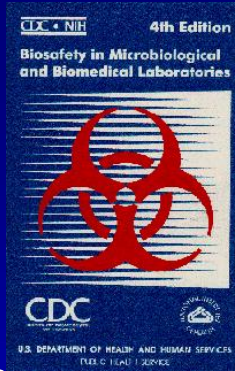


Biosafety in Microbiological and Biomedical Laboratories



- DHHS publication providing CDC/NIH guidelines for the safe handling of infectious agents in laboratories
- Updated and published every 5 years
- 5th edition due to be published in the Fall of 2005
 - Updated Agent Summary Statement for Influenza
- CDC/NIH recommendations are advisory
 - To provide a basis for individual laboratory risk assessment



Revisions to the Influenza Agent Summary Statement for 5th ed BMBL

- **SME Subcommittee formed April 2004**
- **Subcommittee members:**
 - CDC and NIH personnel
 - USDA personnel
 - Influenza experts from Academic community
 - NIH grantees
- **Subcommittee role:**
 - Review the state of knowledge
 - Provide guidance to the Steering Committee
 - Provide a peer review for the document preparation
- **Steering Committee members and role:**
 - CDC and NIH representatives
 - Makes final decisions on recommendations
 - Provides general oversight to revision process.



Interim CDC/NIH Recommendations Posted

- Draft Agent Summary Statement for Influenza was finalized in April 2005
- Interim CDC-NIH Influenza biosafety recommendations posted on CDC website on May 3, 2005
 - Excerpted from draft
 - Contains all recommendations
- <http://www.cdc.gov/flu/han050305.htm>
- Only minor changes expected before publication in Fall, 2005



Key Changes to Influenza Agent Summary Statement

➤ 4th Edition Recommendations:

- BSL-2 facilities and practices for influenza viruses, including non-contemporary human strains
- Did not address avian HP and LP influenza viruses

➤ 5th Edition Recommendations:

- BSL-2 for contemporary human strains (*A/H1, A/H3 and B*) and **LP avian subtypes** excluding H5 and H7
- BSL-3 and ABSL-3 with respiratory protection for non-contemporary human strains (*wildtype A/H2N2*)
- BSL-3 and ABSL-3 with respiratory protection and shower out) for reassortants possessing **1918 influenza virus** genes and **HP avian influenza viruses**



Influenza Viruses: Laboratory Safety Issues

- **Lab-associated infections rare and generally anecdotal**
 - **Rare literature reports of lab infection with avian strains**
- **Lab hazards include**
 - **Inhalation of virus from aerosols**
 - **Infecting animals**
 - **Manipulating high concentrations of virus**
 - **Inoculation of mucus membranes with contaminated gloves**
- **However, genetic manipulation through reverse genetics has the potential to alter host range, pathogenicity and antigenic composition of a virus**



Non-contemporary Human H2N2 Viruses

- Have not circulated in humans since 1968
 - Large proportion of population is susceptible
 - Pandemic potential
- Sensitive to influenza antivirals; vaccine seed stocks available → BSL-3 agent
- BSL-3 and ABSL-3 facilities, practices and procedures recommended
 - Additional respiratory protection from negative pressure HEPA-filtered respirators or PAPRs
 - Clothing change protocol
- *Exception statement to indicate that cold-adapted live attenuated H2N2 vaccine strains can be handled under BSL-2*



Low Pathogenicity Avian Influenza Viruses

- **Regulated by USDA**
 - All avian influenza viruses require APHIS permit
- **BSL-2 and ABSL-2 for LP avian H1-H4, H6 and H8-H15 (H16)**
 - May have additional APHIS permit driven containment requirements
- **LP H5 and H7 may have additional USDA/APHIS permit driven containment requirements**
 - Manipulation in lab has potential to generate HP strain



Highly Pathogenic Avian Influenza Viruses

- **Regulated by USDA**
 - Agricultural and economic implications
 - Require APHIS permit
 - Agricultural Select Agents
- **Some strains may pose increased risk to laboratory workers**
 - Sensitive to influenza antivirals; vaccines in clinical evaluation → BSL-3 agent
- **BSL-3 and ABSL-3 facilities, practices and procedures recommended**
 - Rigorous adherence to additional respiratory protection and clothing change and shower-out protocols
 - Use of negative pressure HEPA-filtered respirators or PAPRs
 - HEPA filtration of laboratory exhaust air
- **Additional containment facility requirements and personnel practices/procedures may be added as condition of APHIS permit**



1918 Viruses Generated by Reverse Genetics

- Risk to lab worker unknown
 - Potential for enhanced virulence
 - Extent of protective immunity in population not known
 - Pandemic potential
- Additional risk assessment data desirable
- Sensitive to influenza antiviral agents; recombinant vaccine could be made → BSL-3 agent
- BSL-3 and ABSL-3 facilities, practices and procedures recommended
 - Large laboratory animals housed in primary barrier system in ABSL-3
 - Rigorous adherence to additional respiratory protection and clothing change protocols
 - Use of negative pressure HEPA-filtered respirators or PAPRs
 - Use of HEPA filtration for treatment of laboratory exhaust air
 - Personal showers prior to exiting laboratory



Risk Assessment for Work with Recombinant or Reassortant Influenza Viruses

- **Considerations for protocol-driven risk assessment should include:**
 - **Gene constellation used**
 - **Number of years since HA and NA genes circulated among humans**
 - **Biocontainment level recommended for parental strains**
 - **Evidence of clonal purity and phenotypic stability**
 - **Clear evidence of attenuation determined in appropriate animal models**
 - **Demonstration of reduced virus replication compared with wild-type parent**



Occupational Health Considerations

- **Implementation of specific medical surveillance and response plan for work with:**
 - **HPAI**
 - **Other avian viruses that have infected humans**
 - **Non-contemporary strains (excluding ca vaccine donor)**
 - **1918 viruses**
 - **Reassortant or recombinant viruses of above**

- **Plans should include:**
 - **Storage of baseline serum**
 - **Annual vaccination with current vaccine**
 - **Employee counseling on disease symptoms**
 - **Protocol to monitor symptoms in individuals**
 - **Protocol for response to suspected lab-acquired infection**
 - **Availability of influenza antivirals for post-exposure prophylaxis and/or treatment**



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- **Members of Influenza BMBL Subcommittee**

