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Highly Pathogenic Avian Influenza (H5) Virus Vaccines - Introduction

Vaccines and Related Biological Products Advisory Committee (10/10/2024)

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Purpose of Today's VRBPAC Committee Discussion on H5 Vaccines

- Update the VRBPAC about the current influenza H5 situation in the U.S., the status of currently licensed H5 vaccines, and ongoing clinical trials
- Provide clarification about the strain change process and expected data requirements for updating licensed pandemic influenza vaccines during the inter-pandemic period
- Discuss the availability of H5 candidate vaccine strains to be considered for incorporation in updated licensed H5 vaccines

Background

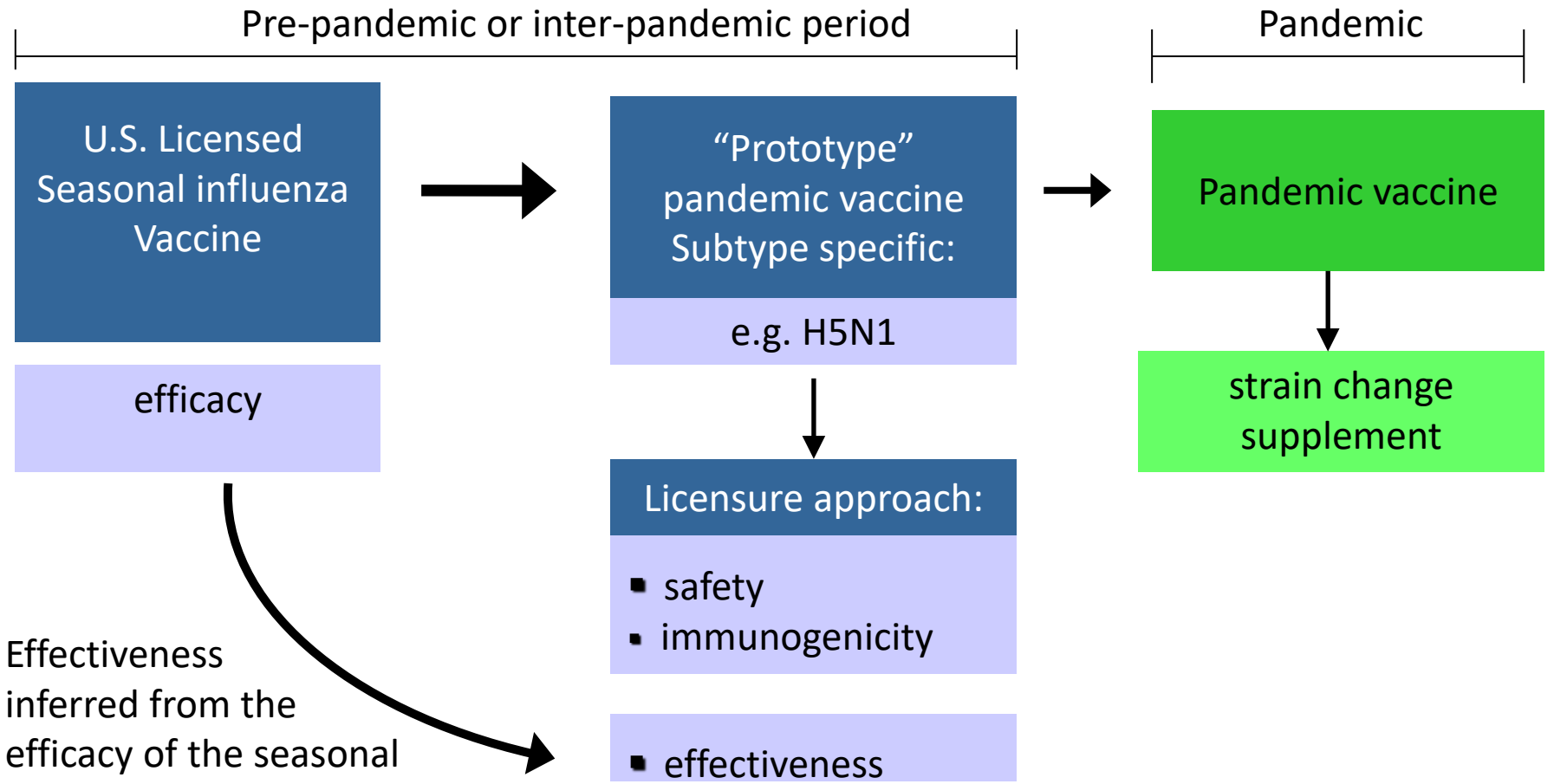
- 2007 – Provided guidance for approaches to facilitate licensure of pandemic influenza virus vaccines in "Guidance for Industry: Clinical data needed to support the licensure of pandemic influenza vaccines"
  - For manufacturers of U.S. licensed seasonal inactivated vaccines
    - Clinical immunogenicity studies to determine dose and schedule
  - For manufacturers of U.S. licensed live attenuated vaccines
    - Noted special concerns regarding clinical studies in advance of a pandemic due to possibility of reassortment
  - For manufacturers without a U.S. licensed seasonal vaccine
    - Noted challenges in identifying an immune surrogate that predicted clinical benefit
- 2007 – Licensure of the first H5 Influenza Virus Vaccine – Sanofi Pasteur
  - Two 90 µg doses i.m., 28 days apart; 18-64 years of age
  - Clade 1 A/Vietnam/1203/2004 vaccine evaluated
- 2009 – H1N1 pandemic
  - H1N1 emergency declared
  - Strain change supplement to BLA allowed fastest availability of vaccine
  - Clinical trials of monovalent vaccines were initiated to confirm immunogenicity and to inform any dose and schedule modifications needed; data submitted post-approval

Background – 2

- 2012 VRBPAC discussion – Licensure of Pandemic Influenza Vaccines: Demonstration of Effectiveness
  - Reiterated that licensure of a pandemic influenza vaccine, e.g., an influenza strain not included in the seasonal influenza vaccine, would be licensed as a new vaccine
  - Safety and immunogenicity data to select the dose and dosing regimen required before licensure
  - Effectiveness inferred from seasonal vaccine
  - Initial licensure was considered as the prototype that would permit a future strain change supplement
  - The committee felt that it was premature to discuss licensure of pandemic influenza vaccines that were not dependent on an HA antibody response
- 2013 – Licensure of adjuvanted H5 Influenza Virus Vaccine – ID Biomedical Corporation of Quebec
  - Two 3.75 µg doses with AS03 adjuvant, i.m., 21 days apart; 18 and older; half dose for 6 months to 17 years of age
  - Clade 2.1.3.2 A/Indonesia/05/2005 evaluated
- 2020 – Licensure of adjuvanted H5 Influenza Virus Vaccine (MDCK) – Seqirus
  - Two 7.5 µg doses with MF59 adjuvant, i.m., 21 days apart; 6 months and older
  - Clade 2.2.1 A/turkey/Turkey/1/2005 evaluated

Current Regulatory Pathway for Licensure of Pandemic Influenza Virus Vaccines

- Process used for currently licensed pandemic vaccines
- Assumes that strain changes recommended by VRBPAC would be implemented during a declared pandemic, and would not require clinical data before approval



Recent Developments

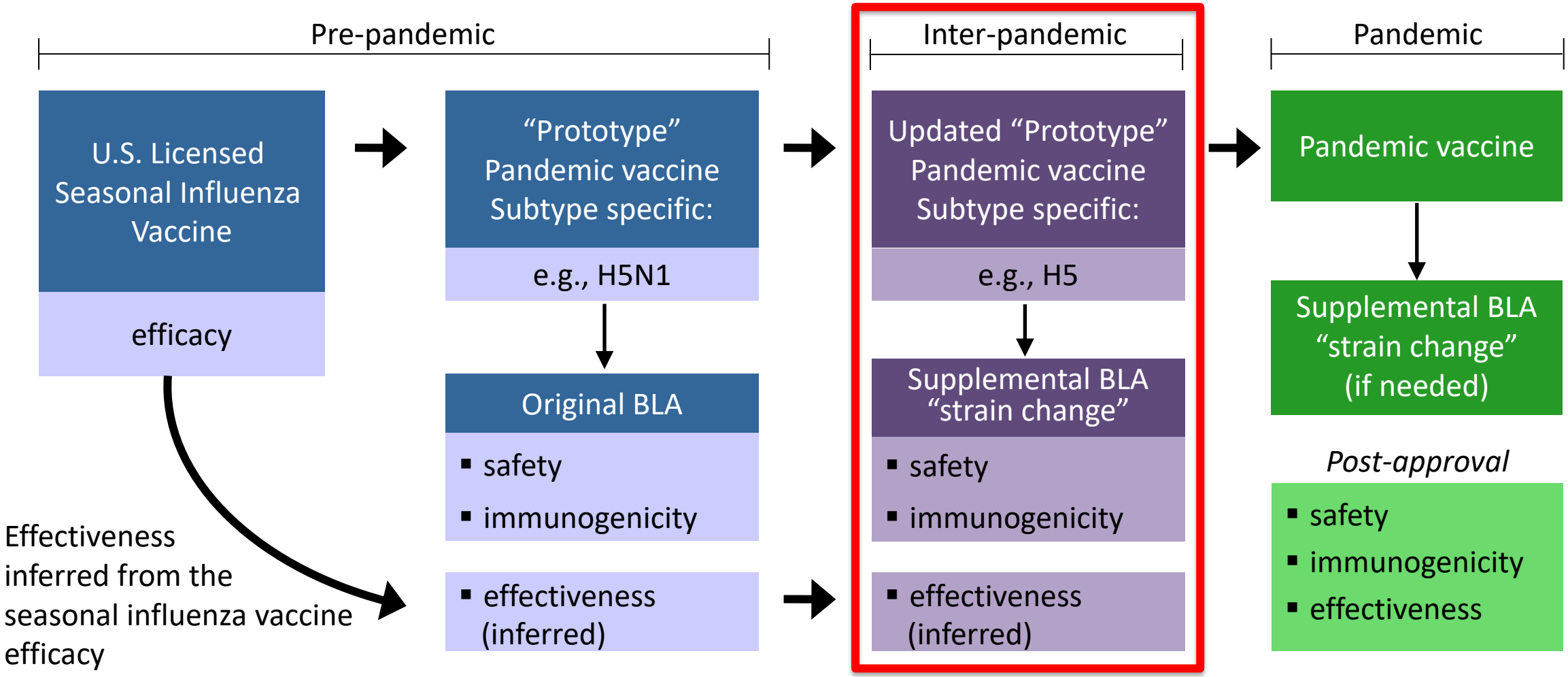
- H5 influenza viruses have continued to diversify genetically and antigenically into multiple clades and sub-clades
  - In recent years, H5 virus isolates have been almost exclusively from clades 2.3.2.1 or 2.3.4.4
- Highly pathogenic avian influenza (HPAI) H5 viruses re-entered North America, and subsequently the United States, at the end of 2021 and early 2022
- These H5 viruses evolved rapidly and resulted in large outbreaks in wild aquatic birds, commercial poultry, marine mammals, and dairy cows; sporadic human infections have also been reported
- Genetic analysis has indicated that these H5 viruses circulating in the U.S. are from the H5N1 clade 2.3.4.4b and that the hemagglutinin is closely related antigenically to the HA of a recent human H5N8 isolate A/Astrakhan/3212/2020 (A/Astrakhan)
- Candidate vaccine viruses have been prepared for A/Astrakhan/3212/2020 and for more recent virus isolates of clade 2.3.4.4b such as A/American Wigeon/South Carolina/22-000345-001/2021
- Manufacturers have requested additional details and clarity about the process for updating the strain composition of pandemic influenza vaccines in the inter-pandemic period

Proposed Process for Updating Pandemic Influenza Vaccines in the Inter-Pandemic Period

- VRBPAC periodically discusses:
  - Whether a change to the current composition of a licensed prototype vaccine is needed for preparedness purposes
  - The appropriateness of currently available candidate vaccine strains for a possible update to licensed prototype vaccines
- Manufacturers of licensed pandemic vaccines prepare a data package for regulatory review of their updated pandemic vaccine, to include:
  - Chemistry, manufacturing, and control data for the updated vaccine to ensure product quality and consistency
  - Clinical immunogenicity and safety data
- VRBPAC would re-convene, if/when an influenza pandemic is declared, to make a final composition recommendation

Updating Pandemic Influenza Vaccines in the Inter-Pandemic Period

- Process assumes continued VRBPAC input
- Timing of supportive data submission differs between inter-pandemic and pandemic situations



Discussion Topics

- Please discuss and provide input on the proposed strain change process during the inter-pandemic period

- Please discuss whether a change to the current composition of licensed prototype vaccines using the proposed process is needed for preparedness purposes and whether candidate vaccine viruses are available that are appropriate to update currently licensed prototype vaccines


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