



**United States Department of  
Health & Human Services  
Office of the Assistant Secretary for Preparedness and Response (ASPR)**

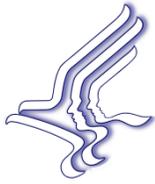
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# **Influenza Vaccine and Adjuvant Stockpiles**

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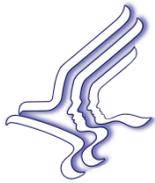


# Influenza Division Stockpiling Mission Is Defined By Several Key Documents:

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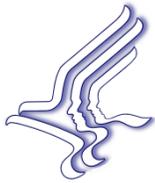
- The National strategy for Pandemic Influenza (November 2005) designated the HHS as the lead agency for public health and preparedness
- Under the HHS Pandemic Influenza Plan (November 2005) the Department's key goals for vaccine preparedness are:
  - » Stockpile enough pre-pandemic influenza vaccines to cover 20 million people in the critical workforce;
  - » Develop sufficient domestic manufacturing capacity to produce pandemic vaccine for the entire US population of 300 persons within six months of pandemic onset.



# Pre-Pandemic H5N1 Vaccine Stockpile Acquisition Strategy



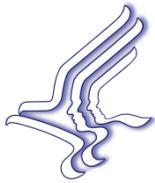
- Utilize manufacturers of US-licensed seasonal inactivated influenza vaccines
- Support commercial scale manufacturing of pre-pandemic vaccines using manufacturing process, facilities, systems and trained personnel for US-licensed seasonal inactivated influenza vaccines
- Support manufacturing during off-season for US-licensed seasonal inactivated influenza vaccines
- Maintain vaccine as bulk product at manufacturers or storage facilities for fill finish when clinical data and circumstances support final container formulations



# Key Considerations When Selecting A Strain For The US Pre-Pandemic Stockpile



- What strains are currently circulating and causing disease?
  - » Human H5N1 infections: frequency and location
  - » HA genetic variation
- What candidate strains are available for vaccine production?
- What is known about the “manufacturability” of the candidate strain?
- What are the manufacturing availability/ capabilities?



# Current Pre-Pandemic Vaccine Stockpile Contracts



- Between 2004 and 2008 nine contracts were awarded to three contractors (GSK-Novartis-Sanofi Pasteur) for the acquisition of pre-pandemic avian influenza H5N1 vaccine
- The USG acquired 152 million doses @ 15 $\mu$ g/ dose (25.3 M doses @ 90 $\mu$ g/ dose)
- Indefinite Delivery/ Indefinite Quantity (ID/IQ) type of contracts were awarded and the manufacturers were requested (if task order issued) to:
  - » Manufacture bulk lots of vaccine
  - » Store bulk vaccine and perform stability testing
  - » Formulate-fill-finish product
  - » Modified for the 2009 H1N1 response

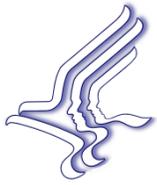


# Current Pre-Pandemic Vaccine Stockpile



H5N1 Bulk Vaccine (Clade)	2005	2006	2007	2008	2009	Totals M doses @ 90 µg/dose
A/VTN/1203/04 (1)	2.27	1.77		0.85		4.89
A/Indo/05/05 (2.1.3)		5.95	2.22	0.04		8.21
A/BHG/QL/1A/05 (2.2)			4.23			4.23
A/Anhui/1/05 (2.3.4)			1.75			1.75
<b>Bulk Vaccine Doses @ 90 µg/dose</b>	<b>2.27</b>	<b>7.72</b>	<b>8.20</b>	<b>0.89</b>		<b>19.08*</b>

• Number of doses adjusted to reflect usage and current potency level of bulk vaccine



# US Pre-Pandemic Adjuvant Stockpile



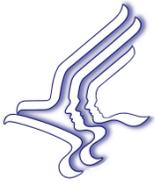
Adjuvant (MF59 and ASO3)	Total Doses (M)
Bulk	120.2
Final Container (FC)	5.2



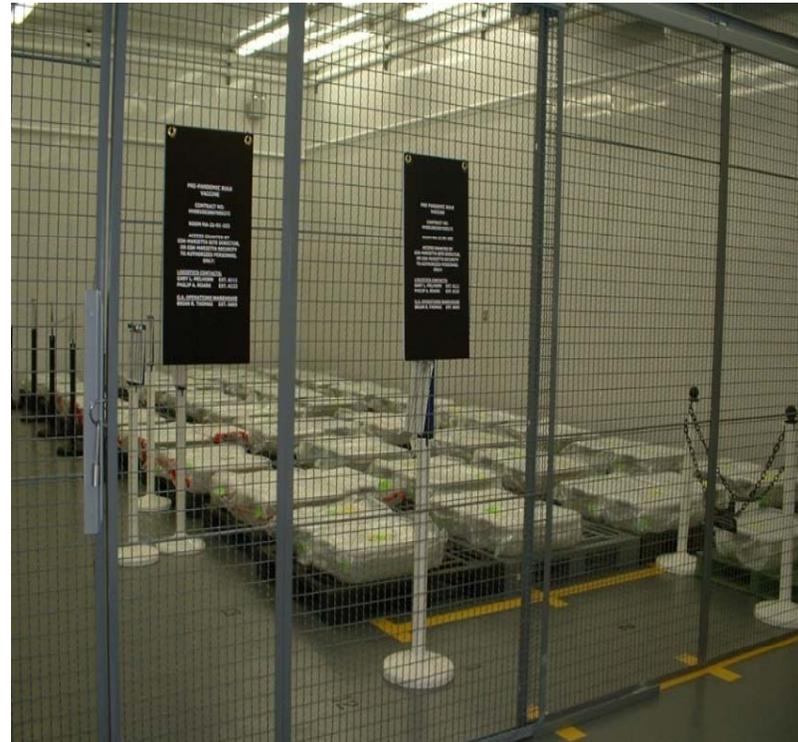
# US Pre-Pandemic Vaccine/Adjuvant Stockpile

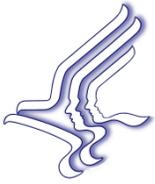


	90 $\mu$ g/dose	7.5 $\mu$ g/dose	3.75 $\mu$ g/dose
A/VTN/1203/04 (1)	4.89	58.6	117.2
A/Indo/05/05 (2.1.3)	8.21	98.5	197
A/BHG/QL/1A/05 (2.2)	4.23	50.7	101.4
A/Anhui/1/05 (2.3.4)	1.75	21.0	42
Total Bulk Vaccine Doses @ 90 $\mu$ g/dose	19.08		
Total Bulk Vaccine Doses @ 7.5 $\mu$ g/dose		228.8	
Total Bulk Vaccine Doses @ 3.75 $\mu$ g/dose			457.6

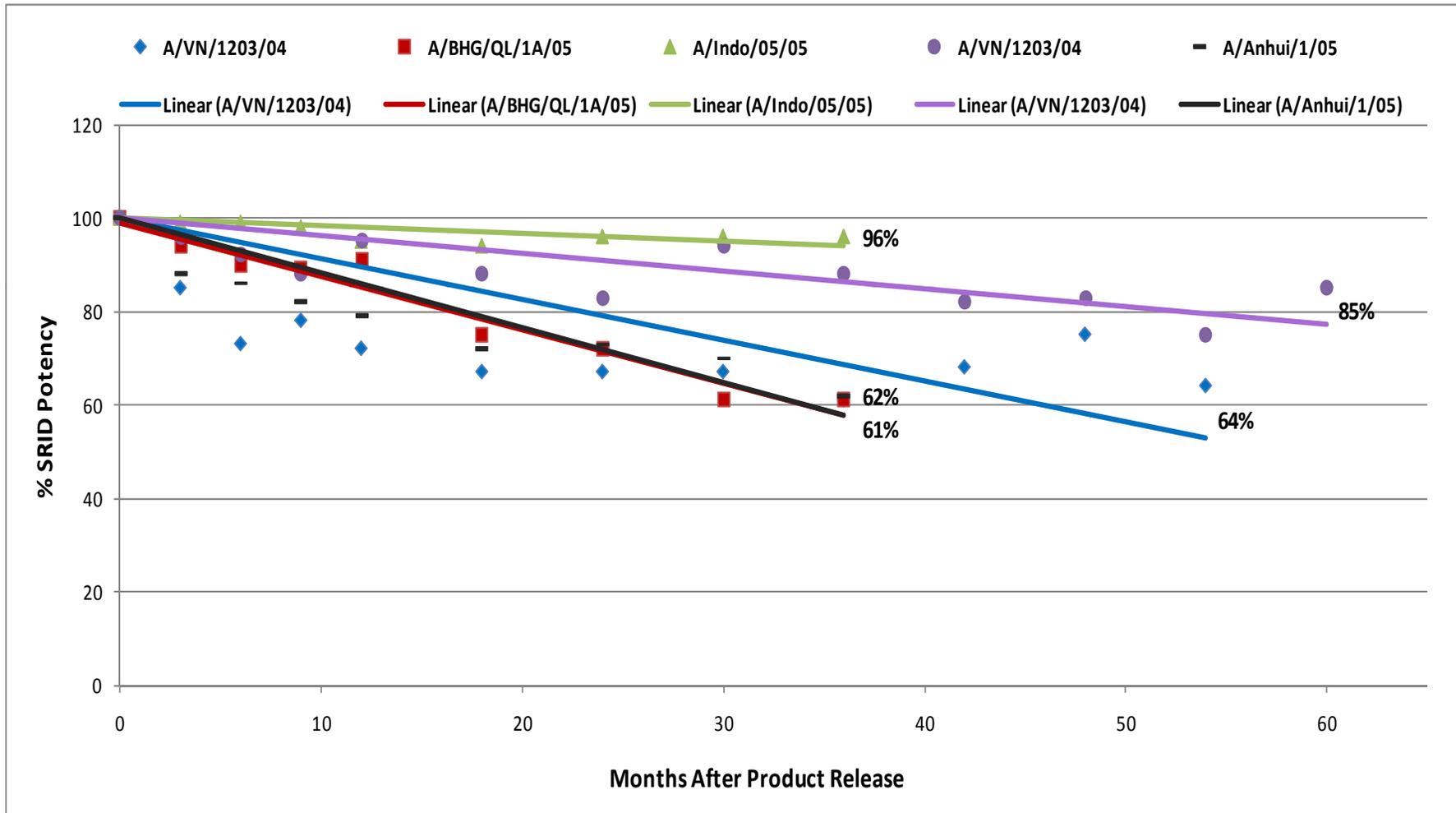


# Pre-pandemic Vaccine Stockpile





# H5N1 Stability Profile



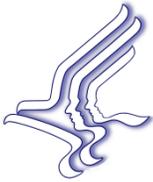


# Importance Of Maintaining The US Pre-Pandemic Vaccine Stockpile

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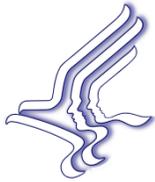
- Large USG investment (~\$1B)
- H5N1 Pre-Pandemic vaccine of several clades/ sub-clades is ready to be FFF in case of pandemic
- Long-term storage influenza vaccine
- Keep monitoring the H5N1 vaccine potency
- Clinical evaluation is needed to confirm stability and provide data for potential EUA



# H1N1 2009 Pandemic



- To respond to the H1N1 2009 pandemic the USG modified the three existing vaccine stockpile contracts and awarded two additional contracts
  - » 230 million bulk doses of H1N1 were supplied by the manufacturers
  - » 186 million doses of H1N1 vaccine were filled by the manufacturers
    - 149 million doses provided to CDC for distribution to public
    - 16 million doses donated internationally
    - 2.7 million doses supplied to the US military
- 120 Million doses of bulk adjuvants (ASO3 and MF59) were also purchased as a contingency



# H1N1 2009 Pandemic – Lesson Learned



- Need to deliver vaccine sooner
  - » Study of high productivity strains to improve candidate viruses
  - » Rapid sterility testing methods to shorten lot release
  - » Improved potency assays that don't require the current wait for reagents
- Need vaccines produced by methods that don't require virus replication
  - » Recombinant vaccine awards
- Need to expand formulation, fill and finish (FFF) capabilities – all manufacturers in 2009 added FFF to respond to the needs for H1N1 vaccine



# Adjuvant-H5N1 Vaccine Antigen “Mix-N-Match Study”

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- **Goal:**

In response to a pandemic, expand the coverage of the influenza vaccine stockpile using the antigen sparing properties of adjuvants. Collaboration between Industry partners and other Federal agencies (NIAID; VTEU's) enhancing response to pandemic.

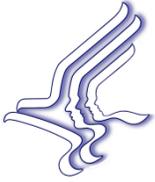
- **Objective:**

To determine whether adjuvants under advanced development by BARDA and H5N1 vaccines stockpiled by the USG can be used safely and effectively during an influenza pandemic under EUA.

- **Products:**

Vaccine: H5N1 A/Indonesia/05/05

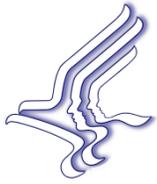
Adjuvants: ASO3 and MF59



# Mix N Match Status



- Physicochemical analysis of adjuvant/antigen mixture
  - » no issues
- Animal immunogenicity studies
  - » no issues
- Rabbit toxicology studies
  - » no issues
- Phase 1 clinical dose-ranging studies for safety and immunogenicity
  - » in progress



# US Pre-Pandemic Vaccine Stockpile Program - Accomplishments



- National stockpile comprised of bulk product forms of H5N1 vaccine antigen and oil-in-water adjuvants
- Multiple vaccine manufacturers
- Multiple sub-clades of H5N1 viruses represented
- Vaccine licensed in U.S. by one manufacturer as antigen-alone formulation (90  $\mu\text{g}$  HA/dose) in 2007
- Two oil-in-water adjuvants with H5N1 and H1N1 vaccine  
Mix-n-Match studies performed with HHS support



# Pre-Pandemic Vaccine Stockpile Future Directions



- Informative Documents
  - » The Public Health Emergency Medical Countermeasures Enterprise Review (August 2010)
  - » President's Council of Advisors on Science and Technology (PCAST) Report to the President on reengineering the influenza vaccine production enterprise to meet the challenges of pandemic influenza (August 2010 )
  
- Future Directions
  - » Investment in technology and methods to produce and release vaccines more rapidly
  - » Improve productivity and expand the number of available candidate viruses for pre-pandemic vaccine production
    - Improve the understanding of the productivity of available candidate viruses
  - » Continued stability monitoring of existing stockpiles
    - Support with clinical testing program