

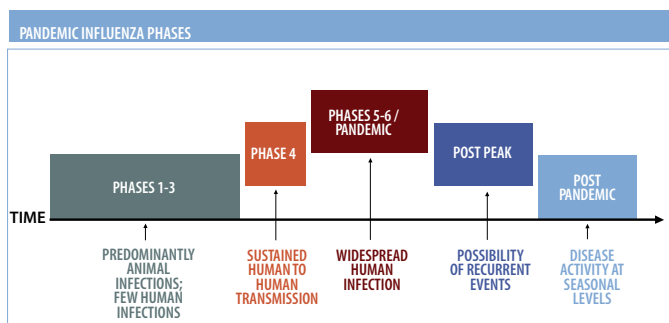
Novel Influenza A H1N1 Pandemic

Introduction

Novel H1N1 (referred to as "swine flu" early on) is a new influenza virus causing illness in people. First detected in people in the United States (US) in April 2009,¹ it is spreading from person to person, probably in much the same way as regular seasonal influenza viruses. It was originally referred to as "swine flu" because laboratory testing showed many of its genes were similar to influenza viruses that normally occur in pigs in North America. Further study has shown this new virus is very different from what normally circulates in North American pigs. It has two genes from flu viruses that normally circulate in pigs in Europe and Asia and also has avian genes and human genes. Scientists call this a "quadruple reassortant."¹

Current state of the pandemic

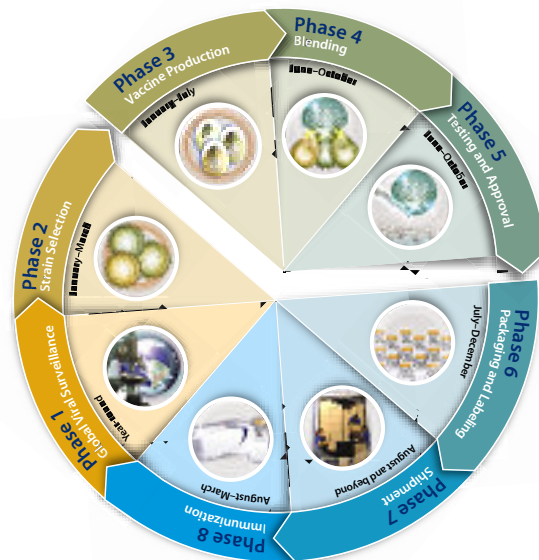
On June 11, the World Health Organization raised the level of influenza novel A (H1N1) pandemic alert to phase 6, as sustained community-level transmission of the virus is taking place in more than one region of the world. The phase does not correlate to severity of disease.



http://www.who.int/csr/disease/avian_influenza/phase/en/

Currently the pandemic is of moderate severity. Most of the cases have been mild, but even mild cases and the current level of severe cases could have a significant impact on health systems and society. The Centers for Disease Control and Prevention (CDC) stated that morbidity (0.4%) is similar to seasonal flu and significantly less than the 1918 influenza pandemic that was associated with morbidity rates of ~1%. According to data reported to the CDC through June 25, there have been 27,717 cases in the US, with 127 deaths across all states. Globally, cases have been reported in over 105 countries.

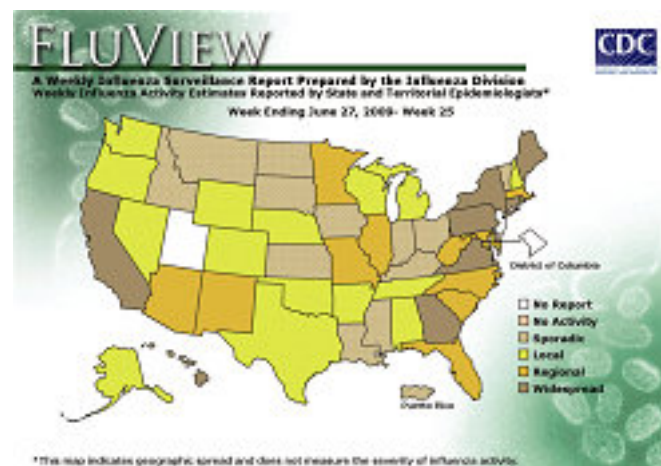
Production Cycle Wheel—Phases 3, 4, and 5 Vaccine Production



Plans for managing novel H1N1

Federal- and state-level public health officials are working together to manage the novel H1N1 pandemic. The Food and Drug Administration (FDA) and Center for Biologics Evaluation and Research (CBER) are working closely with industry to test and license novel H1N1 vaccines in time for the upcoming influenza season. The US Department of Health and Human Services (HHS), CDC, and state public health officials are refining a plan for mass immunizations in the fall, if required. In parallel, the Advisory Committee on Immunization Practices (ACIP) is considering a formal recommendation for H1N1 vaccination. The committee will be meeting late this summer to vote on a recommendation.

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<http://www.cdc.gov/flu/weekly/>

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Several key questions remain:

1. Will it be necessary to vaccinate some or all of the population against the novel H1N1 virus?
2. Which vaccine formulation will be optimal from a safety and efficacy perspective? Adjuvanted or unadjuvanted? Egg based or cell culture based?
3. If required, what is the best way to vaccinate the population? Via the public health system? Via private providers? Utilizing both public and private networks?
4. How can the public best be informed about the novel H1N1 vaccination without causing confusion about the importance of seasonal influenza vaccination?

Role of vaccines in protecting patients from novel H1N1

Currently there is no approved vaccine to protect against the novel A (H1N1) virus. Several are under development, including several candidates from Novartis Vaccines. The FDA will be evaluating the safety, efficacy, and dosing of all the vaccines. Based on the clinical trial data, the FDA will determine the appropriate dosage, how many doses are required, the length of time needed in between dose administration, and if the vaccine will be adjuvanted, unadjuvanted, or both. Finally, the FDA also will decide if the vaccine will be provided under licensure or emergency use authorization. HHS is actively involved in all aspects of developing a novel A (H1N1) vaccine and bringing it to market.

Novartis Vaccines received government orders for our proprietary adjuvant and bulk antigen for the novel A (H1N1) virus, neither of which has been approved for use by the FDA. Novartis is also a leader in developing the next generation of influenza manufacturing technology. Novartis's cell culture (non-egg based) manufacturing platform was the first to produce novel A (H1N1) lots for use in clinical trials. No cell culture vaccine product is currently licensed in the US.

Reference

1. Novel H1N1 Flu (Swine Flu) and You. Centers for Disease Control and Prevention Web site. <http://www.cdc.gov/H1N1flu/qa.htm>. Updated June 30, 2009. Accessed July 6, 2009.

The vaccine production process, with the egg-based method and the cell-based method

The majority of influenza vaccines are typically produced using embryonated egg cultures, which require long production lead times. Typically, eggs must be ordered 1 year in advance of vaccine delivery date.

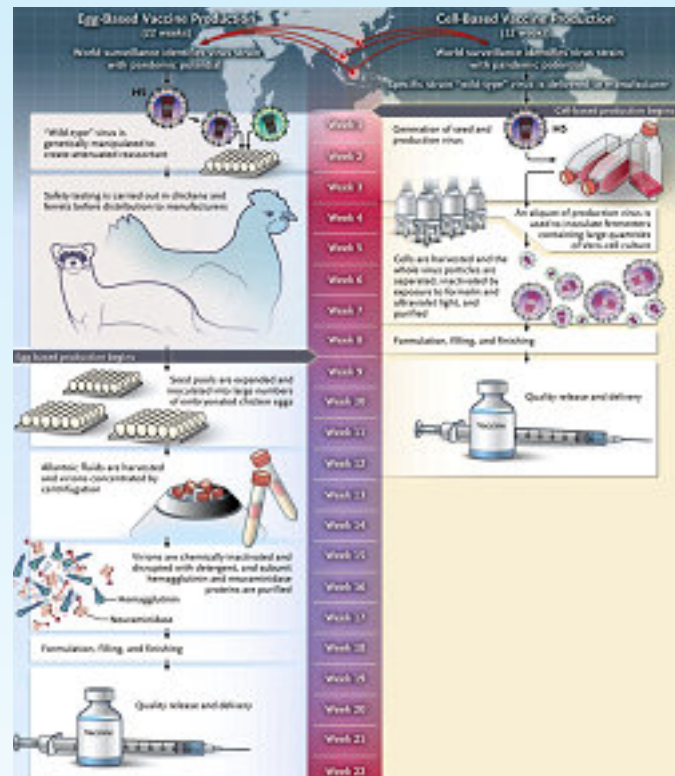


Figure from Peter W Wright. Vaccine preparedness—are we ready for the next influenza pandemic? *N Engl J Med*. 2008;358:2540-2543. Permission pending.

Vaccine production using cell cultures can be more flexible than with egg cultures. Cells are readily available and production can be adjusted to meet changes in demand.¹

Reference

1. Audsley JM, Tannock GA. Cell-based influenza vaccines progress to date. *Drugs*. 2008;68(11):1483-1491.

NOVARTIS HAS BEEN AWARDED A GRANT FOR A STATE-OF-THE-ART CELL CULTURE INFLUENZA VACCINE MANUFACTURING FACILITY



In January 2009, the HHS Biomedical Advanced Research and Development Authority (BARDA) awarded Novartis Vaccines a contract for up to USD 486 million over 8 years to support the development of cell-based influenza vaccine manufacturing facilities in Holly Springs, NC. Once completed and approved, it is expected to have the capacity to provide a pre-pandemic supply of influenza vaccine. The anticipated capacity is 150 million doses of pandemic vaccine within 6 months of declaration of an influenza pandemic.

Seasonal influenza vaccine production is also planned at this facility.