supplement 6
vaccine distribution and use

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SUMMARY OF PUBLIC HEALTH ROLES AND RESPONSIBILITIES FOR VACCINE DISTRIBUTION AND USE

The roles and responsibilities of healthcare partners in vaccine distribution and use are described in **Supplement 3**.

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

State and local health departments:

- Work with healthcare partners and other stakeholders to develop state-based plans for vaccine effectiveness, safety, distribution and use.

HHS agencies:

- Work with manufacturers to expedite public-sector vaccine purchasing contracts during a pandemic.
- Establish mechanisms for vaccine procurement and distribution.
- Develop guidance on priority groups for vaccination.
- Develop and stockpile vaccine for influenza strains with pandemic potential.
- Expedite the rapid development, licensure, and production of new influenza vaccines, as well as evaluate dose optimization strategies to maximize use of limited vaccine stocks.
- Estimate rates of reports of mild and severe adverse events following immunization (AEFIs) that may occur with mass influenza vaccination, and improve capacity for responding to them.
- Identify mechanisms and define protocols for conducting vaccine-effectiveness studies.
- Develop a system for monitoring state-specific vaccine coverage rates at regular intervals, using a pre-existing population-based survey.
- Develop reporting specifications for tracking data on vaccine administration and provide a vaccine database for optional use by states.
- Develop and distribute communication and education materials for use by states and other stakeholders.

PANDEMIC PERIOD

After the first reports of pandemic influenza are confirmed and before a pandemic vaccine becomes available

State and local health departments:

- If stockpiled vaccine of the pandemic subtype is available, work with healthcare partners and other stakeholders to distribute, deliver, and administer vaccines to designated groups.
- Mobilize healthcare partners, and prepare to activate state-based plans for distributing and administering vaccines.
- Keep the healthcare and public health workforce up-to-date on projected timelines for availability of vaccines against pandemic influenza.
- Review modifications, if any, to recommendations on vaccinating priority groups.
- Accelerate training in vaccination and vaccine monitoring for public health staff and for partners responsible for vaccinating priority groups.

PANDEMIC PERIOD (CONT.)

- Work with other governmental agencies and non-governmental organizations to ensure effective public health communications.

HHS agencies:

- Facilitate vaccine procurement, distribution, and tracking, working with private partners.
- Revise recommendations on vaccination of priority groups, guided by epidemiologic information about the pandemic virus (e.g., virulence, transmissibility, drug resistance, geographic spread, age-specific attack rates, morbidity and mortality rates).
- Provide state and local partners with guidance on reporting specifications for tracking administration of vaccine doses, to be used when vaccine becomes available.
- Provide state and local partners with guidance on Investigational New Drug (IND) and Emergency Use Authorization (EUA) procedures if new types of influenza vaccines for pandemic purposes are developed but not yet FDA approved.
- Provide guidance to state and local health departments on which adverse event reports are highest priority for investigation.
- Provide regulatory guidance to vaccine manufacturers for the manufacture and shipment of pandemic vaccines.

After a vaccine becomes available

State and local health departments:

- Work with healthcare partners and other stakeholders to distribute, deliver, and administer pandemic vaccines to priority groups.
- Monitor vaccine supplies, distribution, and use.
- Monitor and investigate adverse events.
- Phase-in vaccination of the rest of the population after priority groups have been vaccinated.
- Provide updated information to the public via the news media.
- Work with federal partners to evaluate vaccine-related response activities when the pandemic is over.

HHS agencies:

- Provide forecasts of pandemic vaccine availability from manufacturers.
- Continue to provide input into appropriate strain selection for seasonal influenza vaccine.
- Distribute public stocks of vaccines to state and large city health departments and to federal agencies with direct patient care responsibility, as needed.
- Implement protocols for assessing vaccine effectiveness.
- Monitor vaccine coverage rates.

S6-I. RATIONALE

The initial response to an influenza pandemic will include medical care, community containment and personal protective measures, and targeted use of antiviral drugs. Before a vaccine containing the circulating pandemic virus strain becomes available, pre-pandemic vaccine from stockpiles (if available for the pandemic subtype or partially cross-protective to the circulating virus) may be considered for persons in designated priority groups. Once a vaccine against the circulating pandemic virus strain becomes available, its distribution and delivery will be a major focus of pandemic response efforts.

Public health goals for vaccination during an influenza pandemic include:

- Developing pre-pandemic strategies for vaccine manufacturing and stockpiling that will maximize manufacturing capability
- Stockpiling influenza vaccine for strains and subtypes with pandemic potential
- Expediting development of a pandemic virus reference strain and distribution of the strain to vaccine manufacturers
- Accelerating production of a pandemic vaccine
- Maximizing the immune response to the vaccine
- Ensuring efficient and equitable distribution of pandemic vaccine, according to priority lists
- Rapidly determining vaccine effectiveness
- Providing ongoing and timely monitoring of vaccine coverage
- Providing ongoing and timely monitoring of vaccine safety

S6-II. OVERVIEW

Supplement 6 provides recommendations to state and local partners and other stakeholders on planning for the different elements of a pandemic vaccination program. The recommendations for the Interpandemic and Pandemic Alert Periods focus on planning for vaccine distribution, vaccination of priority groups, monitoring of adverse events, tracking of vaccine supply and administration, vaccine coverage and effectiveness studies, communications, legal preparedness, and training. The recommendations for the Pandemic Period focus on working with healthcare partners to implement plans for vaccination against pandemic influenza and initiate monitoring activities.

The activities described below are primarily the responsibility of government health authorities at the state, federal, local, and tribal levels. Additional issues that might be of interest to healthcare partners that administer vaccine are addressed in **Supplement 3**.

S6-III. RECOMMENDATIONS FOR THE INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Vaccination against seasonal influenza virus strains

During the Interpandemic Period, state and local health departments should work with healthcare partners to enhance levels of 1) seasonal influenza vaccination in groups at risk for severe influenza and in healthcare workers, and 2) pneumococcal polysaccharide vaccination among those for whom it is recommended.

The success of the pandemic influenza vaccination program will be determined in large part by the strength of state and local vaccination programs during the Interpandemic Period. Higher annual vaccination rates will foster increased familiarity with

and public confidence in influenza vaccines, increased manufacturing capacity for influenza vaccines, and strengthened distribution channels. HHS is working with industry partners to ensure that influenza vaccine can be produced on an emergency basis at any time throughout the year (see Box 1).

Increased use of pneumococcal polysaccharide vaccine may decrease rates of secondary bacterial infections during a pandemic. Because large-scale pneumococcal vaccination might not be feasible once a pandemic occurs, the Interpandemic Period and Pandemic Alert is the ideal time to deliver this preventive measure. Pneumococcal vaccine is indicated for most persons for whom influenza vaccine is recommended. For specific guidelines on the prevention of pneumococcal disease, please see the Recommendations of the Advisory Committee on Immunization Practices (ACIP) (http://www.cdc.gov/mmwr/pdf/rr/rr4608.pdf).

B. Preparedness planning for vaccination against a pandemic influenza virus

A limited amount of avian influenza A (H5N1) vaccine is being stockpiled and will be considered for early use in the event of an H5N1 pandemic. Development of vaccines against other strains with pandemic potential is also being considered. A monovalent vaccine directed against the circulating pandemic virus strain of influenza should begin to be available within 4-6 months after identification of the new pandemic virus strain (Box 1). The number of persons who may be protected by vaccination depends on the manufacturing capacity, the amount of antigen per dose needed for a protective immune response, and the number of doses required. Although annual influenza vaccine is immunogenic in older children and adults with a single 15 microgram (µg) dose, a higher antigen concentration and/or two doses may be needed for pandemic vaccine where persons have no previous exposure to the influenza subtype and lack any immunity. Preliminary results from a recent clinical trial of an H5N1 vaccine in healthy adults suggested that two doses of 90 µg were required. Additional clinical trials are ongoing to evaluate possible ways to improve the immune response to lower the amounts of vaccine antigen needed for protection.

Initial pandemic vaccine stocks will be used to vaccinate designated priority groups (Part 1, Appendix D). After vaccination of these priority groups, vaccination of all those who desire it will be phased in depending on available supplies.

In working with healthcare partners to develop state-based plans for distributing vaccines, state and local health departments might use existing state-based plans for emergency mass distribution of medical supplies as the basis for developing local pandemic vaccination plans (e.g., smallpox and bioterrorism response plans).

1. Vaccination of priority groups

A list of priority groups for receiving vaccination and the rationale for prioritization is provided in Part 1, Appendix D, as interim recommendations. In addition, during a pandemic, changes may be made based on the characteristics of the causative virus (e.g., transmissibility, virulence, initial geographic distribution, age-specific attack rates, complication rates) and on vaccine effectiveness.

To prepare for vaccination of priority groups, state and local health departments should:

- Identify a process for reviewing national recommendations for pandemic influenza vaccination and developing state-specific modifications or refinements in priority groups, depending on local circumstances.
- Develop specific definitions for priority groups (e.g., public safety workers, essential service providers) identifying occupational categories and sub-categories, as needed, within each broad priority.
- Estimate the size of relevant priority groups.
- Develop a plan on how persons in priority groups would be identified at vaccination clinics and how vaccine would most efficiently be provided to those groups.
- Educate professional organizations and other stakeholders about the need for priority groups and the rationale for the groups currently recommended.

2. Vaccine production, procurement and distribution

HHS is working to expand pandemic influenza vaccine production capacity and will signal to manufacturers when to shift from annual to pandemic vaccine production and assure that pandemic vaccine is produced at full capacity.

At the onset of an influenza pandemic, HHS, in concert with the Congress in collaboration with the States, will work with the pharmaceutical industry to acquire vaccine directed against the pandemic strain. Distribution of pandemic vaccine to health departments and providers will occur via private-sector vaccine distributors or directly via manufacturer. (Only stockpiled pre-pandemic vaccine would be distributed by the federal government, if used.)

Each state and federal agency with direct patient care responsibility will receive available vaccine in proportion to the size of its population in defined priority groups. For priority groups that have been identified, state and local health departments should:

- Determine whether vaccine will be shipped directly from the manufacturer to vaccine providers or to public health clinics for further distribution
- Identify organizations that will provide vaccination to persons in priority groups (e.g., local health departments, occupational health clinics, private clinics identified by the employer or union of an occupational group)
- Identify contacts in and obtain written commitments from each clinic or facility responsible for vaccinating a priority group
- Work with these contacts to develop strategies for rapid distribution and administration of vaccines, taking into account vaccine security issues, cold chain requirements, and transport and storage issues
- Estimate the size of the priority groups that will be vaccinated based on extrapolation from national data or on local data, where available
- Identify locations for vaccination clinics that will be operated by health departments and enter into memoranda of agreement with organizations that agree to provide vaccinators or other staff
- Develop procedures for collecting, removing, and disposing of used syringes, needles, and other vaccination supplies
- Develop a plan for training vaccinators and other staff responsible for mass vaccination
- Develop strategies for vaccinating hard-to-reach populations

State and local health departments' plans should also specifically address the delivery of pandemic vaccine to medically underserved and migrant populations to improve equity in access within priority groups and, later, the general population.

If vaccinations are provided by private-sector organizations or providers at offices, clinics, or other sites, state and local health departments should:

- Develop mechanisms to allocate vaccine based on projected need.
- Develop mechanisms to collect unused vaccine (if any) from healthcare providers who have met their priority vaccination goals and distribute the vaccine to those who have not.
- Provide vaccination information to healthcare providers. This may best be accomplished by developing a communications plan for private-sector vaccine use.
- Monitor that vaccine administration follows existing plans on priority groups.

a) Second-dose vaccination

A vaccine against pandemic influenza will likely require two doses, administered at least a month apart, to provide a level of immunity comparable to that obtained with seasonal influenza vaccines. Recommendations on the number of required doses and the timing of the second dose will be issued once immunogenicity trials have been completed.

If two doses are required to achieve immunity, it will be necessary to ensure that vaccinated persons return for the second dose. State and local planners should do the following:

- Arrange for information about the need for a second dose to be provided at the time of vaccination.
- Ensure that planning for vaccine procurement and distribution to clinics and other facilities accounts for the need to use portions of future shipments for second doses, thus reducing the number of available first doses.
- Consider implementing a call-back system or immunization registry that would accomplish the goals of pandemic vaccination (see 3.b below).

b) Contingency planning for Investigational New Drug use

State and local health departments should be prepared to distribute unlicensed vaccines (if needed) under FDA's Investigational New Drug (IND) provisions. Unlicensed vaccines might be needed, for example, if pandemic spread is rapid and standard vaccine efficacy and safety tests are not completed in time to play a role in the response.

IND provisions require strict inventory control and record-keeping, completion of a signed consent form from each vaccinee, and mandatory reporting of specified types of adverse events. IND provisions also require approval from Institutional Review Boards (IRBs) in hospitals, health departments, and other vaccine-distribution venues. The FDA regulations permit the use of a national or "central" IRB. A treatment IND is one IND mechanism that FDA has available for use and is especially suited for large scale use of investigational products (http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfr_99.html).

As an alternative to IND use of an unapproved antiviral drug, HHS may utilize the drug product under Emergency Use Authorization procedures as described in the FDA draft Guidance "Emergency Use Authorization of Medical Products" (http://www.fda.gov/cber/gdlns/emeruse.pdf).

3. Vaccine monitoring and data collection

To ensure optimal use of a new pandemic influenza vaccine, state and local health departments should be prepared to collect data on vaccine effectiveness, vaccine supply and distribution, vaccine coverage, and vaccine safety.

a) Vaccine effectiveness

Vaccine effectiveness will be assessed by comparing rates of influenza-related illness, hospitalization, and/or death among vaccinated and unvaccinated persons. These studies will be implemented by CDC in collaboration with healthcare and university partners and with state and local health departments that participate in influenza surveillance systems.

b) Vaccine supply and distribution

Mechanisms for tracking vaccine supply and distribution will depend on how vaccine is purchased and distributed. Tracking will be implemented by state and local health authorities-who will have major responsibility for allocation decisions-working in association with CDC and vaccine producers. Data also will be obtained from vaccine producers and commercial distributors.

- Vaccine tracking and coverage information may be used by federal, state, and local decision-makers to estimate adverse event rates based on the number of doses administered and to determine if vaccine is being administered according to established priority groups for pandemic vaccine (especially in the early phases of vaccination). Data will be collected from individual providers, collated at the local and state levels, and reported to federal authorities on a scheduled routine basis.

- States with immunization registries may adapt them for use in tracking coverage with pandemic influenza vaccine. Or, states may use a vaccine database that will be supplied by CDC. At a minimum, tracking data should include:
  - Number of doses administered, by date and age, priority group, and state or county (or zip code)
  - Number of doses that represent second doses, as applicable
- State and local authorities may consider additional data requirements for their own needs.

c) Vaccine coverage

CDC will work with states to develop a system for monitoring vaccination rates at regular intervals, using a pre-existing population-based survey tool (e.g., Behavioral Risk Factor Surveillance System) that provides national and state-level estimates and complements the vaccine tracking systems described above.

d) Vaccine safety

State and local health departments should develop a system to report and investigate adverse events following immunization (AEFI) with a pandemic influenza vaccine. Planning steps might include:

- Designating a state-level coordinator to plan for and implement adverse-events reporting and outreach to and education of providers (e.g., adapting and distributing federally developed Dear Doctor letters and materials for vaccine recipients) and who will serve as the state's contact with federal government staff overseeing the Vaccine Adverse Event and Reporting System (VAERS) (www.vaers.hhs.gov).
- Reviewing existing policies for AEFI reporting and follow-up to ensure timeliness of reporting.
- Developing a plan to ensure timely reporting of and communication about large numbers of AEFI reports.
- Reviewing procedures for and familiarizing program staff with the strengths, limitations, and objectives of VAERS. VAERS typically involves direct reporting by individual healthcare providers, with periodic feedback to the states. During a pandemic, some state health departments may wish to receive direct reports of AEFI to conduct investigations of adverse events and minimize duplicate reporting of adverse events to VAERS. State-level AEFI reporting can build on the infrastructure and experience developed during the 2003 smallpox vaccination program.

  Adverse events related to use of IND vaccines may be reported through other mechanisms in addition to or in place of VAERS, in accordance with specific regulatory or policy requirements. Adverse events will also be monitored through the Vaccine Safety Datalink (www.cdc.gov/nip/vacsafe/default.htm#VSD), a network of seven geographically diverse health maintenance organizations through which active surveillance vaccine safety studies are conducted. Another potential resource for vaccine safety research is CDC's Clinical Immunization Safety Assessment (CISA) network (www.vaccinesafety.org/CISA/index.htm).

4. Public health communications

The provision of vaccine information will be an important component of ongoing public health communication during a pandemic (see Supplement 10).

- State and local health departments should work with federal partners to disseminate accurate, useful, and consistent public health messages and should tailor information to local needs as indicated.
- Health departments should provide information to healthcare providers, state and local government officials, and the news media on:
  - Rationale for prioritization and list of priority groups (see Part 1, Appendix D)
  - Phasing of vaccination, if any, after priority groups have been vaccinated
  - When and where vaccination is available

- Importance of vaccination given likelihood of subsequent pandemic waves, particularly if public interest in vaccination has decreased

- As noted above, state and local health departments should be prepared to disseminate information on vaccine use to healthcare providers who purchase private stocks of pandemic influenza vaccine. In addition, all vaccine providers will need vaccine information sheets that describe the risks and benefits of, and contraindications to, vaccination.

5. Coordination with bordering jurisdictions

State and local health departments should review and coordinate vaccine distribution plans with health authorities in bordering jurisdictions, including neighboring states, tribal governments and other unique populations.

6. Legal preparedness

State and local health departments should ensure that appropriate legal authorities are in place to facilitate implementation of plans for distributing pandemic influenza vaccines. Health departments might undertake these legal preparedness steps:

- Ensure that plans for distribution of vaccines are reviewed by appropriate legal authorities.
- Determine whether state and local laws allow non-licensed volunteers or healthcare workers from other jurisdictions to administer influenza vaccines.
- Work with professional organizations and unions to consider options for emergency performance of tasks outside of standard job descriptions.
- Determine whether state and local laws allow mandatory vaccination to the protect public health, if needed.

7. Training

State and local health departments can assist healthcare partners in conducting training exercises to facilitate rapid and effective delivery and use of vaccines (see Supplement 3). Exercises and drills are essential to ensure that emergency procedures are in place and that roles and responsibilities are well understood. It may be useful, for example, to practice emergency implementation of mass vaccination (e.g., receiving large quantities of vaccine; storing and handling vaccine; setting up and staffing clinics; administering vaccine; testing information management systems; educating the public, media, and medical providers; targeting specific priority groups).

S6-IV. RECOMMENDATIONS FOR THE PANDEMIC PERIOD

A. Before a vaccine is available

Before a vaccine becomes available—state and local health departments should do the following:

- Meet with partners and stakeholders to review the major elements of the state's vaccine distribution plan.
- Modify the plan to account for possible updated interim recommendations on priority groups, projected vaccine supplies and timelines for availability, and staffing estimates for mass vaccination.
- Notify the medical community about the status of the plan and the expected availability of vaccines.
- If stockpiled vaccine of the pandemic subtype is available, work with healthcare partners and other stakeholders to distribute, deliver, and administer vaccines to designated groups.
- Update and disseminate public information on the production, distribution, and use of pandemic influenza vaccine before it becomes available (see **Supplement 10**).
- Conduct training for public health staff and partners involved in distributing and administering vaccines.

B. When a vaccine becomes available

- Once a vaccine is ready for distribution, state and local health departments should work with healthcare and community partners to activate plans to:
  - Vaccinate persons in priority groups, in accordance with existing recommendations.
  - Provide a second dose, if required for immunity.
  - Monitor vaccine supply, distribution, and use.
  - Monitor and investigate adverse events.
  - Continue communication with partners and the public.
- After priority groups have been vaccinated and additional vaccine stocks become available, public health authorities should phase-in vaccination of the rest of the population, based on age or other criteria that will ensure fair, equitable, and orderly distribution (see III.B). HHS will issue national recommendations to aid in this process.
- After the pandemic has ended, state and local health departments should evaluate all response activities, including vaccine tracking and delivery, adverse event monitoring, and communications.

BOX 1. DEVELOPMENT OF VACCINES AGAINST PANDEMIC STRAINS OF INFLUENZA

HHS is working with industry partners to ensure that influenza vaccine can be produced on an emergency basis at any time throughout the year (http://www.HHS.gov/nvpo/pandemicplan/) and to facilitate the development of cell- and recombinant-based interpandemic and pandemic influenza vaccines towards FDA licensure in U.S.-based manufacturing facilities. Activities in support of these goals include:

- Stimulating expanded manufacturing capacity by increasing annual demand for influenza vaccines by the CMS and CDC
- Securing a year-round egg supply for production of inactivated egg-based influenza vaccines
- Promoting the development of new technologies that:
  - Shorten the time required to develop a vaccine against a new strain of influenza.
  - Facilitate rapid expansion of vaccine production during a pandemic.
  - Optimize the use of limited vaccine supplies (e.g., antigen-sparing strategies).

HHS is also spearheading the development of human vaccines against avian influenza A (H5N1) and against other influenza A viruses with pandemic potential. HHS is providing funding to develop and manufacture pilot investigational lots of these vaccines at licensed influenza vaccine manufacturers and to evaluate their safety and immunogenicity in NIH-sponsored clinical trials in healthy adult, elderly, and pediatric populations.

HHS is acquiring commercial scale lots of influenza A (H5N1) vaccine to provide vaccine manufacturers with experience initially and then to establish and maintain stockpiles of pre-pandemic H5N1 vaccine.

APPENDIX. RESOURCES FOR MASS VACCINATION AGAINST PANDEMIC INFLUENZA

- **Department of Health and Human Services**
  - Guidelines for large-scale influenza vaccination clinic planning. Developed by CDC's National Immunization Program in response to the 2004 influenza vaccine shortage, this document was prepared to assist in planning for large vaccination clinics. It provides a general overview and guidelines for establishing and running a mass dispensing clinic (http://www.cdc.gov/flu/professionals/vaccination/pdf/vaxclinicplanning0405.pdf).
  - Guidelines for large-scale smallpox vaccination clinics. Although this document is specific to smallpox, most of the content is applicable to and can be adapted to other mass vaccination clinics (http://www.bt.cdc.gov/agent/smallpox/response-plan/files/annex-2.pdf).
  - Information on Investigational New Drug (IND) use and Emergency Use Authorization (EUA). Regulations governing IND applications are described in 21 CFR 312 (http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfr312_99.html). Draft guidance for EUA is provided at http://www.fda.gov/cber/gdlns/emeruse.pdf.
- **Private-sector partners**
  - Community-based mass prophylaxis: a planning guide for public health preparedness. This report from Cornell University's Weill Medical College describes the five components of a mass prophylaxis/vaccination response to an epidemic (http://www.ahrq.gov/research/cbmprophyl/cbmpro.htm).