

23 June 2009

This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.

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Chem-Bio News – Pandemic Influenza Edition #66

1. CONGRESS APPROVES \$7.65 BILLION FOR PANDEMIC FLU RESPONSE:

“Responding to lobbying by the Obama administration and public health advocates, Congress last week approved \$7.65 billion for battling pandemic influenza, more than three times what the House and Senate had earlier proposed.”

2. THE ROLE OF THE DEPARTMENT OF DEFENSE DURING A FLU PANDEMIC: *“This report will focus largely on the role of the Department of Defense (DOD) in supporting the nation's domestic response effort, although it will also touch on DOD's international role.”*

3. FUNCTIONAL SIGNIFICANCE OF THE HEMADSORPTION ACTIVITY OF INFLUENZA VIRUS NEURAMINIDASE AND ITS ALTERATION IN PANDEMIC

VIRUSES: *“Our data indicate that the hemadsorption site serves to enhance the catalytic efficiency of NA and they suggest that, in addition to changes in the receptor-binding specificity of the hemagglutinin, alterations of the NA are needed for the emergence of pandemic influenza viruses.”*

4. OPTIMAL DOSING AND DYNAMIC DISTRIBUTION OF VACCINES IN AN INFLUENZA PANDEMIC:

“However, if prevalence at vaccination is above 1%, effectiveness is much reduced, emphasizing the need for other control measures.”

5. NONREPLICATING VACCINIA VIRUS VECTORS EXPRESSING THE H5 INFLUENZA VIRUS HEMAGGLUTININ PRODUCED IN MODIFIED VERO CELLS INDUCE ROBUST

PROTECTION: *“Thus, the nonreplicating recombinant vaccinia virus vectors are promising vaccine candidates that induce a broad immune response and can be produced in an egg-independent and adjuvant-independent manner in a proven vector system.”*

6. RUSSIA 'TO FACE SWINE FLU WAVE IN NOVEMBER': *“Russia will face a wave of A/H1N1 influenza cases in November, the head of the Russian Academy of Sciences' Influenza Research Institute said Monday.”*

CB Daily Report

CONGRESS APPROVES \$7.65 BILLION FOR PANDEMIC FLU RESPONSE

By Robert Roos

CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)

June 22, 2009

“Responding to lobbying by the Obama administration and public health advocates, Congress last week approved \$7.65 billion for battling pandemic influenza, more than three times what the House and Senate had earlier proposed.

The money was included in a \$106 billion supplemental appropriation bill dedicated mostly to funding the military campaigns in Iraq and Afghanistan. The Senate passed the bill Jun 18, following House passage 2 days earlier.

Most of the pandemic money is for activities by the Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC), but the bill includes \$350 million to boost state and local capacity for responding to the novel H1N1 flu pandemic.

According to a House Appropriations Committee summary of the legislation, it provides \$1.5 billion in fiscal year 2009 money and \$5.8 billion in "contingent emergency appropriations" for HHS and the CDC.

The funds are to be used for expanding surveillance, increasing federal stockpiles of drugs and medical supplies, and developing, buying, and administering vaccines.

The bill also includes \$50 million for distribution by the US Agency for International Development to help countries respond to pandemic flu.”

The full article can be found at: <http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/jun2209funding.html>

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THE ROLE OF THE DEPARTMENT OF DEFENSE DURING A FLU PANDEMIC

By Lawrence Kapp and Don J. Jansen

Congressional Research Service

June 04, 2009

“A flu pandemic is a worldwide epidemic of an influenza virus. As such, the United States’ response to a flu pandemic would have both international and domestic components. Additionally, the domestic response effort would include contributions from every governmental level (local, state, tribal, and federal), non-governmental organizations, and the private sector. This report will focus largely on the role of the Department of Defense (DOD) in supporting the nation’s domestic response effort, although it will also touch on

DOD's international role.

The Department of State would lead the federal government's international response efforts, while the Department of Homeland Security and the Department of Health and Human Services would lead the federal government's domestic response. The Department of Defense would likely be called upon to support both the international and domestic efforts. An analysis of the tasks assigned by the National Strategy for Pandemic Influenza Implementation Plan indicates that DOD's role during a flu pandemic would center on the following objectives: assisting in disease surveillance; assisting partner nations, particularly through military-to-military assistance; protecting and treating US forces and dependents; and providing support to civil authorities in the United States.

With respect to providing support to civil authorities in the United States, the types of defense support which would likely be in greatest demand during a flu pandemic include: providing disease surveillance and laboratory diagnostics; transporting response teams, vaccines, medical equipment, supplies, diagnostic devices, pharmaceuticals and blood products; treating patients; evacuating the ill and injured; processing and tracking patients; providing base and installation support to federal, state, local, and tribal agencies; controlling movement into and out of areas, or across borders, with affected populations; supporting law enforcement; supporting quarantine enforcement; restoring damaged public utilities; and providing mortuary services. Note, however, that DOD's ability to support these requests would be limited by its national defense and force protection responsibilities. The two principal ways in which defense support could be provided to civil authorities are by way of an "immediate response," or in response to a formal "request for assistance" (RFA). Additionally, in extreme circumstances the federal government may expedite or suspend the RFA process and initiate a "proactive federal response."

National Guard personnel would almost certainly be involved in domestic response efforts as members of their state militia under the control of their governor. Current DOD plans do not anticipate federal mobilization of the National Guard or Reserves to respond to a flu pandemic. However, these plans could be modified if circumstances warranted it (for example, if the severity of the pandemic significantly exceeded DOD's planning assumptions). In the event such a federal mobilization is contemplated, an important consideration would be the impact it would have on any response efforts that were already occurring at the state and local levels. For example, the activation of Reserve and National Guard medical personnel may pull them out of local hospitals where they are already engaged in the response effort, thereby undermining state and local response efforts."

The full article can be found at: http://assets.opencrs.com/rpts/R40619_20090604.pdf

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FUNCTIONAL SIGNIFICANCE OF THE HEMADSORPTION ACTIVITY OF INFLUENZA VIRUS NEURAMINIDASE AND ITS ALTERATION IN PANDEMIC VIRUSES

Biotech Week
June 24, 2009

"Human influenza viruses derive their genes from avian viruses. The neuraminidase (NA) of the avian viruses has, in addition to the catalytic site, a separate sialic acid binding site (hemadsorption site) that is not present in human viruses."

"The biological significance of the NA hemadsorption activity in avian influenza viruses remained elusive. A sequence database analysis revealed that the NAs of the majority of human H2N2 viruses isolated during the influenza pandemic of 1957 differ from their putative avian precursor by amino acid substitutions in the hemadsorption site. We found that the NA of a representative pandemic virus A/Singapore/1/57 (H2N2) lacks hemadsorption activity and that a single reversion to the avian-virus-like sequence (N367S) restores hemadsorption. Using this hemadsorption-positive NA, we generated three NA variants with substitutions S370L, N400S and W403R that have been found in the hemadsorption site of human H2N2 viruses. Each substitution abolished hemadsorption activity. Although, there was no correlation between hemadsorption activity of the NA variants and their enzymatic activity with respect to monovalent substrates, all four hemadsorption-negative NAs desialylated macromolecular substrates significantly slower than did the hemadsorption-positive counterpart. The NA of the 1918 pandemic virus A/Brevig Mission/1/18 (H1N1) also differed from avian N1 NAs by reduced hemadsorption activity and less efficient hydrolysis of macromolecular substrates."

"Our data indicate that the hemadsorption site serves to enhance the catalytic efficiency of NA and they suggest that, in addition to changes in the receptor-binding specificity of the hemagglutinin, alterations of the NA are needed for the emergence of pandemic influenza viruses."

The full article can be found at: (J. Uhlenhorff, et. al., "Functional significance of the hemadsorption activity of influenza virus neuraminidase and its alteration in pandemic viruses". Archives of Virology, 2009; 154(6):945-57). Link not available.

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OPTIMAL DOSING AND DYNAMIC DISTRIBUTION OF VACCINES IN AN INFLUENZA PANDEMIC

Drug Week

June 26, 2009

"According to recent research from Australia, "Limited production capacity and delays inherent in vaccine development are major hurdles to the widespread use of vaccines to mitigate the effects of a new influenza pandemic. Antigen-sparing vaccines have the most potential to increase population coverage but may be less efficacious."

"The authors explored this trade-off by applying simple models of influenza transmission and dose response to recent clinical trial data. In this paper, these data are used to illustrate an approach to comparing vaccines on the basis of antigen supply and inferred efficacy. The effects of delays in matched vaccine availability and seroconversion on epidemic size during pandemic phase 6 were also studied. The authors infer from trial data that population benefits stem from the use of low-antigen vaccines. Delayed availability of a matched

vaccine could be partially alleviated by using a 1-dose vaccination program with increased coverage and reduced time to full protection. Although less immunogenic, an overall attack rate of up to 6% lower than a 2-dose program could be achieved."

"However, if prevalence at vaccination is above 1%, effectiveness is much reduced, emphasizing the need for other control measures."

The full article can be found at: (J. Wood, et. al., "Optimal dosing and dynamic distribution of vaccines in an influenza pandemic". American Journal of Epidemiology, 2009; 169 (12):1517-24). Link not available.

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NONREPLICATING VACCINIA VIRUS VECTORS EXPRESSING THE H5 INFLUENZA VIRUS HEMAGGLUTININ PRODUCED IN MODIFIED VERO CELLS INDUCE ROBUST PROTECTION

Medicine & Law Weekly
June 26, 2009

"The timely development of safe and effective vaccines against avian influenza virus of the H5N1 subtype will be of the utmost importance in the event of a pandemic. Our aim was first to develop a safe live vaccine which induces both humoral and cell-mediated immune responses against human H5N1 influenza viruses and second, since the supply of embryonated eggs for traditional influenza vaccine production may be endangered in a pandemic, an egg-independent production procedure based on a permanent cell line."

"In the present article, the generation of a complementing Vero cell line suitable for the production of safe poxviral vaccines is described. This cell line was used to produce a replication-deficient vaccinia virus vector H5N1 live vaccine, dVV-HA5, expressing the hemagglutinin of a virulent clade 1 H5N1 strain. This experimental vaccine was compared with a formalin-inactivated whole-virus vaccine based on the same clade and with different replicating poxvirus-vectored vaccines. Mice were immunized to assess protective immunity after high-dose challenge with the highly virulent A/Vietnam/1203/2004(H5N1) strain. A single dose of the defective live vaccine induced complete protection from lethal homologous virus challenge and also full cross-protection against clade 0 and 2 challenge viruses. Neutralizing antibody levels were comparable to those induced by the inactivated vaccine. Unlike the whole-virus vaccine, the dVV-HA5 vaccine induced substantial amounts of gamma interferon-secreting CD8 T cells."

"Thus, the nonreplicating recombinant vaccinia virus vectors are promising vaccine candidates that induce a broad immune response and can be produced in an egg-independent and adjuvant-independent manner in a proven vector system."

The full article can be found at: (J. Mayrhofer, et. al., "Nonreplicating Vaccinia Virus Vectors Expressing the H5 Influenza Virus Hemagglutinin Produced in Modified Vero Cells Induce Robust Protection". Journal of Virology, 2009; 83(10):5192-5203). Link not available.

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RUSSIA 'TO FACE SWINE FLU WAVE IN NOVEMBER'

RIA Novosti

June 22, 2009

"Russia will face a wave of A/H1N1 influenza cases in November, the head of the Russian Academy of Sciences' Influenza Research Institute said Monday.

"Summer is not the time for flu in Russia... In November we will see the first real wave," Oleg Kiselyov told journalists."

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