

**Update: Status of pandemic influenza vaccine manufacturing capacity,
pre-pandemic stockpile, and planning for vaccine distribution**
November 26, 2007

The Department of Health and Human Services (HHS) continues to work with vaccine manufacturers to develop a stockpile of pre-pandemic vaccine and to increase domestic manufacturing capacity for pre-pandemic and pandemic influenza vaccines. This document is an update to the Pandemic Influenza Vaccination: A Guide for State, Local and Territorial and Tribal Planners sent out in December 2006. It provides updates on aspects of vaccine distribution planning, as well as current planning assumptions, and a brief discussion of key planning considerations. Finally, we are requesting that you confirm the number of ship-to sites you plan to use for pre-pandemic and pandemic vaccine (see section IV).

I. Updates

Pre-pandemic vaccine

There are currently 3 manufacturers of pre-pandemic influenza (H5N1) vaccine; sanofi pasteur, Novartis, and GlaxoSmithKline (GSK). Since 2004 the U.S. has accumulated a pre-pandemic influenza vaccine stockpile of approximately 14.8 million doses. The present goal is to have 20 million 2-dose courses by 2008. However, with advances in antigen sparing techniques such as adjuvants and increased manufacturing capacity, the supply of pre-pandemic influenza vaccine may soon be substantially larger than originally anticipated and may be available to more persons at the onset of an influenza pandemic (Leroux-Roels I, Borkowski A, Vanwollegem T, Dramé M, Clement F, Hons E, Devaster JM, Leroux-Roels G. Antigen sparing and cross-reactive immunity with an adjuvanted rH5N1 prototype pandemic influenza vaccine: a randomised controlled trial. *Lancet*. 2007;370:580-589).

Pandemic vaccine

Should a pandemic occur today, egg-based influenza vaccine production will be the primary method of manufacturing pandemic influenza vaccine in the U.S. until approximately 2010, when domestic cell-based influenza vaccine manufacturing capabilities become operational. Regardless of the technology used, there will be a production lag of approximately 4-5 months from the time the pandemic virus is isolated until the time formulated and filled vaccine will be available from manufacturers for distribution.

Adjuvant

The antigen sparing potential of adjuvants could substantially increase the number of doses of pre-pandemic and pandemic influenza vaccine, when it becomes available. Mix-and-match adjuvant/antigen studies are being planned to examine the feasibility of combining adjuvants from one manufacturer with antigen from another. Because of the less rigorous storage and handling requirements for adjuvants (room temperature storage

with a five year shelf life) and the potential for mix-and-match, in many cases adjuvant may be filled and shipped separately from antigen. Adjuvant and antigen would then be mixed and administered at the point of dispensing (POD). We encourage Project Areas to begin considering planning options for receiving, storing, allocating, repackaging, and redistributing adjuvant to PODs.

Distribution planning

CDC has been working with HHS, the Department of Homeland Security (DHS), and vaccine manufacturers to develop a vaccine distribution plan for pre-pandemic and pandemic influenza vaccines. At this time, planning and exercises are underway with vaccine manufacturers for distribution of pre-pandemic and pandemic influenza vaccines.

Priority groups

Federal guidelines for pre-pandemic and pandemic influenza vaccine prioritization are being updated in light of vaccine technology advances and domestic capacity building. These recommendations will represent a departure from the recommendations published in the 2005 HHS pandemic influenza plan, and will take into account the need to support critical infrastructure. Draft recommendations are posted for public comment at: www.pandemicflu.gov/vaccine/prioritization.html.

Needles and syringes

Preliminary discussions are underway about plans for procuring and distributing needles and syringes to support vaccine administration. At present, the Federal government plans to provide Project Areas with needles and syringes for administration of up to 20 million courses of pre-pandemic influenza vaccine. Decisions regarding providing needles and syringes for larger amounts of pre-pandemic vaccine (see below, section II,1) and for pandemic vaccine are pending.

II. Planning assumptions:

1) Pre-pandemic vaccine

- The pre-pandemic vaccine stockpile is being produced by 3 manufacturers: sanofi pasteur, Novartis, and GSK. Other manufacturers are working on developing vaccines as well.
- 3 planning scenarios
 - 20 million 2 dose courses – for critical infrastructure personnel, as defined by national guidelines
 - 120 million 2 dose courses – target population to be defined
 - 280 million 2 dose courses – for entire U.S. population
- Allocation: Under the scenario where 20 million 2 dose courses are available, a yet to be determined amount of the pre-pandemic vaccine will be allocated at the national level for federal critical infrastructure and the remainder will be distributed to Project Areas for their critical infrastructure, generally in proportion to their population size. If larger amounts of pre-pandemic vaccine are available,

use will be expanded beyond critical infrastructure, but allocation will remain generally in proportion to population.

- Shipping of vaccine:
 - Current: Each of the 3 manufacturers of pre-pandemic vaccine will ship their vaccine (or collaborate with a chosen distributor to ship their vaccine) to Project Area-designated ship-to sites, taking into account the Project Area's allocation, and if multiple ship-to sites within the Project Area, taking into account the state allocation among ship-to sites. Each ship-to site will therefore receive shipments from each of the 3 manufacturers.
 - Future: Centralized distribution will be considered once VMBIP is fully functioning throughout the country
- Number of shipments: pre-pandemic vaccine will be shipped in 3-4 shipments: 1) stockpiled vaccine already filled in multidose vials; 2) stockpiled bulk vaccine to be filled (takes approximately 3 weeks to fill vaccine – this will be the largest shipment); 3) additional pre-pandemic vaccine production, if any, before start of production of pandemic vaccine
- Packaging of vaccine (see **Appendix A** for additional packaging information):
 - Vaccine will be shipped primarily in increments of 100 vial master cartons.
 - The dimensions and weight of the shipping containers for the master cartons are 12.0 inches x 6.5 inches x 6.0 inches and 5.5 lbs; and a pallet consists of 147 master cartons, with dimensions and weight of 48.0 inches x 40.0 inches x 45.5 inches and 850-900 lbs.

2) Pandemic vaccine

- At present sanofi pasteur will be the only manufacturer of pandemic vaccine for the U.S. Starting 2010, it is anticipated additional manufacturers will produce for the U.S. using a cell-based production process.
- 3 planning scenarios
 - 90 microgram doses, 5 dose vials, 660,000 doses per week
 - 15 microgram doses, 10 dose vials, 9 million doses per week
 - 7.5 microgram doses, 20 dose vials, 26 million doses per week
- Allocation: generally in proportion to Project Area population size (for early pandemic vaccine, a yet to be determined amount will be allocated at the national level for federal critical infrastructure).
- Shipping of vaccine:
 - As long as there is a single manufacturer of pandemic vaccine (currently sanofi pasteur), vaccine will be shipped to designated ship-to sites via commercial carrier.
 - Once more than one manufacturer is producing pandemic vaccine, anticipated starting 2010: vaccine from the different manufacturers will be consolidated using a centralized distribution system (for example CDC's Vaccine Management Business Improvement Project currently being

- Using RSS sites as ship-to sites: many project areas plan to use RSS sites to receive vaccine. A number of factors should be carefully considered in making this decision:
 - RSS sites need to be able to receive weekly shipments over a period of many months, in contrast to their usual function which is to receive a one-time shipment in response to a catastrophic event
 - RSS sites need to have sufficient cold storage space to accommodate storage of vaccine. Vaccine should be maintained at 36F -46F (2-8C)
 - Project areas that lease space for RSS sites must have contingency plans for storage in the event their lease ends prior to the completion of the final stage of distribution of vaccine .

- Security: DHS is the Federal agency responsible for coordinating security (with Federal and SLTT law enforcement) when vaccine is under Federal control. Once vaccine is turned over to SLTT officials at ship-to sites, SLTT governments will assume responsibility for security.

- Changes in infrastructure of childhood immunization program: Planners must be cognizant of changes to the childhood immunization program which is transitioning to a centralized distribution system. In this system, vaccine is shipped directly from the central distributor to physician offices, clinics, or public administration sites. Once this system is fully deployed, no states will receive childhood vaccines in a central warehouse. Many states will then no longer maintain central warehouses, and so this infrastructure may no longer be available for receipt of pandemic vaccine.

- Planning for monitoring vaccine doses administered: Monitoring pre-pandemic and pandemic vaccine doses administered will occur through the CDC's Countermeasure and Response Administration (CRA) system. Planners must coordinate with appropriate staff within their Project Area to develop and implement a consolidated plan for collecting, aggregating, and submitting data to the CDC on administration of pre-pandemic and pandemic influenza vaccine. If the location of ship-to sites differs from the sites of administration, a system needs to be in place to effectively and efficiently collect aggregate data and submit doses administered data via your Project Area's selected option through the CRA. Project Areas have designated Vaccine Tracking Coordinators to manage data collection and transmission in the event of a pandemic.

- Immunization officials should plan to provide some form of verification of vaccination to employers of critical infrastructure workers. This will provide a means of tracking the status of employee vaccinations by those employers who want to.

IV. Confirmation of number of ship-to sites:

So that sanofi pasteur can proceed with their planning for distribution of pandemic vaccine, CDC needs to supply them with the total number of ship-to sites that Project Areas plan to designate. Project Areas will have opportunities to change their plans in terms of number of ship-to sites, but due to planning required on sanofi pasteur's part, depending on the situation changes may only be possible during designated time periods.

We have extracted information about planned number of ship-to sites for vaccine from the pandemic plans submitted in April 2007. Based on this information we have created for each Project Area a questionnaire asking for confirmation or updating of this information. We are requesting that each Project Area contact Toscha Stanley with the Division of Immunization Services to obtain their questionnaire. It must be completed and returned to her by **January 4, 2008**.

Toscha Stanley can be reached by email at TStanley@cdc.gov, and by phone at 404-639-6248. You should also contact her if you have any questions about the information provided in this update.

Appendix A: Dimensions and weight of 90 microgram unadjuvanted pre-pandemic vaccine packaging options

Single Unit (5-ml vials) - Packed into Polystyrene Containers			
BOX	5-ml Vials	Dimensions (In)	Weight (lbs)
Box 1	1 - 12	12.2 x 9.7 x 10.2	6
Box 2	13 - 48	15.3 x 12.3 x 11.7	12
Box 3	49 - 132	20.3 x 15.3 x 13.6	23
Box 4	133 - 199	21.2 x 20.7 x 14.0	40

Master Cartons - Packed into Polyurathane Containers			
BOX	Master Cartons (1=100 x 5ml Vials)	Dimensions (In)	Weight (lbs)
E186	2 - 4	23.2 x 19.2 x 19.2	51 - 62
E568	4 - 13	27.0 x 25.7 x 28.2	117 - 166
EF1500	13 - 24	39.5 x 31.8 x 45.7	253 - 314
EF2700	24 - 36	47.0 x 40.2 x 50.0	394 - 460

Full (Refrigerated) Truckload			
	Contents	Dimension (In)	Weight (lbs)
1 Master Carton	= 100 x 5ml vials	12.0 x 6.5 x 6.0	5.5
1 Pallet	= 147 Master Cartons = 14,700 x 5ml vials	48.0 x 40.0 x 45.5	850 - 900
1 Refrigerated Truck	= 24 Pallets = 3,528 Master Cartons = 352,800 x 5ml vials	---	---