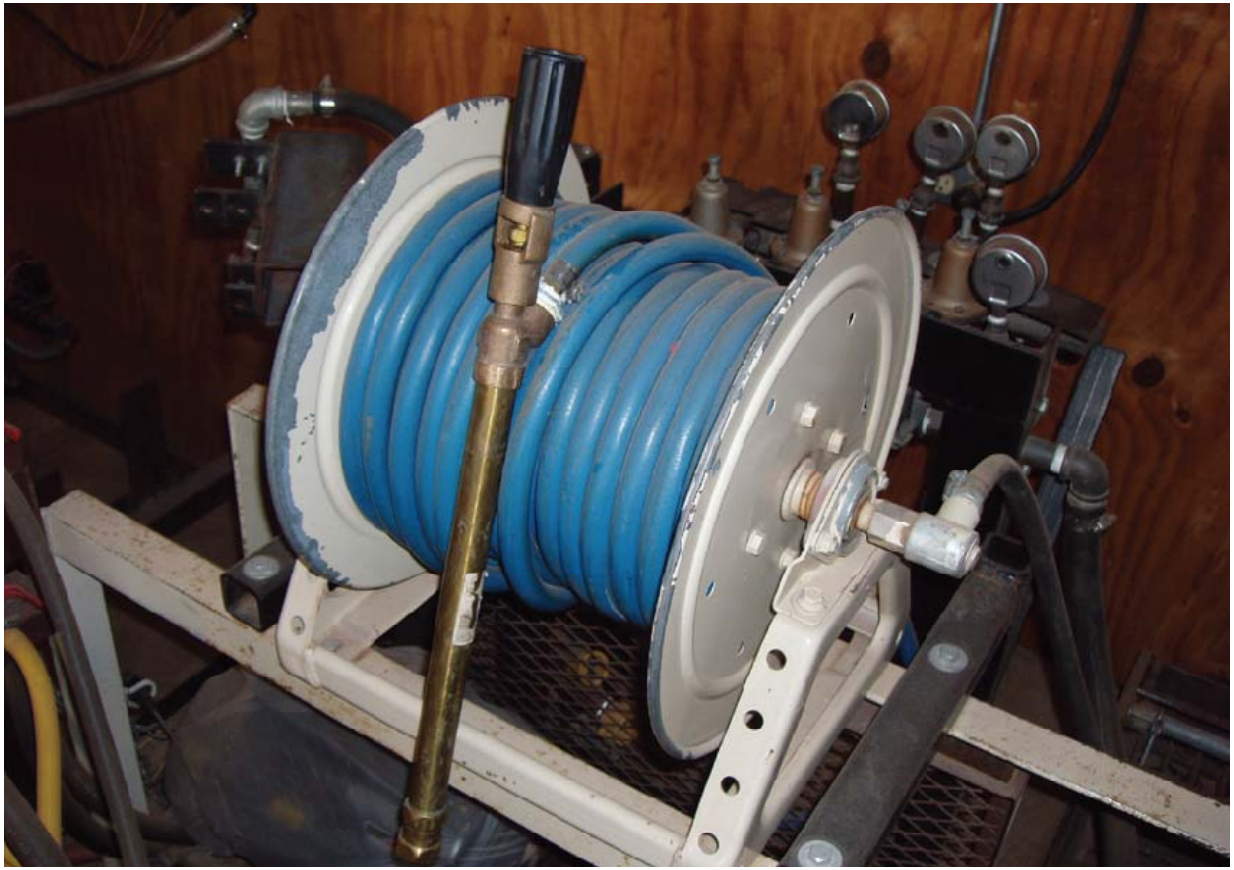
Scenario Definition, Backpack Sprayers

Backpack Sprayers Used in ROW

Scenario Definition, handgun sprayers

- Handgun ROW sprayers (applying only)
  - Consists of a handgun (wand) operated from vehicles equipped with 100 to 1,500 gallon tanks
  - Connected to the tank by hoses up to 2000 feet in length

Hose Reel and Handgun (wand)



Handgun Truck

Vegetation control in ROW using handgun

- Applications may be made directly from the vehicle or to areas having road access

Proposed Surrogate Pesticides

- Four widely used herbicides requiring the minimum personal protective equipment (PPE)
  - Imazapyr (maximum rate 24 lbs ai)
  - Fosamine (maximum rate 1.5 lbs ai)
  - Glyphosate
  - 2,4-D
- Important to have a wide range of applications to accommodate the amount active ingredient handled (AaiH) strata

Proposed Surrogate Pesticides

- 2,4-D and glyphosate have reliable analytical methods and have been successfully used as surrogates in other AHETF exposure monitoring studies
- Fosamine and imazapyr are new surrogates for the AHETF. However, they have been successfully used in other human exposure monitoring studies.
  - *Confirmation of analytical methods is required prior to study initiation*

Surrogate Criteria

- Low Volatility
  - Fosamine $4x10^{-6}$ mm Hg @ 25°C, Imazapyr $2x10^{-7}$ mm Hg@ 20°C
- Environmental Stability
  - Stable under conditions of the study
    - Confirmed during method development and GLP method validation. Also through field fortification measurements
- Analytical Methods: 70–120% recovery; coefficient of variation 20% or lower
- Field recovery: 50-120%; coefficient of variation: 25% or lower.
- Low limits of quantification dermal: 1 µg/section; Inhalation 0.01 µg
- Requires minimal PPE, relatively low toxicity
  - Fosamine and glyphosate: no mammalian toxicity observed

Proposed AaiH Strata

- All exposure durations will be at least 4 hours
- Each subject will apply at *least* 3 tanks of spray
- Three strata of AaiH for each monitoring area (i.e., cluster):

Backpack ROW	Handgun Sprayer ROW
0.5 to less than 1.5 pounds	1 to less than 3.5 pounds
1.5 to less than 15 pounds	3.5 to less than 35 pounds
15 to 50 pounds	35 to 125 pounds

Proposed AaiH Strata

- The AHETF strives to ensure that no two participants be in the same AaiH stratum per monitoring area
  - AHETF believes this may not always be feasible
- Therefore, for these two scenarios, it is stated that it is *preferable* that no two participants be in the same stratum per monitoring area

Application Rate Calculations

- Application rates based on maximum acres treated per day and maximum volume sprayed per day
  - Backpack: EPA assessments generally assume 2 acres treated per day or 40 gallons sprayed per day
  - Handgun: EPA assumes 10 acres treated per day or 1000 gallons sprayed per day
- Confirmed by experts interviewed by the task force

Study Design

- For both scenarios the objective is to design a study that has as many conditions that can influence exposure (directly or indirectly) as possible
  - It is accomplished in these studies this by:
    - Stratifying the range of AaiH and requiring a minimum of three tank loads to be sprayed
    - Diversifying the number of participants and study sites (monitoring areas)
      - Different work habits, climate vegetation/terrain

Study Design

- Both ROW study designs are referred to as efficient configurations intended to achieve two objectives
  - Primary objective: A 'K' value or relative fold factor of 3 for AM, GM and 95th percentile 95% of the time
  - Secondary objective: the ability to test the data to determine if exposure is proportional to AaiH
- For agricultural scenarios, the AHETF typically relies on a study configuration having 5 sites with 5 participants monitored per site (n=25)
- For these two scenarios the AHETF has 7 sites and 3 participants per site (n=21)

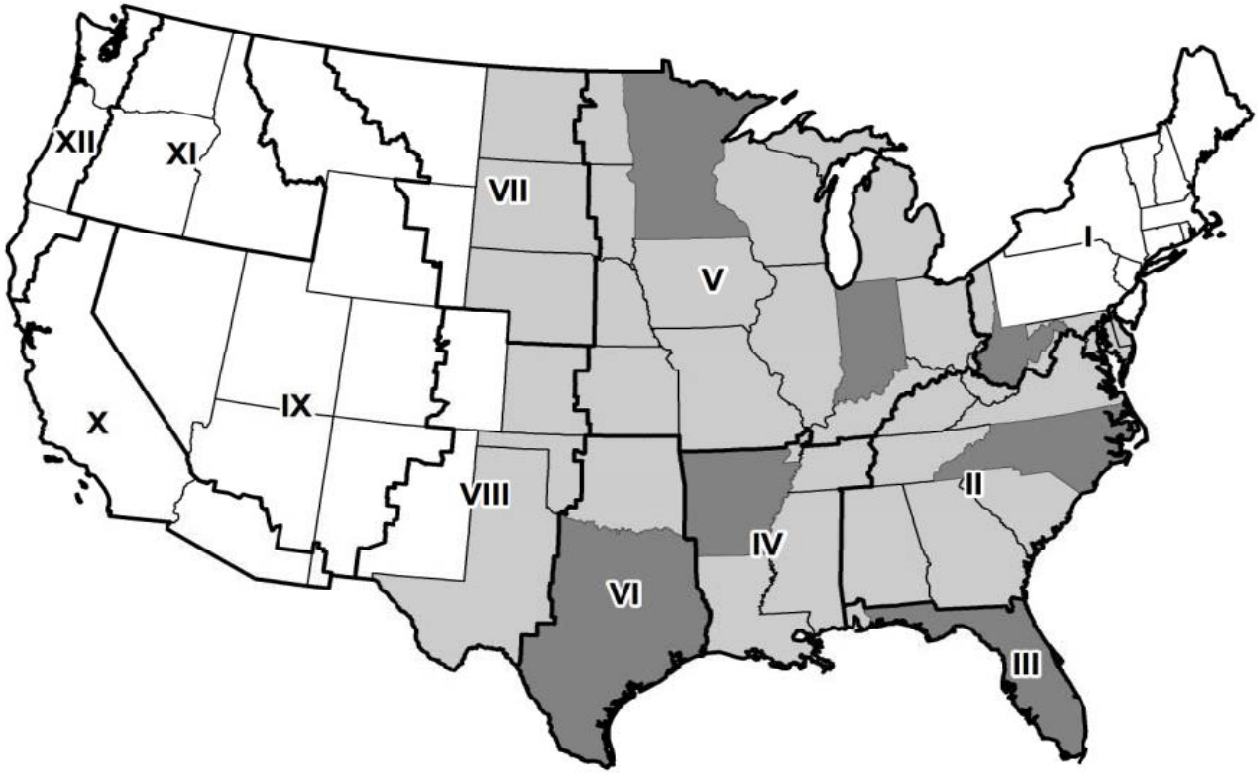
Study Design

- Efficient configuration for both scenarios is 7 monitoring areas with 3 participants per area (per scenario)
  - Focus on eastern portion of the country requiring more vegetation treatments and
  - having areas large enough to treat so they can find and a sufficient pool of participants
- Many utility companies contract out the spraying of ROW and many contract companies operate in several regions throughout the country

Study Design

- For the agricultural scenarios and through consultation with the Board, the AHETF allow only one participant per company/employer
- Because of the smaller pool of employers the AHETF is proposing to allow:
  - Only one participant per company per site (monitoring area)
  - But to permit more than one participant per company per scenario as long as the participants are in different monitoring areas

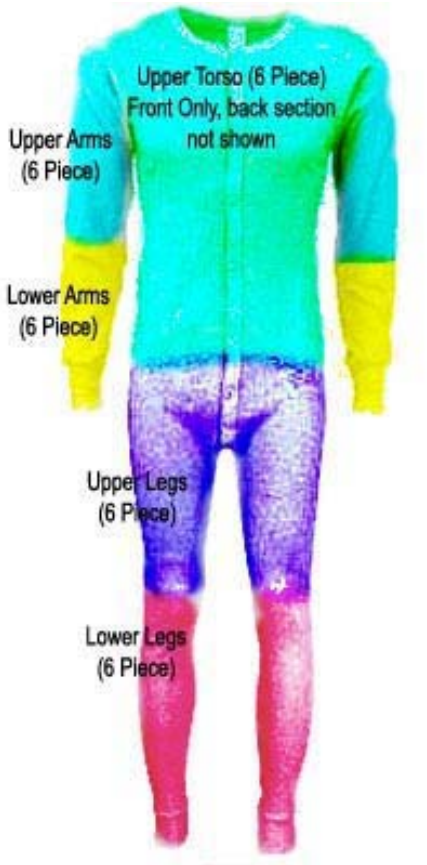
Proposed Monitoring Areas



Dosimetry

- Dermal exposure is measured with cotton union suits which act as a skin surrogate.
  - Worn beneath participants typical work clothing (also acts as an additional layer of protection for the subject)
    - After monitoring period, the garment will be cut into 6 sections
    - Socks will also be included for measurement of exposure to the feet

Inner Dosimeter Example



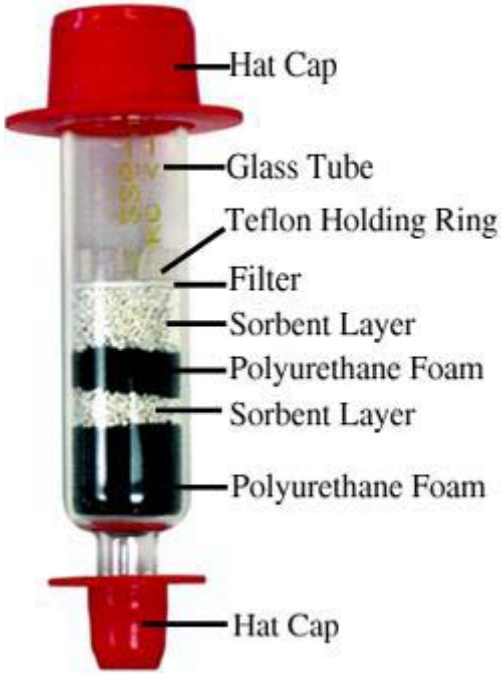
Hand Rinse

Face/Neck Wipe Technique

Inhalation pumps

Inhalation Exposure Monitoring

OSHA Versatile Sampling tube



Backpack Sprayer MOE for Max AaiH (50 lbs)

Surrogate	Dermal MOE	Inhalation MOE	Combined MOE
Imazapyr	218	11,667	214
2,4-D	218	1,167	154
Fosamine	*No observed mammalian toxicity*		
Glyphosate	*No observed mammalian toxicity*		

Handgun Sprayer MOE for Max AaiH (125 lbs)

Surrogate	Dermal MOE	Inhalation MOE	Combined MOE
Imazapyr	484	35,897	477
2,4-D	484	3,590	426
Fosamine	*No observed mammalian toxicity*		
Glyphosate	*No observed mammalian toxicity*		

Existing Data

- EPA currently relies on Pesticide Handlers Exposure Database (PHED) for both backpack and handgun sprayer exposure assessments
  - Backpack studies include those having measurements to coveralls only (requiring estimates of clothing penetration) or studies that do not have measurements of hand exposure for participants wearing gloves
    - None are based on individuals making ROW treatments
  - Handgun sprayer studies include a wide variety of studies, many of which are not specific to ROW treatments
    - One ROW handgun spray study does not have measurements of hand exposure for participants wearing gloves

Conclusions of Science Assessment

- EPA agrees with the AHETF's definition of and approach to diversify these two scenarios
- The AHETF's proposal for 21 subjects collected in 7 different monitoring areas having 3 participants each is appropriate for each scenario as it ensures a wide variety of vegetation, terrain and worker habits is reasonable
- Stress that all attempts be made to measure participants applying AaiH from each of the three stratum per monitoring area
  - Mindful of the AHETFs ability to achieve all AaiH strata in all regions with respect to achieving primary and secondary objectives
- Diversity will be achieved—randomly or purposively—in the course of assigning Amount active ingredient Handled (AaiH) strata within each cluster

Conclusions of Science Assessment

- The Field and Laboratory QA/QC aspects for glyphosate and 2,4-D are robust
  - Confirmation of analytical methods are required fosamine and imazapyr
- The Scenarios are well defined and are likely to produce reliable applicator data for these ROW application methods

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Ethics Assessment

Kelly Sherman
Office of the Director
Office of Pesticide Programs

Value to Society

- Data needed to support EPA risk assessments
- Studies will constitute the entire exposure data set for these scenarios in the Agricultural Handler Exposure Database (AHED®)
- Data will be used to estimate dermal and inhalation exposure for a wide range of pesticides

Recruiting Process

- Subjects will be recruited from eligible companies that make pesticide spray applications to utility ROWs
- Subjects will be recruited who:
  - Have experience within the last year applying liquid sprays to ROWs
  - Meet the other subject eligibility criteria
- Employees are protected from potential employer coercion

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

Respect for Subjects

- Payments to subjects reasonable
- Subjects free to withdraw at any time, for any reason
- Individual results will be provided to subjects upon request
- Medical care for research-related injuries will be provided at no cost to the subjects

Recruiting and Consent

- ☑ Equitable subject selection
- ☑ Fully informed choice
- ☑ Fully voluntary choice
- ☑ Respect for subjects

Risks

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

Risk-Benefit Balance

- Risks have been fully identified and effectively minimized
- No direct benefits to subjects
- Risks to subjects are reasonable in light of potential societal benefits

Responsiveness to Previous EPA & HSRB Recommendations

- Accuracy of Spanish translations
- Method of providing individual exposure information to subjects who request it
- Analysis of representativeness
  - Important characteristics identified
  - Characteristics associated with each monitored worker sent to experts
  - Experts asked if characteristics of monitored workers are representative of workers who operate in the areas where the monitoring occurred

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" 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)

EPA Ethics Assessment

- Protocol meets the applicable ethical requirements of 40 CFR 26, subparts K and L
- No deficiencies noted by EPA

Charge Questions

If the proposed AHETF Rights-of-Way application scenario and field study proposal AHE400 is revised as suggested in EPA's reviews and is performed as described:

1. Is the research likely to generate scientifically reliable data, useful for assessing the exposure of workers who apply pesticides in utility rights of way using backpack or handgun sprayers?

2. Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?