Influenza Vaccine Manufacturing

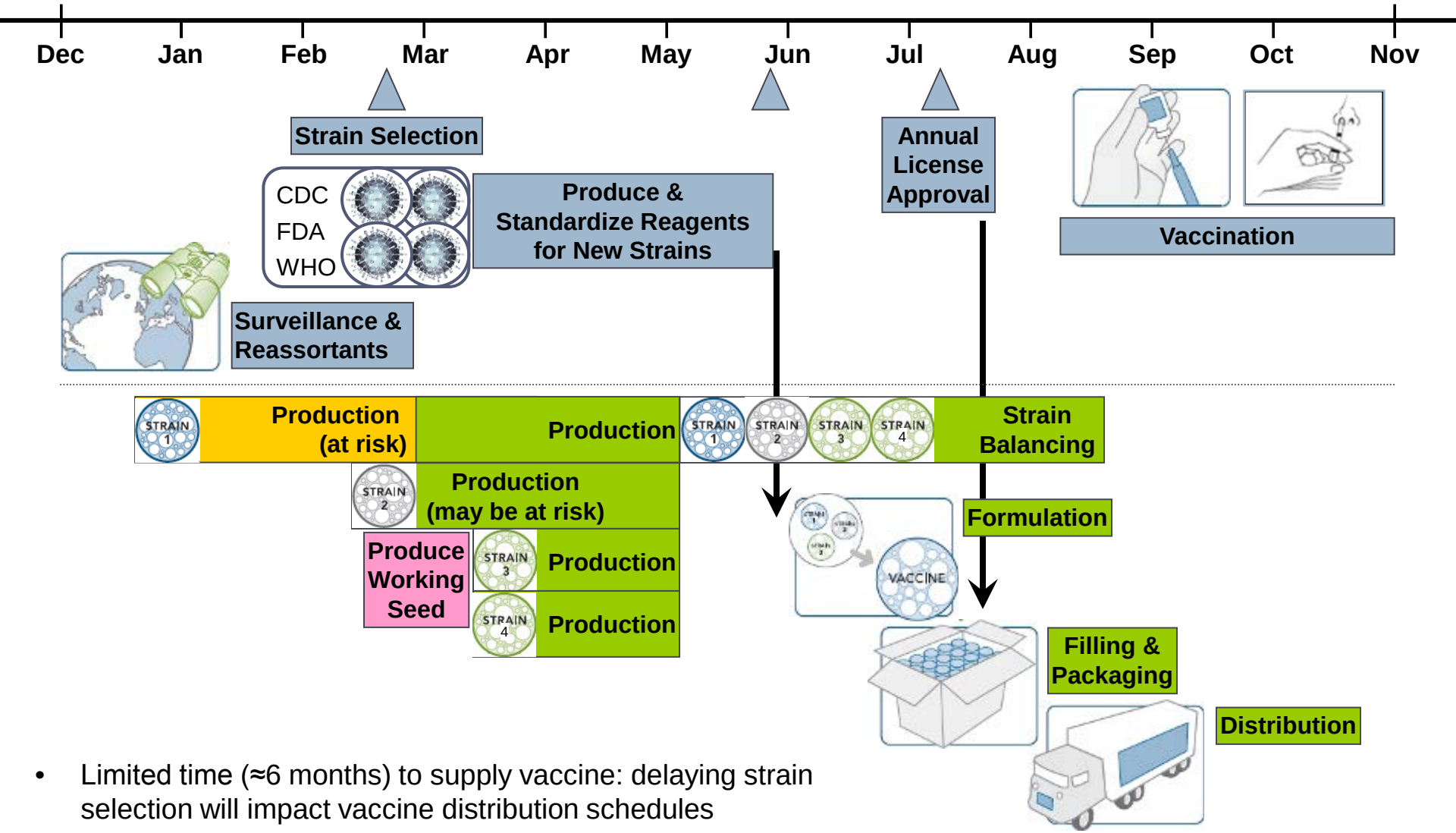
Industry Perspective for 2016-17 Northern Hemisphere Influenza Vaccine Supply

Vaccines and Related Biological Products Advisory Committee

04 March 2016

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

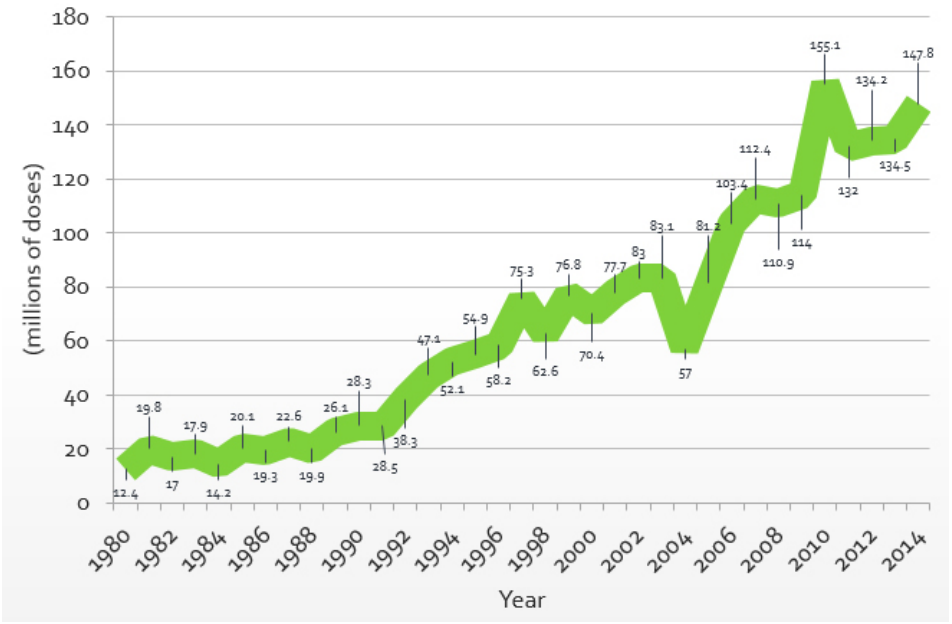
Annual Influenza Vaccine US Supply Timeline



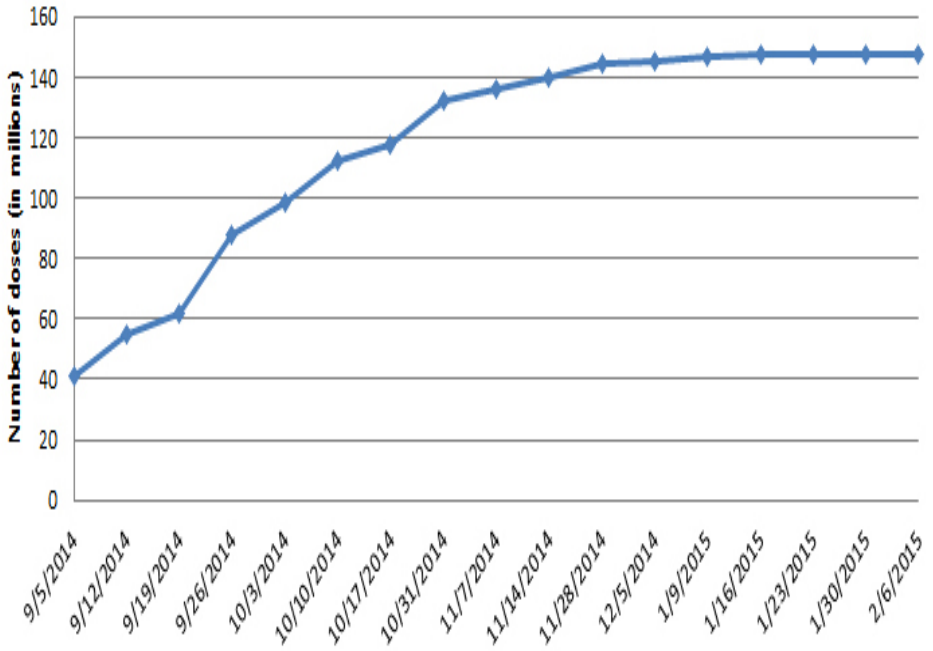
- Limited time (≈6 months) to supply vaccine: delaying strain selection will impact vaccine distribution schedules

US Influenza Vaccine Distribution: 1980-2016*

1980-2014 Seasons – Total Doses



2014-2015 Season – Total Doses



- 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

Influenza Strains Evaluated for NH 2016-2017*

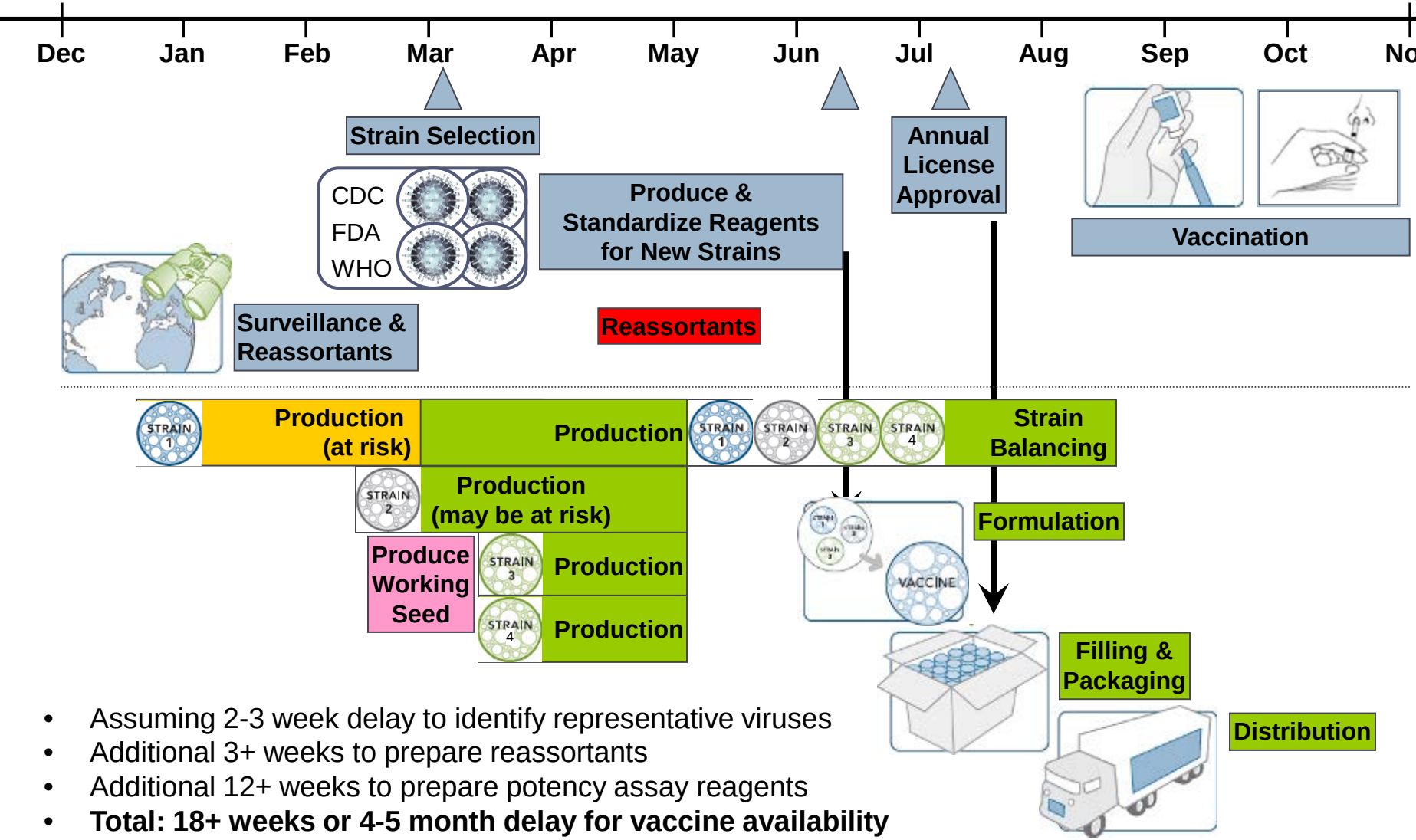
- **A(H1N1):** A/California/07/09-like
  - A/Brisbane/10/10
  - A/Bolivia/559/13
  - A/South Africa/3626/13
  - A/New Caledonia/58/14
  - A/Florida/62/14
  - A/Minnesota/32/15
  - A/Slovenia/2903/15
  - A/St. Petersburg/61/15
  - A/Michigan/45/15 (6B.1)
  - A/Iowa/53/16 (6B.2)
- **B Victoria:** B/Brisbane/60/08-like
  - B/Texas/2/13
  - B/Indiana/25/15
  - B/Brisbane/46/15
- **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 Yamagata:** B/Phuket/3073/13-like
  - B/Brisbane/9/14
  - B/Utah/09/14
  - B/Maryland/12/15
  - B/California/12/15

*WHO recommended strains for 2016-2017 highlighted in red http://www.who.int/influenza/vaccines/virus/recommendations/2016_17_north/en/

Concerns Regarding Late-Emerging H1N1 Genetic Subgroup/s

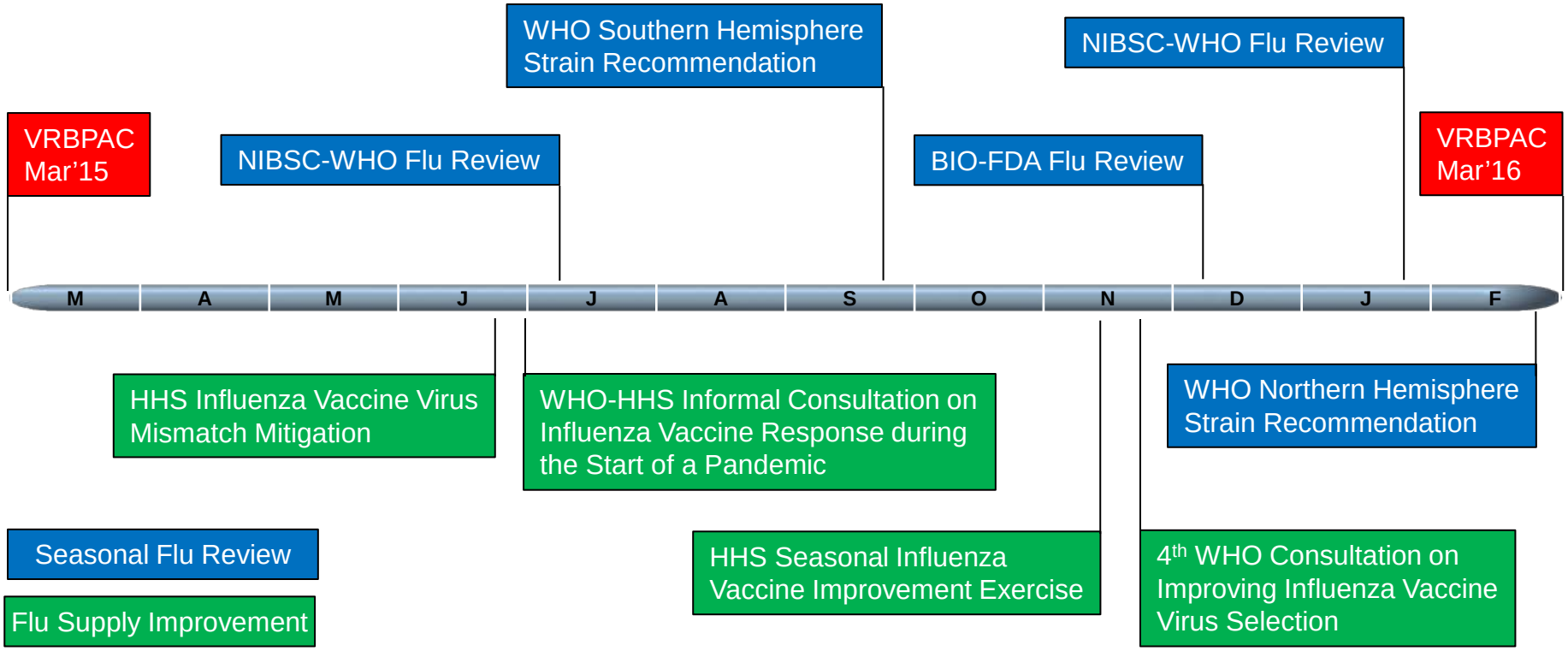
- A(H1N1) viruses typically are lower yielding strains than A(H3N2) viruses – require longer manufacturing campaigns
- Currently, no new representative viruses or CVVs confirmed
- No high-growth reassortants identified
- No potency assay reagents available
- Many manufacturers may have already produced (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)
  - Adopted October 2010, ratified July 2014, came in to force October 2014
  - Access to genetic resources and related traditional knowledge for potential research and utilization purposes
  - 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
  - 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…