

13 January 2009

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## **Chem-Bio News – Pandemic Influenza Edition # 43**

**1. HHS REPORTS PROGRESS ON CELL-BASED PANDEMIC VACCINES:** *“The 19-page progress report by HHS Secretary Mike Leavitt, posted yesterday on the HHS Web site, also says that biotechnology companies hope to have point-of-care tests that can distinguish between pandemic and seasonal flu viruses ready to submit to the Food and Drug Administration (FDA) by the end of this year.”*

**2. NO DANGEROUS CHANGES SEEN IN HONG KONG H9N2 VIRUS:** *“Hong Kong health officials reported today that the H9N2 avian influenza virus that recently infected a 2-month-old girl from mainland China has not acquired any genes from human-adapted flu viruses, implying that it is unlikely to pose a major danger to humans.”*

**3. GUIDANCE FOR INDUSTRY POSTMARKETING ADVERSE EVENT REPORTING FOR MEDICAL PRODUCTS AND DIETARY SUPPLEMENTS DURING AN INFLUENZA PANDEMIC:** *“FDA anticipates that during an influenza pandemic, industry and FDA workforces may be reduced, while reporting of adverse events<sup>2</sup> related to widespread use of influenza-related products may increase.”*

**4. CDC DIRECTOR OUT JAN. 20:** *“Obama's team asked for Gerberding's resignation; chief operating officer will be in charge until new director is named.”*

**5. COMPATIBILITY AMONG POLYMERASE SUBUNIT PROTEINS IS A RESTRICTING FACTOR IN REASSORTMENT BETWEEN EQUINE H7N7 AND HUMAN H3N2 INFLUENZA VIRUSES:** *“These results indicate substantial incompatibility among the gene products of the two test viruses, a critical role for the RNP complex in the generation of reassortant viruses, and a functional interaction of PB2 and PA.”*

**6. ONGOING EVOLUTION OF SWINE INFLUENZA VIRUSES: A NOVEL REASSORTANT:** *“Analysis of GenBank sequence data reveals numerous reassortment events in recent years, demonstrating ongoing evolution of swine influenza viruses.”*

**7. EXPERIMENTAL EVOLUTION OF HUMAN INFLUENZA VIRUS H3 HEMAGGLUTININ**

**IN THE MOUSE LUNG IDENTIFIES ADAPTIVE REGIONS IN HA1 AND HA2:** *"This study has identified adaptive sites and regions within the HA1 and HA2 subunits that may guide future studies of viral adaptation and evolution in nature."*

## CB Daily Report

### Chem-Bio News

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#### **HHS REPORTS PROGRESS ON CELL-BASED PANDEMIC VACCINES**

By Lisa Schnirring and Robert Roos

CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)  
January 9, 2009

"In a progress report on federal pandemic influenza planning efforts, the US Department of Health and Human Services (HHS) says several companies working under federal contracts are on track to develop cell culture–based pandemic flu vaccines.

The 19-page progress report by HHS Secretary Mike Leavitt, posted yesterday on the HHS Web site, also says that biotechnology companies hope to have point-of-care tests that can distinguish between pandemic and seasonal flu viruses ready to submit to the Food and Drug Administration (FDA) by the end of this year.

The report is the sixth progress update since March 2006 and comes as Leavitt nears the end of his tenure as secretary. In his introduction, Leavitt wrote that HHS has accomplished a great deal over the past 33 months but still has much to do. "Preparation is a continuum. Each day that we prepare brings us closer to being ready," he said.

The report says that all six companies that HHS contracted with in 2006 to develop cell-based flu vaccines are moving toward FDA approval of their vaccines and that five are on target for reaching their contract milestones."

The full article can be found at: <http://www.cidrap.umn.edu/cidrap/content/influenza/panflu/news/jan0909planning-br.html>

[Return to Top](#)

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#### **GENE SEQUENCING OF H9N2 VIRUS SHOWS AVIAN ORIGIN**

Department of Health, The Government of the Hong Kong Special Administrative Region  
News Release  
January 7, 2009

"The Centre for Health Protection (CHP) of the Department of Health today (January 7) completed gene sequencing on an influenza A (H9N2) virus found in a two-month-old girl in December 2008 and the results indicated all the genes were of avian origin."

"The epidemiological and genetic findings so far suggest that the H9N2 virus has shown no signs of increased risk for human-to-human transmission," the spokesman said."

The full article can be found at: <http://www.dh.gov.hk/english/press/2009/090107-2.html>

[Return to Top](#)

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## **GUIDANCE FOR INDUSTRY POSTMARKETING ADVERSE EVENT REPORTING FOR MEDICAL PRODUCTS AND DIETARY SUPPLEMENTS DURING AN INFLUENZA PANDEMIC**

US Food and Drug Administration Draft Guidance  
December 2008

"This guidance provides recommendations to industry regarding postmarketing adverse event reporting for drugs, biologics, medical devices and dietary supplements during an influenza pandemic. FDA anticipates that during an influenza pandemic, industry and FDA workforces may be reduced, while reporting of adverse events<sup>2</sup> related to widespread use of influenza-related products may increase. The extent of these possible changes is unknown. This guidance discusses FDA's intended approach to enforcement of adverse event reporting requirements for medical products and dietary supplements during the Federal Government Response Stages<sup>3</sup> of an influenza pandemic. FDA believes this approach will make it possible for firms with reporting responsibilities to focus their limited resources on reports related to influenza-related products and other specific types of reports indicated in this guidance, as well as on reports related to any other products presenting special concerns as specified by FDA.<sup>4</sup>"

The full article can be found at: <http://www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-D-0610-gdl.pdf>

[Return to Top](#)

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## **CDC DIRECTOR OUT JAN. 20**

By Alison Young  
The Atlanta Journal-Constitution  
January 10, 2009

"Obama's team asked for Gerberding's resignation; chief operating officer will be in charge until new director is named.

The controversial tenure of CDC Director Julie Gerberding will end Jan. 20 — after Barack Obama is sworn in as president, employees of the Atlanta-based agency were informed in an e-mail sent late Friday evening.

Until a new director is named, the Centers for Disease Control and Prevention's chief

operating officer, Bill Gimson, will be acting director, the e-mail said."

"Gerberding's six years leading one of the nation's most trusted institutions were marked by numerous controversies, from allegations that she allowed politics to interfere with science to concerns that her strategic decisions incapacitated the agency's ability to respond in a public health crisis.

Through it all, Gerberding maintained that the changes she initiated at the agency had made it stronger and better able to do its job in a post-9/11 world. During her tenure, she has expressed pride in the agency's response to outbreaks of SARS and monkeypox, its groundbreaking research into avian influenza and other diseases. In the past year, she increasingly spoke out on topics related to health care reform — a key topic in the presidential election — and the importance of preventing disease before it needs treatment."

The full article can be found at: <http://www.ajc.com/search/content/news/stories/2009/01/10/cdc.html>

[Return to Top](#)

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## **COMPATIBILITY AMONG POLYMERASE SUBUNIT PROTEINS IS A RESTRICTING FACTOR IN REASSORTMENT BETWEEN EQUINE H7N7 AND HUMAN H3N2 INFLUENZA VIRUSES**

Biotech Week

January 14, 2009

"To identify factors that restrict the generation of reassortant viruses, we cotransfected human embryonic kidney cells with plasmids for the synthesis of viral RNAs of both A/equine/Prague/1/56 (Prague; H7N7) and A/Yokohama/2017/03 (Yokohama; H3N2) viruses together with the supporting protein expression plasmids."

"Of the possible 256 genotypes, we identified 29 genotypes in 120 randomly plaque-picked reassortants examined. Analyses of these reassortants suggested that the formation of functional ribonucleoprotein (RNP) complexes was a restricting factor, a finding that correlated with the activities of RNP complexes composed of different combinations of the proteins from the two viruses, as measured in a minigenome assay. For at least one nonfunctional RNP complex (i.e., Prague PB2, Prague PB1, Yokohama PA, and Prague NP), the lack of activity was due to the inability of the three polymerase subunit proteins to form a heterotrimer. Adaptation of viruses possessing a gene encoding a chimera of the PA proteins of the two viruses and the remaining genes from Prague virus resulted in compensatory mutations in the PB2 and/or PA protein."

"These results indicate substantial incompatibility among the gene products of the two test viruses, a critical role for the RNP complex in the generation of reassortant viruses, and a functional interaction of PB2 and PA."

The full article can be found at: (C.J. Li, et. al., "Compatibility among Polymerase Subunit Proteins Is a Restricting Factor in Reassortment between Equine H7N7 and Human H3N2

Influenza Viruses". *Journal of Virology*, 2008;82(23):11880-11888). Link not available.

[Return to Top](#)

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## **ONGOING EVOLUTION OF SWINE INFLUENZA VIRUSES: A NOVEL REASSORTANT**

Health & Medicine Week

January 12, 2009

"A novel H3N2 influenza virus strain isolated in Germany from pigs with clinical symptoms of influenza is described. It was characterised by neutralisation test, hemagglutination inhibition test and complete sequencing of the genome."

"The data demonstrate the emergence of a H3N2 reassortant with the human-like HAH3 gene of prevalent European porcine H3N2 influenza viruses and a NAN2 gene of the European porcine H1N2 viruses. The gene segments of the internal proteins are avian-like, consistent with European porcine influenza viruses."

"Analysis of GenBank sequence data reveals numerous reassortment events in recent years, demonstrating ongoing evolution of swine influenza viruses."

The full article can be found at: (R. Zell, et. al., "Ongoing evolution of swine influenza viruses: a novel reassortant". *Archives of Virology*, 2008;153(11):2085-2092). Link not available.

[Return to Top](#)

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## **EXPERIMENTAL EVOLUTION OF HUMAN INFLUENZA VIRUS H3 HEMAGGLUTININ IN THE MOUSE LUNG IDENTIFIES ADAPTIVE REGIONS IN HA1 AND HA2**

Health & Medicine Week

January 12, 2009

"The genetic basis for virulence and host switching in influenza A viruses (FLUAV) is largely unknown. Because the hemagglutinin (HA) protein is a determinant of these properties, HA evolution was mapped in an experimental model of mouse lung adaptation."

"Variants of prototype A/Hong Kong/1/68 (H3N2) (wild-type [wt] HK) human virus were selected in both longitudinal and parallel studies of lung adaptation. Mapping of HA mutations found in 11 independently derived mouse-adapted populations of wt HK identified 27 mutations that clustered within two distinct regions in or near the globular frameworks of the HA1 and HA2 subunits. The adaptive mutations demonstrated multiple instances of convergent evolution involving four amino acid positions (162, 210, and 218 in HA1 and 154 in HA2). By use of reverse genetics, convergent HA mutations were shown to affect cell tropism by enhancing infection and replication in primary mouse tracheal epithelial cells in vitro and mouse lung tissue in vivo. Adaptive HA mutations were multifunctional, affecting both median pH of fusion and receptor specificity. Specific mutations within both adaptive

regions were shown to increase virulence in a mouse lung model. The occurrence of mutations in the HA1 and HA2 adaptive regions of natural FLUAV host range and virulent variants of avian and mammalian viruses is discussed."

"This study has identified adaptive sites and regions within the HA1 and HA2 subunits that may guide future studies of viral adaptation and evolution in nature."

The full article can be found at: (L. Keleta, et. al., "Experimental Evolution of Human Influenza Virus H3 Hemagglutinin in the Mouse Lung Identifies Adaptive Regions in HA1 and HA2. *Journal of Virology*", 2008; 82(23): 11599-11608). Link not available.

[Return to Top](#)

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