



US Vaccine Production for the 2009 H1N1 Pandemic

Biomedical Advanced Research and Development Authority (BARDA)

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HHS/ASPR/BARDA**



Today



- **State of influenza preparedness in the US with emphasis on influenza vaccine production.**
- **General structure(s) for vaccine production and delivery for the pandemic.**
- **H1N1 vaccine production to date**
- **Clinical trials highlights**



What is BARDA?



- **BARDA is an operating division within HHS/ASPR**
- **BARDA's mission is to provide countermeasures for CBRN threats, pandemic influenza, and emerging infectious diseases by product requirement setting, product development, stockpile acquisition/building, manufacturing infrastructure building, and product innovation.**



Other Countermeasures

Antimicrobials

Diagnostics

Vaccines

Therapeutics



Under what authorities?



THE WHITE HOUSE
MEMORANDUM
November 18, 2007

PUBLIC LAW 110-417—DEC. 10, 2008 110 STAT. 2801

THE WHITE HOUSE
FOUNDED 1789
ESTABLISHED BY CONGRESS IN 1800

Federal Register (Vol. 22, No. 51, Tuesday, March 20, 2007) Notices 12108

Federal Register (Vol. 22, No. 17, Monday, April 23, 2007) Notices 28917

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Biomedical Advanced Research and Development Authority (BARDA)
Office of the Assistant Secretary for Preparedness and Response (ASPR)
U.S. Department of Health and Human Services (HHS)

**Draft BARDA Strategic Plan
for Medical Countermeasure
Research, Development, and Procurement**

July 2007

Background: The White House memorandum discusses the need for medical countermeasures to protect the American people. The ASPR will lead the development of medical countermeasures to protect the American people and coordinate the development of these products. The ASPR will also coordinate the development of these products.

Subject: BARDA will lead the development of medical countermeasures to protect the American people and coordinate the development of these products. The ASPR will also coordinate the development of these products.

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NATIONAL STRATEGY FOR
**PANDEMIC
INFLUENZA**

HOMELA

**HHS Pandemic
Influenza Plan**

NATIONAL STRATEGY FOR
**PANDEMIC
INFLUENZA**

IMPLEMENTATION PLAN

HOMELAND SECURITY COUNCIL
MAY 2006



U.S. Influenza Vaccine Landscape 2004-2005



Seasonal Vaccine Supply

- Two Inactivated Split Vaccines
- One Live Attenuated Vaccine

Pandemic Vaccines

- None

U.S. Influenza Vaccine Manufacturing

- Egg-based TIV (30M seasonal doses/yr)

Seasonal Vaccine Technology

- Trivalent formulation
- Egg-based Manufacturing

Pandemic Vaccine Technology

- NA



swH1N1 Pandemic Major Questions



- **Should we provide novel H1N1 vaccine for entire US population?**
- **Who can provide vaccine? In what forms?**
- **How long will it take to produce, license, deliver? How do we speed this up?**
- **How immunogenic will it be? One dose (like seasonal) or 2 doses (like H5N1). Will we need to provide adjuvant and if so how?**
- **What are the ways we can make the vaccine go further if needed?**
- **What will the uptake be?**



Initial Manufacturing Assessments



- **Strategy overview**
- **Review and tiering**
- **Regulatory considerations**
- **Importation and distribution issues**
- **Clinical trials-funding, evaluation**



Initial Manufacturing Assessments



Strategy overview

- Based on US pandemic plan, epidemiology, virus characteristics, etc
- Experiences, contracts with H5 and Seasonal influenza

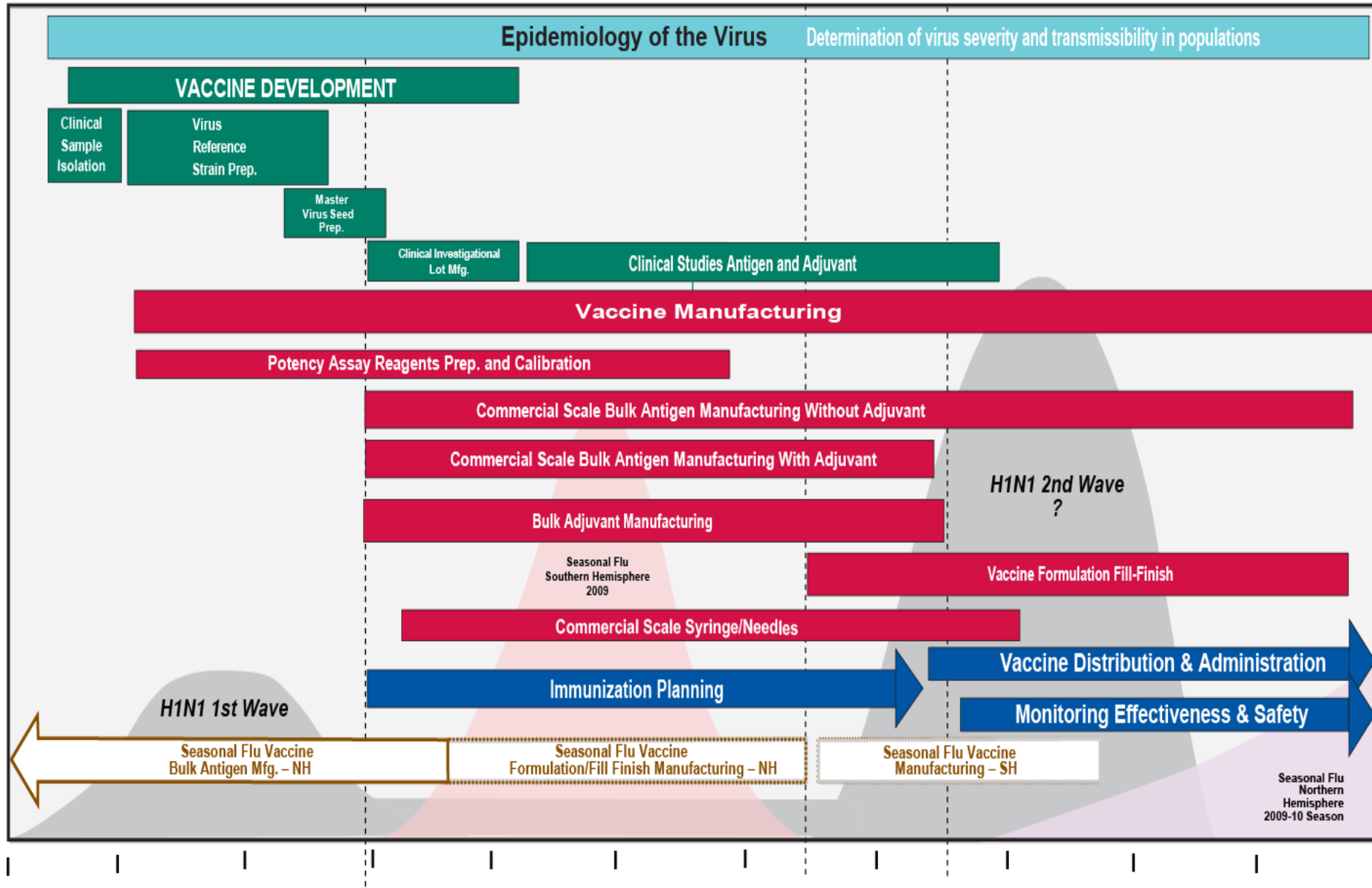
Review and tiering

Regulatory considerations

Importation and distribution issues

Clinical trials-funding, evaluation

U.S. 2009-H1N1 Vaccine Strategy





Initial Manufacturing Assessments



Strategy overview

Review and tiering

- Tier 1: Licensed US producers and facilities
- Tier 2: Reasonable pathway to EUA-producers/facilities
- Tier 3: <TRL 7 technologies

Regulatory considerations

Importation and distribution

Clinical trials-funding, evaluation



Initial Manufacturing Assessments



Strategy overview

Review and tiering

**Regulatory
considerations**

- Top to bottom input
- Historical involvement of FDA

Importation and
distribution

Clinical trials-
funding, evaluation



Initial Manufacturing Assessments



Strategy overview

Review and tiering

Regulatory considerations

Importation and distribution

- Only domestic production in Pa
- Animal virus-USDA involvement

Clinical trials-
funding, evaluation



Initial Manufacturing Assessments



Strategy overview

Review and tiering

Regulatory considerations

Importation and distribution

**Clinical trials-
funding, evaluation**

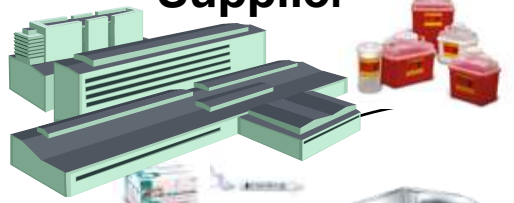
- Capability
- Time
- Costs



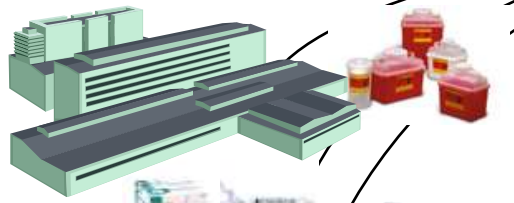
Results

- **Provide vaccine for entire US population.**
- **Prepare as rapidly as possible to meet 5 ACIP target groups 42M then 159M.**
- **Contracts with only US-licensed mfgs**
- **Prepare appropriate contingency EUA's**
- **Retain flexibility for presentations/purchase of vaccine**
- **Purchased 250+M doses of bulk**
- **Fill/finish 160+M**
- **4 presentations-total of 9 licensed products.**

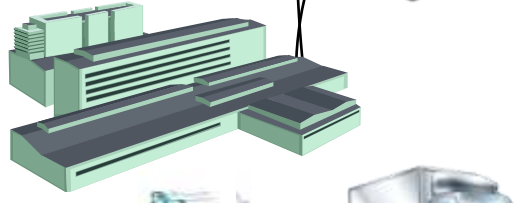
Ancillary Component Supplier



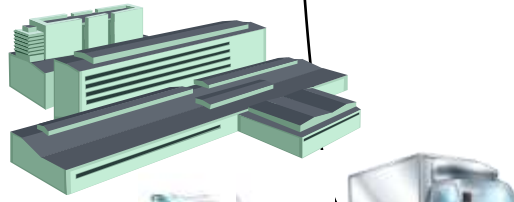
BD



COV



RTI



SM

Kitting and Repackaging

1

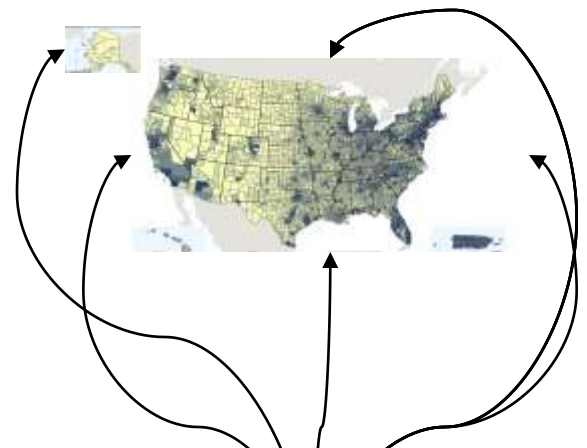


2



PUSH

6 M Kits
~2100 Trucks



3



TX



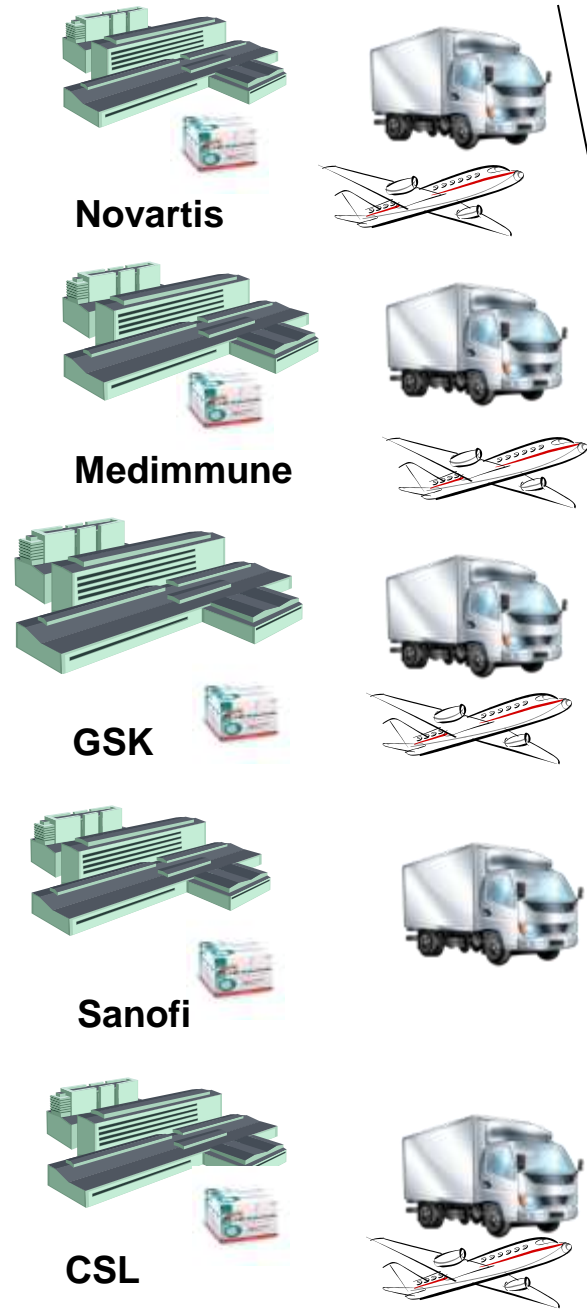
OH

CDC

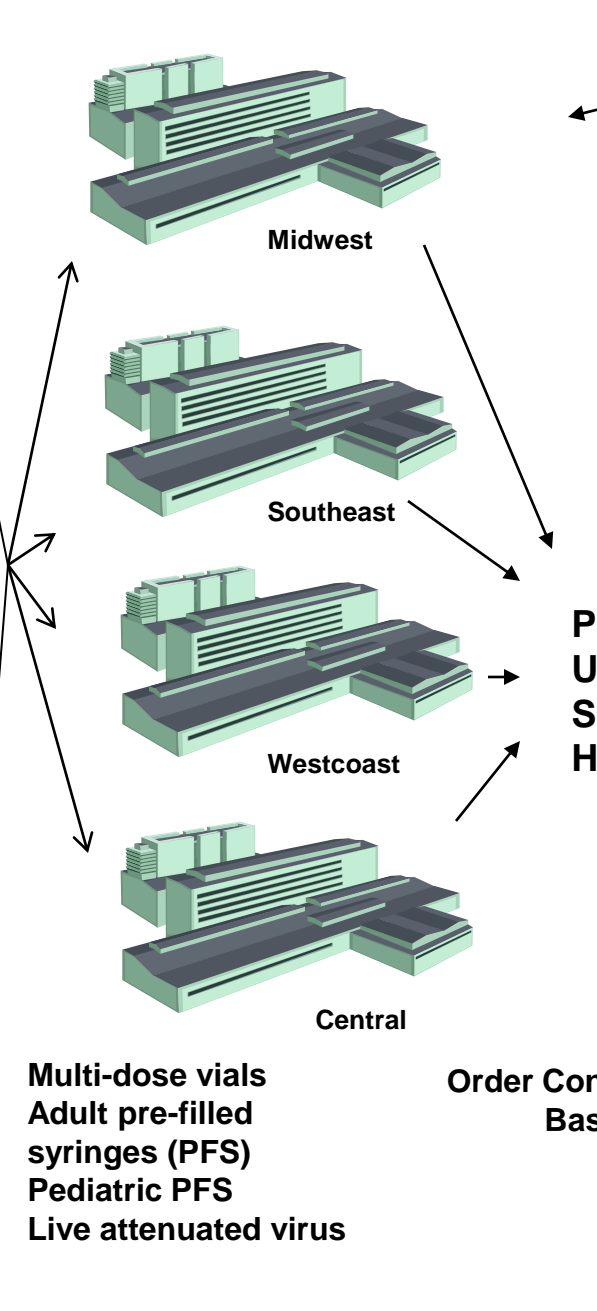
Order Consolidation & Distribution



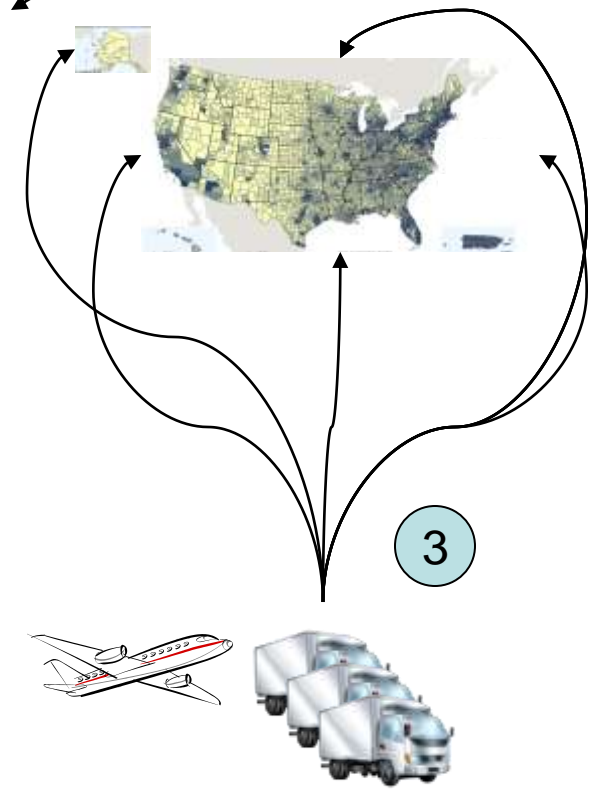
1 Vaccine suppliers and Fillers



2 Distributor sites



Kits for multi-dose vials & PFS



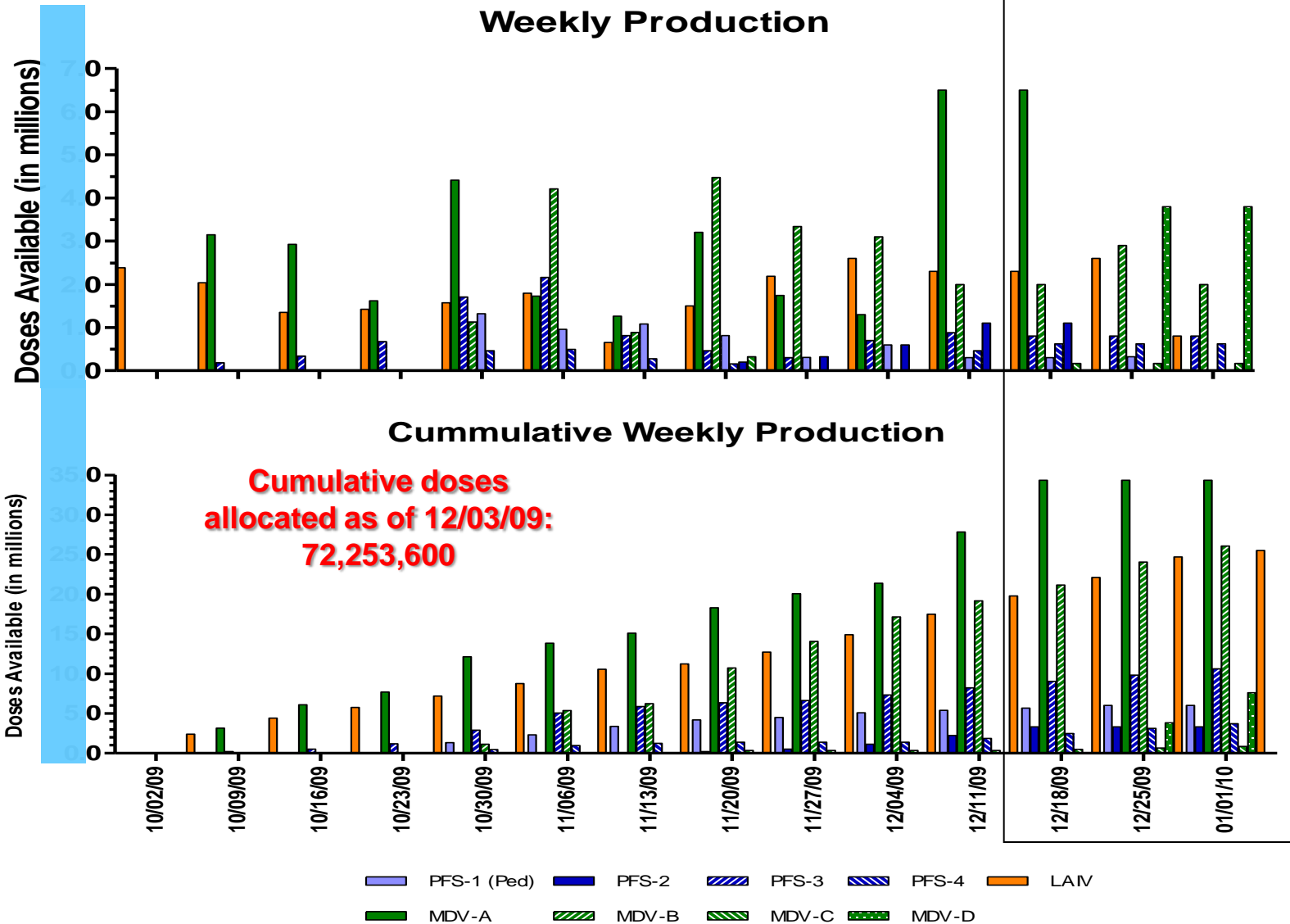
PUSH



Summary H1N1 Production since October 09



Projected*





2009 H1N1 Human Vaccine Trials Supported by BARDA



- **BARDA/ASPR provided funds through production contracts to 5 manufacturers to carry out trials**
- **13 trials in US and Costa Rica; 11,352 subjects 6 months to over 65 years old, All 3 adjuvants evaluated.**
- **10,352 to receive inactivated and 500 live attenuated vaccine; 6,098 to receive inactivated vaccine without adjuvant and 4,254 to receive vaccine with adjuvant**
- **Small placebo group in trials without adjuvant; comparator for adjuvanted vaccine trials is vaccine without adjuvant**
- **Almost all trials now fully enrolled, 1 or 2 doses administered to all subjects, safety follow-up for 6 months (no adjuvant) or 12 months (adjuvant)**



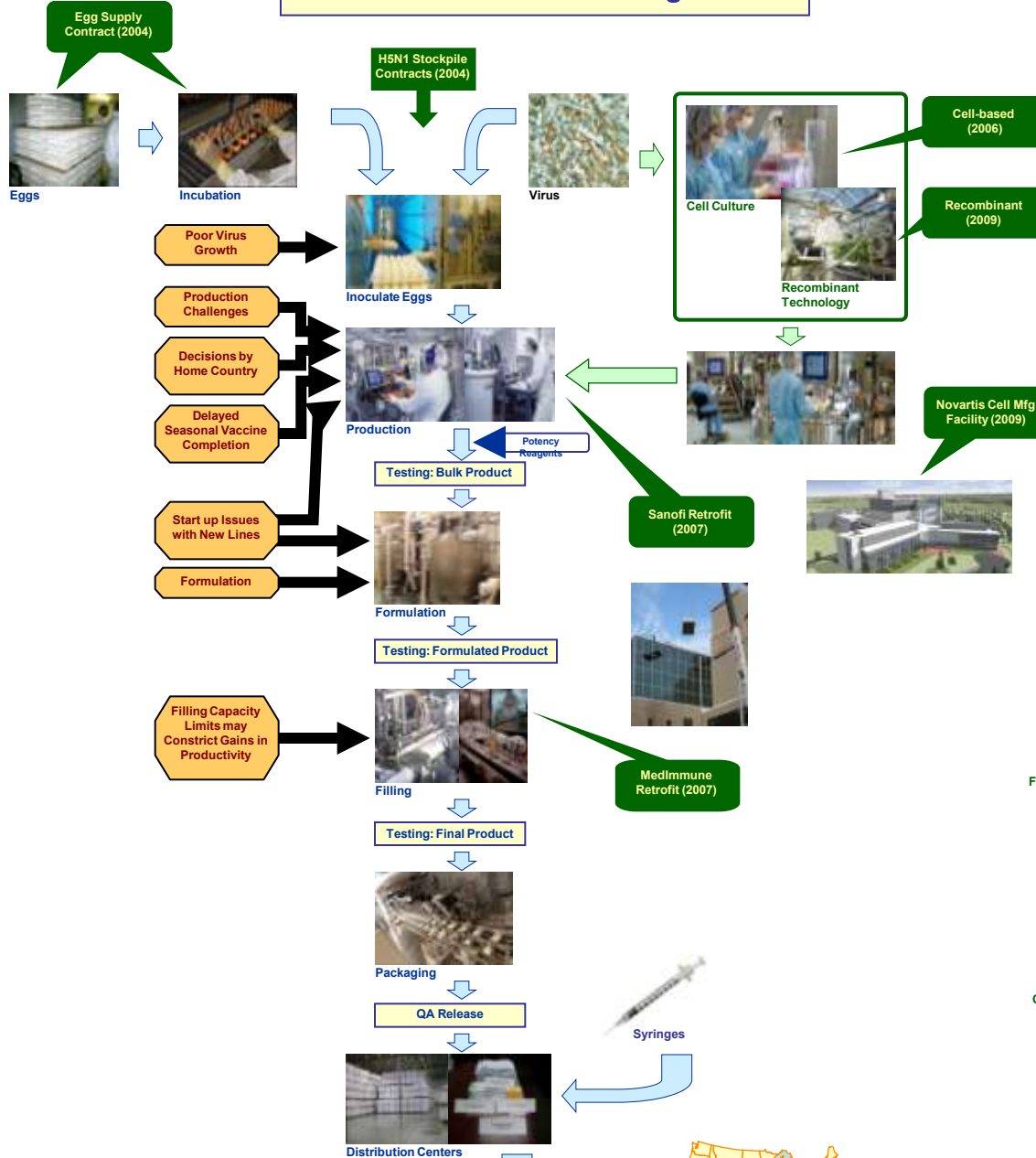
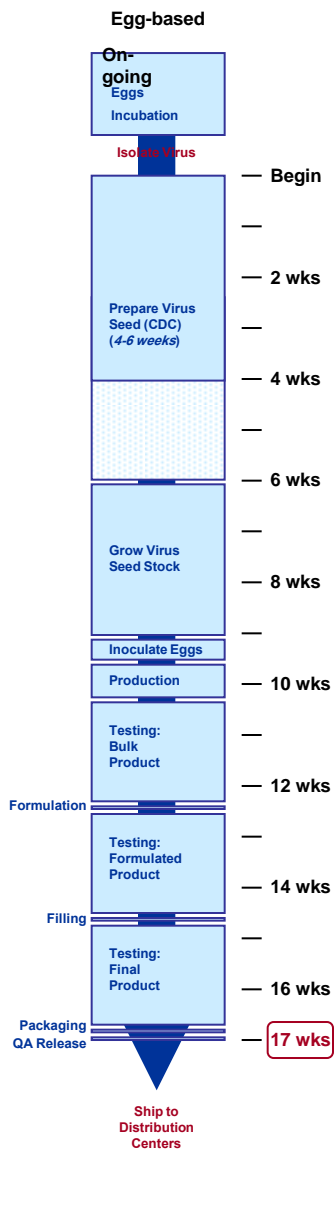
2009 H1N1 Vaccine Trials Supported by BARDA



- **Without adjuvant, 1 dose at 15 μg in adults and 2 doses in children <10 resulted in protective antibody levels (FDA criteria), in some studies as early as 8-10 days**
- **In trials with adjuvant, an even stronger immune response, with significant dose sparing, but more local and systemic reactivity**
- **Safety results consistent with seasonal vaccine clinical trials**
- **No SAEs definitely related to vaccine and no increase over expected cases of immune-mediated disorders**
- **BARDA also collaborating with NIAID on Mix-and-Match study, combining antigen and adjuvant from different manufacturers**

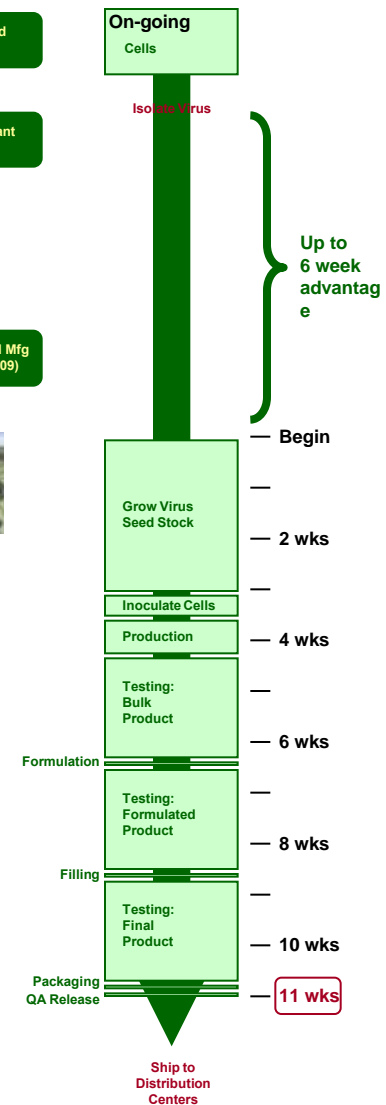
H1N1 Vaccine Manufacturing Process

Current Technology



Future Technology

Cell- and Recombinant-based





BARDA-IEDD and other HHS International Support



- **Vaccines**
 - \$24.4 M provided to WHO through cooperative agreement grants: 6 countries originally funded including Vietnam (IVAC)-total of 10 countries to be funded.
 - \$1M direct HHS grant to VABIOTECH in Vietnam.
 - \$3.5M awarded to WHO for further support of LAIV development.
 - \$8M awarded to PATH in 2009 for clinical trials in Vietnam with international pre-pandemic vaccine candidates.
 - US will donate 10% of H1N1 vaccine produced for US to WHO
- **Anti-virals**
 - HHS provided antivirals to WHO international stockpile and to H1N1 outbreak in Mexico-continues to maintain intl. stockpile
- **Diagnostics**
 - HHS/BARDA provided \$4M to support deployment of HHS funded contractor diagnostics POC to domestic & international sites.
- **Other Countermeasures**
 - HHS has supported a wide range of activities through CDC, NIH etc..

National Strategy for Pandemic Influenza (Nov 2005) and HHS Pandemic Influenza Plan (Nov 2005) www.pandemicflu.gov

Pandemic and All-Hazards Preparedness Act- Title IV, sec. 401

IPAPI initiative



www.vaccineworkshop.hhs.gov

U.S. Influenza Vaccine Landscape 2008-2009

Seasonal Vaccine Supply

- Five Inactivated Split Vaccines
- **Four Inactivated Split Vaccines in Clin Dev**
- **One Live Attenuated Vaccine**

Pandemic Vaccines

- One Inactivated Split Vaccine
- Three Inactivated Split Vaccines in Clin Dev

U.S. Influenza Vaccine Manufacturing

- Egg-based TIV (90M seasonal doses/yr)
- **Cell-based TIV (UC) (50M seasonal doses/yr)**
- **Egg-based LAV (15M seasonal doses)**
- **Adjuvant (UC)**

Seasonal Vaccine Technology

- Trivalent formulation
- Egg-based Manufacturing
- Cell-based Manufacturing

Pandemic Vaccine Technology

- Antigen-only formulation
- Adjuvanted formulations in Clin Dev
- Antigen-sparing
- Cross-protective formulations
- Mix N Match



Merci beaucoup