

11 August 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 #73

1. PANDEMIC INFLUENZA VACCINE MANUFACTURING PROCESS AND TIMELINE:

"It takes approximately five to six months for the first supplies of approved vaccine to become available once a new strain of influenza virus with pandemic potential is identified and isolated."

2. STATES TO DESIGNATE PROVIDERS TO GIVE H1N1 VACCINES: *"State health departments will decide which providers will administer the pandemic H1N1 influenza vaccine this fall, and a single company will be the distributor for all the doses, it was announced today."*

3. ORIGINS AND EVOLUTIONARY GENOMICS OF THE 2009 SWINE-ORIGIN H1N1 INFLUENZA A EPIDEMIC: *"We show that it was derived from several viruses circulating in swine, and that the initial transmission to humans occurred several months before recognition of the outbreak."*

4. CDC ADVISES AGAINST CLOSING SCHOOLS DURING H1N1 OUTBREAKS: *"Federal officials recommended today that schools should not close down during novel H1N1 influenza outbreaks, though they emphasized that the advice is a guideline and that decisions should be made based on local conditions."*

5. ASSESSMENT OF LOCAL PUBLIC HEALTH WORKERS' WILLINGNESS TO RESPOND TO PANDEMIC INFLUENZA THROUGH APPLICATION OF THE EXTENDED PARALLEL PROCESS MODEL [EXTENDED PARALLEL PROCESS MODEL]: *"Local health department employees with a perception of high threat and high efficacy – i.e., those fitting a 'concerned and confident' profile in the EPPM analysis – had the highest declared rates of willingness to respond to an influenza pandemic if required by their agency, which was 31.7 times higher than those fitting a 'low threat/low efficacy' EPPM profile."*

6. POSSIBLE FIX FOUND FOR PROBLEM OF LOW YIELD IN PANDEMIC VACCINE PRODUCTION: *"John Wood of the U.K.'s National Institute for Biological Standards and Control said an improved version of the seed strain his lab produced in May seems to generate a virus yield that is on a par with what manufacturers get when they make seasonal flu vaccine."*

7. IRAN BANS PILGRIMS FROM ATTENDING HAJJ: *“The Iranian health ministry has banned Iranian pilgrims from attending the annual Hajj pilgrimage in Saudi Arabia, due to the risk of the spread of swine flu, state media reported Thursday.”*

CB Daily Report

Chem-Bio News

PANDEMIC INFLUENZA VACCINE MANUFACTURING PROCESS AND TIMELINE

World Health Organization

August 06, 2009

“It takes approximately five to six months for the first supplies of approved vaccine to become available once a new strain of influenza virus with pandemic potential is identified and isolated. These months are needed because the process of producing a new vaccine involves many sequential steps, and each of these steps requires a certain amount of time to complete. The vaccine development process from start (obtaining a virus sample) to end (availability of vaccine for use) is summarized below.

Activities at WHO Collaborating Centers

1. Identification of a new virus: As part of a network set up for surveillance, laboratories around the world routinely collect samples of circulating influenza viruses and submit these to WHO Collaborating Centres for Reference and Research on Influenza for analysis. The first step towards the production of a pandemic vaccine starts when a Centre detects a novel influenza virus that differs significantly from circulating strains and reports this finding to WHO.
2. Preparation of the vaccine strain (called vaccine virus): The virus must first be adapted for use in manufacturing vaccine. To make the vaccine virus less dangerous and better able to grow in hen's eggs (the production method used by most manufacturers), the virus is mixed with a standard laboratory virus strain and the two are allowed to grow together. After a while, a hybrid is formed which contains the inner components of the laboratory strain, and the outer components of the pandemic strain. It takes roughly three weeks to prepare the hybrid virus.
3. Verification of the vaccine strain: After its preparation, the hybrid virus needs to be tested to make sure that it truly produces the outer proteins of the pandemic strain, is safe and grows in eggs. Upon completion of this process, which takes roughly another three weeks, the vaccine strain is distributed to vaccine manufacturers.
4. Preparation of reagents to test the vaccine (with reference reagents): In parallel, WHO Collaborating Centres produce standardized substances (called reagents) that are given to all vaccine manufacturers to enable them to measure how much virus they are producing, and to ensure they are all packaging the correct dose of vaccine. This requires at least three months and often represents a bottleneck for manufacturers.

Activities at vaccine manufacturers

1. Optimization of virus growth conditions: The vaccine manufacturer takes the hybrid vaccine virus that it has received from the WHO laboratories, and tests different growth conditions in eggs to find the best conditions. This process requires roughly three weeks.
2. Vaccine bulk manufacture: For most influenza vaccine production, this is performed in nine to twelve-days old fertilized hen's eggs. The vaccine virus is injected into thousands of eggs, and the eggs are then incubated for two to three days during which time the virus multiplies. The egg white, which now contains many millions of vaccine viruses, is then harvested, and the virus is separated from the egg white. The partially pure virus is killed with chemicals. The outer proteins of the virus are then purified and the result is several hundred or thousand liters of purified virus protein that is referred to as antigen, the active ingredient in the vaccine. Producing each batch, or lot, of antigen takes approximately two weeks, and a new batch can be started every few days. The size of the batch depends on how many eggs a manufacturer can obtain, inoculate and incubate. Another factor is the yield per egg. When one batch has been produced, the process is repeated as often as needed to generate the required amount of vaccine.
3. Quality control: This can only begin once the reagents for testing the vaccine are supplied by WHO laboratories, as described above. Each batch is tested and the sterility of bulk antigen is verified. This process takes two weeks.
4. Vaccine filling and release: The batch of vaccine is diluted to give the desired concentration of antigen, and put into vials or syringes, and labeled. A number of these are then tested:
 - * for sterility
 - * to confirm the protein concentration and
 - * for safety by testing in animals.

This process takes two weeks.

5. Clinical studies: In certain countries, each new influenza vaccine has to be tested in a few people to show that it performs as expected. This requires at least four weeks. In some countries this may not be required as many clinical trials were done with similar annual vaccine preparation, and the assumption is that the new pandemic vaccine will behave similarly.

Activities at regulatory agencies - regulatory approval

Before the vaccine can be sold or administered to people, regulatory approval is required. Each country has its own regulatory agency and rules. If the vaccine is made with the same processes as the seasonal influenza vaccine, and in the same manufacturing plant, this can be very rapid (one to two days). Regulatory agencies in some countries may require clinical testing before approving the vaccine, which adds to the time before the vaccine is available.

The full process, in a best case scenario, can be completed in five to six months. Then the first final pandemic vaccine lot would be available for distribution and use."

The full article can be found at: http://www.who.int/csr/disease/swineflu/notes/h1n1_vaccine_20090806/en/index.html

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STATES TO DESIGNATE PROVIDERS TO GIVE H1N1 VACCINES

By Robert Roos

CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)
August 10, 2009

"State health departments will decide which providers will administer the pandemic H1N1 influenza vaccine this fall, and a single company will be the distributor for all the doses, it was announced today.

McKesson Corp., based in San Francisco, announced it will be the central distributor of H1N1 vaccines under a contract with the Centers for Disease Control and Prevention (CDC). McKesson currently distributes vaccines under the CDC's Vaccines for Children (VFC) program.

"McKesson's role will be to distribute the vaccine to sites designated by state health departments across the country," the company said in a press release. "Each state will designate the providers who will receive and administer the vaccine."

That's different from how seasonal flu vaccines are handled, noted Jim Blumenstock, chief program officer for public health practice at the Association of State and Territorial Health Officials in Washington, DC.

"This is a government-controlled program, so it'll be the state agencies working with local partners and the CDC that will make the determination as to where the public will be able to get vaccine," Blumenstock said. "This is not like your seasonal flu [vaccination] program where healthcare providers decide whether or not they want to do it and then submit private orders."

The full article can be found at: <http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/aug1009vaccine.html>

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ORIGINS AND EVOLUTIONARY GENOMICS OF THE 2009 SWINE-ORIGIN H1N1 INFLUENZA A EPIDEMIC

Biotech Law Weekly
August 7, 2009

"In March and early April 2009, a new swine-origin influenza A (H1N1) virus (S-OIV)

emerged in Mexico and the United States(1). During the first few weeks of surveillance, the virus spread worldwide to 30 countries (as of May 11) by human-to-human transmission, causing the World Health Organization to raise its pandemic alert to level 5 of 6. This virus has the potential to develop into the first influenza pandemic of the twenty-first century."

"Here we use evolutionary analysis to estimate the time-scale of the origins and the early development of the S-OIV epidemic. We show that it was derived from several viruses circulating in swine, and that the initial transmission to humans occurred several months before recognition of the outbreak. A phylogenetic estimate of the gaps in genetic surveillance indicates a long period of unsampled ancestry before the S-OIV outbreak, suggesting that the reassortment of swine lineages may have occurred years before emergence in humans, and that the multiple genetic ancestry of S-OIV is not indicative of an artificial origin. Furthermore, the unsampled history of the epidemic means that the nature and location of the genetically closest swine viruses reveal little about the immediate origin of the epidemic, despite the fact that we included a panel of closely related and previously unpublished swine influenza isolates."

The full article can be found at: (G.J.D. Smith, et. al., "Origins and evolutionary genomics of the 2009 swine-origin H1N1 influenza A epidemic". Nature, 2009; 459(7250): 1122-U107).
Link not available.

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CDC ADVISES AGAINST CLOSING SCHOOLS DURING H1N1 OUTBREAKS

By Maryn McKenna

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

August 07, 2009

"Federal officials recommended today that schools should not close down during novel H1N1 influenza outbreaks, though they emphasized that the advice is a guideline and that decisions should be made based on local conditions.

The guidelines, composed by the Centers for Disease Control and Prevention (CDC) and released at a press briefing by the Department of Health and Human Services, build on revised guidance that the CDC issued in May. Early in the pandemic's spring wave, schools were told to close for up to 2 weeks, but the CDC changed its advice shortly afterward to say that schools should focus on keeping sick students and staff out of school.

The new advice is being issued because "once you close a school, as we saw last spring, that creates a very significant ripple effect" on parents and businesses, Janet Napolitano, secretary of the Department of Homeland Security, said during the briefing.

However, the officials said, some schools will be justified in closing if they have a high rate of infection or large numbers of students with the underlying conditions that make the virus more dangerous. "We hope no schools will have to close, but realistically, some schools will close this fall," Department of Education Secretary Arne Duncan said."

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

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ASSESSMENT OF LOCAL PUBLIC HEALTH WORKERS' WILLINGNESS TO RESPOND TO PANDEMIC INFLUENZA THROUGH APPLICATION OF THE EXTENDED PARALLEL PROCESS MODEL [EXTENDED PARALLEL PROCESS MODEL]

By Daniel J., Ran D. Balicer, Carol B. Thompson, J. Douglas Storey, Saad B. Omer, Natalie L. Semon, Steve Bayer, Lorraine V. Cheek, Kerry W. Gateley, Kathryn M. Lanza, Jane A. Norbin, Catherine C. Slemp, Jonathan M. Links

PLoS One

July 24, 2009

"We administered an online, EPPM-based survey about attitudes/beliefs toward emergency response (Johns Hopkins~Public Health Infrastructure Response Survey Tool), to local public health employees in three states between November 2006 – December 2007. A total of 1835 responses were collected for an overall response rate of 83%. With some regional variation, overall 16% of the workers in 2006-7 were not willing to "respond to a pandemic flu emergency regardless of its severity". Local health department employees with a perception of high threat and high efficacy – i.e., those fitting a 'concerned and confident' profile in the EPPM analysis – had the highest declared rates of willingness to respond to an influenza pandemic if required by their agency, which was 31.7 times higher than those fitting a 'low threat/low efficacy' EPPM profile."

The full article can be found at: <http://www.plosone.org/article/info:doi/10.1371/journal.pone.0006365>

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POSSIBLE FIX FOUND FOR PROBLEM OF LOW YIELD IN PANDEMIC VACCINE PRODUCTION

By Helen Branswell

The Canadian Press on Google News

August 06, 2009

"A British laboratory may have found a fix for the low yield problem that has been plaguing companies making swine flu vaccine, a scientist from the lab revealed Wednesday.

John Wood of the U.K.'s National Institute for Biological Standards and Control said an improved version of the seed strain his lab produced in May seems to generate a virus yield that is on a par with what manufacturers get when they make seasonal flu vaccine.

While Wood cautioned the increased yield has to be confirmed by manufacturers, any improvement would be welcome news. Manufacturers have been clamouring for the new seed strain, which the lab started shipping out Wednesday.

"Oh, they are," Wood said in an interview from Potters Bar, England, where NIBSC is located. "We have a lot of orders in the wings ready to get all the paperwork in place."

The full article can be found at: <http://www.google.com/hostednews/canadianpress/article/ALeqM5jLZrJztuTevHm9vPrqhBNbLODnyw>

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IRAN BANS PILGRIMS FROM ATTENDING HAJJ

Associated Press in the Khaleej Times

August 06, 2009

"The Iranian health ministry has banned Iranian pilgrims from attending the annual Hajj pilgrimage in Saudi Arabia, due to the risk of the spread of swine flu, state media reported Thursday.

Health Minister Kamran Baqeri-Lankarani said that the presence of over 3 million pilgrims from all over the world - including many from Iran - in Mecca and Medina would increase the risk of mass infections."

The full article can be found at: http://www.khaleejtimes.com/displayarticle.asp?xfile=data/middleeast/2009/August/middleeast_August142.xml§ion=middleeast&col=

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