

Risk-based Containment of Agricultural Pathogens

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Agricultural Risk Assessment

Three main agricultural research activities
involved in the conduct of risk analysis

- Animal and plant pests, noxious weeds and invasive species.
- Biological control activities
- Genetically Modified Organisms



Public Health Risk
Assessment

Is Different Than

Agricultural Risk
Assessment



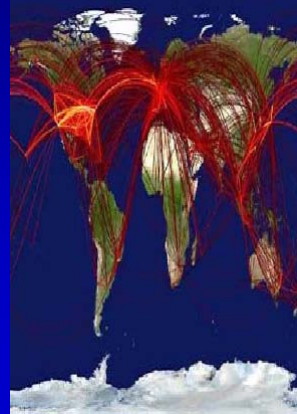
Agricultural Risk Classification

- In contrast to risk classification of human pathogens, risk classification of Agricultural pathogens considers:
 - economic impact
 - effects on trade
 - variables of geographic regions
 - susceptibility of multiple animal or crop species.
 - disease status between countries and regions within countries
- These factors and others have made development of universal criteria difficult to achieve.

Exotic/Foreign Diseases

Challenge: Protecting Agriculture in an age of:

- Global Trade
- Extensive International Travel
- Porous Borders
- Agro-Terrorism



What's a Foreign Animal Disease (FAD)?

A FAD is defined as those animal diseases that have never been present in the "Country Du Jour" or that were eradicated through intensive, expensive control programs

Animal Diseases Eradicated From the U.S.

1892 Contagious Bovine Pleuropneumonia	1959 & 1966 Screwworm (SE & SW respectively)
1929 Foot-and-Mouth Disease	1971 VEE
1929 Fowl Plague	1973 Sheep Scabies
1934 Glanders	1974 Exotic Newcastle Disease*
1942 Dourine	1978 Classical Swine Fever (Hog Cholera)
1943 Texas Cattle Fever	1985 Highly Pathogenic Avian Influenza*
1959 Vesicular Exanthema	

ECONOMIC IMPACTS OF FADs

- Hypothetical
 - FMD in USA: **\$10.4 – 33.6 Billion**
 - CSF in USA: **\$3.2 Billion**
- Actual
 - HPAI 1983: **\$349 Million**
 - END in CA in 2003: **\$ 360 Million**
 - FMD UK 2001: **\$15 Billion** (6 million stock culled)
 - CSF in Netherlands 1997: **\$3.4 Billion**



ECONOMIC IMPACT OF FOREIGN ANIMAL DISEASES



Ranking Factors of Foreign Animal Diseases, APHIS, 1983

Economic risks

Vulnerability

Epidemiological risks

Availability of tests and reagents

Research needs

FAD Risk Classification Factors

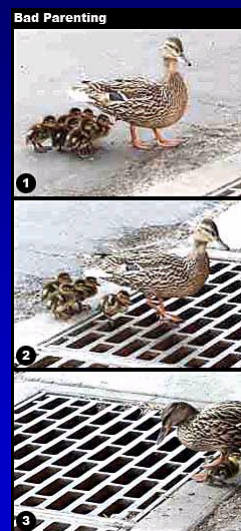
- **Virulence & Pathogenicity**
- **Route of Transmission/Infection**
- **Agent Stability – biological decay, conditions to prolong survival**
- **Infectious dose**
- **Shedding patterns – known and understood? Variables of stress?**
- **Quality and/or Concentration**

FAD Risk Classification Factors

- Endemic or foreign to the region
- Availability of data – Morbidity & Mortality
- Effective prophylaxis, treatment or vaccines
- Active control or eradication programs for the disease
- Animal (large or small) or laboratory animal studies
- Host range
- Surveillance testing

Requirements for Infection or Disease Production

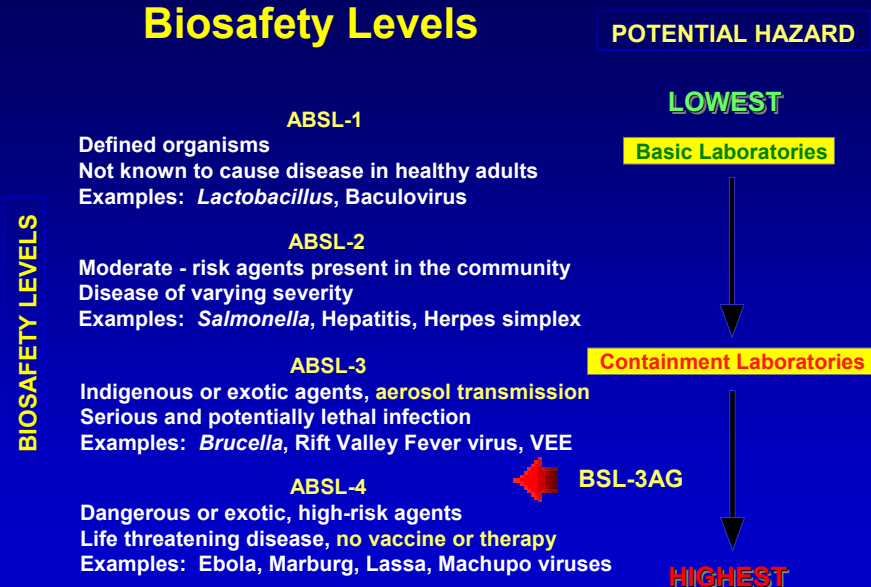
- Sufficient number of organisms to cause infection
- Susceptible host
- Access to proper portal of entry (ie. respiratory or enteric tissue etc.)
- Ability of the organism to produce pathology in the host



So What is the Correct Biocontainment Level?

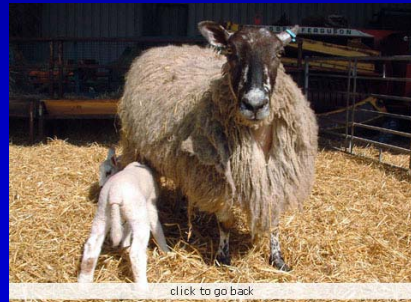
- Do a thorough on site risk assessment
- Determine an appropriate biocontainment level
- Consider further enhancements (equipment or procedural) that may mitigate risk
- Evaluate the process and modify further as needed

Biosafety Levels



Proposed BioSafety Levels for work with Livestock Pathogens

- Similar to BMBL BSL and ABSL levels
- Proposed 4 BSL levels
- Proposed 4 ABSL levels
- Define the ABSL-3-Ag level



BSL-1

- Facility and practices appropriate for work with well-characterized, **low risk agents** not known to cause disease in **healthy animals** that represent no potential **economic loss to agricultural industries**. (E.g. E. coli)
- No specialized practices other than good microbiological technique are utilized.
 - Facilities should be easily cleanable,
 - sink for hand washing
 - conform to the facility requirements described in the BMBL for BSL-1.
- These laboratories are typical of undergraduate or secondary education teaching laboratories.

BSL-2

- Facility, safety equipment and practices appropriate for agents of **moderate** potential hazard to **animals, or agriculture** that are generally endemic, cause illness of varying degree, and are typically treatable or preventable. (E.g. Salmonella, BVD)
- Most research and diagnostic laboratories that work with food borne pathogens and domestic diseases are designed to perform work at this level.

BSL-3

- Facility, safety equipment, and practices applicable to clinical, diagnostic, research, or production facilities in which work is done with indigenous or exotic agents with a potential for transmission, and which may cause **serious and potentially lethal infections or grave economic consequences if released**. (E.g. Brucella, PRRS)
- Laboratory facility and practices include inward directional airflow, separation from non-laboratory areas, special laboratory protective clothing, and decontamination of laboratory waste.

BSL-3 Enhancements

- For *in vitro* work with some highly infectious agriculture agents (E.g. CSF, NDV), BSL-3 may be modified further with enhancements specifically designed to protect the environment such as:
 - HEPA filtration of supply and exhaust air,
 - laboratory liquid effluent/sewage decontamination,
 - personnel exit showers,
 - facility integrity testing (soap bubble test, etc).

BSL-4

- Facility, safety equipment and practices appropriate for research on dangerous and exotic agents that pose a high individual risk of human life-threatening disease, which may be transmitted via the aerosol route and for which there is no available vaccine or treatment.
- While there is no BSL-4 requirement solely for agricultural agents, recently two viruses have been discovered that are lethal for agricultural species and for humans (Nipah and Hendra viruses) and for which there are no vaccines.

ABSL-1

- Facility and practices appropriate for work with well-characterized, **low risk agents** not known to cause disease in healthy animals. No specialized practices other than good microbiological technique are utilized.
- These facilities are typical of University or industry research farms.

ABSL-2

- Facility, safety equipment and practices appropriate for agents of **moderate potential hazard to animals, or agriculture** that are generally **endemic**, cause illness of varying degree, and are typically treatable or preventable.
- Most research and diagnostic vivariums that work with food borne pathogens and domestic diseases are designed to perform work at this level.

ABSL-3

- Facility, safety equipment, and practices applicable to clinical, diagnostic, research, or production facilities in which work is done with indigenous or exotic agents with a potential for transmission, and which may cause **serious and potentially lethal infections or grave economic consequences if released**.
- Vivarium facility and practices include:
 - inward directional airflow,
 - separation from uninfected animal areas,
 - special laboratory protective clothing,
 - decontamination of laboratory waste.

ABSL-3 Enhancements

- For *in vivo* work with some **highly infectious agriculture agents**, ABSL-3 may be modified further with enhancements specifically designed to **protect the environment** such as:
 - placing animals in isolation containers (e.g. isolets, flexible film isolators, etc.) with HEPA filtration of supply and exhaust air,
 - sewage decontamination,
 - personnel exit showers

ABSL-4

- Facility, safety equipment and practices appropriate for research on **dangerous and exotic zoonotic agents** that pose a high individual **risk of human life-threatening disease**, which may be transmitted via the aerosol route and for which there is **no available vaccine or treatment**.
- This standard would have all of the features of a BSL-3-Ag facility with added worker protection.
- No BSL-4 requirement solely for agricultural agents, however agents that are lethal for agricultural species and for humans (Nipah and Hendra viruses) can only be manipulated in vivaria having ABSL-4 capability.
- Currently no ABSL-4 in U.S. with large animal capacity

BSL-3-Ag

- USDA-ARS defined enhanced ABSL-3 facilities, safety equipment and practices particular to agriculture research where the **facility barriers**, usually considered secondary barriers, **now act as primary barriers**.
- Standard is used when **large animals** (cows, pigs, bison, deer, etc.) are infected with **high consequence livestock pathogens** and **cannot** be placed inside of **any other animal isolation device**.
- ABSL-3 facility (as defined in the BMBL) with a number of enhancements specifically designed to protect the environment:
 - HEPA filtration of supply and exhaust air,
 - Central sewage decontamination,
 - Exit personnel showers,
 - Facility integrity testing (pressure decay test).
- FMD, CSF and HPAI are representative of agricultural agents assigned to this biosafety level.

Animal Diseases Requiring BSL3-Ag

- African swine fever virus
- Avian influenza virus (highly pathogenic)
- Classical swine fever
- Foot and mouth disease virus
- Lumpy skin disease virus
- Contagious bovine pleuropneumonia
- Contagious caprine pleuropneumonia
- Newcastle disease virus
- Peste des petits ruminants
- Rift Valley fever virus
- Rinderpest virus



Biosafety Matrix Livestock & Poultry Animal Pathogens

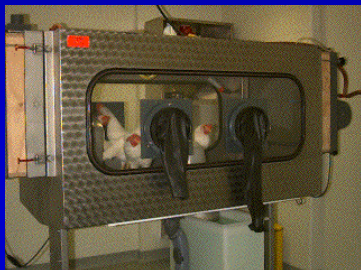
Livestock Pathogen Description	Laboratory Biocontainment	Animal Biocontainment	
		Small	Large
Disease producing organisms which are enzootic but not subject to official control.	BSL-1	ABSL-1	ABSL-1
Disease producing organisms which are either exotic or enzootic but subject to official control and which have a low risk of spread from the laboratory/vivarium.	BSL-2	ABSL-2	ABSL-2
Disease producing organisms which are either exotic or enzootic but subject to official control and which have a moderate risk of spread from the laboratory/vivarium.	BSL-3	ABSL-3	ABSL-3
Disease producing organisms which are either exotic or enzootic but subject to official control and which have a high risk of spread from the laboratory/vivarium.	BSL-3 enhanced	ABSL-3 enhanced	BSL-3-Ag
Disease producing organisms which are either exotic or enzootic but subject to official control and which have a high risk of spread from the laboratory/vivarium and are zoonotic.	BSL-4	ABSL-4	BSL-3-Ag with PPE or ABSL-4

Unique issues arise in containment evaluation for agricultural animals used in research



BSL-3 – Ag Considerations

- No Primary Containment (loose housed)
- Large Infected Species (any)
- Environmental Protection
- Potential Internal Transmission (room to room)
- What agent and how the agent will be used!!!



BSL-3 Agriculture

- APPLIES TO LOOSE HOUSED ANIMALS INFECTED WITH SOME AGENTS
- Building design features incorporate many ABSL-4 requirements to include.
- Rigorous certification and validation requirements (i.e. Pressure Decay Testing of animal rooms)



Secondary Barriers (Facility)

- ABSL-3-Ag facilities have special engineering and design features to prevent microorganism escape to environment
- Overhead floor(s) - Houses sophisticated ventilation, HEPA-filtered supply and exhaust systems
- Underlying floor(s) - Houses sophisticated plumbing, effluent collection, and treatment systems
- Laboratory entrance and exit through:
 - clean change room, personal shower, dirty change room, suit chemical shower room (if needed)
- Additional measures are effected to control access (e.g., 24-hour guard and check in / out system).

BSL-3-Ag Large Animal Facility

MECHANICAL MEZZANINE

MECHANICAL MEZZANINE

MECHANICAL MEZZANINE

PROGRAM FLOOR

CRANE SPACE

ENTRANCE

RECEIVING AREA

LABORATORY

STORAGE

RECEIVING AREA

LABORATORY

STORAGE

ENTRANCE

BSL-3-Ag Large Animal Facility

53,314 SF program space; 156,623 SF total space

The floor plan illustrates the layout of the BSL-3-Ag Large Animal Facility. The facility is divided into several functional areas, each color-coded according to its containment level:

- BSL-3AG (Light Blue):** This area includes the central corridor, the large animal housing units on the left and right, and the central laboratory and support spaces.
- BSL-3 ENHANCED (Green):** This area is located along the perimeter of the facility, primarily on the left and right sides, and includes the central laboratory and support spaces.
- CONTAINABLE (Purple):** This area is located in the central laboratory and support spaces, specifically in the central corridor and the central laboratory area.
- CLEAN (Orange):** This area is located in the central laboratory and support spaces, specifically in the central corridor and the central laboratory area.

The facility also includes a central laboratory and support space, a central corridor, and a central laboratory and support space.

APR Doors



AIR, LIQUIDS and SOLIDS



SPECIAL PRACTICES

- Emphasis on SOPs, training, manuals
- Severe access limitation (select agents)
- Emphasis on decontamination of people, waste, equipment
- Personal quarantine (5-7 days)
- PPE as dictated by the agent used

Change room



FLU ANYONE?



Highly Pathogenic Avian Influenza

Enhancements for in vitro work involving propagation of HPAIV:

- Shower out for all personnel exiting the containment area
- HEPA-filtration of all exhaust air derived from the containment area
- Collection and treatment (heat or chemical) of all liquid effluents (except shower run-off) originating from the containment area prior to discharge
- Written confirmation of a personnel quarantine or restrictions policy

HPAI In Vivo Work

Use of Primary Containment: Animals housed in isolator units.

- Require the same 4 enhancements for in vitro work -- PLUS the following two additional enhancements:
 - Heat treatment of all solid animal wastes and tissues prior to leaving the containment area
 - Bio-isolators are HEPA-filtered out

No Primary Containment: Animals loosely housed.

- BSL-3 Agriculture required
- 5-day personnel quarantine or restrictions policy

SUMMARY

- An onsite risk assessment is vital to determining the level of containment required to work with Agriculture agents of concern.
- Biocontainment levels are a continuum with 8 levels defined as starting points.
- Work with Ag agents of concern in the laboratory does NOT require BSL3-Ag
- Work with loose-housed animals with some (11) Ag agents requires BSL3-Ag

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