

US EPA ARCHIVE DOCUMENT



EPA Review of Completed AEATF II Mop Study

Dermal and inhalation monitoring of
workers mopping floors
with an antimicrobial product

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Organization of Presentation

- Background and Context
- Science Assessment
- Ethics Assessment



Different Questions for Completed Study

- Was the proposal appropriately amended after review?
 - Responsiveness to EPA and HSRB comments?
 - Approved by IIRB and CDPR?
- Was the protocol faithfully executed?
 - Did recruiting follow the design?
 - Were needed amendments properly handled?
 - Did deviations compromise the research or the subjects?
- What were the results? Were the objectives achieved?
- Was the research conducted ethically?



Scope of Mop Scenario

- One of 17 AEATF II antimicrobial handler exposure scenarios
- Includes mopping floors with a dilute solution of antimicrobial product in water, and emptying each mop bucket
- Excludes pouring concentrated product into mop buckets and mixing with water
 - Many variations
 - Will be monitored as a different scenario



Mop Study: Basics

- Conducted in 3 randomly selected vacant buildings in Fresno, CA
 - Site 1: Office building
 - Site 2: Retail space (Rite Aid)
 - Site 3: Meeting space (Retired Teacher's Memorial Building)
- To ensure diversity of individual exposures, at each site one enrolled subject was assigned to each of six "Monitoring Events" (MEs), defined by the planned duration of mopping

ME	Planned Duration
1	30 - <40 min
2	40 - <50
3	50 - <60
4	60 - <70
5	70 - <80
6	80 - 90



Intended Diversity Was Achieved

ME	Planned Duration	Actual Duration		
		Site 1	Site 2	Site 3
1	30 - <40 min	31	38	38
2	40 - <50	45	51	49
3	50 - <60	59	63	59
4	60 - <70	67	69	69
5	70 - <80	53	79	79
6	80 - 90	85	90	89



Mop Study: Basics

- Monitored dermal and inhalation exposure of 6 subjects at each of 3 sites (N=18) to didecyl ammonium chloride (DDAC) formulated as Buckeye Sanicare Lemon Quat
- Subjects wore outer/inner dermal exposure dosimeters:
 - Long pants, long-sleeved shirt, shoes, socks, and no gloves
 - Whole body dosimeters (WBD) underneath clothing
- Subjects also wore breathing zone OVS air samplers, with pump on belt
- Subjects mopped floors using a string mop and a bucket with wringer, and emptied spent mop water



Macro Schedule: AEATF II Mop Study

	2008				2009				2010			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Protocol Review	■	■	■									
Protocol Revision					■	■	■					
Recruiting/Enrollment						■	■	■				
Field Monitoring							■	■				
Sample Analysis							■	■				
Closeout/QA/Reporting								■	■	■	■	■
EPA/HSRB Post-Review											■	■



Study Submission to EPA

- 31 Aug 10 AEATF II submits Final Report (MRID 48210201)
- 20 Sep 10 AEATF II submits Supplement 1 (MRID 48231201)
- 21 Sep 10 AEATF II submits Supplement 2 (MRID 48231901)
- 30 Sep 10 GPL submits demographic data
- 18 Oct 10 GPL submits e-mail responses to EPA questions



Documents Considered in EPA Reviews

- Primary Study Report MRID 48210201
 - Supplement 1 MRID 48231201
 - Supplement 2 MRID 48231901
 - Demographic Data Spreadsheet "Subject Info all 32"
- EPA Science & Ethics Review of Mop Protocol (10 Mar 08)
- HSRB 25 Jun 08 Report of April 08 review of Mop Protocol



Scope of Revisions & Amendments

- Protocol revisions of 26 Feb 09 addressed most EPA and HSRB comments
- Amendments
 1. Refine criteria for site selection
 2. Clarify details in protocol; Revise consent form
 3. Permit enrollment of subjects one-by-one
 4. Add newspaper advertisements
 5. Randomize assignment of enrolled subjects to MEs
 6. Revise specification for analytical phase
 7. Change Field Study Coordinator and Associate; Revise consent form to conform

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Science Assessment AEATF II Mop Study

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October 28, 2010



Overview

- Study Objective
- Responsiveness to EPA and HSRB Comments
- Protocol Deviations
- DDAC Residue Removal Efficiency Study
- Sectioning of WBD (Inner & Outer)
- Dermal Unit Exposures Represent 3 Clothing Configurations
- Summary of Key Study Parameters
- QA/QC Results
- Statistical Analysis
- Conclusions



Study Objective

- Collect mopping exposure data in which the upper and lower 95% confidence limits will be no more than 3-fold ($K=3$) higher or lower than the geometric mean, arithmetic mean, and 95th percentile of the unit exposures



Responsiveness to EPA Comments

- Redefine the scenario to include disposing of spent mop water
 - *Done in revised protocol of Feb 09*
- Provide data on recovery efficiency of hand-wash/face-wipe methods for DDAC
 - *Provided existing study on efficiency of DDAC residue removal from hands*



Responsiveness to HSRB Comments

- Consider repeat measurements
 - *Trade-off of knowledge about within-worker variability for more samples of between-worker variability*
- Use longer monitoring duration
 - *Additional industry information indicates 90 minutes of mopping per day represents the reasonable upper range*
- Consider defining ME by AaiH vs duration
 - *Best information available for mopping is based on duration*
- Review proportionality between exposure and AaiH
 - *AEATF II deferred to EPA*



Protocol Deviations

- 22 reported protocol deviations, including
 - Air sampling related issues
 - Light levels not monitored at sites
 - Participant re-mopped an area previously mopped
 - Chain of custody documentation lost for 1 sample
- 1 unreported deviation (change in type of mop bucket)
- None of the deviations negate the use of the exposure results



Proposed Brite 6185 EZMT Mop Bucket with 6127-01 Wringer



- “EZMT” foot pedal permits user to empty bucket into floor drain without lifting it
- This product discontinued by manufacturer in 2006 in favor of a bucket with baffles to reduce sloshing



35-Qt SplashGuard™ Mop Bucket used in Mop Study

- CON 335-3YW Bucket
- CON SW7YW Down-Press Wringer

No foot pedal for emptying
without lifting

Internal baffles to reduce
sloshing

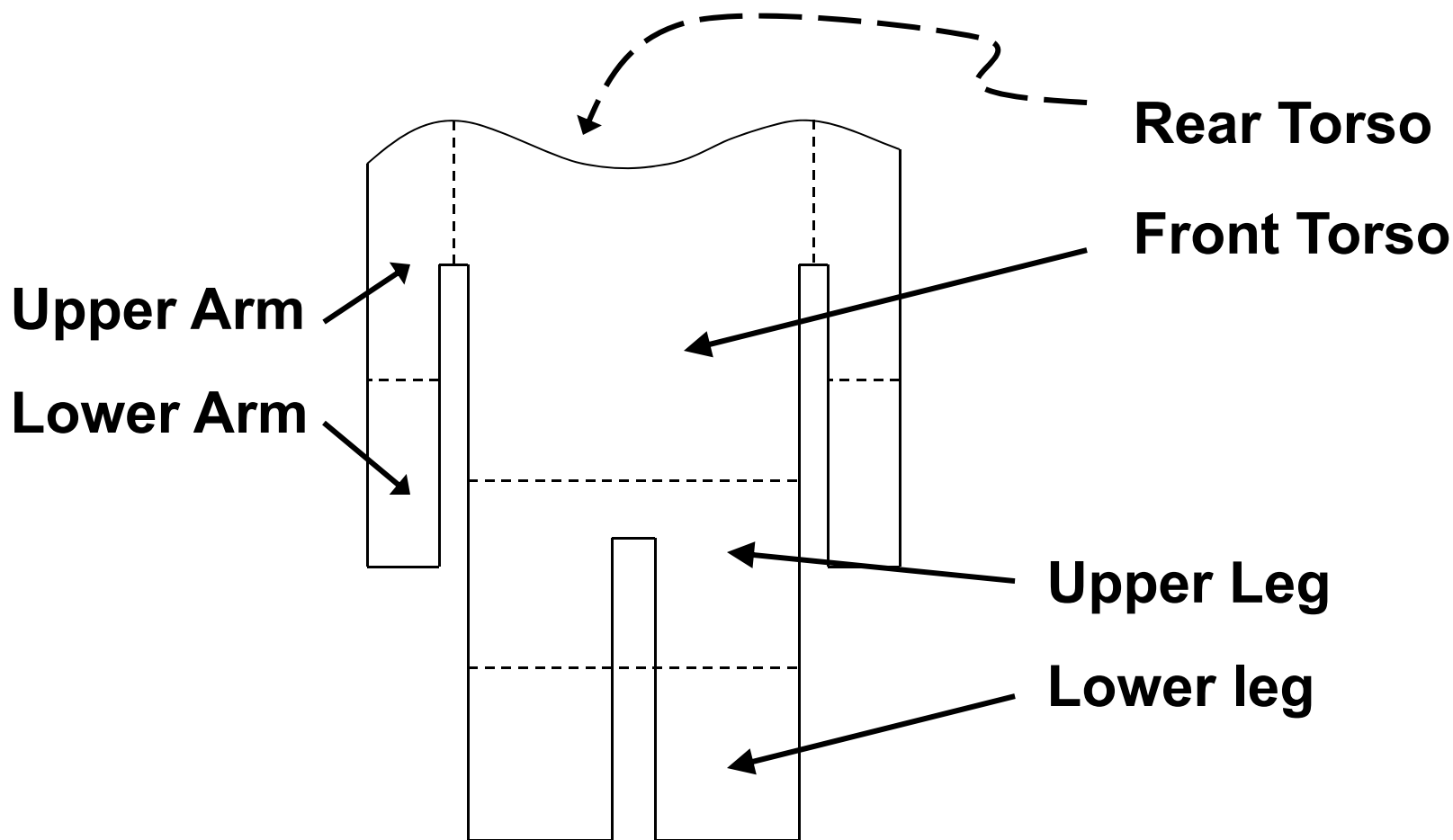


DDAC Residue Removal Efficiency Study

- MRIDs 47214801, 48270301; Pre-Rule study
- Removal efficiency study summary
 - Hand fortified (pipette to palm) with 5 or 100 ug/50uL/hand; n=10 for each fortification level
 - Allowed to dry for 30 min, then washed/rinsed with 50% IPA in water
 - Residues remaining after initial hand wash wiped from hand using dressing sponges moistened with 50% IPA in water
- Mop study hand wash and face/neck wipe procedures similar
- Removal efficiencies
 - Hand wash = ~90%; Used to correct mop hand residue results
 - Hand wipes = ~60%; Used to correct mop face/neck residue results



Sectioning of WBD (inner & outer)





Dermal Unit Exposures Represent 3 Clothing Configurations

- Study participants wore **long** pants, **long**-sleeved shirts, **shoes/socks, no gloves** over WBDs
- For each ME, residues were analyzed from both outer clothing and inner WBD, sectioned by body part
- Clothing configurations that can be estimated for each ME:
 - (1) **long** pants, **long**-sleeved shirt [**shoes/socks, and no gloves**]
 - (2) **long** pants, **short**-sleeved shirt [**shoes/socks, and no gloves**]
 - (3) **short** pants, **short**-sleeved shirt [**shoes/socks, and no gloves**]
- Estimates for “shorts” are obtained by adding the inner and outer lower arm (short-sleeved shirt), or by adding the inner and outer lower leg (short pants)



Summary of Key Study Parameters

Parameter	Low	High	Mean
Pounds AI Handled	0.00308	0.0183	0.00634
Mopping Duration (min)	31	90	62
Area Mopped (ft ²)	3,324	14,191	5,516
No. Buckets Used	2	6	4
No. Gallons Applied	~1	5.5	~2
DDAC Concentration (% AI)	0.025	0.035	0.029



QA/QC Results

Sample	LOQ
Air	10 ng
Neck/face	50 ng
Hands	1 ug
WBD sections	3 ug
Socks	1 ug

- Controls
 - All lab and field blanks were < LOQ
- Laboratory Recoveries
 - Range for mean \pm std for all 3 clusters $95\pm 4\%$ to $113\pm 3\%$
- Field Recoveries
 - Range for mean \pm std for all 3 clusters $91\pm 8\%$ to $109\pm 8\%$
 - Field recoveries were used to correct field samples (dosimeters)



Statistical Analysis–Unit Exposures (UE)

- 3 methods were used to estimate UEs
 - Empirical estimates
 - Simple random sample (SRS)
 - Mixed model
- Mixed model selected to best represent the UE results



Unit Exposures (UE) for Mopping Scenario

Exposure Route	Clothing	AEATF II (n=18)	
		Arithmetic Mean	95th Percentile
Dermal (mg/lb ai)	Long pants/long-sleeves, shoes/socks, no gloves	23.2 (17.4, 31.4)	50.8 (33.3, 77.3)
	Long pants/short-sleeves, shoes/socks, no gloves	26.3 (20.3, 34.6)	54.7 (37.2, 80.3)
	Short pants/short-sleeves, shoes/socks, no gloves	82.1 (55.1, 125.5)	215 (124, 373)
Inhalation ($\mu\text{g}/\text{m}^3/\text{lb ai}$)	Breathing zone	52.4 (27.0, 105.7)	130 (54.8, 318)



Was the Sample Large Enough?

- The benchmark objective of 3-fold relative accuracy ($K \leq 3$) was met for the mixed-model results using the 3 cluster x 6 ME study design
 - Relative accuracy (K) ranged from 1.3 to 1.7 for the mixed model results
 - $K < 3$ indicates enough samples ($n=18$) were collected to satisfy EPA's needs
- No additional mop MEs are needed



Intra-Cluster Correlation (ICC)

- Based on analogy to earlier studies for similar tasks, an estimated ICC of 0.3 was used to determine the number of clusters and MEs in the study design
- The ICC calculated from this mop study is 0
- This indicates that individual behavior affects exposure more than does building type or floor configuration



Proportionality of Exposure to AaiH

- Proportionality between exposure and AaiH is an assumption EPA uses in handler exposure assessments



Does the Mop Study Support or Confound the Assumption of Proportionality?

- The Mop Study provides:
 - Evidence of proportionality between dermal exposure and AaiH
 - No evidence of proportionality between inhalation exposure and AaiH
- Minimal exposure was expected from this mopping scenario (low VP and low potential for aerosols) and monitored exposure was very low (mean 0.000263 mg/m³)
- We did not learn anything that would lead us to abandon the assumption of proportionality



Limitations on Data Generalization

- Mop study population is not a true random sample
 - Assumes exposure is independent of location
 - Bias of volunteer pool unknown
- Statistical inference from these results to the universe of moppers is not justifiable



EPA Plan for Use of Mop Study Data

- Use unit exposure data generically to estimate potential exposure to low- or moderate-volatility pesticides use in mopping scenarios
 - String mop is worst case, representing all mops, including RTU, sponge, or microfiber mops
 - Dermal UEs available for various clothing configurations
 - UEs normalized by AaiH
- Use chemical-specific hazard and dermal absorption data to estimate internal dose and risk



Example: New AI with Low Volatility

- Assume product has these relevant characteristics
 - Acute toxicity profile is consistent with short-sleeved shirts with long pants, no gloves
 - 10% active ingredient in concentrated product
 - Dilution rate 0.5 ounce per gallon water, from automatic dispenser
- Estimate daily exposure = $UE \times AaiH$
 - Dermal UE from long pants/short-sleeved shirt, socks, no gloves
 - Inhalation UE = air concentration (mg/m³/pound AI)
 - $AaiH = 0.5 \text{ fl oz} * 1 \text{ gal}/128 \text{ fl oz} * \text{density } 8.34 \text{ lb/gal} * 5 \text{ gallons/day} * 0.1 \text{ ai in concentrated product}$



Calculation of AaiH

- AaiH =
 - Volume of concentrated product in fluid ounces, converted first to gallons, and then to weight
 - * Number of gallons mopped per day
 - * Concentration of AI in product
- $AaiH = 0.5 \text{ fl oz/gal} * 1 \text{ gal}/128 \text{ fl oz} * \text{density } 8.34 \text{ lb/gal} * 5 \text{ gallons/day} * 0.1 \text{ ai}$



Conclusions

- Study results are sound enough to support estimates of dermal and inhalation unit exposures in the mopping scenario
- Enough samples were collected: no additional mop MEs are required
- Data limitations must be acknowledged in assessments

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Ethics Assessment AEATF II Mop Study

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October 28, 2010



Overview

- Responsiveness to protocol reviews
- IRB oversight
- Recruiting and subject demographics
- Deviations of potential ethical significance
- Completeness of documentation
- Substantive acceptance standards
- Findings
- Conclusions



Responsiveness to EPA Comments

- Better provision for interviewing and consenting Spanish-speaking subjects
 - *References to translators replaced by references to bilingual investigators in protocol of 26 Feb 09*
- Express “normal business hours” in local time
 - *Changed to Pacific Time in revised consent form, ESBOR, and flyer*



Responsiveness to HSRB Comments

- Consider using a tracer rather than pesticide
- Used pesticide, per EPA advice
- Ensure CF is readable; simplify
- Negligible change in readability
- Explain how community will be engaged/involved
- Revised in protocol; planned meetings with employers did not take place
- Ensure Spanish translations are in appropriate dialect
- All translations done by CA translator, part of research team



IRB Oversight

- Initial protocol reviewed by convened IIRB, Inc. in Jan 08
- All subsequent IIRB, Inc. reviews conducted under expedited procedures, without minutes or other records
- Investigators complied fully with IIRB, Inc., procedures and requirements



Accounting for Recruiting Processes

24-Apr-09	Janitorial Services Companies Identified	322
	Janitorial Services Contacted	?
	Janitorial Services Agreeing to Post Flyer	65
13-Jul-09	Callers Responding to Flyers	21
Amendment 3	Subjects Enrolled	7
Amendment 4	Callers Responding to Newspaper Ads	~35
	Enrolled from Newspaper Ads	25
24-Jul-09	Total Subjects Enrolled	32
	Withdrawn: Sensitive to Alcohol Rinse	2
	Total Subjects Randomized	30
	Withdrawn: Moved Away	1
	Randomized to MEs	18
	Randomized to Alternate MEs	6
	Other alternates	5



Recruiting Summary

- Recruiting process was equitable, and free of coercion or undue influence
- Recruiting was conducted consistent with the protocol, at each stage of amendment
- Subject recruiting and selection processes were consistent with EPA's policy direction to incorporate random elements whenever feasible



Subject Demographics

		All Enrolled Subjects	Monitored Subjects
Sex	Male	15 (47%)	10 (56%)
	Female	17 (53%)	8 (44%)
Language	English	20 (63%)	11 (61%)
	Spanish	12 (37%)	7 (39%)
Range of Experience		3 mos - 40 yrs	3 mos - 40 yrs
Mean Experience		8.8 yrs	11.1 yrs
Age Range		18 - 53	18 - 53
Mean Age		36.8 yrs	38.1 yrs
Health	"Excellent"	18 (56%)	10 (56%)
	"Good"	12 (38%)	7 (39%)
	"Fair"	2 (6%)	1 (6%)
Requested Results		25 (78%)	15 (83%)



Deviations of Ethical Significance

- Reported deviations:
 - Omitted/shortened rest breaks
 - Photos showing subjects' faces at one site
- Unreported deviations:
 - Enrollment of 2 subjects with self-described "fair" health
 - Creation and retention of additional records linking subject names to ID codes



Completeness of Documentation—1

- Initial “Final Report” (MRID 48210201)
 - Significant omissions
 - Protocol with tracked changes
 - Documentation of IRB approvals
 - Appendices Q and R full of irrelevant, duplicative material, completely unindexed
- Supplement 1 (MRID 48231201)
 - Substantively complete
 - Irrelevant, duplicative material deleted from Appendices Q and R; both appendices fully indexed



Completeness – 2

- Other deficiencies:
 - Rationale for defining MEs by duration (provided in Supplement 2—MRID 48231901)
 - Subject demographics (provided in spreadsheet 30 Sep 10)
 - Accounting for pre-enrollment recruiting process (provided in email 18 Oct 10)
 - IIRB procedures and roster (provided directly by IIRB, Inc.)
- Requirements of 26.1303 substantially satisfied



Substantive Acceptance Standards

- 40 CFR 26.1703
 - Prohibits reliance on data involving intentional exposure of pregnant or nursing women or of children

- 40 CFR 26.1705
 - Prohibits reliance on data unless EPA has adequate information to determine substantial compliance with subparts A through L for 40 CFR 26

- FIFRA 12(a)(2)(P)
 - Makes it unlawful to use a pesticide in human tests without fully informed, fully voluntary consent



Findings

- All subjects were at least 18; pregnant or nursing women were excluded; all females were tested for pregnancy
- No noteworthy deficiencies in the ethical conduct of the research
- Protocol was faithfully executed, and amended when needed; minor deviations did not compromise safety or consent of subjects
- Subjects were fully informed and their consent was fully voluntary, without coercion or undue influence



Conclusion

- Available information indicates that the AEATF II Mop Study was conducted in substantial compliance with subparts K and L of 40 CFR part 26



AEATF II Mop Study: Charge Questions

- a. Was the research reported in the Antimicrobial Exposure Assessment Task Force II (AEATF–II) completed study report AEA03 and associated supplemental reports faithful to the design and objectives of the protocol and governing document of AEATF-II?
- b. Has the Agency adequately characterized, from a scientific perspective, the limitations on these data that should be considered when using the data in estimating exposure of those who apply antimicrobial floor-cleaning products with mop and bucket?
- c. Does available information support a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR Part 26?