

NATIONAL INSTITUTES OF HEALTH
RECOMBINANT DNA ADVISORY COMMITTEE
BIOSAFETY WORKING GROUP

Risk Group Classification and Risk Assessment for Research with Non-
Contemporary Strains of Human Influenza Viruses, and Highly Pathogenic Avian
Influenza Viruses

Building 1, Wilson Hall
NIH Campus
June 24, 2008

Agenda

- 10:30 AM **Call to Order and Opening Remarks**
- Jacqueline A. Corrigan-Curay, J.D., M.D., Office of the Director, National Institutes of Health (NIH), Bethesda, MD
- Session I* ***Non-Contemporary Strains of Influenza Viruses H2N2 and 1918***
- 10:40 AM **Epidemiology of Non-Contemporary Strains of Influenza Viruses: H2N2 and 1918 Influenza Viruses**
- Disease burden
 - Morbidity and mortality
- Jeffrey K. Taubenberger, M.D., Ph.D., National Institute of Allergy and Infectious Diseases (NIAID), NIH, Bethesda, MD
- 11:00 AM **H2N2: Review of Data on Effectiveness of Antivirals and Vaccines**
- John Treanor, M.D., University of Rochester, Rochester, NY
- 11:20 AM **1918 Influenza Virus and Biosafety**
- Review of Centers for Disease Control and Prevention oversight of research with fully reconstructed 1918 influenza virus
 - Review of recommendations in the *Biosafety in Microbiological and Biomedical Laboratories* manual for research with fully reconstructed 1918 influenza and recombinant viruses containing 1918 sequence
- Jacqueline M. Katz, Ph.D., Centers for Disease Control and Prevention (CDC), Atlanta, GA

11:40 AM

Data on Efficacy of Antivirals for 1918 Influenza Virus

- Summary of data on effectiveness of antivirals for fully reconstructed 1918 and/or recombinant influenza viruses containing 1918 sequence

Terrence M. Tumpey, Ph.D., CDC, Atlanta, GA

12 NOON

Immunogenicity of Influenza Viruses with Genes from 1918 Influenza Virus: Implications for Vaccines

Terrence M. Tumpey, Ph.D., CDC, Atlanta, GA

12:20 PM

BREAK/DISTRIBUTION OF LUNCH

12:40 PM

Working Lunch Discussion Questions

Moderator: Howard J. Federoff, M.D., Ph.D., Georgetown University Medical Center, Washington, DC

- What are the advantages and limitations of specific animal models (e.g., mouse, ferret, nonhuman primate) to predict the effectiveness of antivirals or vaccines on 1918 and H2N2 influenza viral infection in humans?
 - How comparable are the data from studies performed in different types of animals?
 - How likely are the data in animal models to predict effectiveness in humans?
- Do the available animal data indicate that antivirals would be effective in humans with influenza containing segments in addition to the HA/NA from 1918 influenza virus?
- A study with macaques (Kobasa D. et al., *Nature* 445:319) indicates that there may be differences in the regulation of type I interferon responses with 1918 influenza virus compared with contemporary influenza virus. Are there data to indicate whether this response would alter the effectiveness of antivirals?
 - Are additional antiviral studies needed in other animal models using fully reconstructed 1918 influenza or recombinant virus containing 1918 sequence (e.g., NS1) that evoke this specific cytokine effect?
- What data exist regarding whether preexisting immunity to other strains of H1N1 (either by natural infection or by contemporary vaccines) can protect against infection with 1918 influenza virus?
- Are there additional experiments that would be useful to determine the impact of antivirals or vaccines on infection with non-contemporary strains of human influenza viruses?
- What was the impact of the reemergence of H1N1 in 1977, and what insights might this provide for the potential reemergence of H2N2?

1:40 PM

BREAK

1:50 PM

Recombinant Work with 1918 and Other Influenza Viruses: Review of Data on Molecular Determinants of Virulence

Peter Palese, Ph.D., Mount Sinai School of Medicine, New York, NY

2:10 PM

Questions

Moderator: Howard J. Federoff, M.D., Ph.D.

- What is known about whether viral segments/genes other than those already identified as 1918 influenza virus virulence factors (i.e., HA, NA, NS1, PB-1-F2) might contribute to the virulence of influenza viruses?
- Is the mouse model adequate for testing virulence, or are additional data on virulence and pathogenicity using 1:7 (1 gene segment 1918) constructs needed from ferret studies?
- What additional studies would be useful to identify virulence factors?
- Are sufficient data available to determine containment levels for 1918 recombinants constructed from circulating influenza strains and certain segments, genes, or sequences of 1918 influenza virus?
- Are certain experiments particularly high risk (e.g., recombinants using certain 1918 segments with segments from certain avian or human influenza viruses)?
- Would it be possible to develop criteria to determine when containment could be lowered for research with novel 1918 viral recombinants (e.g., similar to select agent exclusion data for attenuated influenza viruses)?

3:00 PM

BREAK

Session II

Highly Pathogenic Avian Influenza Viruses

3:10 PM

Highly Pathogenic Avian Influenza Viruses: U.S. Department of Agriculture (USDA) Oversight

- Definition of highly pathogenic avian influenza viruses
- Animal and Plant Health Inspection Service (APHIS) permitting process and determination of biosafety levels
- Oversight of research with recombinant viruses containing one or more genes from highly pathogenic avian influenza viruses
- Summary of available animal models and their prediction of virulence

Frederick Doddy, D.V.M., M.S., APHIS, USDA, Riverdale, MD
David E. Swayne, D.V.M., Ph.D., Agricultural Research Service, USDA, Athens, GA

3:40 PM

H5N1 and Human Disease

- Review of cases to date
- Evidence of person-to-person transmission

Tim Uyeki, M.D., M.P.H., M.P.P., CDC, Atlanta, GA

4:10 PM

Antivirals and Vaccines for H5N1

- What is known about the genetic basis of virulence
- Preclinical and clinical data to date on effectiveness of antivirals
- Vaccine work for H5N1

Kanta Subbarao, M.D., M.P.H., NIAID, NIH, Bethesda, MD

4:30 PM

Questions

- What other pathogenic animal/avian strains of influenza virus might merit a higher risk group designation in Appendix B of the *NIH Guidelines*?
- Are there sufficient data on H5N1 virulence factors to be able to determine containment levels for certain recombinant viruses, or are additional studies needed?

5:00 PM

RAC Biosafety Working Group Discussion

Moderator: Steven Dewhurst, Ph.D., University of Rochester Medical Center, Rochester, NY

- Are additional data needed to determine whether preventive or therapeutic measures would be available for H2N2? 1918? H5N1?
- For recombinant work with each of these agents in which genes may be placed into a lower risk group of influenza virus, are there experiments that need to be done to help establish virulence up front, and if so, at what level of containment should initial research be performed?

5:30 PM

ADJOURNMENT