ASPR
ADMINISTRATION FOR STRATEGIC PREPAREDNESS AND RESPONSE

BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY
BARDA

Vaccines for Pandemic Influenza Preparedness and Response

Presentation to the Vaccines and Related Biological Products Advisory Committee (VRBPAC)

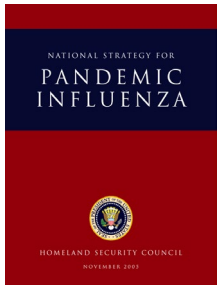
10 October 2024

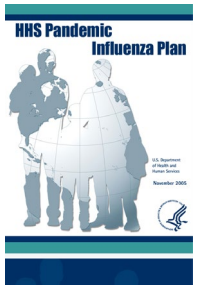
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U.S. Department of Health and Human Services (HHS)

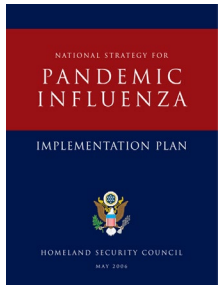
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Pandemic Preparedness Policy

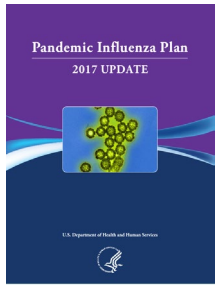
The U.S. government has established several pandemic preparedness goals under plans, such as:



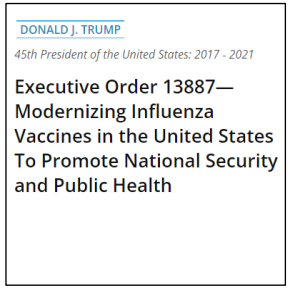


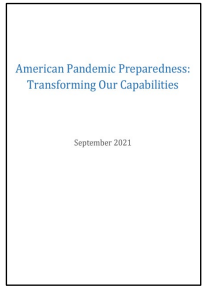


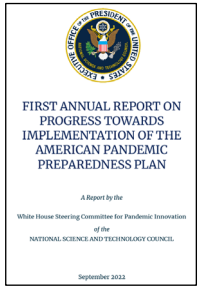


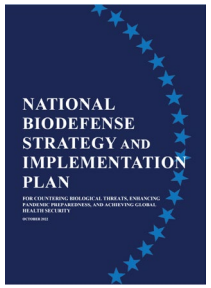


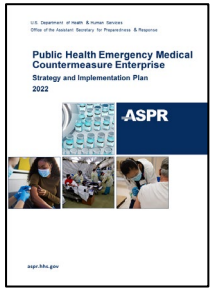












These goals include:

- Delivery of first finished doses of pandemic vaccine within 3 months of a pandemic declaration;
- Having a sufficient supply to meet public demand within 4 months of a pandemic declaration; and
- Manufacture, fill, finish, release, and deliver enough vaccine for the entire U.S. population within 6 months of a Public Health Emergency (PHE) declaration.

To enable rapid response and meet these goals, BARDA continuously maintains influenza virus vaccine seed lots and small quantities of antigen and adjuvant, manufactures clinical trial vaccine lots, and conducts clinical trials to understand the immune response.



Goal 1: Preparedness
Rapidly develop safe, effective medical countermeasures accessible to all Americans

Goal 2: Response
Maintain a sustainable, mission-ready response posture

Goal 3: Partnerships
Leverage mechanisms to foster flexible partnerships

https://www.cdc.gov/pandemic-flu/php/national-strategy/index.html
https://medicalcountermeasures.gov/barda/strategic-plan/

Vaccine Medical Countermeasures (MCMs) for Pandemic Influenza and Emerging Diseases Preparedness and Response Program

- The U.S. National Pre-pandemic Influenza Vaccine Stockpile (NPIVS) was formally initiated in 2005 and leverages existing infrastructures and capabilities to support preparedness and response

- BARDA has maintained contracts with FDA-licensed influenza vaccine manufacturers without interruption since 2005 to allow:
  - Fast and continuous updates of pre-pandemic influenza virus vaccine seed lots, production of influenza virus vaccine for conduct of clinical trials, and as funding allows, manufacture of bulk and/or final container antigen and adjuvants stockpiled for pandemic preparedness;
  - Continuous storage and monitoring of stability of stockpiled pre-pandemic antigens and adjuvants; and
  - Quick response (contracts in place) in case of a pandemic event

- The NPIVS is currently composed of adjuvants (AS03, MF59) and pre-pandemic influenza virus bulk antigen and final containers of vaccine manufactured from candidate vaccine viruses representing virus subtypes regarded to have the greatest potential to cause a pandemic
  - **CSL Seqirus** – cell-based, egg-based (**OCONUS**), and MF59 adjuvant; **domestic**
  - **GSK** – egg-based (**OCONUS**), AS03 adjuvant; **domestic**
  - **Sanofi** – egg-based and recombinant protein; **domestic**

- Utilizes facilities that currently produce domestic and licensed seasonal influenza vaccine for immediate response capability at commercial scale

Current Pandemic Influenza Virus Vaccine Response Plan*

- **CSL Seqirus**: cell-based influenza virus vaccine antigen + MF59 adjuvant
  - AUDENZ is approved for use in persons 6 months of age and older
  - Co-formulated antigen and MF59 adjuvant in pre-filled syringes or multidose vials

- **Sanofi, GSK**: Sanofi egg-based influenza virus vaccine antigen + GSK AS03 adjuvant
  - Sanofi is the largest supplier of influenza virus vaccine antigen in the U.S.
  - Sanofi influenza A(H5) virus vaccine (antigen only) is indicated for use in persons 18 to 64 years of age
  - Will require clinical data to support an emergency use authorization (EUA)
  - Will require a bedside mix of antigen and adjuvant

- **GSK**: GSK egg-based antigen is not a major part of the response plan in the U.S.
  - Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted is approved for use in persons 6 months of age and older
  - Antigen is manufactured outside the U.S., with pandemic commitments to other markets; however, the U.S. has procured some antigen final containers and bulk antigen.

- mRNA-based vaccines are not a part of the current preparedness activities; however, BARDA is planning for potential future responses.
  - Nucleic acid-based seasonal influenza virus vaccines are not licensed yet in the U.S.
  - If the vaccines become licensed in the U.S., pandemic influenza vaccine response plans will be re-assessed

***subject to funding availability**

Making Decisions about Pre-Pandemic Influenza Vaccines

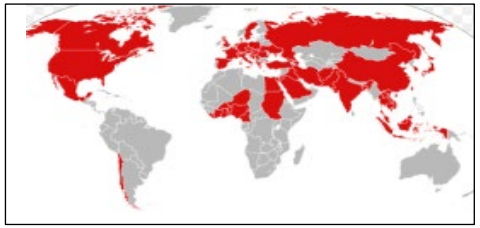
Interagency decision – making body

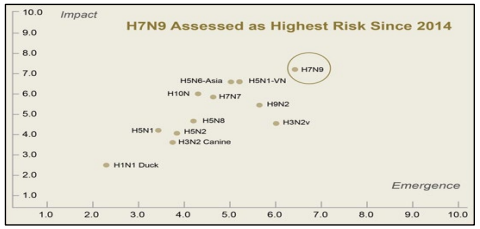
Surveillance – Epi data

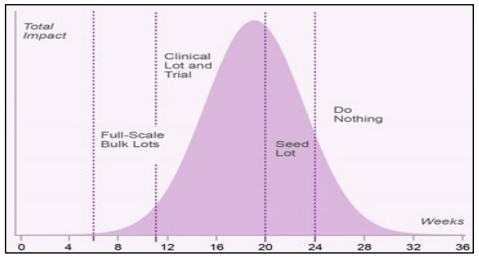
Decision using a metered response approach

Implementation









Influenza A(H5) Virus Clade 2.3.4.4b Preparedness in the U.S.

2022

JANUARY
» 1st influenza A(H5) clade 2.3.4.4b found in wild birds in the U.S.

FEBRUARY
» Influenza A(H5) found in U.S. commercial poultry (first since 2020)

MARCH
» BARDA contracted FDA licensed influenza vaccine manufacturers to prepare A/Astrakhan (H5) virus vaccine seeds

APRIL
» 1st human H5N1 case reported in the U.S.

MAY
» Sporadic influenza A(H5) virus infections reported in small mammals in U.S.
» H5 vaccine seed lots manufactured at the FDA licensed influenza vaccine manufacturers

JUNE – JULY
» H5N1 found in large aquatic mammals in the U.S.

SEPTEMBER
» Two influenza A(H5) vaccine clinical trials contracts awarded – (**CSL Seqirus & GSK**)

OCTOBER – DECEMBER
» Influenza A(H5) continues to be found in mammals in the U.S.

2023

JANUARY – JULY
» Additional H5 antigen procured

AUGUST
» CSL Seqirus H5 vaccine clinical trial fully enrolled

SEPTEMBER
» H5 vaccine ‘Mix-N-Match’ Clinical Trial contract awarded (BARDA)

OCTOBER
» GSK H5 vaccine clinical trial fully enrolled

DECEMBER
» Ongoing H5N1 circulation in wild birds, poultry, and mammals in North America

2024

APRIL-MAY
» Awarded task orders to fill/finish influenza (H5) virus vaccine in final containers

AUGUST
» Enrollment underway in the BARDA-sponsored H5 vaccine ‘Mix-N-Match’ Clinical Trial

AUGUST-SEPTEMBER
» Additional procurement of finished vaccine, bulk antigen, vaccine seed lots
» MF59 Vendor Managed Inventory fully invested

Sources:
1. CDC - Highlights in the History of Avian Influenza (Bird Flu) Timeline – 2020-2023 | Avian Influenza (Flu) (cdc.gov)
2. USDA/ APHIS - USDA APHIS | 2022-2023 Confirmations of Highly Pathogenic Avian Influenza in Commercial and Backyard Flocks
3. USGS - Distribution of Highly Pathogenic Avian Influenza in North America, 2021/2022 | U.S. Geological Survey (usgs.gov)

Pandemic Readiness: Influenza A(H5) Virus Vaccine Clinical Trials, i.

Sponsor: GSK

Protocol Title: A Phase I/II Observer-blind, Randomized, Multi-center Trial to Evaluate the Safety and Immunogenicity of Different Formulations of Monovalent Influenza A/Astrakhan/3212/2020 Like (H5N8) Virus Vaccine With AS03 Adjuvant System (Referred to as Q-Pan H5N8), Given as a Two-dose Series to Adults 18 to 64 Years of Age and 65 Years of Age and Older

Status: Enrollment complete

Study Group (2 doses 21 days apart)	18–64 years*	>65 years*
3.75mcg HA + AS03 (half dose)	65	65
3.75mcg HA + AS03 (full dose)	65	65
7.5mcg HA + AS03 (half dose)	65	65
7.5mcg HA + AS03 (full dose)	65	65

**Number of Participants*

Outcomes

- Safety: safety and reactogenicity of different formulations adjuvanted with full or half dose of AS03
- Immunogenicity: hemagglutination inhibition (HAI) antibody responses and microneutralization (MN) antibody responses against influenza A/Astrakhan/3212/2020 (H5N8)-like virus at days 1, 22, 43, 6 months following last dose

NCT05975840

Pandemic Readiness: Influenza A(H5) Virus Vaccine Clinical Trials, ii.

Sponsor: CSL Seqirus

Protocol Title: A Phase 2, Multi-Center, Randomized, Observer-Blind Study, to Evaluate Safety and Immunogenicity of Homologous or Heterologous Priming and Booster Vaccinations With H5N8 or H5N6 MF59-adjuvanted, Cell Culture-derived Influenza Vaccine in Healthy Subjects ≥18 Years of Age

Status: Enrollment complete

Study Group	Dose 1 (Day 1)	Dose 2 (Day 22)	Dose 3 (6 months)	18–64 years*	>65 years*
1	aH5N8c	aH5N8c	aH5N8c	120	120
2	aH5N8c	aH5N6c	aH5N8c	60	60
3	aH5N6c	aH5N8c	aH5N8c	60	60

**Number of Participants*

Outcomes

- Safety: safety and reactogenicity of different homologous and heterologous prime boosting regimens adjuvanted with MF59
- Immunogenicity: hemagglutination inhibition (HAI) antibody responses and microneutralization (MN) antibody responses against influenza A/Astrakhan/3212/2020 (H5N8)-like virus and influenza A/Guangdong/18SF020/2018 (H5N6)-like virus at Days 1, 22, 43, 6 months, and days 1 and 21 post dose #3

NCT05874713

Pandemic Readiness: Influenza A(H5) Virus Vaccine Clinical Trials, iii.

Sponsor: Biomedical Advanced Research and Development Authority (BARDA)

Protocol Title: Randomized, Double-Blind, Phase 2 Study to Assess Safety and Immunogenicity of A/H5 Inactivated Monovalent Influenza Vaccines at Different Antigen Dose Levels Adjuvanted with AS03® or MF59®

Status: Recruiting

Sanofi Egg-based Antigen	Adjuvant	Antigen Dose	18–64 years*	≥65 years*
A/Astrakhan/3212/2020 (H5N8)	AS03 Full Dose	3.75 µg	60	0
		7.5 µg	60	60
		15 µg	60	60
A/Astrakhan/3212/2020 (H5N8)	AS03 Half Dose	3.75 µg	60	0
		7.5 µg	60	60
		15 µg	60	60
A/Astrakhan/3212/2020 (H5N8)	MF59	3.75 µg	60	0
		7.5 µg	60	60
		15 µg	60	60
A/bar-headed goose/Qinghai/1A/2005 (H5N1)	AS03 Full Dose	3.75 µg	60	0
		7.5 µg	60	60
		15 µg	0	60
A/bar-headed goose/Qinghai/1A/2005 (H5N1)	MF59	3.75 µg	60	0
		7.5 µg	60	60
		15 µg	0	60

*Number of Participants

NCT06560151

Outcomes

- Safety: safety and reactogenicity following each vaccination of different antigens and antigen doses of vaccine given with AS03 full dose, AS03 half dose, or MF59 adjuvant
- Immunogenicity: hemagglutination inhibition (HAI) antibody responses and microneutralization (MN) antibody responses against influenza A/Astrakhan/3212/2020 (H5N8)-like virus and influenza A/bar-headed goose/Qinghai/1A/2005 (H5N1)-like virus at days 1, 22, 43, 6 months following last dose



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https://medicalcountermeasures.gov/barda/influenza-and-emerging-infectious-diseases/