# Experience with the United States Department Of Agriculture (USDA) Center for Grain & Animal Health Research (CGAHR) Arthropod-Borne Animal Diseases Research Unit (ABADRU):

## Looking at Rift Valley fever virus and Occupational Biosafety and Hazard Practices

Masters of Public Health Field Experience
Kansas State University

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USDA United States Department of Agriculture

Agricultural Research Service

CGAHR

ABADRU

# Outline

- Introduction
- Overview of Rift Valley fever virus (RVFV)
- Overview of Occupational Biosafety
- Field Experience
  - Biosafety Training Module
  - Rift Valley fever virus and Bluetongue virus Module
- Assessment of Biosafety for Needle-free Delivery
  - Objectives
  - Materials and Methods
  - Results
  - Summary
  - Conclusion
- Acknowledgements

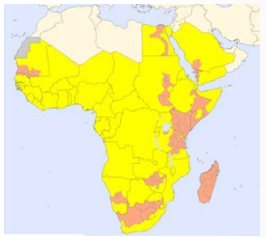
# Introduction

- Zoonotic threat of Rift Valley fever virus (RVFV)
  - Epidemic and financial impact (Clements, *et al*, 2007; Sindato, *et al*, 2011)
  - An Arthropod-Borne - Arbovirus 
  - Medically and Agriculturally important in Africa (Hughes-Fraire, *et al*, 2011)
  - Causes outbreaks impact both human and animal health (Ikegami & Makino, 2011)
    - Bans on movement of animals and products

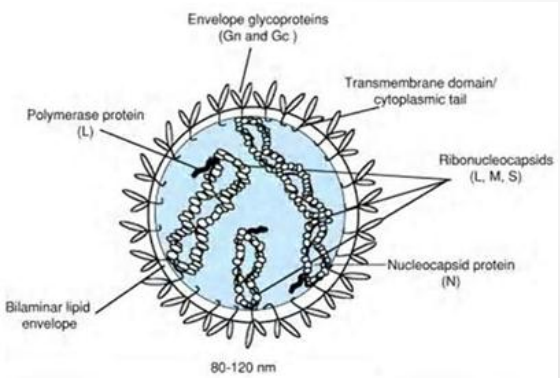

- Organizations and researchers
  - Concern of occupational biosafety (NICD, 2011)
  - Constitutes an important public health issue (Archer, *et al*, 2011)
  - Potential to be globally significant (Strauss & Strauss, 2008)

# Overview
# Rift Valley fever virus

- Isolated from lamb in Kenya, Africa's Rift Valley (Daubney, *et al*, 1931)
- Responsible for severe disease in sub-Saharan Africa for over 70 years (Hartley, *et al*, 2011)
  - In 2010 (NICD, 2011)
    - 238 human infections, 26 deaths
    - 14,342 animal infections, 8,877 confirmed deaths
    - Subclinical cases difficult to quantify



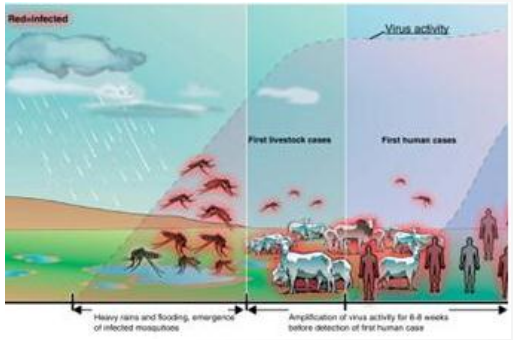
- Rift Valley fever virus (Sindato, *et al*, 2011)
  - Family: *Bunyaviridae* Genus: *Phlebovirus*
  - Single *stranded, negative RNA virus*
  - *Genome*
    - *M*ade up of S- M- and L- segments each containing a separate nucleocapsid within the virion




Adapted from Geisbert, *et al*, 2001

# Overview
# Rift Valley fever virus

- Epidemiology
  - As mentioned RVFV is a mosquito transmitted disease
    - Virus can be transmitted (vertically) from mother to eggs (Hartley, *et al*, 2011)
    - Commonly transmitted by *Aedes*, *Culex*, and *Culicoides* sp. (Turell, *et al*, 2008)
    - Humans and Ruminants amplify virus (Sindato, *et al*, 2011)




  - Humans also infect via (Hartley, *et al*, 2011)
    - Contact of infected blood or tissue
    - Inhalation of aerosol during slaughter of infected livestock

# Overview
# Rift Valley fever virus

- Human Health (Sindato, *et al*, 2011)
  - Incubation period 2-6 days
- Clinical Signs
  - Flu-like syndrome, hemorrhagic fever (37.8-40°C), strong headaches, body pain, dizziness, nausea, epigastric discomfort, photophobia-retinitis, anorexia, and hemorrhage from body cavities
  - <2% can progress from illness to death
- Recovery within 4-7 days

# Overview
# Rift Valley fever virus

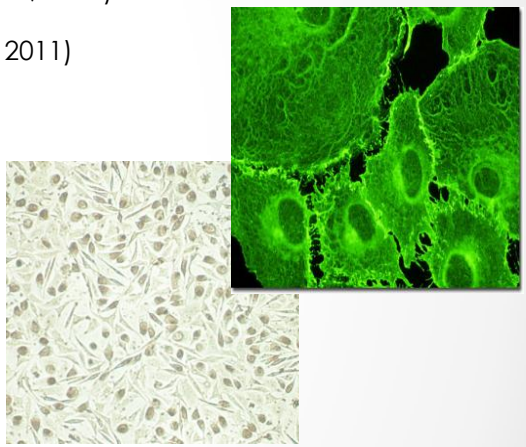
- Animal Health (Spickler & Roth, 2006)
  - Incubation
    - 12-36 hours in newborn lambs
    - Up to 72 hours in sheep, cattle, and dogs

- Clinical Signs
  - Fever (40-42°C), anorexia, lymphadenopathy, weakness, nasal discharge, and usually death within 36 hrs

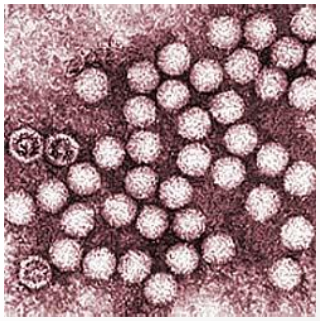
- Recovery
  - Lambs: 90-100% mortality
  - Cattle: 10-70% mortality
  - Abortion is typical in 90-100% of affect ewes and cattle

# Overview of Rift Valley fever virus

- Diagnosis
  - RVFV treated as emergency (Archer, *et al*, 2011)
  - Dependent on virus or nucleic acid isolation (Clements, *et al*, 2007)
    - Via RT-PCR or isolation in mice or cell culture (NICD, 2011)
      - Vero E6 (African green monkey) cells
      - BHK-21 (baby hamster kidney) cells



  - Immunoassay
    - Antigen detection
    - Antibody detection

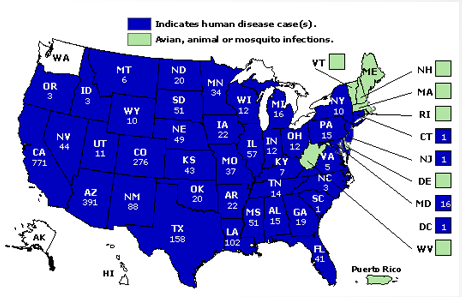



# Overview
# Rift Valley fever virus

- Prevention and control
  - Attenuated and Killed Vaccines
  - Vector control
    - Insecticides
    - Repellants
    - Clothing

- Treatment
  - None – supportive care

# Overview
# Rift Valley fever virus




- Importance (Murray, *et al*, 2010 & Hartley, et al, 2011)
  - West Nile virus (WNV) in 1999-present
    - Exotic arbovirus endemic in North America
    - Due to presence competent mosquito vector
  - Outbreaks confirmed in Yemen and Saudi Arabia in 2000
    - Turell, *et al*, 2008
      - Demonstrated the vector competence of North American mosquito species
        - Competent vector
          - *Culex tarsalis*
          - *Aedes vexans* from Louisiana and Florida

  - Hughes-Fraire, *et al*, 2011
    - Epidemic/economic model determined a potential loss of $120 million– $2.3 billion

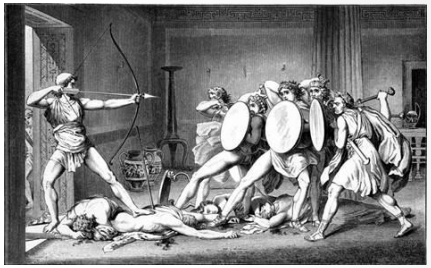
# Overview Occupational Biosafety

- Introduction (CDC, 2009; Harding & Byers, 2006)

  - Biosafety
    - Consistent application of safety measures
  - Biohazard
    - Biological agent or condition that causes a hazard
  - Biosecurity
    - Designed to prevent misuse of microorganisms


# Overview
# Occupational Biosafety

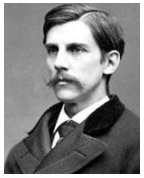
- History
  - Biosafety limited to last 150 years
    - Empirical practices go to ancient times (Block, 2001)
      - The Odyssey – Homer (Rieu, 1952)
      - Susruta – Hindu Physician
      - Black Plague Middle Ages
      - Venice Magistry, 1438
      - Many others…



Susruta

Holmes

Pasteur



Lister

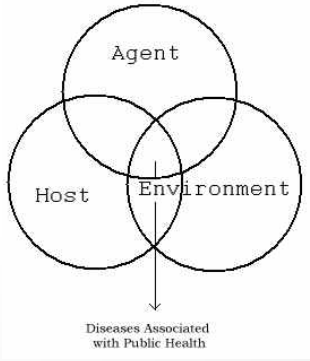
Koch

# Overview
# Occupational Biosafety

- Laboratory acquired infections (LAI) (CDC, 2009)
  - Due a break down in microbiological practices



- Risk of LAI
  - Transmission hazards
    - Mouth pipettes, syringe and needle, spills and splashes, etc…
  - Reported late 1880's
    - Brucellosis, glanders, diphtheria, cholera, tetanus, & Typhoid fever
  - Epidemiological review
    - Kisskalt, 1915

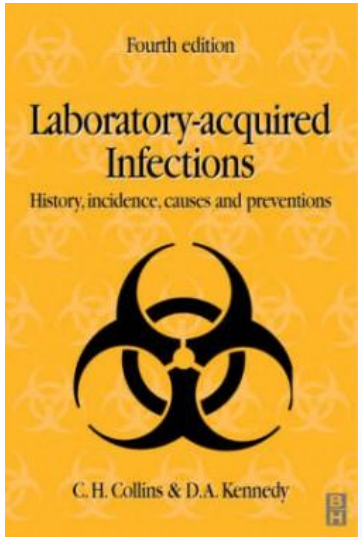



# Overview Occupational Biosafety

- Studies of LAIs

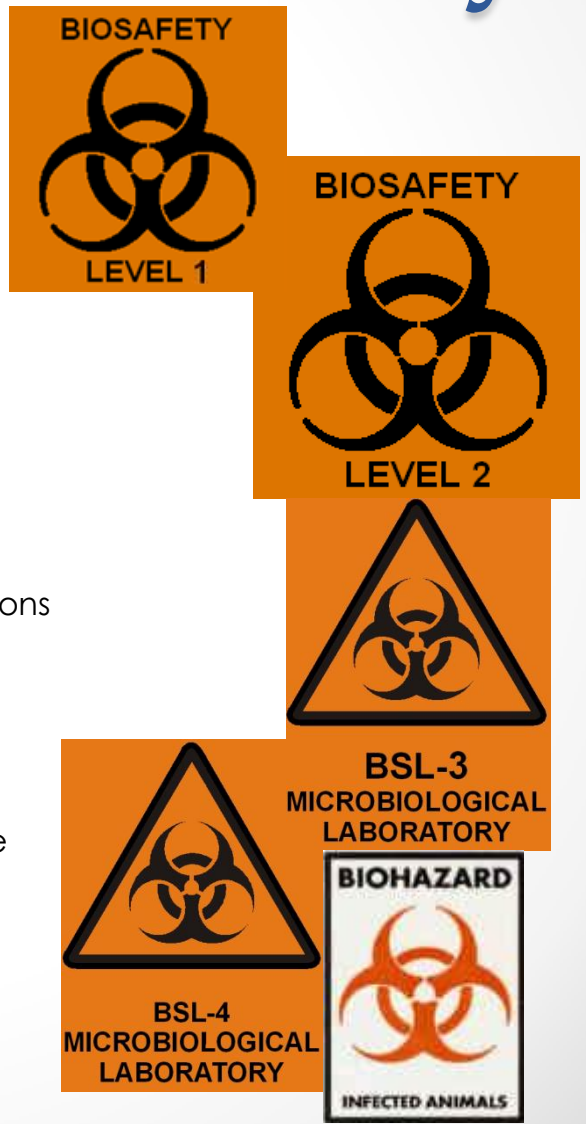
  - Pike & Sulkin (1935-1978)
    - 4,079 reported infections
    - 168 fatalities
  - Harding & Byers (1979-2005)
    - 1,141 reported infections
    - 24 fatalities

*Not all LAIs reported



# Overview
# Occupational Biosafety

- BSL-1: Student training/teaching labs
  - Agents are well-defined and characterized
    - Not known to cause disease
- BSL-2: Clinical/diagnostic labs
  - Agents are considered moderate-risk agents
    - Associated with human disease (varying severity)
  - Open bench
    - Standard microbiological techniques
      - Probability of splashes and aerosols is low
- BSL-3: Research/production facilities
  - Agents may be indigenous or exotic
    - Associated with serious and potentially lethal infections
    - Potential for respiratory transmission
      - High transmissibility by aerosols
- BSL-4: Dangerous/exotic laboratories
  - Agents pose high individual risk of life-threatening disease
    - Vaccine or therapy may not be available



# Field Experience

- Organization History
  - Arthropod-Borne Animal Disease Research Unit (ABADRU)
  - Moved from Laramie, WY → Manhattan, KS
    - Cooperative with K-State researchers
    - Biosecurity Research Institute (BRI)
  - Study animal diseases transmitted by arthropods
    - Bluetongue virus (BTV)
    - Vesicular Stomatitis virus (VSV)
    - Epizootic Hemorrhagic Disease virus (EHDV)
    - Rift Valley fever virus (RVFV)

USDA United States Department of Agriculture

ABADRU

BRI Biosecurity Research Institute

- Importance
  - Public health and U.S. livestock

Public Health

# Field Experience

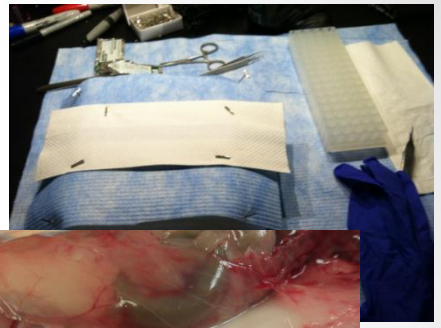
- Role & Objectives
  - USDA ABADRU
    - Rift Valley fever virus
    - Zoonotic disease research
    - Occupational hazard guidelines
    - Laboratory biosafety

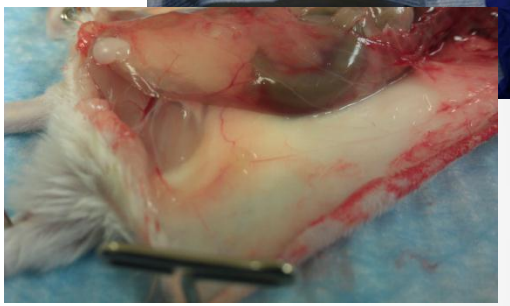
ABADRU

USDA United States Department of Agriculture

# Field Experience

## Student Activities





- Mouse work
  - *Culicoides sonorensis*
  - *Immunologic response from feeding*
- Lab work
  - Methods and procedures
  - Occupational hazards and biosafety


# Field Experience

## Student Activities

- Frontier Field Trip
  - U.S.-Mexico Border Port of Entry (USPOE) in Santa Teresa, NM
    - Border control interdiction and trade security
    - Immigration Policy Border Communities Conference
    - NM Border Authority
    - U.S. Customs and Border Protection (USCBP)
    - Food and Drug Administration (FDA)
    - New Mexico Department of Agriculture, at the Chihuahua Regional Cattle Union Livestock Facilities

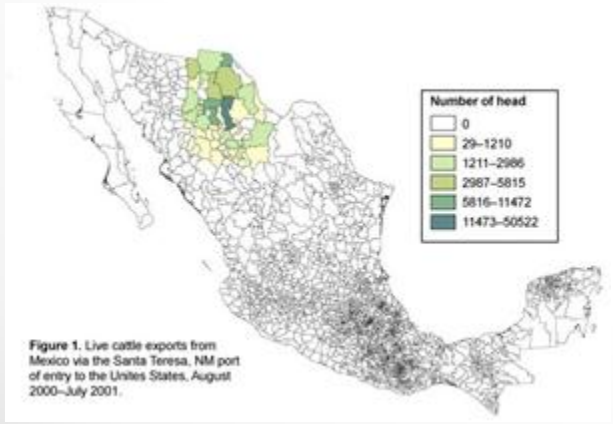


Figure 1. Live cattle exports from Mexico via the Santa Teresa, NM port of entry to the Unites States, August 2000–July 2001.

# Field Experience

## Student Activities

- Product
  - Biosafety Training PowerPoints
- Need
  - No tutorials specific to the BSL-2 Laboratory
- Use
  - Provide safety information
  - Knowledge to be proactive during training period
  - Completion of presentation
    - Quiz to provide certificate of completion

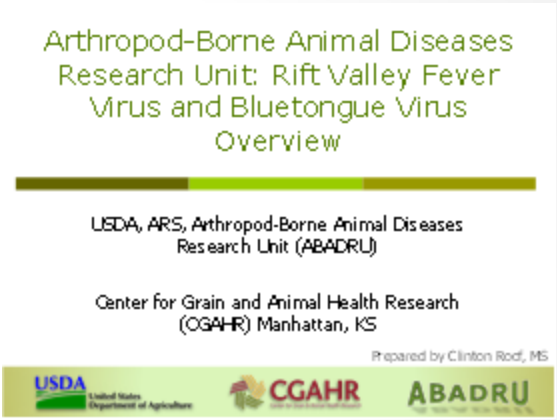





# Field Experience

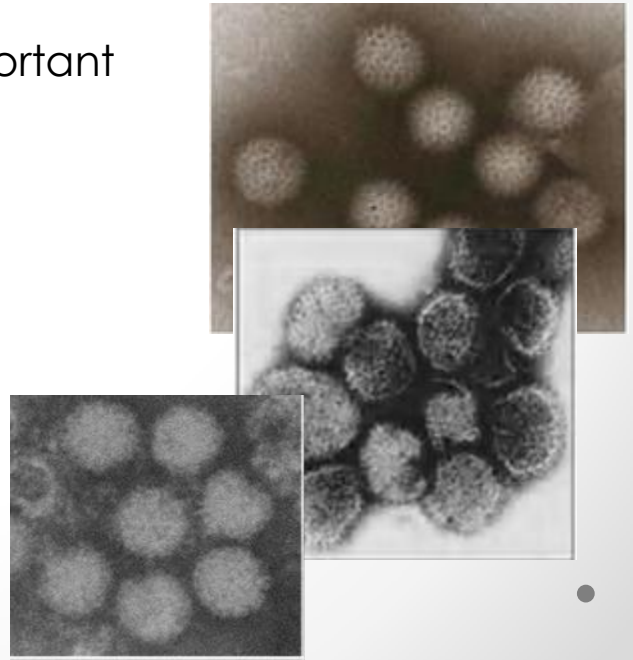
## Student Activities

- Product
  - Virus Overview Training PowerPoint
    - Rift Valley fever virus
    - Bluetongue virus




- Benefit
  - Student and temp-works need basic virology
  - Understand why the ABADRU research is important

- Use
  - Health impact and risks of viruses
  - Self-vigilance to increase biosafety
  - Completion of presentation
    - Quiz to provide certificate of completion



# Field Experience

## Student Activities

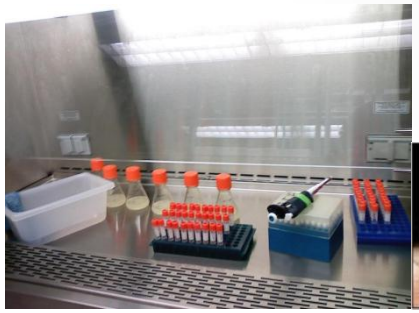
- Product
  - Preliminary evaluation of P50 Microdose NeedleFree Injection System© in BSL-2 laboratory

- Benefit
  - Increase worker biosafety
  - Improve the immunologic response from vaccines
  - Reduce the need to raise *Culicoides sonorensis* (midge) strains for research

- Use in a controlled research facility
  - Administer modified live vaccines (such as MP-12)
  - Live Rift Valley fever virus

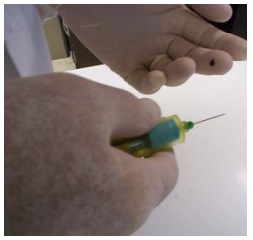
# Assessment of Biosafety for Needle-free Intradermal Delivery

- Occupational biosafety
  - Workers in bioresearch laboratories
    - Zoonotic agents



- Simulate transmission method of arthropod vectors

- Risks and safety (Deng, *et al*, 2012; Mitragotri, 2005)
  - Compared to traditional needle and syringe



- Risks of aerosol generation (Zehrung, & Kristensen, 2009)

# Objectives

To characterize potential risks of the P50 Microdose NeedleFree Injection System© for intradermal injection of infectious agents or modified live vaccines in BSL-2 and BSL-3 laboratories

To evaluate differences in surface splatter and wetness for test dose and pressure combinations

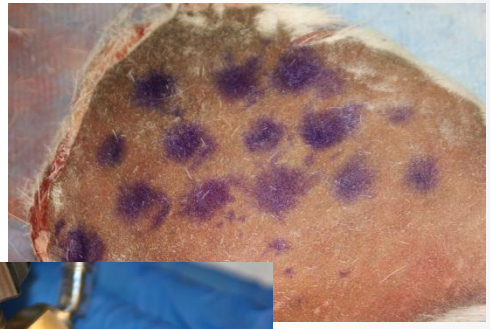
# Materials & Methods

- Donated Boer goat forelimbs with intact hide
  - Stored in a sealed bag at -20°C

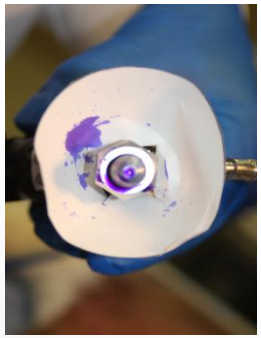
- P50 Microdose NeedleFree Injection System©
  - Compressed $C0_2$ as a power source

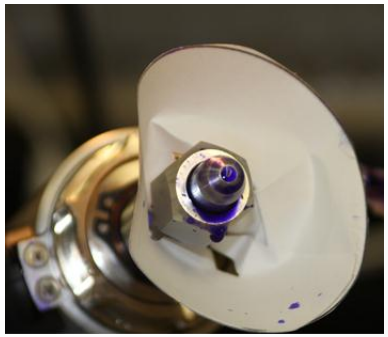
# Materials & Methods

- Two Solutions
  - 5% Crystal Violet
  - Germ Juice®

- Doses/pressure
  - 50 µL/100 psi
  - 100 µL/90 psi
  - 250 µL/90 psi





# Results

## Germ Juice® Solution

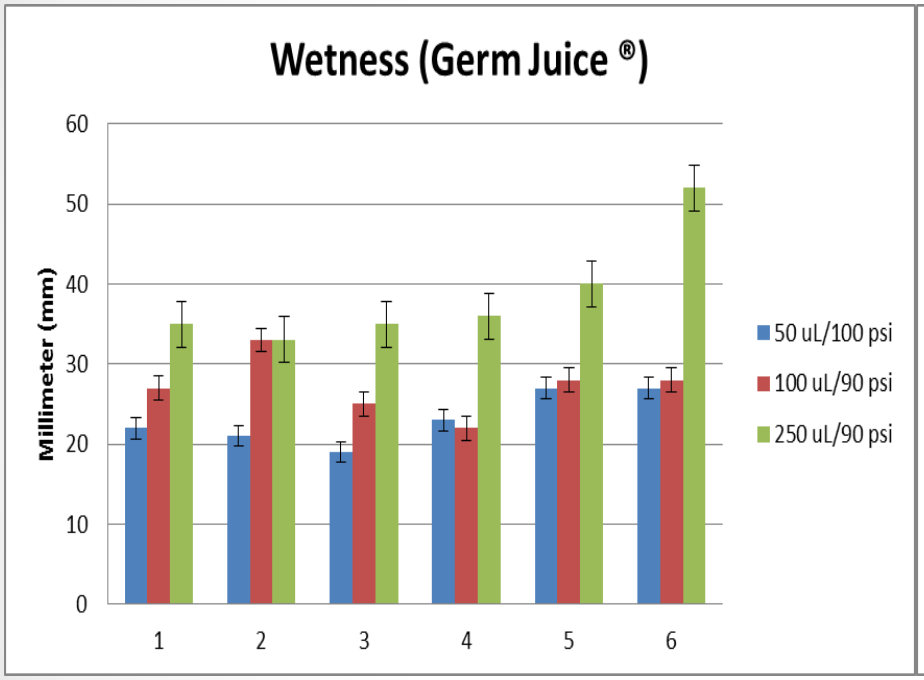
| Limb Location | Right Front | Data Points | | | | | | Mean |
|---|---|---|---|---|---|---|---|---|
| Wetness (mm) | 50 uL/100 psi | 22 | 21 | 19 | 23* | 27* | 27* | 23.2 |
| Pooling (y/n) | 50 uL/100 psi | 0 | 0 | 0 | 0* | 0* | 0* | 0.0% |
| Surface splatter (mm) | 50 uL/100 psi | 19 | 0 | 14 | 20* | 22* | 25* | 16.7 |
| Aerosolization (y/n) | 50 uL/100 psi | . | . | . | 0* | 0* | 1* | 33.3% |
| Wetness (mm) | 100 uL/90 psi | 27 | 33 | 25 | 22* | 28* | 28* | 27.2 |
| Pooling (y/n) | 100 uL/90 psi | 1 | 0 | 1 | 1* | 0* | 1* | 66.7% |
| Surface splatter (mm) | 100 uL/90 psi | 25 | 20 | 20 | 26* | 24* | 29* | 24.0 |
| Aerosolization (y/n) | 100 uL/90 psi | . | . | . | 1* | 1* | 1* | 100.0% |
| Wetness (mm) | 250 uL/90 psi | 35 | 33 | 35 | 36* | 40* | 52* | 38.5 |
| Pooling (y/n) | 250 uL/90 psi | 1 | 0 | 1 | 1* | 1* | 1* | 83.3% |
| Surface splatter (mm) | 250 uL/90 psi | 0 | 0 | 70 | 35* | 31* | 0* | 22.7 |
| Aerosolization (y/n) | 250 uL/90 psi | . | . | . | 1* | 1* | 1* | 100.0% |

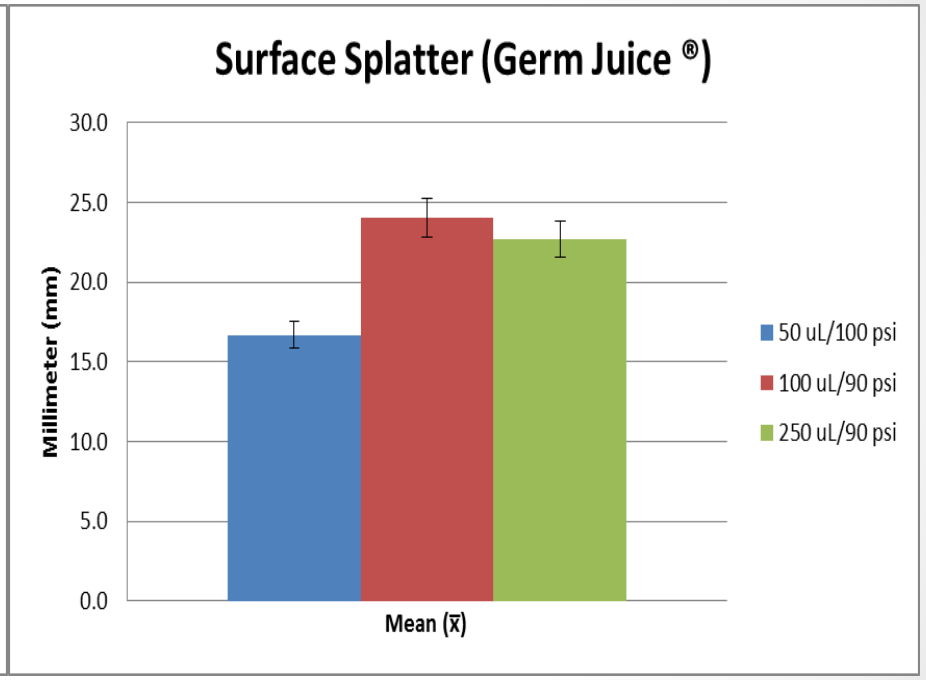
# Results

## Crystal Violet Solution

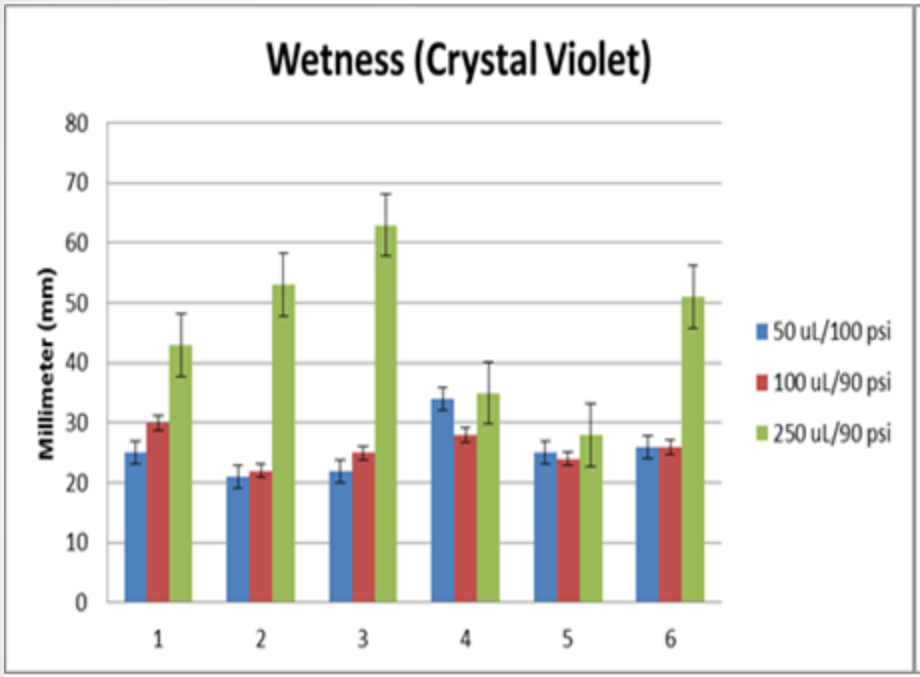
| Limb Location | Left Front | Data Points | | | | | | Mean |
|---|---|---|---|---|---|---|---|---|
| Wetness (mm) | 50 uL/100 psi | 25 | 21 | 22 | 34* | 25* | 26* | 25.5 |
| Pooling (y/n) | 50 uL/100 psi | 0 | 1 | 0 | 1* | 1* | 0* | 50.0% |
| Surface splatter (mm) | 50 uL/100 psi | 0 | 0 | 0 | 0* | 0* | 0* | 0.0 |
| Aerosolization (y/n) | 50 uL/100 psi | . | . | . | 0* | 0* | 0* | 0.0% |
| Wetness (mm) | 100 uL/90 psi | 30 | 22 | 25 | 28* | 24* | 26* | 25.8 |
| Pooling (y/n) | 100 uL/90 psi | 0 | 1 | 1 | 1* | 1* | 1* | 83.3% |
| Surface splatter (mm) | 100 uL/90 psi | 0 | 30 | 20 | 25* | 20* | 21* | 19.3 |
| Aerosolization (y/n) | 100 uL/90 psi | . | . | . | 1* | 1* | 1* | 100.0% |
| Wetness (mm) | 250 uL/90 psi | 43 | 53 | 63 | 35* | 28* | 51* | 45.5 |
| Pooling (y/n) | 250 uL/90 psi | 1 | 0 | 1 | 1* | 0* | 1* | 66.7% |
| Surface splatter (mm) | 250 uL/90 psi | 0 | 0 | 0 | 27* | 24* | 37* | 14.7 |
| Aerosolization (y/n) | 250 uL/90 psi | . | . | . | 1* | 1* | 1* | 100.0% |

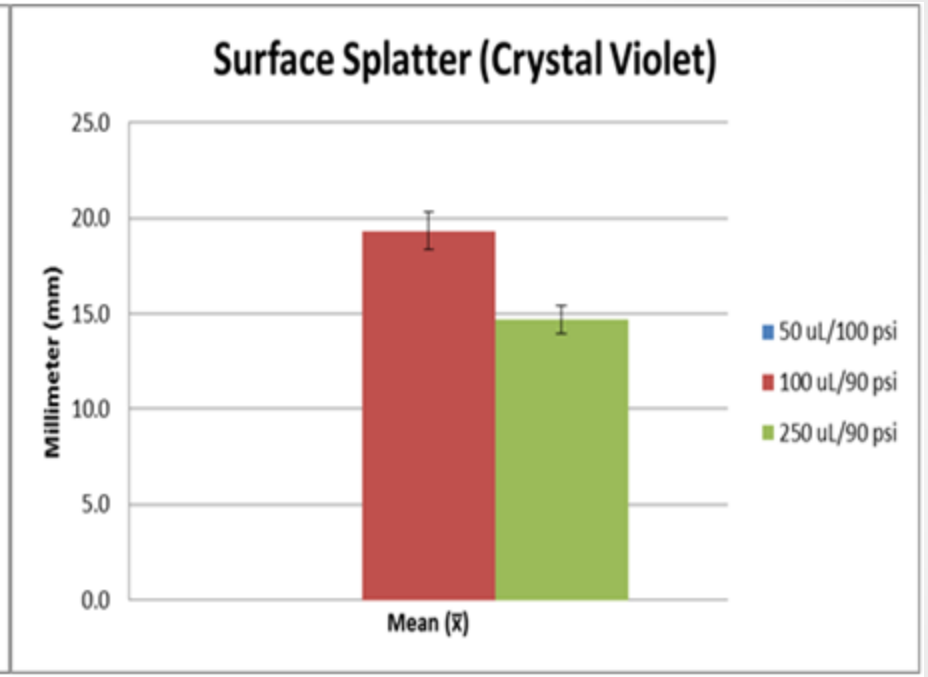
# Results


Wetness (Germ Juice ®)
Millimeter (mm)
60
50
40
30
20
10
0
1
2
3
4
5
6
50 uL/100 psi
100 uL/90 psi
250 uL/90 psi

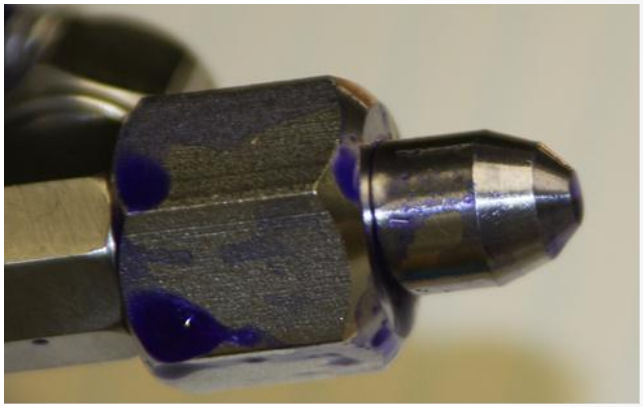

Surface Splatter (Germ Juice ®)
Millimeter (mm)
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Mean (x̄)
50 uL/100 psi
100 uL/90 psi
250 uL/90 psi

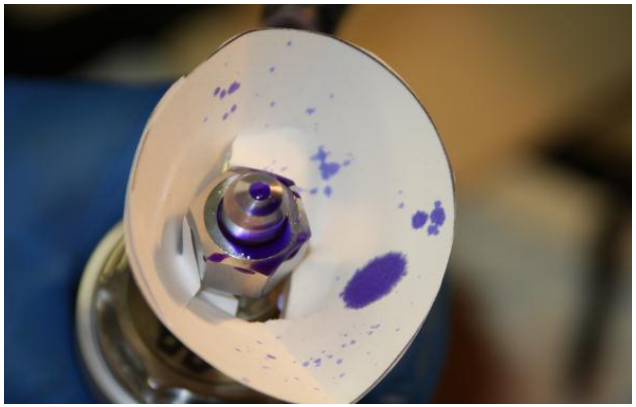
# Results


Wetness (Crystal Violet)
Millimeter (mm)
80
70
60
50
40
30
20
10
0
1
2
3
4
5
6
50 uL/100 psi
100 uL/90 psi
250 uL/90 psi

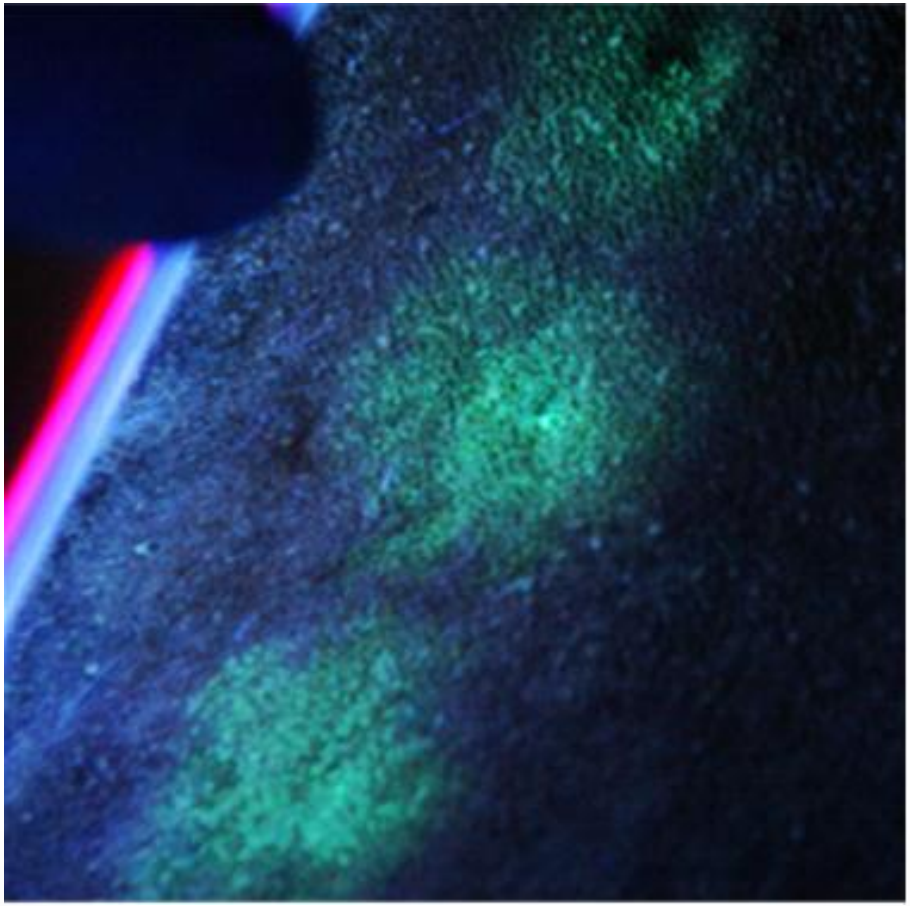

Surface Splatter (Crystal Violet)
Millimeter (mm)
25.0
20.0
15.0
10.0
5.0
0.0
Mean (x̄)
50 uL/100 psi
100 uL/90 psi
250 uL/90 psi

# Results

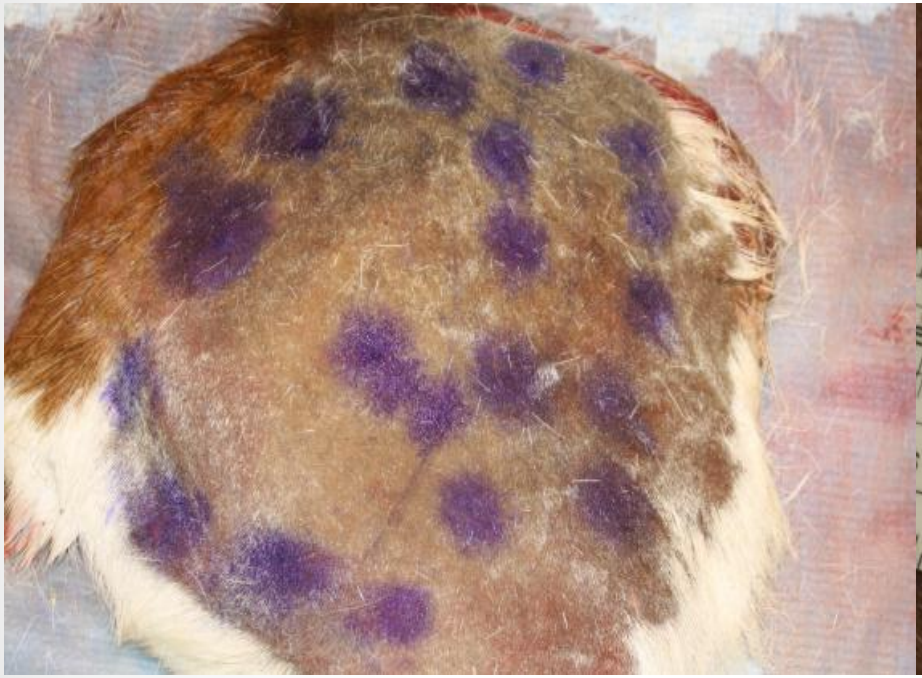


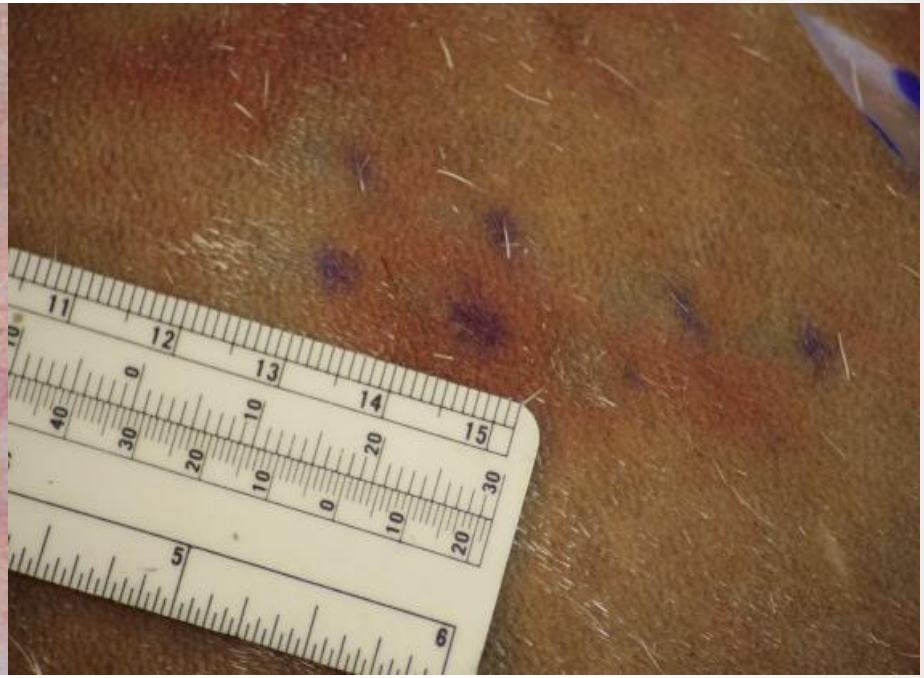


# Results

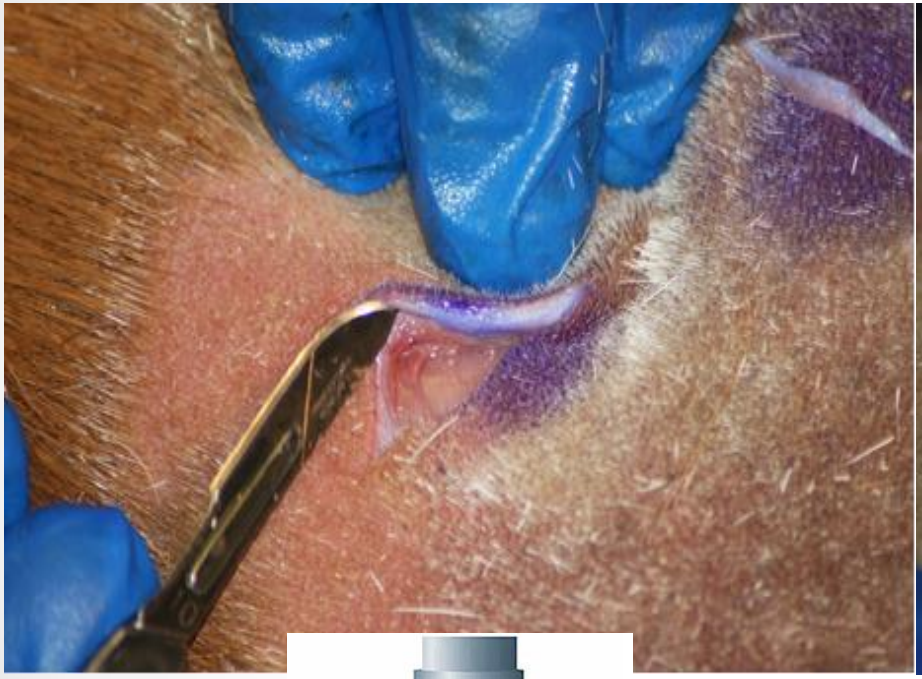


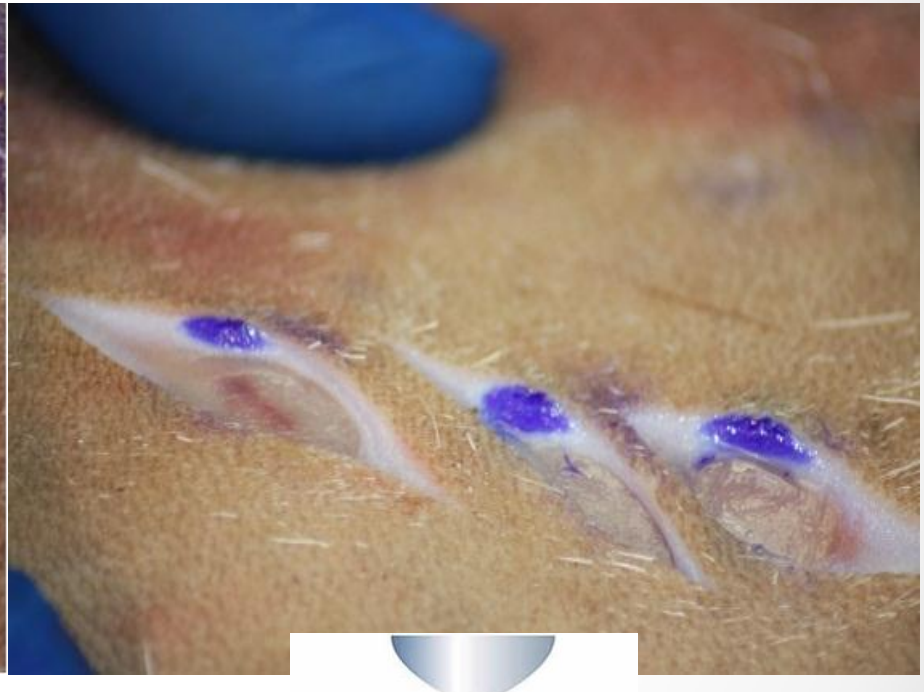
# Results

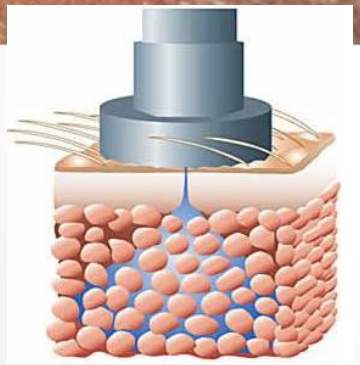


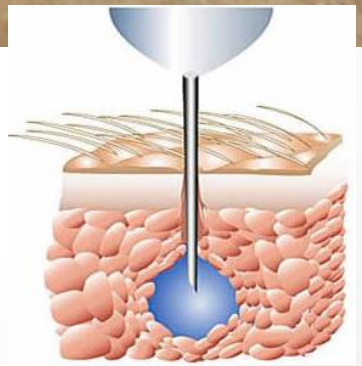


# Results







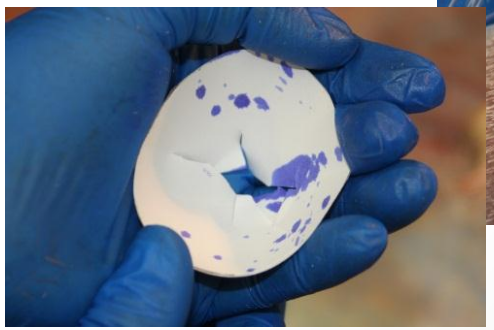


# Conclusion

- Advances in technology
  - Evaluate the safety
  - Practical application


- Success of the device
  - Subcutaneous and intramuscular injections
  - Accuracy of intradermal delivery
  - Interest for research purposes

- More data points needed
  - Statistical difference
  - Other devices

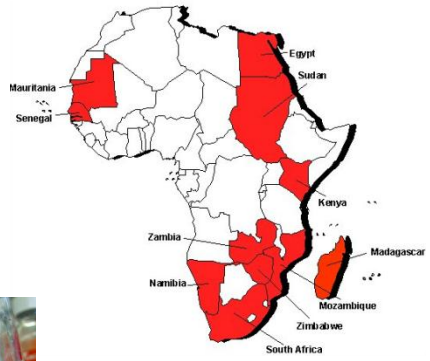


- Safety of device
  - Needle-less use
  - Aerosolization

# Summary

- Gains
  - Knowledge
  - Understanding
  - Risks and hazards
- Disciplines
  - Public health
  - Animal health







ABADRU

KANSAS STATE UNIVERSITY

CGAHR
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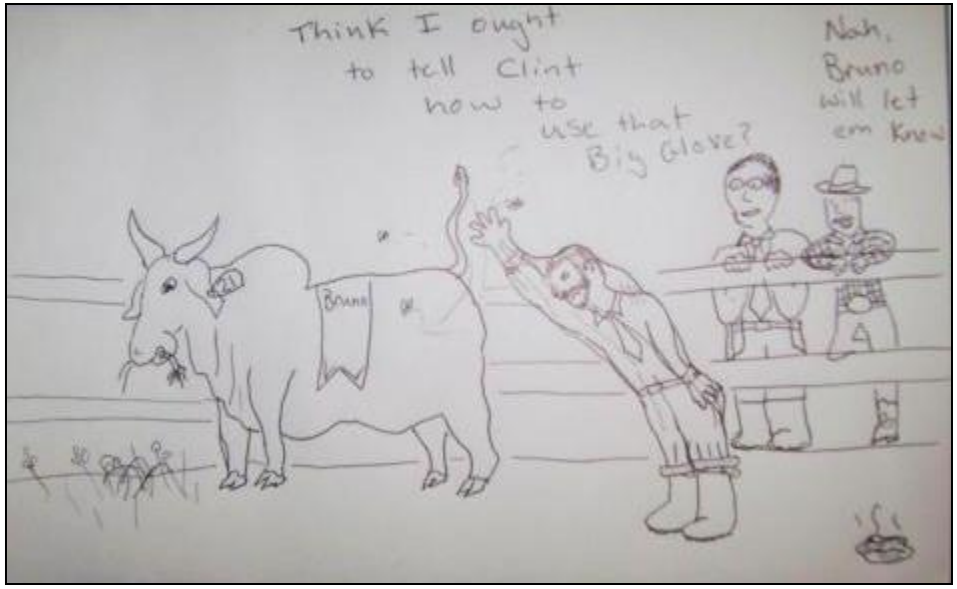
# Questions




Thanks to my brother Levi Roof