The FDA CBER requested this annual summary of information from influenza vaccine manufacturers supplying the U.S., for purposes of a general presentation to the VRBPAC. This summary has been prepared from a variety of public sources, and was reviewed by Sanofi Pasteur, Seqirus, GSK, Protein Sciences and AZ/MedImmune.
Annual Influenza Vaccine US Supply Timeline

- **Surveillance & Reassortants**
  - CDC
  - FDA
  - WHO

- **Strain Selection**
  - CDC
  - FDA
  - WHO

- **Produce & Standardize Reagents for New Strains**

- **Annual License Approval**

- **Produce Working Seed**

- **Production (may be at risk)**

- **Production**

- **Strain Balancing**

- **Formulation**

- **Filling & Packaging**

- **Distribution**

- **Vaccination**

- **Surveillance & Reassortants**

- **Limited time (∼6 months) to supply vaccine: delaying strain selection will impact vaccine distribution schedules**

Industry Comments, VRBPAC 04 March 2016
US Influenza Vaccine Distribution: 1980-2016*

Vaccine supply requires well-matched strains, sufficient quantities, timely pre-season delivery

To date (19Feb’16) 146.4 million doses distributed: initiated 04Sep’15

End of Mar’14 (not Feb’14) strain selection would have delayed initial dose supply to Oct’14

*Reported to CDC by manufacturers and selected distributors [http://www.cdc.gov/flu/professionals/vaccination/vaccinesupply.htm](http://www.cdc.gov/flu/professionals/vaccination/vaccinesupply.htm)
Influenza Strains Evaluated for NH 2016-2017*

- **A(H1N1):** A/California/07/09-like
  - A/Brisbane/10/10
  - A/Bolivia/559/13
  - A/South Africa/3626/13
  - A/New Caledonia/58/14
  - A/Florida/62/14
  - A/Minnesota/32/15
  - A/Slovenia/2903/15
  - A/St. Petersburg/61/15
  - A/Michigan/45/15 (6B.1)
  - A/Iowa/53/16 (6B.2)

- **A(H3N2):** A/Hong Kong/4801/14-like
  - A/Hong Kong/7127/14
  - A/New Caledonia/71/14
  - A/Norway/2178/14
  - A/Montana/28/15
  - A/South Australia/09/15
  - A/Brisbane/47/15 & /82/15

- **B Victoria:** B/Brisbane/60/08-like
  - B/Texas/2/13
  - B/Indiana/25/15
  - B/Brisbane/46/15

- **B Yamagata:** B/Phuket/3073/13-like
  - B/Brisbane/9/14
  - B/Utah/09/14
  - B/Maryland/12/15
  - B/California/12/15


Industry Comments, VRBPAC 04 March 2016
Concerns Regarding Late-Emerging H1N1 Genetic Subgroup/s

- A(H1N1) viruses typically are lower yielding strains than A(H3N2) viruses – require longer manufacturing campaigns
- Currently, no new representative viruses or CVVs confirmed
- No high-growth reassortants identified
- No potency assay reagents available
- Many manufacturers may have already produced (at risk) significant H1N1 amounts for 2016 which will further impact timing and quantity of supply
A 2-3 Week Delay of H1N1 Strain Selection Now Would Delay Influenza Vaccine US Supply by at Least 4 Months

- Assuming 2-3 week delay to identify representative viruses
- Additional 3+ weeks to prepare reassortants
- Additional 12+ weeks to prepare potency assay reagents
- Total: 18+ weeks or 4-5 month delay for vaccine availability
Industry Engagement with WHO and HHS to Improve Seasonal Influenza Vaccine Supply

- Improving influenza vaccine supply, support requirements, risk management
- Response strategies to supply “late”/mismatched strains e.g. H3N2 drift (2014-2015)
- Assessing seasonal vaccine supply impact of adherence to the Nagoya Protocol
Seasonal Influenza Vaccine Improvement

- Given H3N2 drift (2014-'15) HHS hosted meetings (Jun & Nov’15) with HHS/BARDA, FDA, CDC, NIBSC, industry representatives
  - Surveillance, characterization, vaccine improvements, supply mitigation options
- Delayed candidate vaccine strain availability scenarios:
  - To April: delays vaccine availability, impacts immunization programme schedules
  - To July: manufacture in-process, potentially two different vaccines in same campaign, reduced uptake of late vaccine
- In rare circumstances of a late emerging strain: delaying selection to mid-late March acceptable if: appropriate CVVs available; assay reagents in process
- In the rare circumstance of a significant delay then this will need to be centrally coordinated (akin to the 2009 H1N1 pandemic response)

Given the multiple challenges, preference is for no strain selection delay
Nagoya Protocol: Background & Potential Impact

• Developed from access-and-benefit sharing discussions at the Convention on Biodiversity (2010)
  o Adopted October 2010, ratified July 2014, came into force October 2014
  o Access to genetic resources and related traditional knowledge for potential research and utilization purposes
    o Users and providers of genetic resources and related traditional knowledge, agree on fair and equitable sharing of benefits arising from their utilization
• Potentially impacting seasonal influenza strain availability as pathogens are included
• Obligations under the NP will require negotiating terms of pathogen use

Unknown impact on influenza vaccine availability for the US market
Concluding Comments

• Timely vaccine supply requires close collaboration and communication between multiple stakeholders to ensure sufficient provision of well-matched vaccine

• Timely strain selection ensures vaccine availability and usage
  o Preference is for current strain recommendation timelines and if a change is required, do so for one strain by mid-late March

• Impact of adherence to the Nagoya Protocol may be a delay in seasonal influenza vaccine supply and distribution in the US

Thank you for your attention…