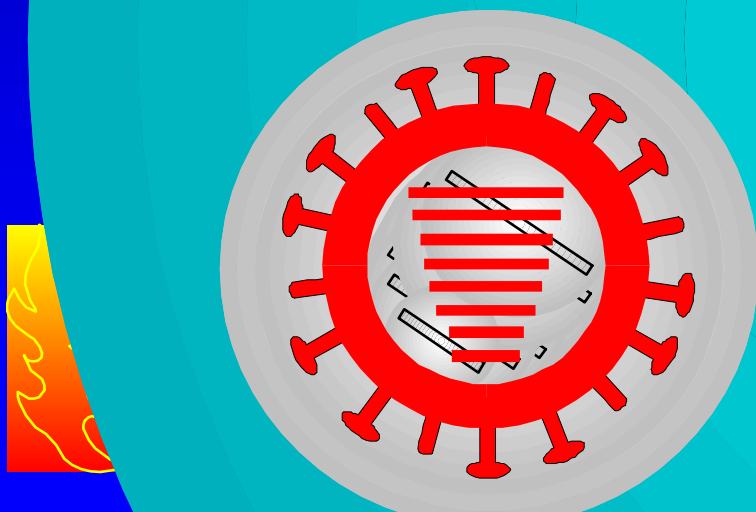


# Avian Influenza - Pandemic Preparedness





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

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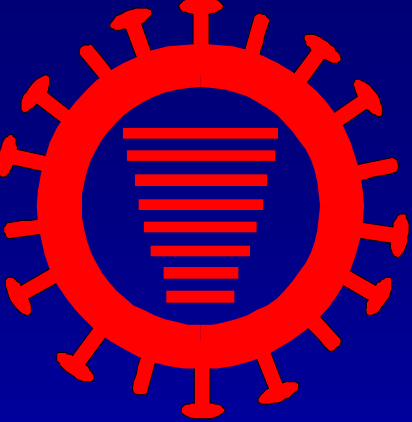
- 20-47 million illnesses
- 18-42 million clinic visits
- Up to 730,000 hospitalizations
- 89,000 to 207,000 deaths

# NIH Workshop: Establishing Preclinical Variables for Evaluation

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- **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

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



# Substrates for Production

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- **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

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- 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



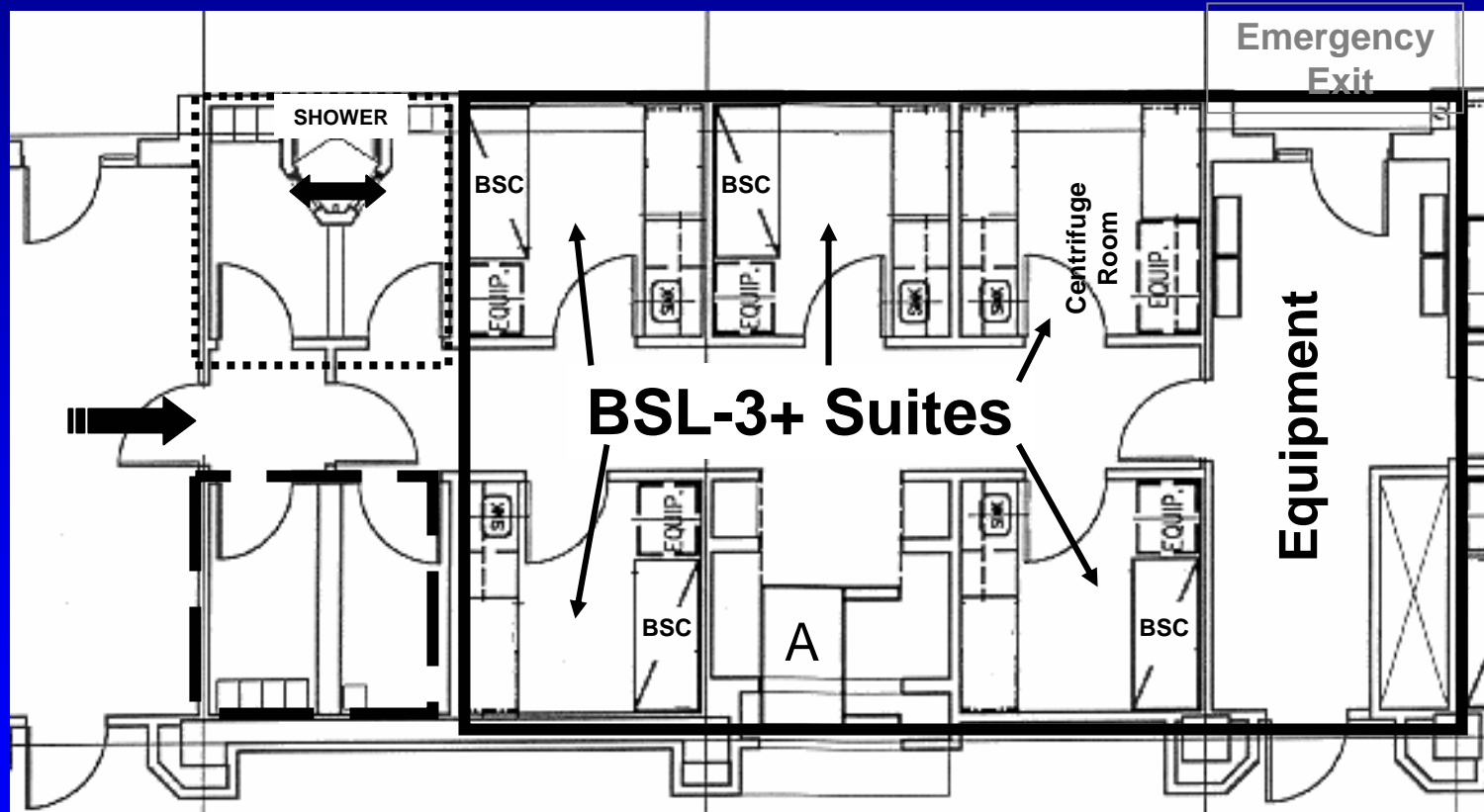
# Safety Considerations

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- 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

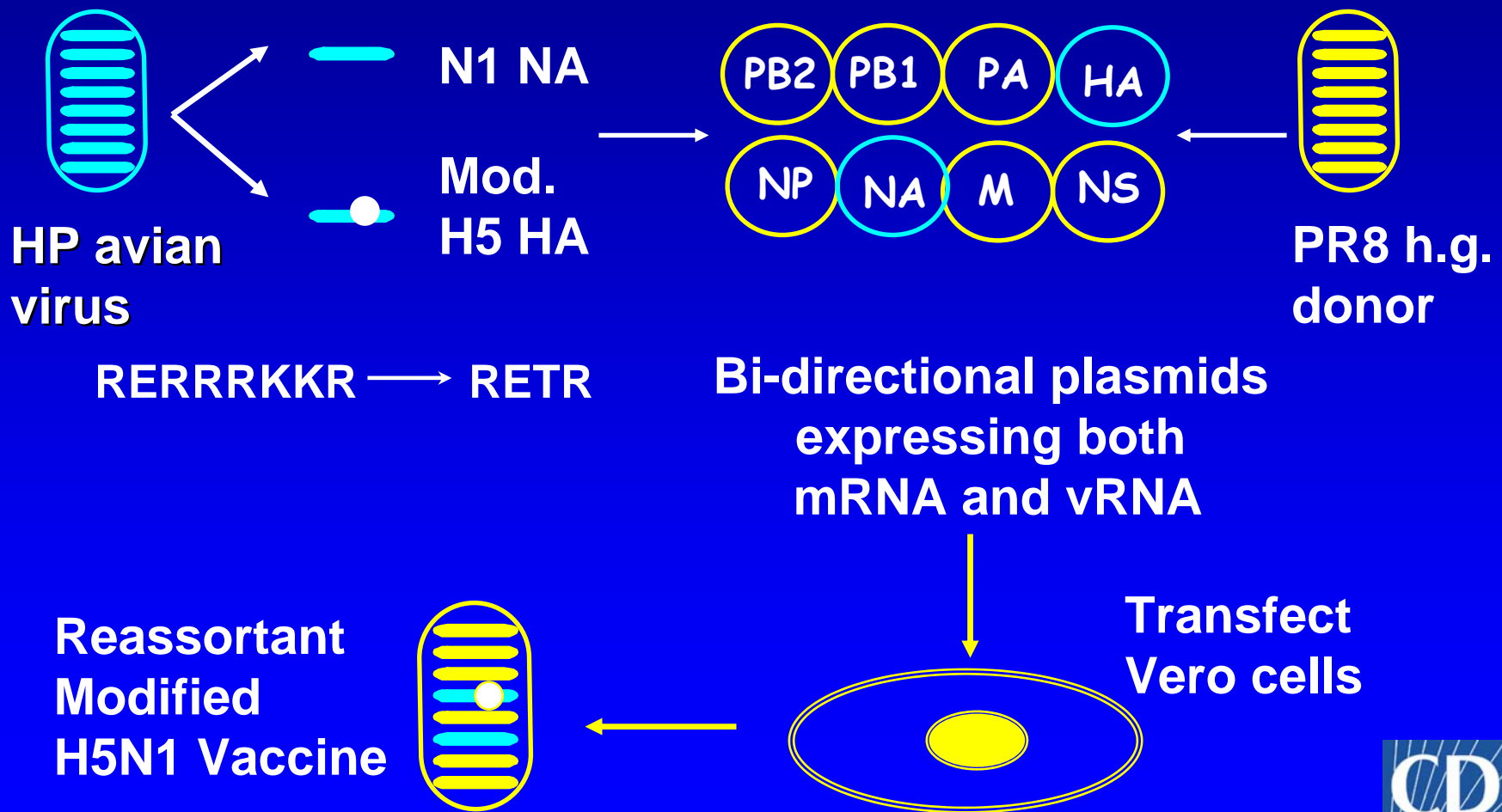


# Other Significant Regulatory Issues and IP Issues

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- **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**

# Generation of “conventional” H5N1 vaccine with modified HA using plasmid-based reverse genetics



# Pandemic Preparedness: We're on a Roll

