SAFETY SYMPOSIUM ON
PUBLIC HEALTH AND BIOSAFETY PRACTICES FOR RESEARCH WITH 1918 H1N1 INFLUENZA VIRUS

Co-Sponsored by the

NIH Recombinant DNA Advisory Committee (RAC)
and
Intragovernmental Select Agent and Toxin Technical Advisory Committee (ISATTAC)

5635 Fishers Lane
Terrace Level
Rockville, MD

December 2, 2008

8:00 AM **Welcome**

Speakers: Hugh Auchincloss, M.D., National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH)
Amy Patterson, M.D., Office of the Director, NIH
Richard Henkel, Ph.D., Division of Select Agents and Toxins, Centers for Disease Control and Prevention (CDC)

8:10 AM **1918 Influenza Virus: An Overview of the Pathogenicity of the 1918 H1N1 and Virulence Factors**

Speakers: Jeffery Taubenberger, M.D., Ph.D., NIAID, NIH
Slide Presentation

Terrence Tumpey, Ph.D., Influenza Division, CDC
Slide Presentation

8:40 AM **Current Containment and Occupational Health Practices for Work with 1918 H1N1: BMBL and CDC Influenza Division Occupational Health Practices**

Speakers: Richard Henkel, Ph.D. -- Slide Presentation

Jacqueline Katz, Ph.D., Influenza Division, CDC
Slide Presentation

9:00 AM **Development of Recommendations under the *NIH Guidelines for Research with Recombinant DNA Molecules* for Research with 1918 H1N1 Influenza Virus**

Speaker: Jacqueline Corrigan-Curay, J.D., M.D., Office of the Director, NIH -- Slide Presentation

Medical, Ethical, and Public Health Considerations in the Use of Antivirals for Prophylaxis During Research with 1918 Influenza Virus

9:10 AM **Safety and Efficacy of Antivirals for Prophylaxis and Treatment of Influenza**

Speakers: Arnold Monto, M.D., University of Michigan
Slide Presentation

Richard Whitley, M.D., University of Alabama
Slide Presentation

9:40 AM **Panel I: Safety and Efficacy of Antiviral Prophylaxis**

Moderator: Howard Federoff, M.D., Ph.D., Georgetown University, RAC Chair

Panelists: Regina Dutkowski, Ph.D., Hoffman La Roche
Arnold Monto, M.D.
Judith Ng-Cashin, M.D., GlaxoSmithKline
Barbara Styrt, M.D., M.P.H., Federal Food and Drug Administration
John Treanor, M.D., University of Rochester
Richard Whitley, M.D.

Questions:

- What is known about the safety of multi-week use of antivirals for prophylaxis against influenza?
- What is known about repeated doses of antivirals as prophylaxis?
- What is known about rotating antiviral use, e.g. oseltamivir, zanamivir, amantadine or rimantadine?
- What is known about inadvertent exposure in early pregnancy?
- Is the efficacy of antiviral post-exposure prophylaxis equivalent to pre-exposure prophylaxis?

- If antivirals are not instituted until symptoms develop, how well does this reduce:
    - Risk of influenza complications
    - Viral shedding and risk of transmission in the community
- What is the risk of fostering resistance in circulating strains of influenza? 1918 H1N1?

10:10 AM **Plenary Discussion of Questions**

11:10 AM **BREAK**

11:25 AM **Ethical Considerations in Mandating Prophylaxis**

Speaker: Thomas May, Ph.D., Medical College of Wisconsin

11:40 AM **Panel II**: **Ethical and Public Health Considerations for Use of Pre-Exposure Antiviral Prophylaxis**

Moderators: Eileen Ostlund, D.V.M, M.S., Ph.D., Animal and Plant Health Inspection Service, U.S. Department of Agriculture
Robyn Shapiro, J.D., Medical College of Wisconsin

Panelists: David Henderson, M.D., Clinical Center, NIH
Thomas May, Ph.D.
Michael Osterholm, Ph.D., M.P.H., University of Minnesota
John Tam, Ph.D., Consultant, Global Influenza Division, World Health Organization
Tim Uyeki, M.D., M.P.H., M.P.P., Influenza Division, CDC (*via teleconference*)

Questions:

- The 1918 H1N1 virus exists only in the laboratory, is associated with significant morbidity and mortality historically in humans and in current animal studies, and is highly transmissible. In light of this, should the public health objective be to prevent <u>any</u> researcher from developing an active case of 1918 H1N1 that could be spread to the public, or is it acceptable to be prepared to contain the infection once in the community? What are the ethical and public health considerations in this regard?
- Is our ethical obligation to protect the public higher because this virus was re-created in the laboratory?

- Scenario: A 1918 influenza researcher living in an urban setting becomes symptomatic and seeks treatment within 24 hours of developing symptoms. At that point he/she may have been infectious for more than 24 hours
    - Would the circle of potential candidates be small enough to contain and outbreak? What if, during the day prior to developing symptoms, the researcher traveled by air or attended a crowded public event?
- Is antiviral prophylaxis warranted absent known exposure?

12:15 PM **Break and Distribution of Lunches**

12:30 PM **Plenary Lunch Discussion of Panel II Questions**

Risk Management: Biosafety Containment, Practices and Infection Control

1:30 PM **NIH Intramural Program: Proposed Biosafety Containment and Use of Prophylaxis for 1918 H1N1**

Speakers: Brian Murphy, Ph.D., NIAID, NIH -- Slide Presentation

Kanta Subbarao, M.D., NIAID, NIH
Slide Presentation

Deborah Wilson, Ph.D., Division of Occupational Health and Safety, NIH -- Slide Presentation

1:45 PM **Panel III: Antiviral Prophylaxis: Implications for Determining Biosafety Containment Level and Practices**

Moderators: Stephen Dewhurst, Ph.D., University of Rochester
Dennis M. Dixon, Ph.D., NIAID, NIH

Panelists: Richard Henkel, Ph.D.
Leslie Hofherr, M.S., M.P.H., Lovelace Respiratory Research Institute
Joseph Kanabrocki, Ph.D., University of Chicago
Michael Osterholm, Ph.D., M.P.H.
Kanta Subbarao, M.D. M.P.H.
David Weber, M.D., M.P.H, University of North Carolina

Questions:

- What do we know about exposures for investigators working at BSL3+ containment:
  - Evidence of subclinical disease from seroconversion
  - Clinical disease
- Define what expected added safety to the individual or to the population can be obtained from the use of antiviral drugs continuously over and above that of BSL3 with enhancements and procedures?
- Assess risk with pre-exposure prophylactic use and added degree of safety achieved with use?
- Assess risk with therapeutic use in conjunction with isolation of infected laboratory worker?
- Should prophylaxis be used for all/any experiments with the entire 1918 H1N1?
- Would researchers be expected to structure their research to be able to take prophylaxis for a certain number of weeks?
- Are there certain high risk experiments that might justify use, for example certain animal studies?
- If use of pre-exposure prophylaxis is not considered to be part of enhanced practices, is BL3 enhanced containment adequate?
- What are the additional protections afforded by BL-4 containment as opposed to BSL3+?

2:25 PM **Plenary Discussion of Questions**

3:25 PM **BREAK**

3:35 PM **Panel IV: Management of known Exposures to 1918 H1N1 and Laboratory Workers with Influenza Like Illness (ILI)**

Moderator: Louis Kirchhoff, M.D., University of Iowa
Deborah Wilson, Ph.D.

Panelists: Leslie Hofherr, M.S., M.P.H
Jonathan McCullers, M.D., St. Jude Children's Research Hospital
James Schmitt, M.D., Division of Occupational Health and Services, NIH
John Treanor, M.D.

Questions:

- In the event of a known or suspected exposure, what measures should be in place for quarantine or isolation?
    - Should facilities be available at the institution for self isolation?
    - Could researchers be sent home to self-isolation?
    - Does the public health threat rise to the level of required quarantine? Under what authority?
- In the event a laboratory worker becomes ill with an influenza-like illness, what should be the protocol?

4:00 PM **Plenary Discussion of Questions**

4:45 PM **Panel V: Prophylaxis for research with recombinant human influenza viruses containing some genes or segments from 1918 H1N1**

Moderator: Stephen Dewhurst, Ph.D., University of Rochester

Panelists: Jonathan McCullers, M.D.
Andrew Pekosz, Ph.D., Johns Hopkins University
Bernard Roizman, Sc.D., University of Chicago
Jeffery Taubenberger, M.D., Ph.D.
Terrence Tumpey, Ph.D.

Questions:

- If pre-exposure prophylaxis is recommended for research with the fully reconstructed 1918 H1N1, should its use be recommended for research with viruses containing only some segments, genes or sequence from 1918 H1N1?
- Should prophylaxis be considered only for constructs containing certain 1918 H1N1 genes associated with virulence (e.g., HA, NA, PB1, M, NP)?
- From a public health perspective, is the HA gene the critical one for pandemic potential?
- Should prophylaxis be required for initial experiments, but may be stopped if the specific constructs can be demonstrated to be attenuated with respect to the parent viruses?
- How could this be determined?

5:15 PM **Plenary Discussion of Questions**

6:10 PM **Closing Remarks**

6:15 PM **ADJOURNMENT**