

Proactive Laboratory Animal Allergy Surveillance and Education (ProLASE)



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Baylor College of Medicine (BCM)

- Private medical school located in the Texas Medical Center
 - 1000 acre complex with 46 independent institutions
- BCM Family
 - 1832 faculty members
 - 1398 students
 - 786 post-doctoral fellows
- Total research support is \$302 million



Center for Comparative Medicine (CCM)

- 8 animal housing facilities
 - One of the nation's largest mouse facilities (35,000 cage capacity)
 - $35,000 \times 5 \text{ mice/cage} = 175,000 \text{ mice}$
- 135 employees
- Animals housed
 - Rodents (mice, rats, guinea pigs)
 - Dogs, Cats
 - Sheep, pigs, rabbits
 - Non-human primates



Lab Animal Allergies (LAA)

- 90,000 – 125,000 workers exposed to lab animals each workday
 - 11-44% of those will develop LAA
- Conjunctivitis, rhinitis, urticaria, and asthma
 - Occurs through inhalation or skin contact
- Significance
 - AAALAC, BMBL, NIOSH



Mouse Urinary Protein (MUP)

- Predominant mouse allergen
 - Attaches to small (3.3 – 10 μm) particles that deposit in the respiratory tract
- Produced by the liver and is excreted primarily via urine
 - Hormonally controlled
- Acceptable levels
 - $>5 \text{ ng/m}^3$ = increased development of LAA
 - $>3 \text{ ng/m}^3$ = sensitization for LAA



Sampling Locations

	Facility A	Facility B	Facility C
Facility Size (sq. ft)	65,000	9,600	32,000
Species Housed	Mouse only	Multi-species	Multi-species
Number of mouse cages	~27,000	~700	~6,532
Cages	Positive pressure	Static	Static, negative and positive
Cage Dumping	Robot, down draft dump station or open bin	Non-vacuumed dump station	Open bins and down draft dump station

Air Samples

- Collected according to industry standard
 - SKC® SURE-SEAL, 37 mm leak free air sampling cassettes
 - 1.0 μm PTFE filters
 - SKC® universal PCXR8 air pumps
 - 120 minutes at a rate of 2L/min
- Captured proteins are eluted
 - PBS/0.5% Tween 20 and stored at -20°C until analysis
- MUP ELISA kit (Indoor Biotechnologies)
 - All samples ran in triplicate and averaged



Preliminary Results (ABSA 2007)

- Elevated levels of MUP were present in dirty cage wash areas
- Allergies (possibly attributed to lab animals) were underreported at BCM
- Significant correlation for development of allergies that were worst at work related to:
 - Failure to wear a mask
 - Working in the facility > 1 year
 - Vietnamese descent





Face Masks/Respirators

Surgical Mask



>99% BFE for particles $\geq 5.0 \mu\text{m}$

Cone Mask



>99% BFE for particles $\geq 4.0 \mu\text{m}$

N95 Respirator



>95% BFE for particles $> 0.3 \mu\text{m}$

Approximate amount of MUP filtered by mask

~50%

~60%

~97%

Approximate amount of MUP remaining on peak TMF day in dirty cage wash (22.63 ng/m³)

11.32 ng/m³

9.05 ng/m³

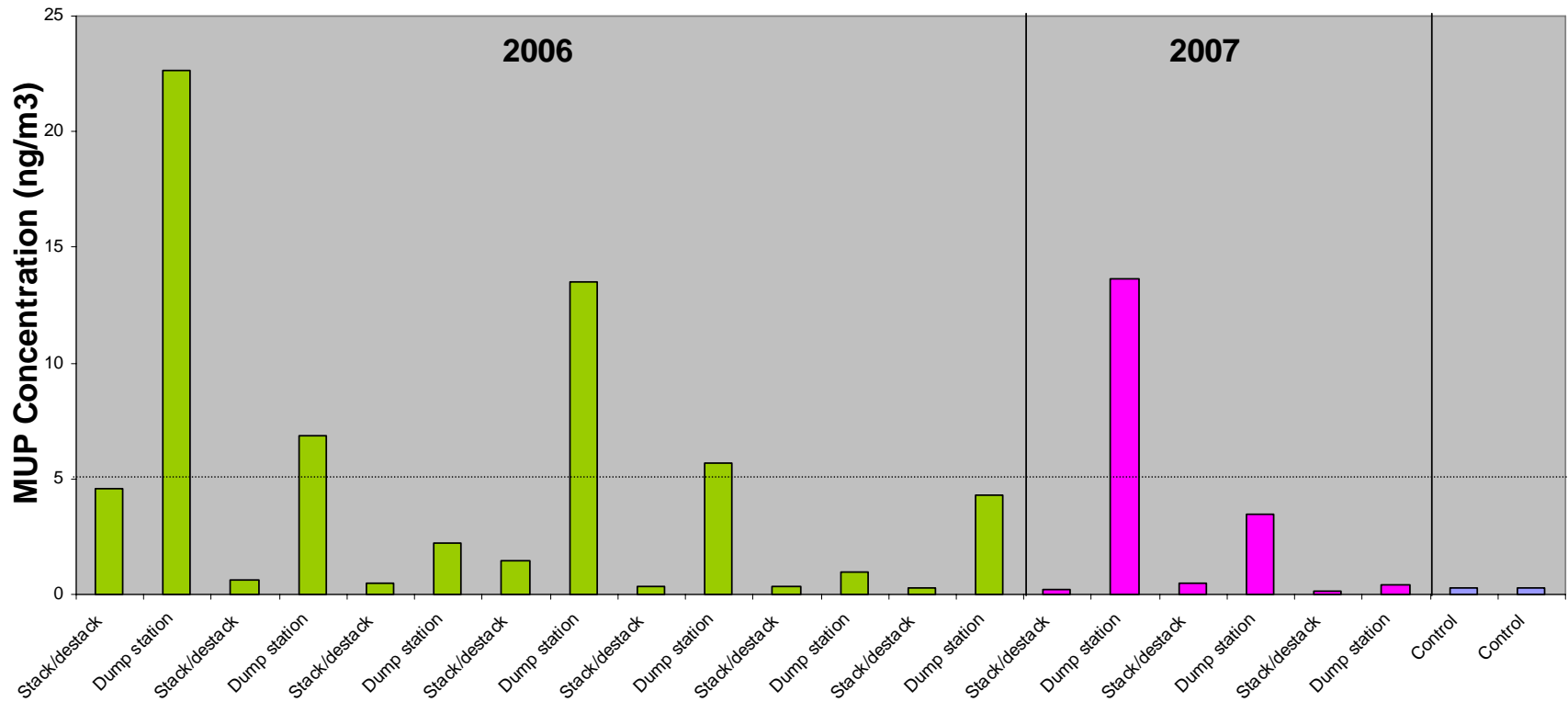
0.68 ng/m³

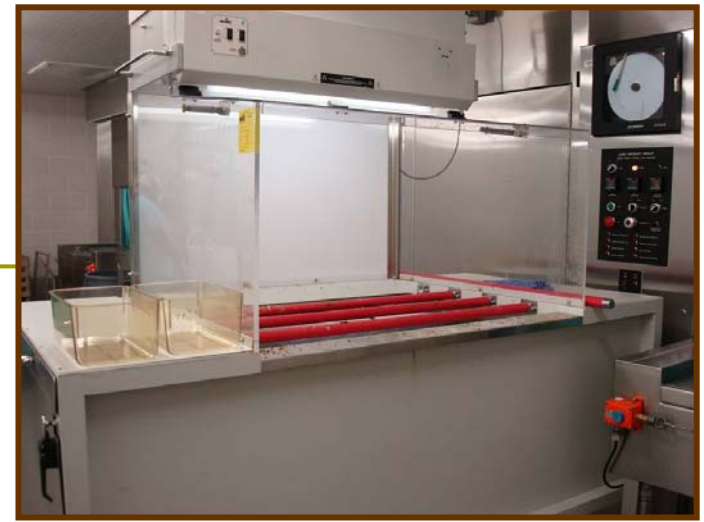
Proactive Laboratory Animal Allergy Surveillance and Education (ProLASE)

- Annually assess facilities for the presence of MUP.
- Recruit volunteers from the animal husbandry program to undergo MUP specific allergy skin tests.
- Provide education to individuals working in the animal facilities.
 - Targeted education for individuals involved in animals husbandry
 - General education for research personnel

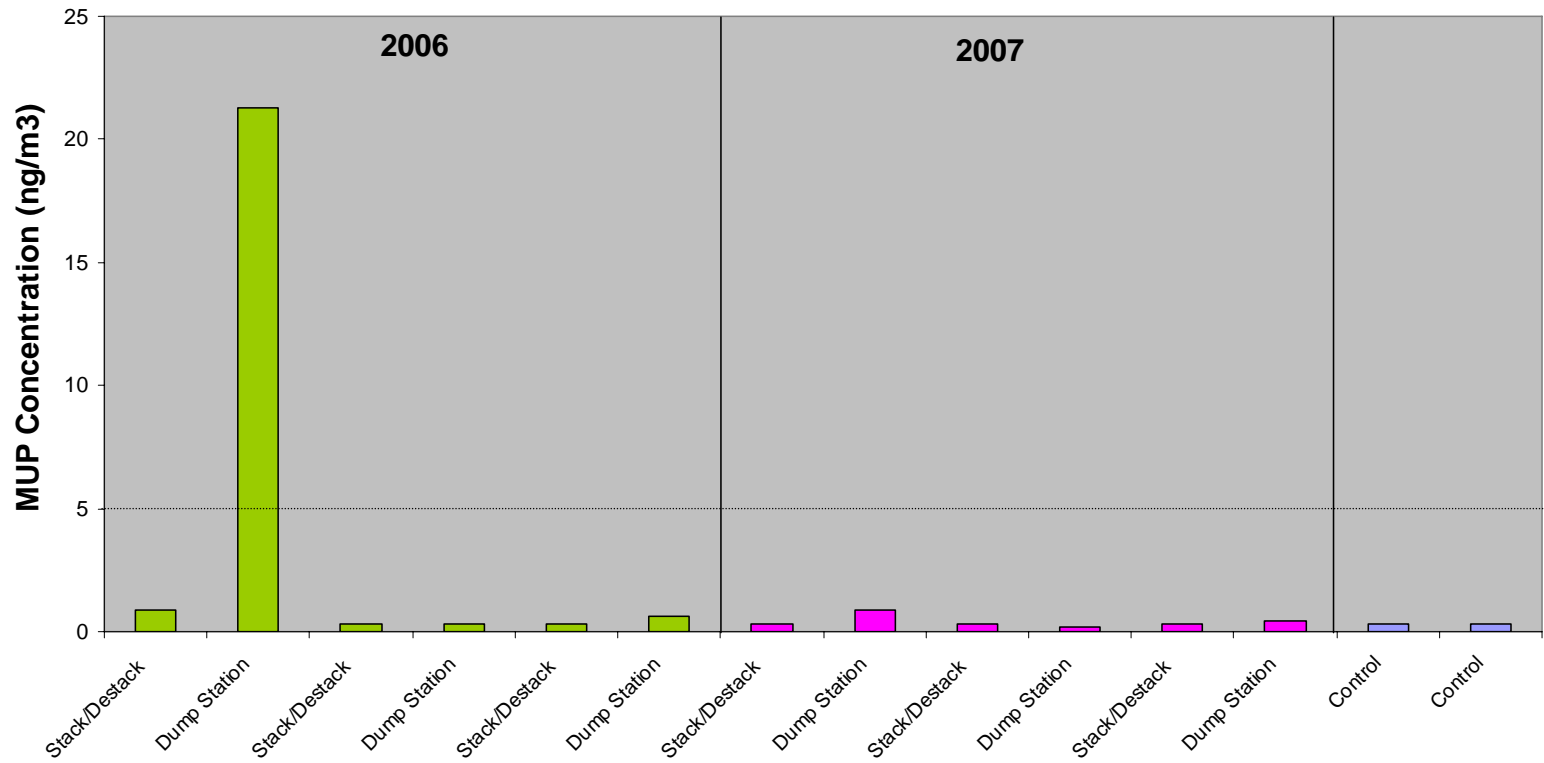


Quantity of Mouse Urinary Protein (MUP) in Facility A Dirty Cage Wash





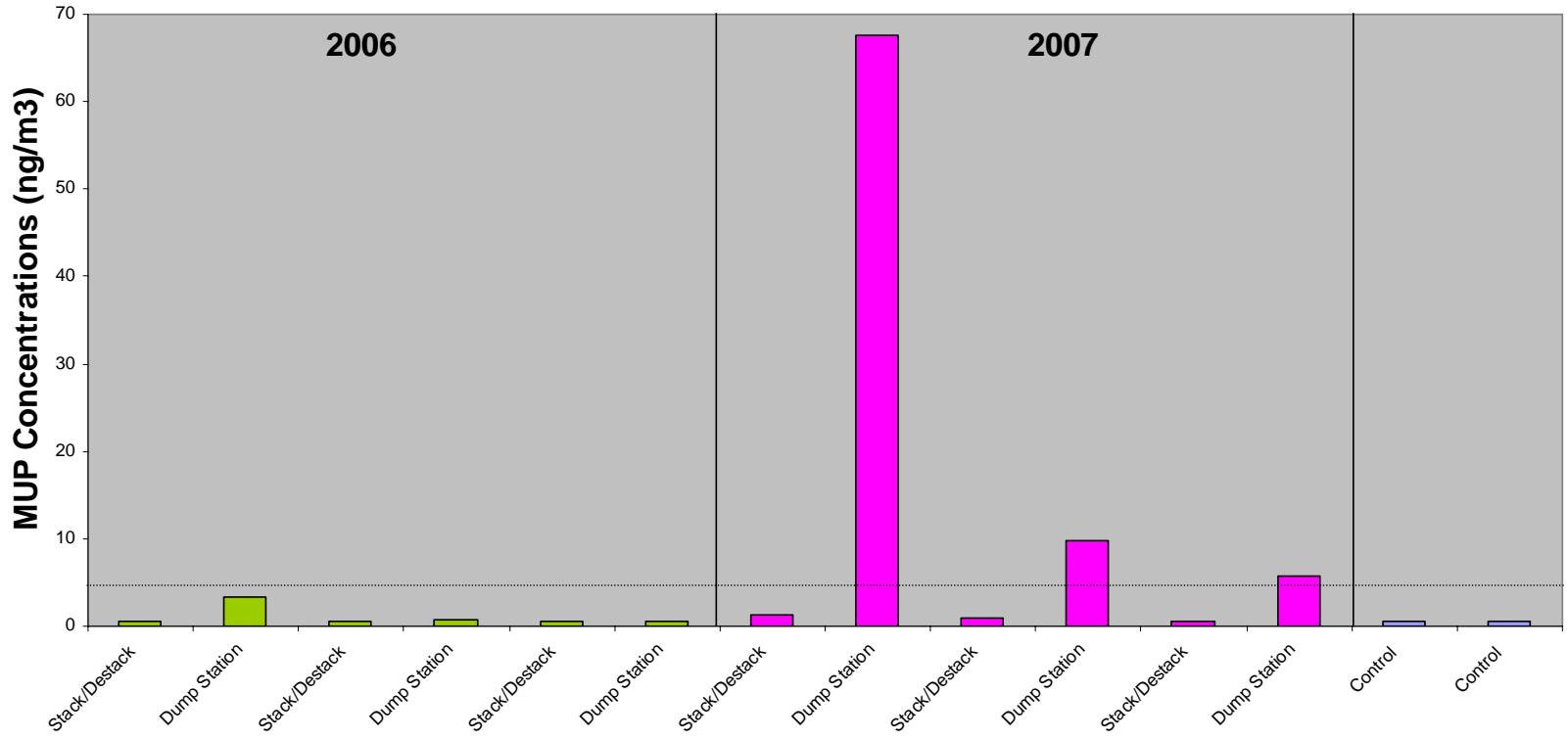
Quantity of Mouse Urinary Protein (MUP) in Facility C Dirty Cage Wash





Failure to Perform Preventative Maintenance!!

Quantity of Mouse Urinary Protein (MUP) in Facility B Dirty Cage Wash



Conclusions

- Elevated levels of MUP are present in dirty cage wash areas on a continuing basis
 - *Engineering controls work extremely well in rooms, corridors, suites*
 - *Dumping of cages in open bins needs to cease*
 - *Pre-filters and filters must be changed at regular intervals.*

Mouse Allergy Skin Tests

- Recruit 50 volunteers from CCM employees
 - Volunteers received a \$10 gift card to BCM cafeteria
- Complete updated survey that included 4 additional questions
- Visit allergy clinic for mouse allergen skin test



Preliminary Skin Test Results

	Age Sex	Race	Allergy Symptoms	Symptoms Worse at Work	Skin Test	Work in Dirty Cage Wash	Facility (species housed)	Years in Current Facility
1	53 M	Asian	No	-	-	Yes	D (multi)	1-3
2	37 F	African	Yes (3/7)	No	-	Yes	D (multi)	< 1
3	18 M	African	Yes (3/7)	Yes	-	Yes	D (multi)	< 1
4	42 F	African	No	-	-	Yes	D (multi)	1-3
5	24 M	Hispanic	Yes (2/7)	No	+	No	C (multi)	1-3
6	37 M	White	Yes (1/7)	No	-	Yes	C (multi)	1-3
7	49 M	White	No	-	-	Yes	C (multi)	1-3
8	63 M	Asian	Yes (4/7)	No	-	No	C (multi)	>5
9	31 M	Hispanic	Yes (7/7)	No	+	Yes	A (mouse only)	>5
10	52 F	Hispanic	No	-	-	No	C (multi)	>5
11	55 M	Asian	No	-	-	No	C (multi)	-
12	48 M	African	Yes (5/7)	No	+	Yes	E (multi)	>5
13	23 M	African	Yes (3/7)	Yes	-	Yes	E (multi)	<1
14	37 M	African	Yes (2/7)	No	-	Yes	E (multi)	<1
15	23 M	Hispanic	Yes (1/7)	No	-	Yes	E (multi)	1-3
16	35 F	African	Yes (2/7)	No	-	Yes	C (multi)	< 1
17	27 F	African	No	-	-	No	C (multi)	1-3
18	25 F	White	No	-	-	No	A (multi)	1-3
19	23 F	White	Yes (2/7)	Yes	-	No	C (multi)	1-3
20	23	Hispanic /White	Yes (2/7)	Yes	-	No	B,D,E,G (multi)	< 1

Volunteer #9



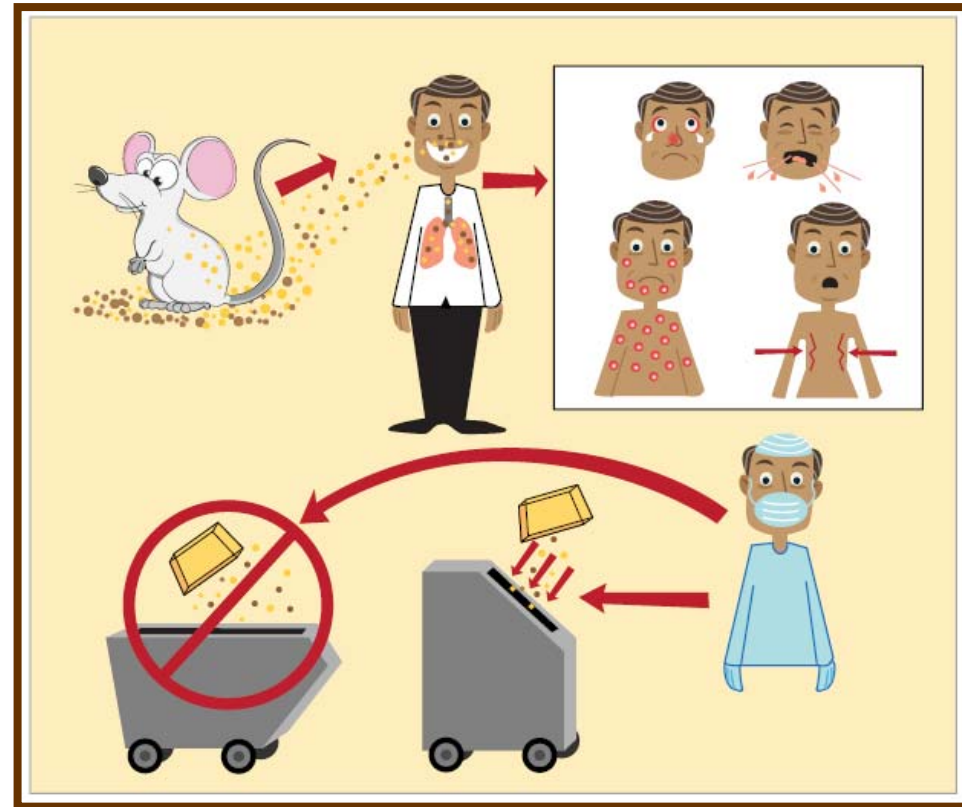
- Reported the following symptoms
 - Watery/itchy eyes
 - Runny or stuffy nose
 - Difficulty swallowing/chest tightness
 - Excessive mucous production
 - Frequent colds
 - Skin problems
- Previously diagnosed with allergies and takes medication on/off
- Recently developed symptoms while at work
- Reported symptoms to
 - Supervisor
 - Coworkers
 - OHP

	Antigen	
	Wheal (mm)	Flare (mm)
Histamine Control	13	45
Saline Control	0	5
Mouse Epithel Greer GE201:20	10	30

Targeted Education

Post literature on site in the animal facilities

- Emphasize importance of LAA
- Significance of early detection
- Need for appropriate PPE
- Symptoms of LAA
- How to report symptoms to OHP



General Education

- Lunch & Learn Seminars
 - Tecniplast sponsored webinar “Managing the challenges of Lab Animal Allergy”
- BCM now requires “animal handling” physicals
 - Annually for animal husbandry staff, every 3 years for researchers
 - Allergy literature distributed at time of physical

Conclusions

- Lab Animal Allergy awareness has increased
 - *Masks are required for animal husbandry staff*
 - *Not N95 respirators*
 - *OHP clearance is now required*
- Involvement in a LAA program cannot be voluntary
 - *Should employers proactively screen individuals to assure those with severe mouse allergies are not working with mice*
 - *Prevent workman's compensation claims*
 - *Lessen the effect of missed work time*

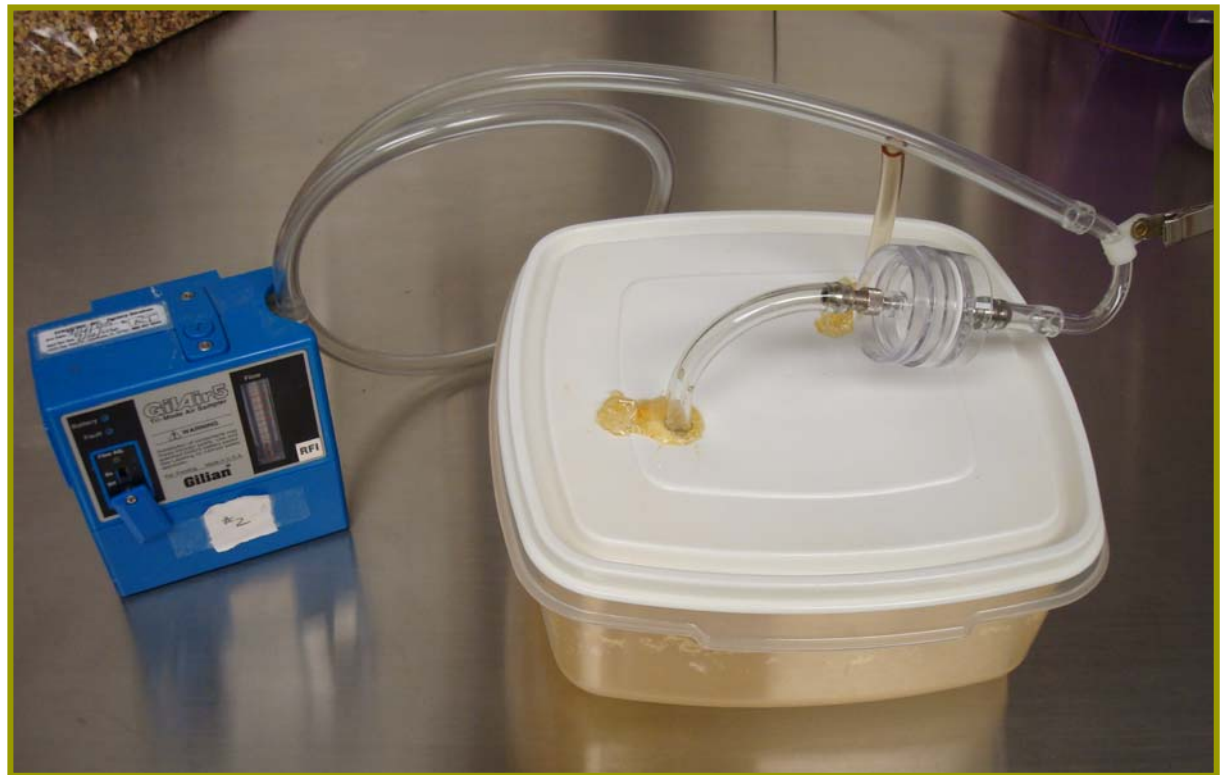


Rodent Bedding and MUP

- Bedding samples obtained from Harlan
- Mice were housed for 8 days with each bedding material
 - 9 cages with 2 mice each
- Dirty bedding collected and subjected to simulated cage dumping
- Air samples collected and analyzed by MUP ELISA
 - Dirty bedding OD – clean bedding OD = released MUP

The “MUPinator”

- Bedding placed in “MUPinator”
- Shake for 30 seconds
- Air samples collected for 2 min



Bedding Samples

- Corn Cob*
- Soft Cob →
- Aspen SaniChip
- Aspen Shredded
- Omega-dri
- Pelleted Paper
- Diamond Soft
- Tek Fresh →
- Isopad



MUP Release from Bedding

Bedding	MUP Specific ELISA OD*
Shredded Aspen	0.019
Isopad	0.059
Aspen SaniChip	0.185
Diamond Soft	0.270
Tek Fresh	0.464
Omega-dri	0.778
Soft Cob	1.081
Corn Cob	1.353
Pellet Paper	1.469

*The higher the OD value, the more MUP that was released from the bedding. OD value for clean bedding (each individual type of bedding) was subtracted from the OD value for dirty bedding.

Acknowledgments

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CCM employees

NIOSH Pilot Project Research Training Award

UT-SPH

Until this happens.....



Picture from Velteck Associates, Inc advertisement