

Skin Decontamination of 49% and 60% Hydrofluoric Acid: Relation Between Burn Model and Decontamination in an Immature Domestic Pig

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Hexafluorine® Pig Probe Studies

- * *Honeywell* has Performed Studies of Treatment of 38% HF Burns in a Similar Pig Model
- * *Prevor* has Performed a 70% HF Decontamination Study in a Rabbit Model

HEXAFLUORINE® Experimental Animal Study: I

- ❖ 120 New Zealand White Rabbits divided into 6 groups of 20;
- ❖ Burn created by application of 1 cm diameter filter paper saturated with 70% HF (< 1% total body surface area); 20 second exposure
- * Methods: 3 types of irrigation tested:
 - Water: 10 L/minute for 5 minutes;
 - Water + Calcium Gluconate: Water 10 L/minute for 3 minutes + inunction of 2.5% calcium gluconate gel;
 - Hexafluorine®: 0.2 L/minute for 3 minutes

HEXAFLUORINE® Experimental Animal Study: II

- Observation of rabbits' skin: exposed areas at 10 minutes; 1 hour; 2 hours; then every 24 hours for 6 days;
- Burns classified as No Burn; Visible Burn; Extensive Burn; Severe Burn.

HEXAFLUORINE® Experimental Animal Study: III Classification of Burn After Decontamination

Time	Water Water	+ Calcium Gluconate	Hexafluorine®
10 min	Visible	No Burn	No Burn
1 Hour	Extensive	No Burn	No Burn
2 Hours	Severe	No Burn	No Burn
Day 1	Severe	Visible	No Burn
Day 2	Severe	Visible	No Burn
Day 3	Severe	Extensive	No Burn
Day 4	Severe	Extensive	No Burn
Day 5	Severe	Extensive	No Burn
Day 6	Severe	Extensive	No Burn







HF Burn Decontamination: Pig Model

- Objective
 - Comparing the Effects of:
 - ❖ No Decontamination
 - **❖** Water Decontamination
 - ♦ Hexafluorine® Decontamination

Following 49% and 60% HF Skin Exposure in an Immature Domestic Pig Model

HF Burn Decontamination: Pig Model

- Study Approved by the Animal Care and Use Committee, WIL Research Laboratories, Ashland, Ohio, USA
- Funding:
 - ❖ Honeywell, Morristown, New Jersey, USA
 - * Laboratoire Prevor, Valmondois, France

HF Burn Decontamination: Pig Model

Species: Domestic White Pig

Supplier: Local Farm, Ohio, USA

* Age: Juvenile

Weight: Approximately 9 - 15 kg

Preparation of Animals

Removal of Hair from Back and Flanks

- Anesthesia used to allow safe & precise clipping
- Clipping performed ~ 48-hrs prior to HF exposure
- After clipping, skin washed with Betadine surgical scrub to prevent infection
- Depilatory agent (Nair®) applied to skin for removal of hair stubble ~ 18-hrs prior to HF exposure
- After depilatory agent application, skin washed with Betadine surgical scrub to prevent infection

Animal Sedation & Anesthesia

- Performed to allow a safe, precise, controlled and humane experiment
- Sedation Atropine (0.05 mg/kg), tetrazol (3 mg/kg) and xylazine (1 mg/kg) administered IM
- Anesthesia Animals intubated and anesthesia maintained with isoflurane
- Animals maintained in a state of surgical anesthesia throughout the experimental period

HF Application Procedure

- Exposure sites Marked with Indelible Ink and/or Tape
- * 49% or 60% HF Applied with a 25 mm Hill Top Chamber®
- * 0.4 mL 49% or 60% HF Applied with this Occlusive System
- Light Uniform Pressure Applied during HF Application

HF Exposure Times and Decontamination Type: Animals Nos. 1 & 3

Flank	Skin Site	HF (%)	Exposure Time (sec)	Decontamination
	1	49	30	No Decontamination
Right	2	49	30	Tap Water
	3	49	30	Hexafluorine®
	4	49	60	Tap Water
	5	49	60	Hexafluorine®

HF Exposure Times and Decontamination Type: Animals Nos. 1 & 3

Skin Site		Exposure Time (sec)	Decontamination
6	60	15	No Decontamination
7	60	15	Tap Water
8	60	15	Hexafluorine®
9	60	30	Tap Water
10	60	30	Hexafluorine®
	Site 6 7 8 9	6 60 7 60 8 60 9 60	Site (%) Time (sec) 6 60 15 7 60 15 8 60 15 9 60 30

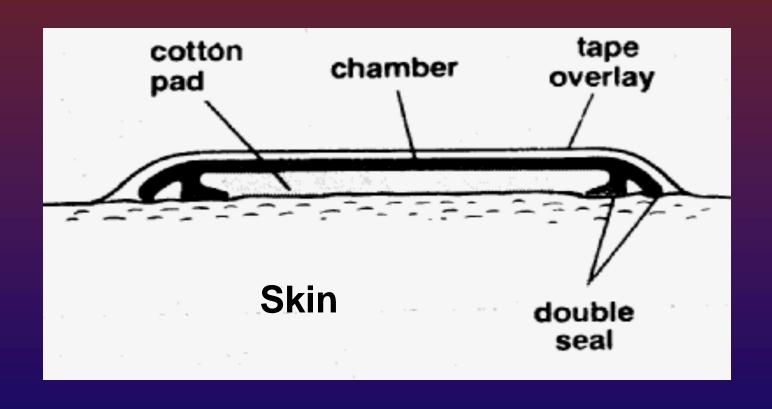
HF Exposure Times and Decontamination Type: Animals Nos. 2 & 4

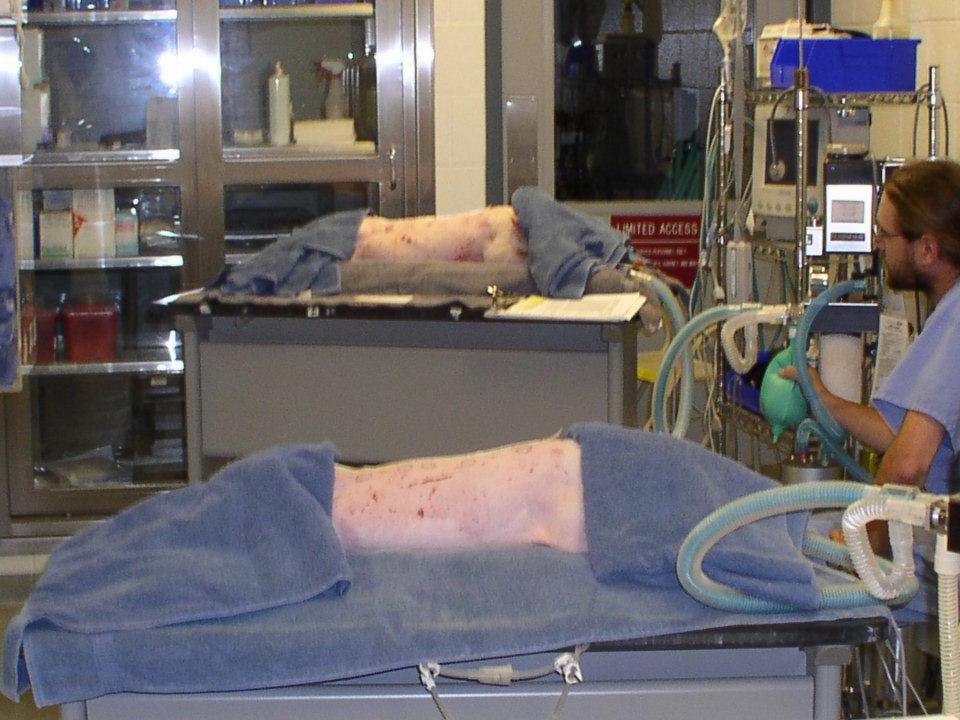
Flank	Skin Site	HF (%)	Exposure Time (sec)	Decontamination
	1	60	15	Tap Water
Right	2	60	15	Hexafluorine®
	3	60	30	Tap Water
	4	60	30	Hexafluorine®
	5	60	30	No Decontamination

HF Exposure Times and Decontamination Type: Animals Nos. 2 & 4

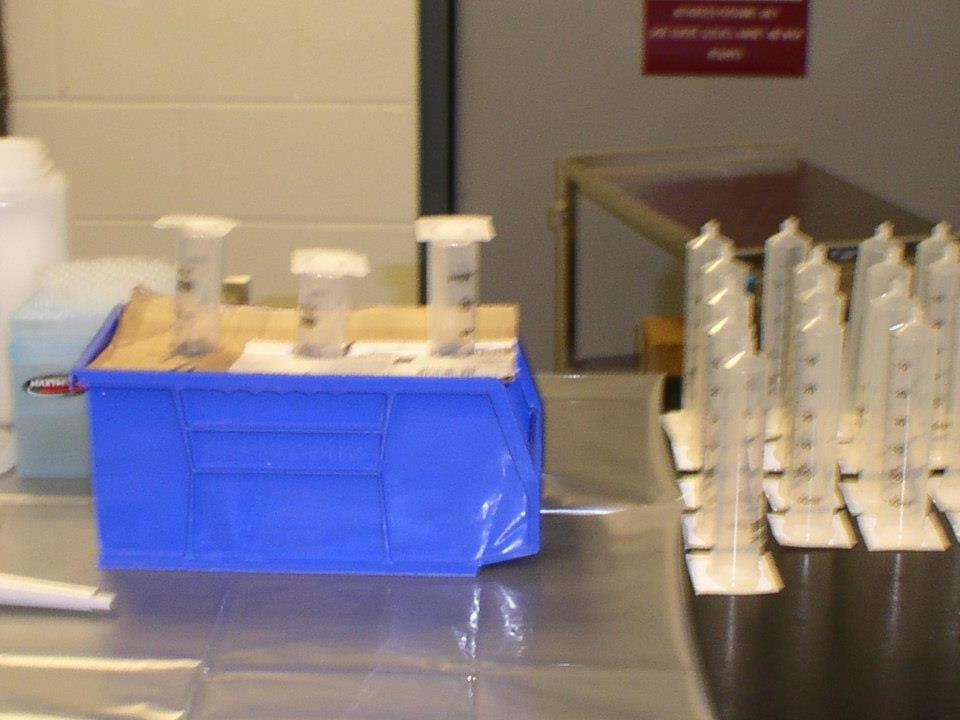
Flank	Skin Site	HF (%)	Exposure Time (sec)	Decontamination
	6	49	30	Tap Water
Left	7	49	30	Hexafluorine®
	8	49	60	Tap Water
	9	49	60	Hexafluorine®
	10	49	60	No Decontamination

Hill Top Chamber®

















❖ ALL HF-Exposed Skin Sites with No Decontamination Developed Severe HF Burns



 Tap Water Decontamination Resulted in Less Severe Burns than No Decontamination

Results

- Hexafluorine® Decontamination Resulted in Less Severe Burns than No Decontamination
 - May have Been Less Severe than when Burns were Decontaminated with Tap Water
 - ❖ Biopsies were similar between Tap Water and Hexafluorine® Decontamination Sites
 - ❖ Results were Not Reproducible from Animal to Animal and Site to Site



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7/11/03

Animal: 38078

Site: 1 49% HF

Prior to dose administration

Exposure Time (sec.): 30

No decontamination

WIL-447007

7/11/03

Animal: 38078

Site: 2 49% HF

Prior to dose administration

Exposure Time (sec.): 30

Tap water (6 minute)

WIL-447007

7/11/03

Animal: 38078

49% HF Site: 3

Prior to dose administration

Exposure Time (sec.): 30

Hexafluorine (6 minute)



WIL-447007

7/10/03

Animal: 38075

Site: 1 49% HF

Prior to dose administration

Exposure Time (sec.): 30

No decontamination

WIL-447007

7/10/03

Animal: 38075

Site: 2 49% HF

Prior to dose administration

Exposure Time (sec.): 30

Tap water (6 minute)

WIL-447007

7/10/03

1.1.1.

Animal: 38075

Site: 3 49% HF

Prior to dose administration

Exposure Time (sec.): 30

Hexafluorine (6 minute)



0mm 10 20 30 40 50 50 WIL-447007 WIL-44

7/11/03

Animal: 38079

Site: 10 49% HF

Prior to dose administration

Exposure Time (sec.): 60

No decontamination

WIL-447007

7/11/03

Animal: 38079

Site: 9 49% HF

Prior to dose administration

Exposure Time (sec.): 60

Hexafluorine (6 minute)

WIL-447007

7/11/03

Animal: 38079

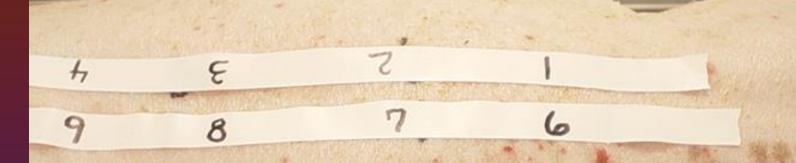
Site: 8 49% HF

Prior to dose administration

Exposure Time (sec.): 60

Tap water (6 minute)





WIL-447007

7/10/03

Animal: 38075

Site B

60% HF

Prior to dose administration

Exposure Time (sec.): 15

No decontamination

WIL-447007

7/10/03

Animal: 38075

Site: 7 60% HF

Prior to dose administration

Exposure Time (sec.): 15

Tap water (6 minute)

WIL-447007

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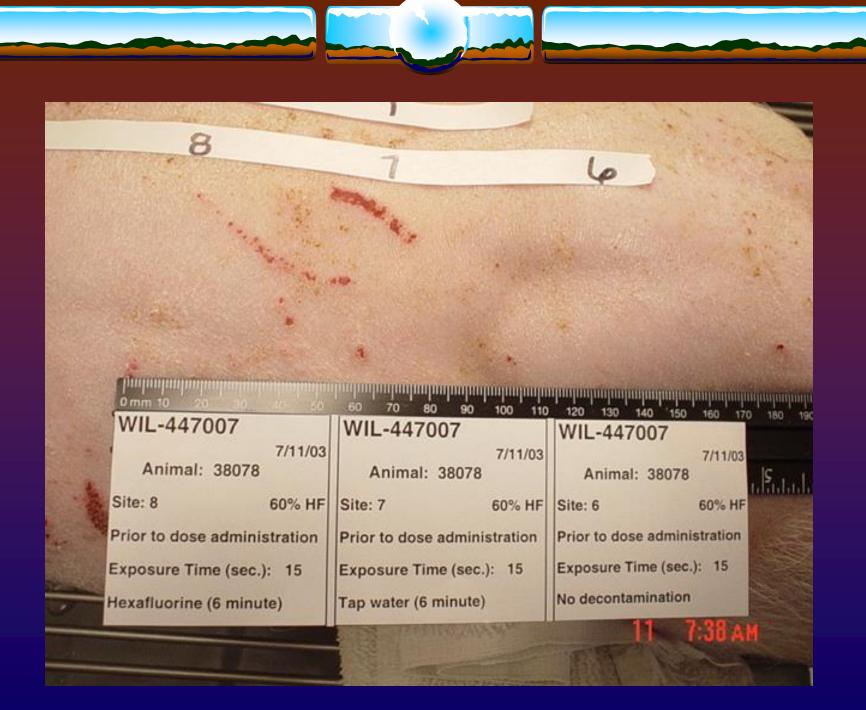
Animal: 38075

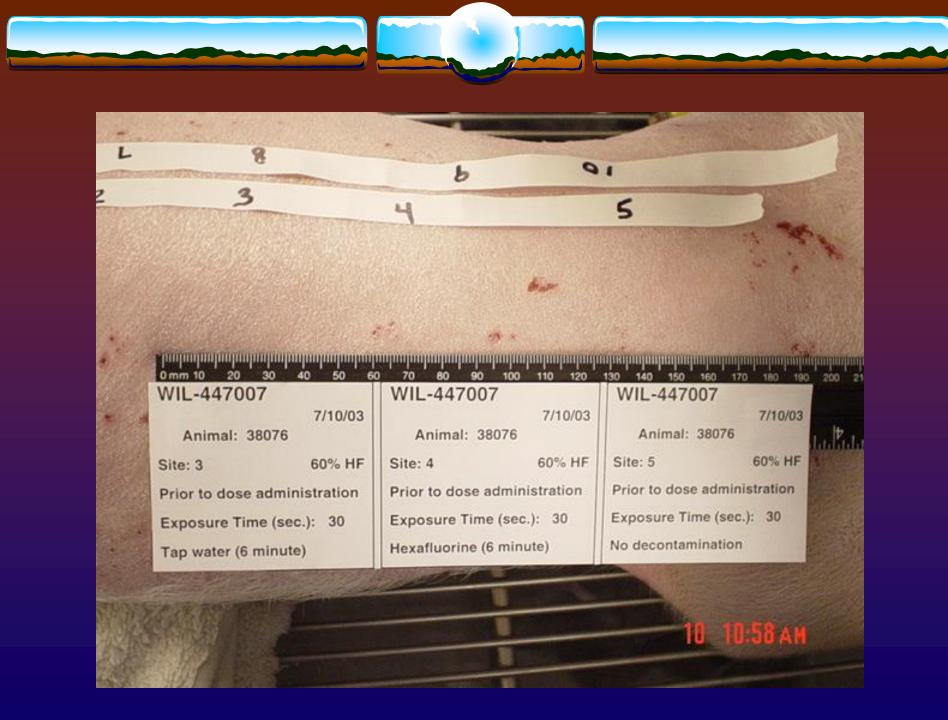
Site: 6 60% HF

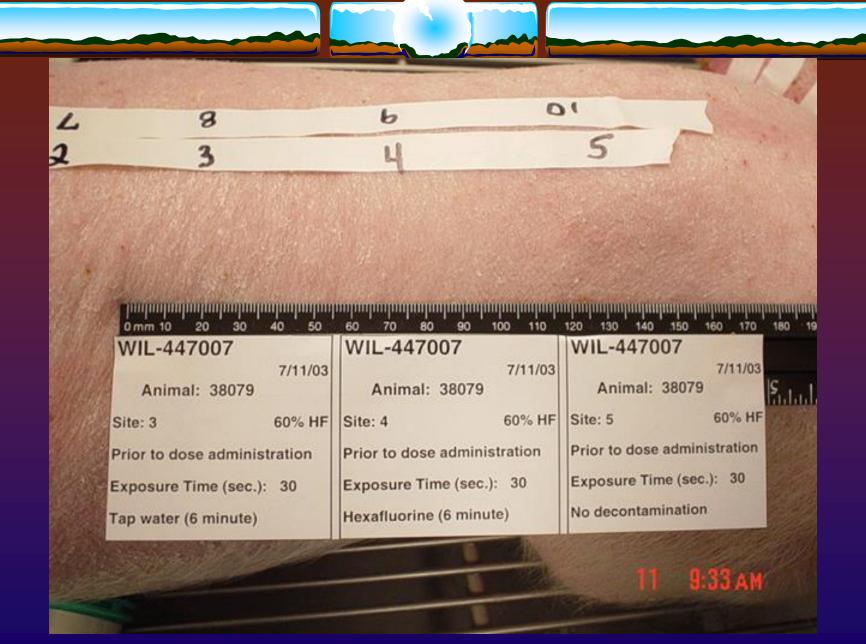
Prior to dose administration

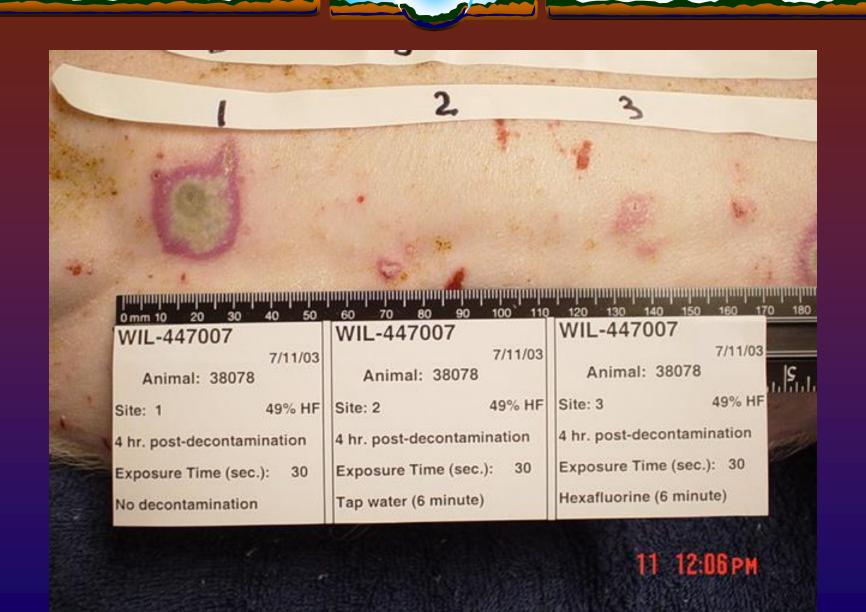
Exposure Time (sec.): 15

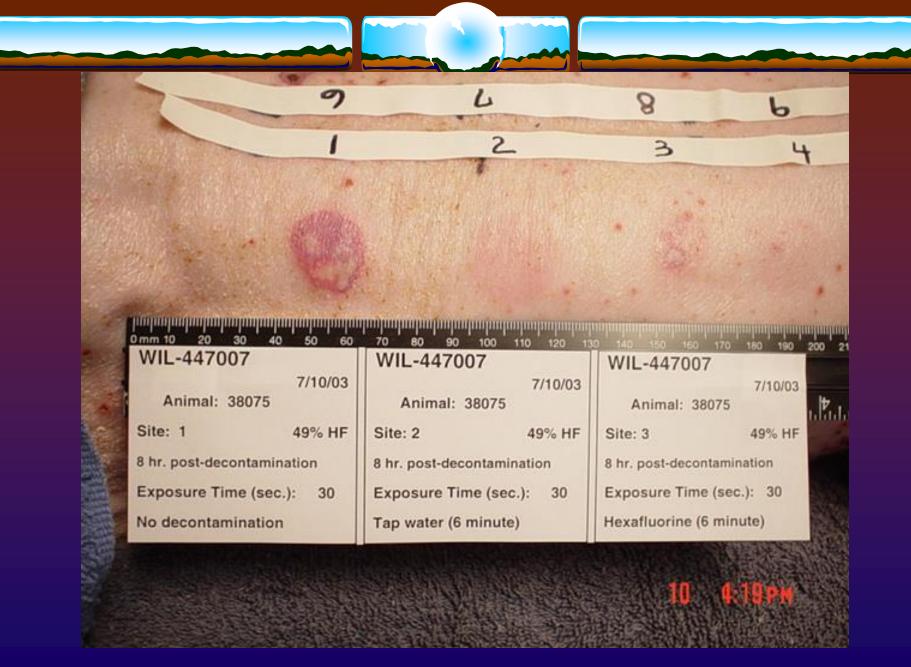
Hexafluorine (6 minute)

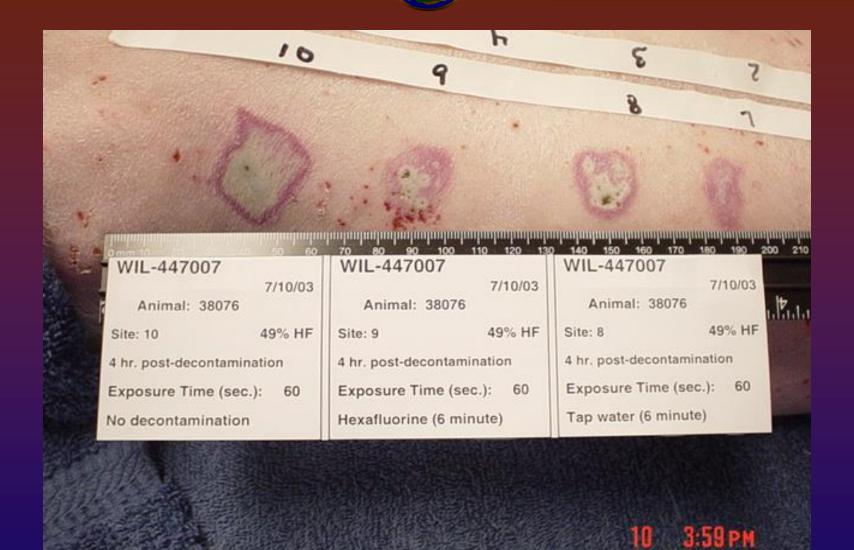


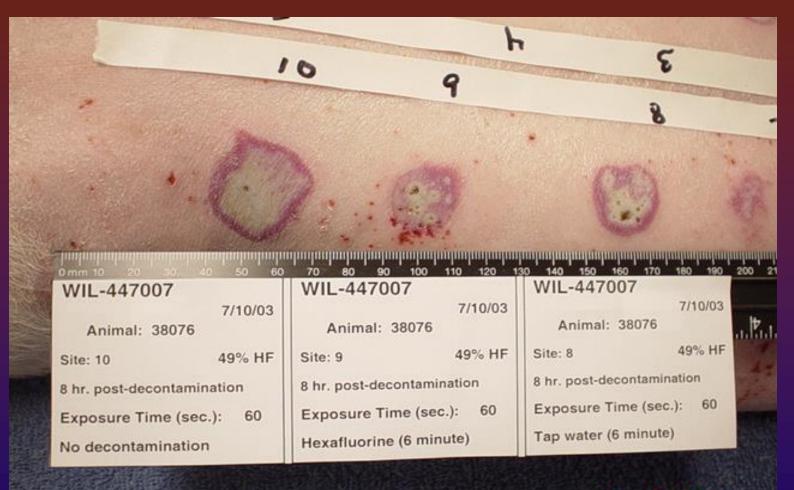






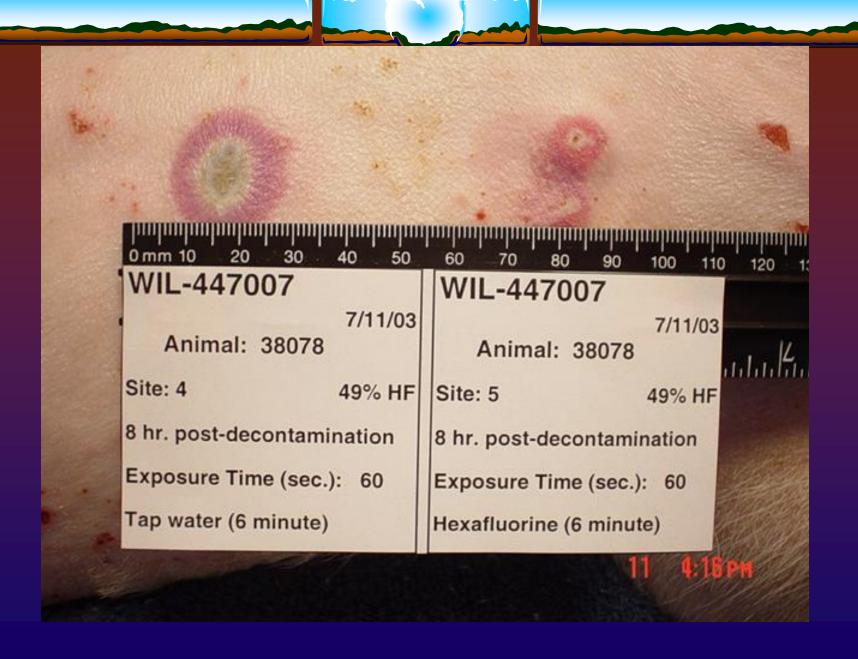






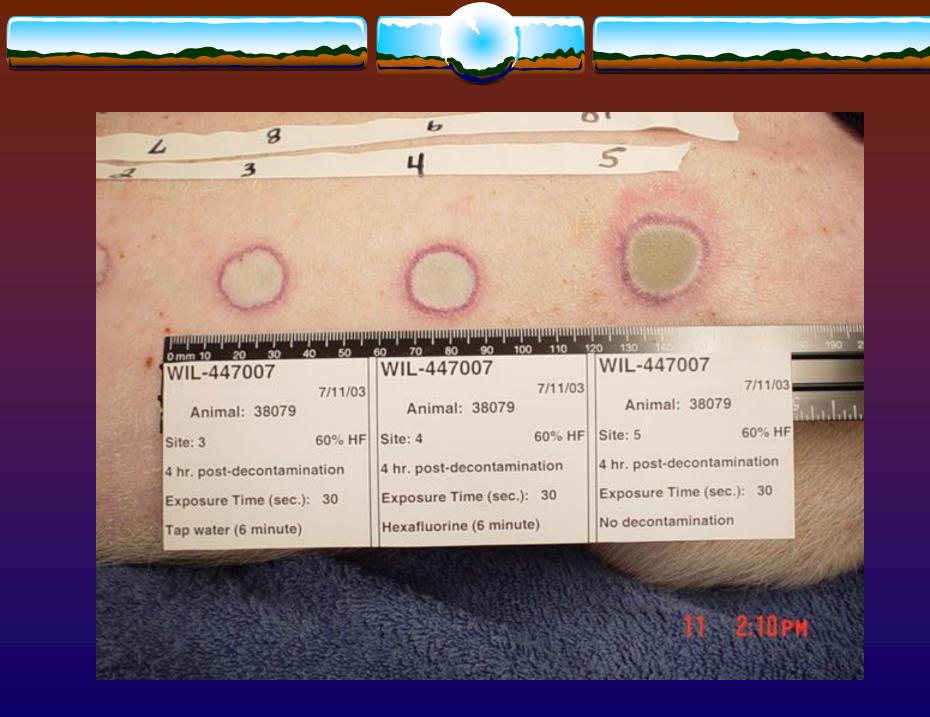


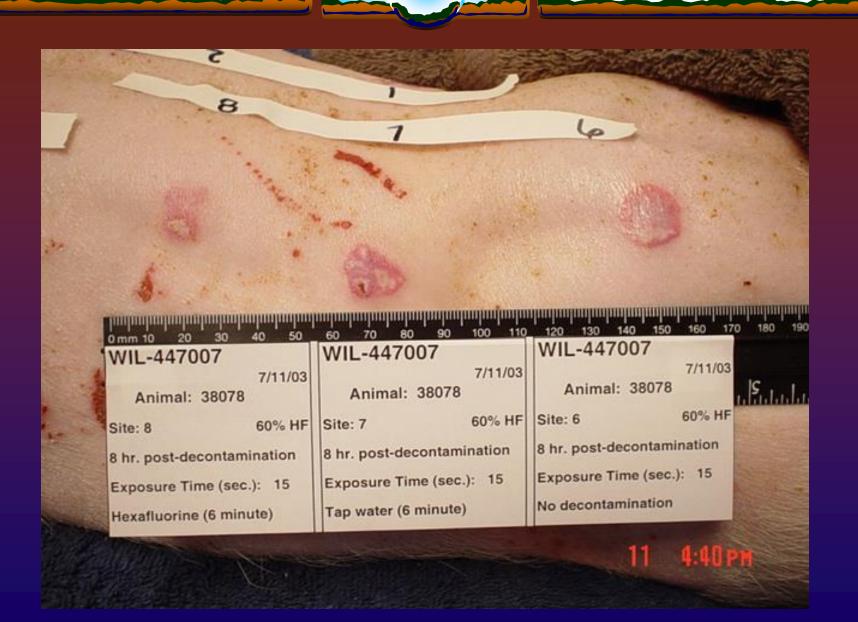












Hexafluorine® Pig Probe Studies: Methods and Materials Study Dates May 2002 – July 2003

% HF	No. of Animals
70	3
60	3
49	5

Hexafluorine® Pig Probe Studies: 70% HF – 3 Animals

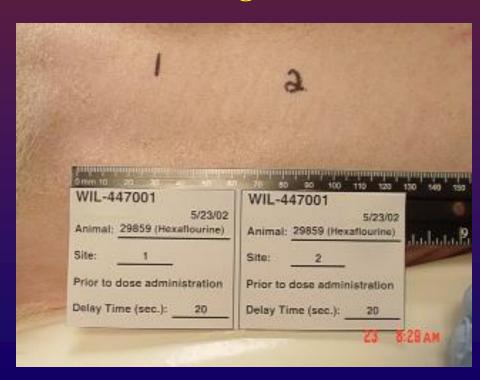
- * No Difference between Hexafluorine® and Water, even with only a 5-Second Delay to Decontamination
- Burns were Already Visible at the Time the Hilltop Chamber was Removed
- * Therefore, it Appeared that in this Model, neither Hexafluorine® nor Water was Efficacious

Study No. 1 – May 2002

Before 20-second contact with 70% HF

Pig #1

Pig #2



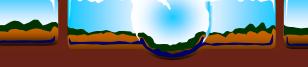
Study No. 1 -- May 2002

20-second contact with 70% HF followed by a 20-second delay to decontamination

Pig # 1 1 Hour after Water Pig #2 1 Hour after Hexafluorine®







Study No. 1 -- May 2002

20-second contact with 70% HF followed by a 20-second delay to decontamination

Pig #1 4 Hours after Water

Pig #2 4 Hours after Hexafluorine®





Study No 1 -- May 2002

20-second contact with 70% HF followed by a 20-second delay to decontamination

Pig #1 8 Hours

after Water

Pig #2 8 Hours after

Hexafluorine®



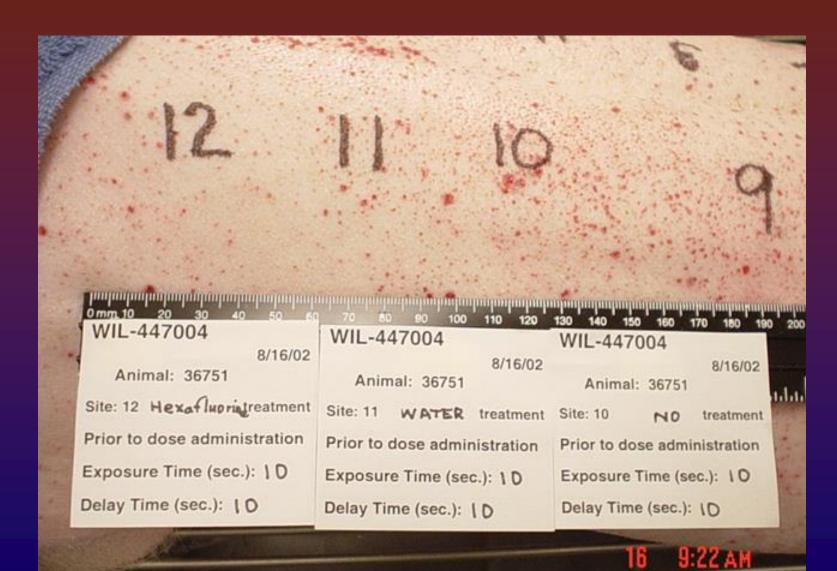


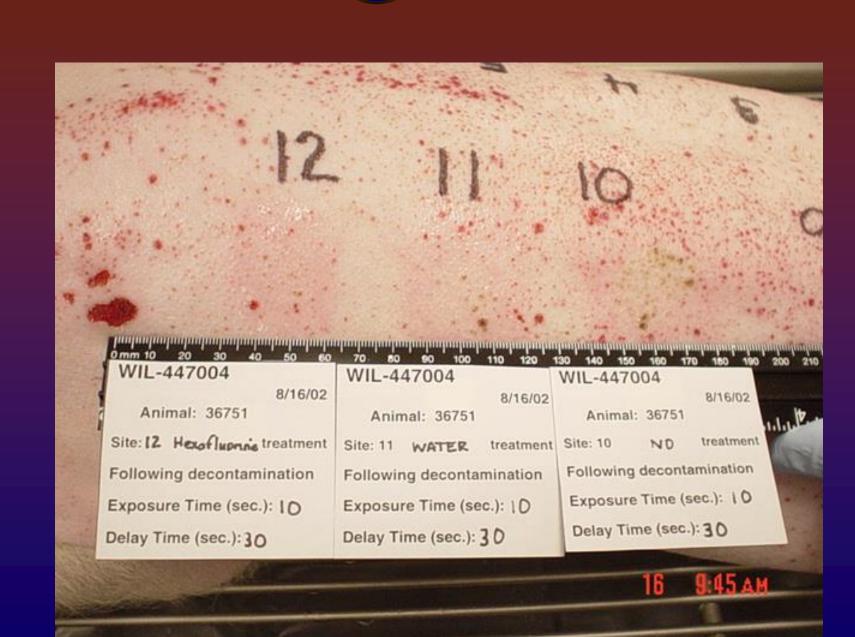
Hexafluorine® Pig Probe Studies: 49% HF – 5 Animals

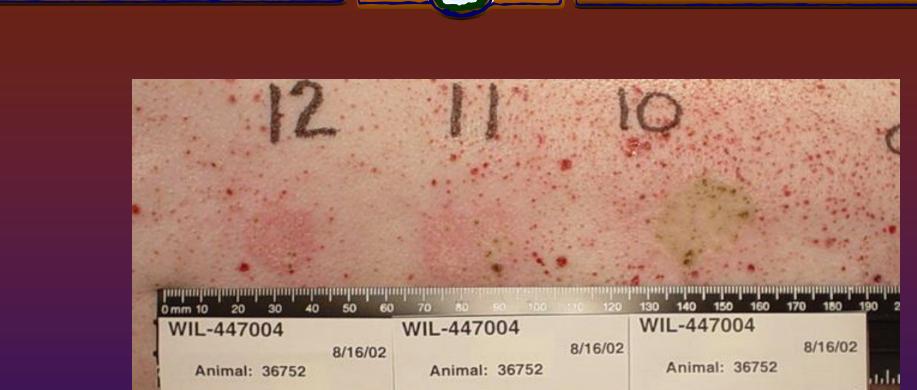
- ❖ August 2002 Study with 1 Pig Showed Efficacy of Hexafluorine®
- ❖ November 2002 Study with 1 Pig was Equivocal
- March 2003 and July 2003 Studies with 3 Pigs were inconsistent
 - Variations from Animal-to-Animal and from Site-to-Site in the Same Animal
 - Hexafluorine® was more Efficacious than Water in some Animals and some Sites, but *not* in others
 - In a few sites Water was more efficacious than Hexafluorine®

Hexafluorine® vs. Water Decontamination Probe Study in an Immature Pig Model

- ❖ The 10 second exposure + 30 second delay to decontamination is a reasonable model:
- ❖ 49% HF exposure causes nearly immediate onset of pain;
- Occupational standards such as ANSI states that decontamination showers/eyewash stations should be immediately available, but in no case should it take an exposed worker than 10 seconds to begin decontamination







Site: 12 Hexafluonne treatment

15 min Post decontamination

Exposure Time (sec.): ID

Delay Time (sec.): 30

Site: 11 WATER treatment

15 min. Post decontamination

Exposure Time (sec.): 10

Delay Time (sec.): 3 D

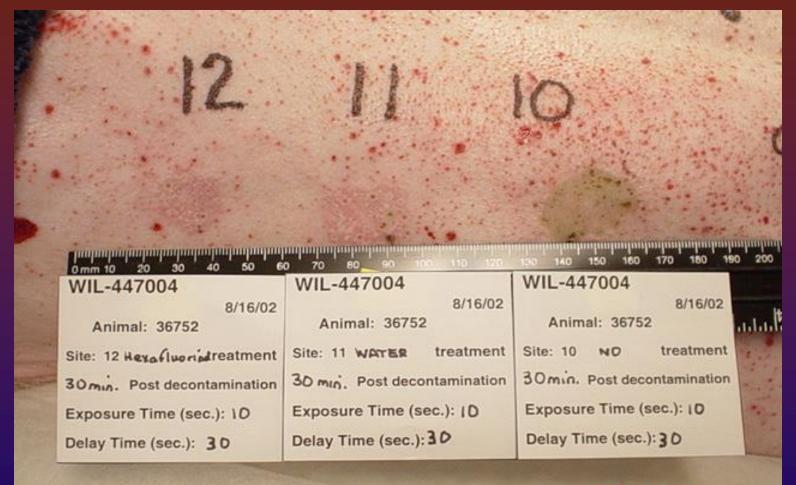
Site: 10 NO treatment

15 min Post decontamination

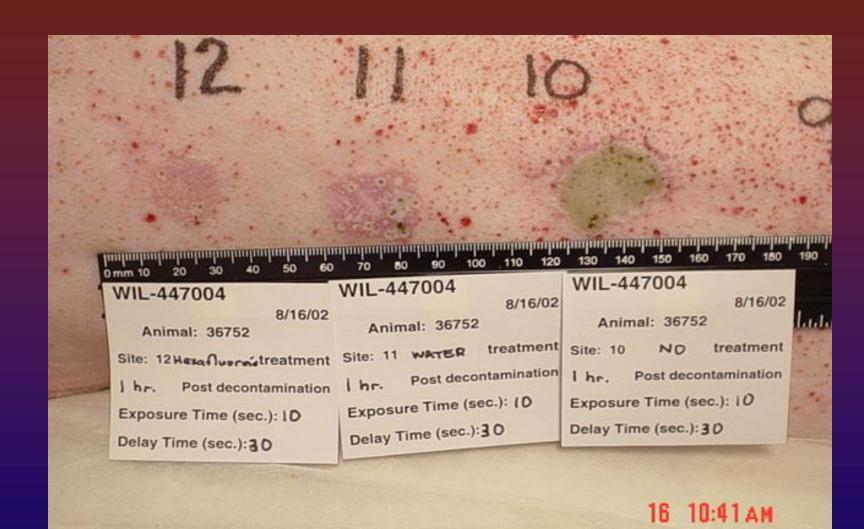
Exposure Time (sec.): 10

Delay Time (sec.): 30





16 10:11 AM





WIL-447004 WIL-447004 WIL-447004 8/16/02 8/16/02 8/16/02 Animal: 36752 Animal: 36752 Animal: 36752 Site: 12 Hexafluonaitreatment Site: 11 WATER treatment treatment Site: 10 Post decontamination 2 br Post decontamination Post decontamination 2 hr. Exposure Time (sec.): 10 Exposure Time (sec.): 10 Exposure Time (sec.): 10 Delay Time (sec.): 30 Delay Time (sec.): 3D Delay Time (sec.): 30





Hexafluorine® Pig Probe Studies

- Overall, the Immature Domestic Pig Model gives *inconsistent* results of whether Hexafluorine® is more Efficacious than Water for Decontamination of 49% and 60% HF Exposures
- ❖ Both Hexafluorine® and Water were Clearly More Efficacious than No Decontamination with 49% and 60% HF
- ❖ There was Some Evidence that Hexafluorine® was More Efficacious than Water with 49% HF
- * No Efficacy of either Hexafluorine® or Water for 70% HF exposure was shown in this model
 - This is in *Distinct Contrast* with the Occupational Experience with *Human* 70% HF Exposure

Hexafluorine® Pig Probe Studies

- * What are the Potential Problems with this Model?
 - While the Pig is Supposed to be the Best Model for Human Skin Exposure, there is a *Discrepancy* between Results of these Probe Studies and actual Human Clinical Experience
 - ❖ It may be that the Methods of Skin Preparation (Removing Hair with Electric Clippers and Depilatory Cream) Somehow Alter the Skin Response to HF Exposure
 - ♦ Pig Skin may *not* Respond to 49, 60, and 70% HF Exposure Similar to Human Skin

Hexafluorine® Pig Probe Studies

- Next Steps Under Consideration
 - *In Vitro* Study of Cultured Cells for the Effects of HF and Potential Alteration with Hexafluorine® or Water
 - Ex Vivo Studies of the Effects of Hexafluorine® or Water following HF Application to Isolated Human or Animal Skin
 - Finding a *Hairless Animal Model* to Avoid the Potential Interferences of Clipping and Depilation

Proposed Clinical Trial of Hexafluorine® for Decontamination of Occupational HF Exposures

Discussions Under Way to have a Clinical Trial at

the Honeywell HF Production Plant in Amherstburg, Ontario, Canada

