A (H1N1) Influenza Vaccine Production Process

A novel A(H1N1) influenza virus strain emerged in April 2009, with cases first reported in Mexico and the U.S. Human-to-human spread of the virus soon reached additional countries while world health officials expressed concern for a potential pandemic. As the world’s leading supplier of influenza vaccine, sanofi pasteur immediately activated its pandemic response plan and began assessing its capabilities to support public health efforts and produce a vaccine against the new strain.

The first step in developing a vaccine for A (H1N1) was obtaining a seed virus. The seed virus is a specially modified version of the virus designed to produce a vaccine in mass quantities. After world health officials analyzed and identified the dominant circulating strain, they selected virus strains and submitted them to contracted laboratories for preparation of the seed virus. The laboratories then distributed seed viruses to manufacturers to begin the production process. The laboratories will then distribute seed viruses to manufacturers to begin the production process. The seed virus is prepared using either conventional reassortment or reverse genetics techniques.

Upon receipt of the seed virus, sanofi pasteur began the development process called “passaging,” to prepare a “working seed.” Passaging is the process for acclimating virus to grow in an egg-based production environment at optimum yield. Millions of specially prepared chicken eggs are used to produce the vaccine. The eggs are delivered to sanofi pasteur and each one is injected with the working seed. The eggs are then incubated allowing the virus to multiply. After incubation, the virus-loaded fluid is harvested followed by multiple purification steps to ensure the virus in inactivated.

Sanofi Pasteur began large-scale production of the novel A/California/7/2009(H1N1) vaccine in our facilities in the United States and France the week of June 22. Production of the vaccine employs egg-based technology. The dosage requirements for the vaccine will be based on clinical trials expected to take place during the summer.

The FDA will determine the clinical trial protocols for testing all pandemic vaccines. Since people may respond differently to pandemic viruses than interpandemic viruses, it is important to determine safety and dosage prior to implementing a large-scale immunization program.

Quality control tests are performed on all batches for purity, sterility and potency in each step of the production process. Doses of the vaccine are formulated and filled in vials and syringes that must be properly packaged and labeled. Samples of every lot of formulated vaccine are sent to the FDA for release. Shipments of pandemic vaccines begin once health authorities authorize it and establish recommendations for immunization.
To ensure safety and purity, vaccine is produced in a clean environment where quality control experts enforce strict standards, continuously monitoring the process.

The majority of time for Bulk Manufacturing and Production and Purification and Testing is dedicated to testing and approval.

Surveillance
- Reference labs around the world collect wild virus carried by humans and characterize the genetic makeup. The virus is continually monitored and tracked by health authorities.

Strain Selection
- World health officials analyze and identify the dominant circulating strain.
- Health officials select virus strains and submit them to contracted laboratories to prepare seed virus.
- Laboratories distribute seed viruses to manufacturers to begin the production process.

Preparation of Seed Virus
- Seed virus is prepared by contracted laboratories using conventional reassortment or reverse genetics methods:
  - Conventional reassortment - Two flu strains with the preferred features for a new vaccine are injected into an egg and the genes reassort naturally.
  - Reverse genetics - Merges selected genetic information of the virus taken from the wild-type virus with the laboratory virus.

Seed Passaging and Selection
- Once the seed virus is received, vaccine manufacturers begin passaging the seed virus in eggs to determine the optimum growth conditions and to improve virus yield by acclimating the virus to growing in eggs.
- The working seed developed by the manufacturer is certified by the FDA.

Bulk Manufacturing and Production
- Millions of specially-prepared chicken eggs are used to produce the vaccine. Throughout the year, fertilized eggs are delivered to the manufacturer. Each egg is injected with the working seed.
- The eggs are incubated for several days to allow the virus to multiply. After incubation, the virus-loaded fluid is harvested.
- Portion of manufactured vaccine is used for clinical trials.
- Clinical trials may occur simultaneously with manufacturing.

Purification and Testing
- Manufacturers test the vaccine concentrate with specially prepared reagents provided by the FDA to determine the potency of the vaccine for immunization.
- Manufacturers begin filling the doses into vials and syringes, which are then sealed and carefully inspected before labels are applied to show the vaccine batch, lot numbers, and expiration date.
- Each lot must be specifically “released” by the FDA before manufacturers can ship supplies.

Formulation, Filling and Packaging
- Viral fragments from strains are collected from different batches, and combined upon completion of quality control tests.
- Upon FDA approval and licensing, the vaccine is released for distribution in time for immunization.
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Shipping
- Vaccine shipments take place over time as vaccine is produced.
- Health authorities determine distribution process.

Vaccination
- Health authorities will establish recommendations and priorities for vaccination.

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Courtesy of sanofi pasteur, May 2009