2015 Annual Conference

KANSAS STATE UNIVERSITY
BRI Biosecurity Research Institute

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Seminar 12 - Biocontainment Facility Design, Commissioning and Certification Strategies

Title: Commissioning and Beyond: Annual Certification and Commissioning of Biocontainment Facilities

Atlanta, Georgia

Learning Objectives

1. Describe the concept of pressure reversal, also known as air flow reversal in containment laboratories and define where the pressure reversals are not allowed, and where they are permitted.
2. Describe the National Institutes of Health and Centers for Disease Control oversight of BSL-3 facilities.
3. Explain differences between biocontainment facility commissioning and annual performance verification and understand the distinction of ANSI Z9.14 and "Select Agent" rules as they relate to performance verification.
4. Understand what options are available to simplify the design of biocontainment facility HVAC to reduce costs.

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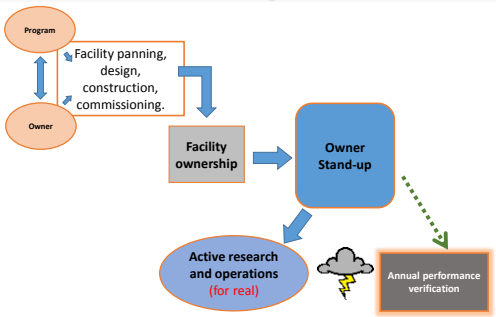
Outline/Agenda



HVAC features & critical components (Biocontainment)

- Important to note that the focus is BSL-3 "ish"
  - Maintenance service records
  - Scheduled PM milestones
  - Redundancy (n+1)
  - Independent supply and exhaust systems interlocked thru BMS
  - Ability to demonstrate performance

Over 1000 BSL-3 Labs in the US

Performance Guidelines & Standards

- DHHS, Centers for Disease Control and Prevention and National Institutes of Health, Biosafety in Microbiological and Biomedical Laboratories (BMBL)BMBL
- **ANSI/ASSE Z9.14 – 2014, Testing and Performance-Verification Methodologies for Ventilation Systems for Biosafety Level 3 (BSL-3) and Animal Biosafety Level 3 (ABSL-3) Facilities**
- USDA, ARS 242.1 Manual, Facilities Design Standards
- National Institutes of Health, Design Requirements Manual
- Association for Assessment and Accreditation of Laboratory Animal Care (AALAC): Guide for the Care and Use of Animals
- **Federal Select Agent Program CDC & USDA**

There are additional reference guides and related standards

Annual requirements

- **BSL-3 / ABSL-3 Annual re-verification**
  - **The BMBL says it and it means what?**
    - Methodologies for testing and performance verification is/was lacking. No "standards" for testing/verification of HVAC performance until …..
  - **ANSI/ASSE Z9.14 – 2014**
    - Focuses on BSL-3 ventilation systems
    - Uses risk assessment and performance based approach
    - Standardizes testing and provides uniformity
      - *still considered a guidance document*

Annual requirements

- **Select Agent** extends beyond HVAC and broadens the concept of annual HVAC performance re-verification
  http://www.selectagents.gov/resources/BSL3%20and%20ABSL3%20Verification%20Guidance.pdf
  - **Confirm means of detecting airflow by occupants. (Suggests annual calibration if applicable)**
  - Confirmation of inward airflow by observation (smoke)
  - **Confirm operation of decontamination systems**
  - BAS performance, storage and alarm function
  - **Confirmation of all other alarms (fire, security, medical, etc.)**
  - Annual HVAC HEPA certification
  - **PM history for fans**
  - **CMMS work order documents**
  - **Verify Inspection and repair of penetrations, and seals, surfaces, etc.**
  - Certification of Biosafety Cabinets (NSF Standard 49)
  - **Inspection of seals on centrifuges**
  - **Document proper operation of drench showers, eyewash stations, hands free sinks**

All documented!!

Biocontainment verification using active research

- **Applies science, real pathogens and experimental design for data collection**
- **Pathogen selected intentionally for assessment of biocontainment capabilities beyond facility testing performance data and written SOP's**
- **Design was to conduct animal disease research, verify biocontainment performance, and exercise operational protocol design to demonstrate contamination control and risk mitigation.**

Acknowledgments

- Dr. Bob Rowland and Associates: College of Veterinary Medicine, Department of Diagnostic Medicine & Pathobiology, Kansas State University
- Research Support Staff, Biosecurity Research Institute, Office of the Vice President for Research, Kansas State University
- Chris Kiley, Merrick & Company

The Pathogens

- Porcine Circo Virus type 2 (PCV2) and Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) are economically important diseases of the U.S. swine population.

  A recent study estimates the cost to be in excess of $560 million in losses each year for the swine industry.

  - Highly infectious to susceptible animals (direct contact and aerosol). i.e., survives well outside the host
  - Neither virus poses risk of infection in human beings.
  - Local isolates of the pathogens are not regulated outside of local institutional biosafety committee approvals for use.

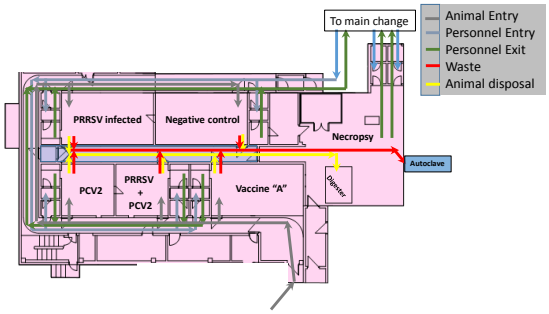
Study Objectives

- **1. Develop a vaccine challenge model of PCVD incorporating PCV2/PRRSV dual infection**.
  - The purpose of this objective is to reproduce this experimental model in conventional pigs under high biosecurity containment.
- **2. Test biocontainment performance of the facility.**
  - PCV2 is highly stable in the environment and easily spread on surfaces and fomites.
  - BL2 – type facilities often do not provide adequate containment of PCV2.
  - PRRSV is highly infectious, with only a few virions needed to initiate a productive infection.
  - PCV2 and PRRSV are not risks to human health so both viruses provide an excellent test for biosecurity systems (biocontainment equipment and protocols).
- **3. Develop and test protocols and procedures for future planned research with high-consequence pathogens.**
  - Numerous and sustained studies in pig models is planned
  - Results to enhance personnel safety, understand capabilities and/or limitations, and add efficiency for future project planning.

Protocols

- **Animal rooms (5) entered in ordered sequence twice per day over a 90 day period**
- **Strict entry and exit procedures followed (clothing change and shower out)**
- **Common entry corridor used for access to all 5 animal holding rooms**
- **All waste materials bagged, topically treated and placed into a common shared corridor from each animal room.**
- **Standard husbandry and daily sanitation practices.**
- **Vapor phase decontamination was not performed until end of study**

Process Flows



Factoids

- 50 Pigs
  - Beginning weight 14 pounds
  - Ending weight average 112 pounds
  - 11,760 pounds of feed
- 5 Groups, i.e., 5 rooms
- 114 days total
- Waste management
  - 97 autoclave loads (clothing {3,072 pounds} and disposables)
  - 100 EDS cycles (400,000 gallons)
  - 5,625 pounds of tissue via TDS
- Animal rooms were opened to common corridor over 450 times during the experiment
- 1,460 (est.) showers taken
- 256+ hours of Biosafety training
- 127+ hours project meetings

Heating, cooling capacity &response.

Typical steam load needs were utilized

Directional airflow and BAS monitoring consistent

Provided regulatory comfort

Experience for operators and users

Project Outcome/Results

- **No cross contamination to adjacent animal rooms in the suite as measured by PCR and serological assays**
  - Negative control animals remained negative
  - PRRSV only room showed no infection of PCV2
  - PCV2 room showed no infection to PRRSV

Study Conclusions

- Facility features for biocontainment sustained experimental control and prevented cross contamination.
- Procedures and protocols sustained experimental control and prevented cross contamination

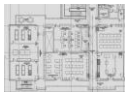
Summary

- **Four primary references for biosafety and biocontainment facility requirements.**
  - CDC/NIH Biosafety in Microbiological and Medical Laboratories (BMBL)
  - ANSI/ASSE Z9.14, Testing and Performance-Verification Methodologies for Ventilation Systems for Biosafety Level 3 (BSL-3) and Animal Biosafety Level 3 (ABSL-3) Facilities
  - USDA, ARS Facility Design Standards Manual 242.1
  - NIH Design Requirements Manual

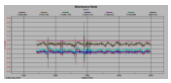
- **"Select Agents" vs BSL-3.**
  - The Federal Select Agent Program oversees the possession, use and transfer of biological select agents and toxins, which have the potential to pose a severe threat to public, animal or plant health or to animal or plant products. Together with Centers for Disease Control and the USDA, Animal and Plant Health Inspection Service, approximately 70 pathogens and toxins are regulated.

Summary

- **Is there a formal biocontainment certification body in the United States?**
  - Not yet. Facilities and research programs receive authorizations and approvals to use, possess, and conduct studies with high consequence pathogens through a combination of institutional and governmental organizations.
    - **ABSA Accreditation**
    - **Biorisk Management System**
    - **Institutional Biosafety Committee**
    - **USDA and CDC (Select Agents and Toxins)**
    - **rDNA Guidelines**
    - **Import/Export Permit**



- **List 3 key components of successful biocontainment facilities?**
  - Facility design
  - Systems performance
  - Operating protocols



Questions?

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