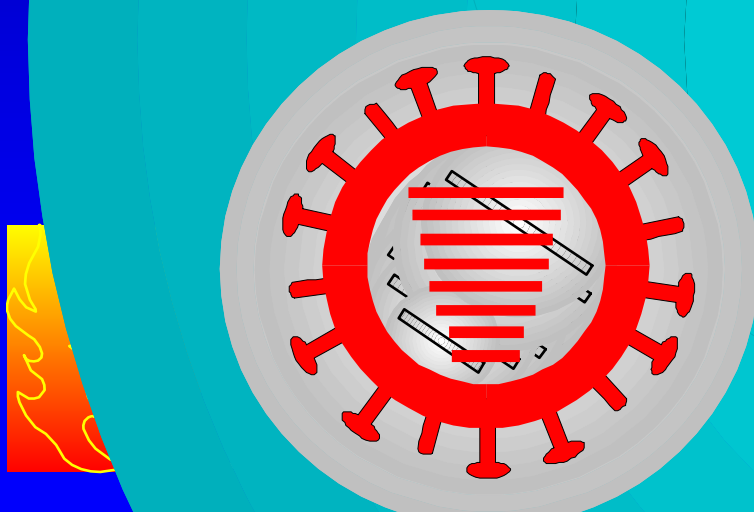


Avian Influenza - Pandemic Preparedness





Avian influenza
STRIKES
Virginia poultry
farms



Pandemic Influenza: The Ever Present Threat



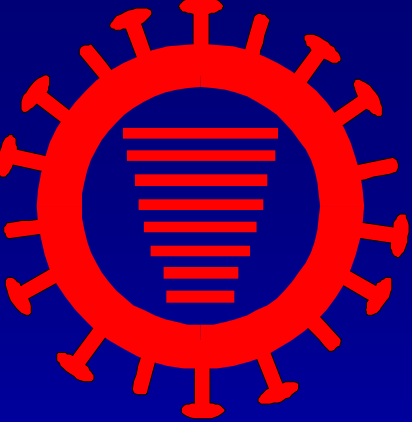
Likely U.S. Impact of an Influenza Pandemic: Estimates from a CDC Model

- 20-47 million illnesses
- 18-42 million clinic visits
- Up to 730,000 hospitalizations
- 89,000 to 207,000 deaths

NIH Workshop: Establishing Preclinical Variables for Evaluation

- **Seed Viruses for
manufacturers**
- **Substrates for
Production**
- **Reagents**
- **Safety
Considerations**
- **Other Regulatory
Issues**





Generation and Characterization of Seed Viruses for Manufacturers

- H5 (multiple antigenic variants); H9N2 (G9 and G1 antigenic variants); H7 (Eurasian and N. American); H2; H6; and other subtypes (H4, H10, H13) as new threats emerge
- Conditions for production of reference seeds for manufacturers
 - SPAFAS eggs
 - Certified cells
- At least two master strain backgrounds:
 - PR8 (H1N1) for high growth production of inactivated vaccine
 - Cold-adapted (ca) A/Ann Arbor (H2N2) for live attenuated intranasal vaccine
- Wild-type virus as reference for manufacturing
 - H9N2 G1-like 1073 human strain

Major Outbreaks of HPAI Avian Viruses Since 1980s

Avian subtype	Country	Year
H5N3	U.S.	1983
H7N7	Australia	1985
H5N2	Mexico	1995/95
H7N3	Pakistan	1995
H5N1	Hong Kong	1997
H5N2	Italy	1997
H7N1	Italy	1999
H5N1	Hong Kong	2001-2003
H7N7	Netherlands	2003



Substrates for Production

- **Egg-based production is primary emphasis at present**
- **Cell-based production of future interest**
 - **Certified Vero Cell Production**
 - **Certified MDCK Cell Production**

Reagent Requirements-Establishing a Library of Reagents

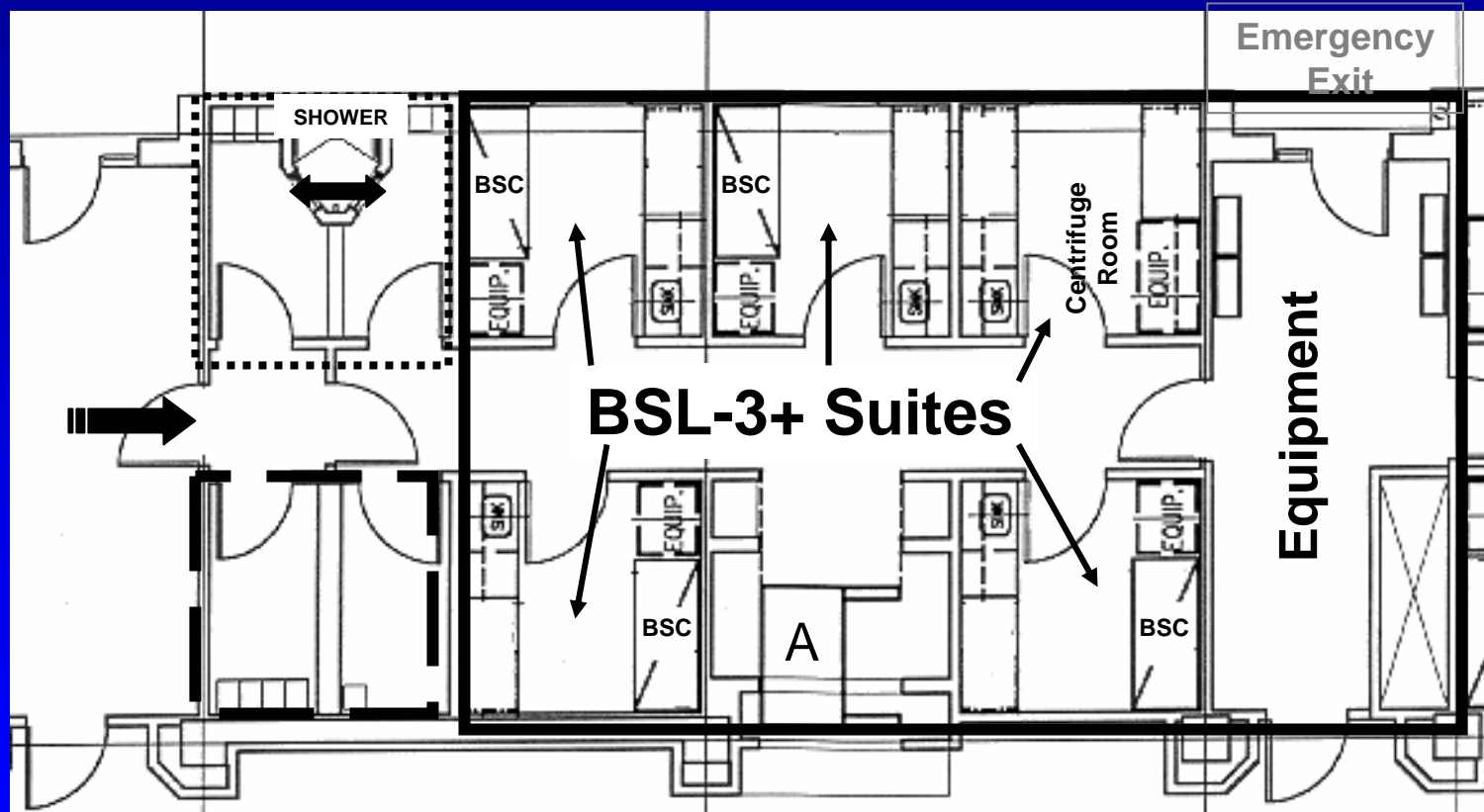
- Post infection or immunization antiserum to generate classical reassortants
- SPAFAS (LAIV) or regular (TIV) eggs
- Certified cell lines for cell-based vaccines
- Cell media components free of TSEs
- Purified HA for production of sheep serum
 - Coordinated with generation of reference viruses
- Sheep serum for vaccine potency testing

Safety Considerations

- Importance of international safety guidelines for international enterprises
- Laboratory Containment Levels
 - Requirements for BSL2, BSL2+, or BSL3+ conditions
- Protection of laboratory staff
- Protection of the environment
- Use of Good Laboratory Practices (GLP) or Good Manufacturing Practices (GMP)
- Safety of reference seeds in chickens, mice, ferrets
- Shipment of reference from BSL3+ environment: international permits and regulations
- Efficacy of vaccines derived from HPAIV



“BSL-3+” Laboratory Layout



Emergency
Exit



Other Significant Regulatory Issues and IP Issues

- **Select Agent Requirements for HPAIV**
 - Paperwork necessary to inventory and track shipment of HPAIV
 - Additional laboratory security
- **Certified cell lines for cell-based production**
- **Intellectual Property issues around plasmid-based reverse genetics generated vaccine candidates**

Pandemic Preparedness: We're on a Roll

