Perspectives in Pandemic Influenza Preparedness
FDA’s Role in the Development and Licensure of Seasonal & Pandemic Influenza vaccines

Marion F. Gruber, PhD
Director, Office of Vaccines Research & Review
FDA/CBA

BARDA Industry Day
October 30, 2018
Washington D.C.
<table>
<thead>
<tr>
<th>Valency</th>
<th>Vaccine type</th>
<th>Trade name</th>
<th>Age range</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trivalent</td>
<td>Inactivated, egg-based</td>
<td>Fluzone</td>
<td>≥ 6 months of age</td>
<td>Sanofi-Pasteur</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluzone High Dose</td>
<td>≥ 65 years of age</td>
<td>Sanofi-Pasteur</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluzone Intradermal</td>
<td>18 – 64 years of age</td>
<td>Sanofi-Pasteur</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluarix</td>
<td>≥ 3 years of age</td>
<td>GSK</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FluLaval</td>
<td>≥ 6 months of age</td>
<td>GSK</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluviron</td>
<td>≥ 4 years of age</td>
<td>Seqirus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Agriflu</td>
<td>≥ 18 years of age</td>
<td>Seqirus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Afluria</td>
<td>≥ 6 months of age</td>
<td>Seqirus Pty Ltd</td>
</tr>
<tr>
<td></td>
<td>Inactivated, adjuvanted</td>
<td>Fluad</td>
<td>≥ 65 years of age</td>
<td>Seqirus</td>
</tr>
<tr>
<td></td>
<td>Inactivated, cell-based</td>
<td>Flucelvax</td>
<td>≥ 4 years of age</td>
<td>Seqirus</td>
</tr>
<tr>
<td></td>
<td>Recombinant Protein</td>
<td>Flublok</td>
<td>≥ 18 years of age</td>
<td>Protein Sciences Corp</td>
</tr>
<tr>
<td></td>
<td>Live attenuated vaccine</td>
<td>FluMist</td>
<td>2 – 49 years of age</td>
<td>Astra Zeneca</td>
</tr>
<tr>
<td>Valency</td>
<td>Vaccine type</td>
<td>Trade name</td>
<td>Age range</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------------------------</td>
<td>------------------------</td>
<td>------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>Quadrivalent (QIV)</td>
<td>Inactivated, egg-based</td>
<td>Fluzone QIV</td>
<td>≥ 6 months of age</td>
<td>Sanofi-Pasteur</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluzone Intradermal QIV</td>
<td>18 – 64 years of age</td>
<td>Sanofi-Pasteur</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FluLaval QIV</td>
<td>≥ 6 months of age</td>
<td>GSK</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Afluria QIV</td>
<td>≥ 6 months of age</td>
<td>Seqirus Pty Ltd</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluarix QIV</td>
<td>≥ 6 months of age</td>
<td>GSK</td>
</tr>
<tr>
<td>Inactivated, cell-based</td>
<td>Flucelvax Quadrivalent</td>
<td>≥ 4 years of age</td>
<td>Seqirus Inc</td>
<td></td>
</tr>
<tr>
<td>Recombinant Protein</td>
<td>Flublok Quadrivalent</td>
<td>≥ 18 years of age</td>
<td>Protein Sciences Corp</td>
<td></td>
</tr>
<tr>
<td>Live attenuated</td>
<td></td>
<td>FluMist QIV</td>
<td>2 – 49 years of age</td>
<td>Astra Zeneca</td>
</tr>
<tr>
<td>Monovalent A/H5N1 (pandemic)</td>
<td>Inactivated, egg-based</td>
<td>n/a</td>
<td>18 – 64 years of age</td>
<td>Sanofi-Pasteur</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 2 doses, 90 μg HA/dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>n/a</td>
<td>• ≥ 18 years of age, 3.75 μg HA with AS03</td>
<td>GSK</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• 6 months -17 years of age, 1.9 ug HA with AS03</td>
<td></td>
</tr>
</tbody>
</table>
Each year, one or more of the vaccine strains may be replaced with a new strain.

FDA convenes VRBPAC to recommend influenza vaccine strains to be included in FDA-licensed vaccines based on WHO consultation on flu vaccine composition.

Submission of a prior approval manufacturing supplement to an existing biologics license application (BLA) is required for annual influenza strain chain.

- "Strain change supplement"
  - Inactivated vaccines: No clinical data
  - Live attenuated: Limited clinical data

Lot release
CBER is a WHO Essential Regulatory Laboratory (ERL): Influenza Product Quality Laboratories

CBER’s ERL activities include
• Yearly flu strain selection
• Antigenic characterization of circulating influenza isolates for strain selection purposes
• Generation of high growth reassortants viruses suitable for use in vaccine production
• Production, calibration and provision of SRID reference reagents to measure vaccine potency
• Antigenic confirmation of production seeds
• Lot release
US -Licensed Pandemic Influenza Vaccines: Influenza A (H1N1) 2009 Vaccines

• Approved as strain change supplements to the seasonal influenza virus vaccine BLAs
  
  • Consistent with licensure of seasonal vaccines
  
  • Consistent with past regulatory actions: 1986 - Influenza A/Taiwan/1/86 H1N1
    • Monovalent vaccines licensed as strain change supplements
    • No clinical data
  
  • Supported by VRBPAC 7/2009
Pre-pandemic period

U.S. Licensed Seasonal influenza vaccine
A, subtype: H1, H3

Licensure approach:
- Safety
- Immunogenicity
- Efficacy

Annual update:
- Strain change supplement

Licensure of "Prototype" pandemic vaccine:
- Adjuvanted
- Unadjuvanted

A, subtype: H5
A, subtype: H7
A, subtype: H9...

Pandemic

Pandemic vaccine update:
- Adjuvanted
- Unadjuvanted

- Strain change supplement

A, subtype: H5
A, subtype: H7
A, subtype: H9...

Annual update:
- Strain change supplement
- Effectiveness inferred from the efficacy of the seasonal flu vaccine
Pandemic Influenza Vaccines manufactured using a process that is not U.S. licensed (with or without adjuvant)

• Demonstration of effectiveness:
  • If the manufacturer develops a seasonal influenza vaccine:
    • Infer effectiveness of the vaccine from the efficacy of the seasonal made by the same process
  • If the manufacturer does not develop a seasonal vaccine:
    • Accelerated Approval: Prelicensure safety and immunogenicity data required to support dose and dosing regimen
    • Manufacturer must verify clinical benefit during the pandemic

Guidance for Industry- Pandemic Influenza vaccines 2007
Preparing for the next Pandemic

Regulatory pathways to licensure are defined

Vaccine availability
- Continue to explore options to accelerate vaccine availability
  - Alternative manufacturing technologies/platforms
    - Cell-based, recombinant, adjuvants and delivery systems

Reagents/potency testing
- Development of alternatives to SRID are ongoing

Development of correlate of protection