



# **Influenza Virus Vaccine 2017-2018 Strain Selection**

**Vaccines and Related Biological Products  
Advisory Committee (3/9/2017)**

*Anissa Cheung, Regulatory Coordinator  
Division of Viral Products/OVRR/CBER/FDA*

# Purpose of Today's VRBPAC Committee Discussion

- Review influenza surveillance and epidemiology data, antigenic characteristics of recent virus isolates, serological responses to current vaccines, and the availability of candidate vaccine strains and reagents
- Make recommendations for the strains of influenza A (H1N1 and H3N2) and B viruses to be included in 2017-2018 influenza vaccines licensed for use in the United States

# Types of Analyses Used for Vaccine Strain Selection

- Epidemiology of circulating strains (*CDC*)
  - Surveillance data from U.S. and around the world
  
- Antigenic relationships among contemporary viruses and candidate vaccine strains (*CDC/DOD*)
  - Hemagglutination inhibition (HI) tests using post-infection ferret sera
  - HI tests using panels of sera from humans receiving recent inactivated influenza vaccines
  - Virus neutralization tests
  - Antigenic cartography
  - Phylogenetic analyses of HA and NA genes
  - Vaccine effectiveness

# Key Challenges for Vaccine Strain Selection

- Vaccine effectiveness depends on the match between the hemagglutinin (HA) of the vaccine and the HA of circulating strains of virus
  - Antigenic drift of HA continuous for influenza A and B
  - Antibody to HA correlated with vaccine efficacy
  
- Timelines for influenza vaccine production are relatively fixed
  - Strain selection in February/March necessary for availability of vaccine for subsequent northern hemisphere winter (influenza season)
  - Manufacturers typically begin production of monovalent of one strain before strain selection recommendations are made (at risk)
  
- Availability of reference strains (candidate vaccine viruses) suitable for vaccine manufacture
  - Vaccine production depends on growth properties of strains used for manufacture
  - Strain-specific reagents needed for potency determination (inactivated and recombinant protein vaccines)

# Seasonal Influenza Vaccine Production Timetable

- This slide is to illustrate the production timeframe of seasonal influenza vaccine starting from surveillance to the administration of vaccine to the general public

Steps	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC	
Surveillance	[Orange bar spanning all months]												
Select Strains	[Orange bar]												
Reference Virus	[Orange bar]												
Reagents	[Orange bar]												
Production		[Orange bar]											
Release							[Orange bar]						
Distribution								[Orange bar]					
Administer								[Orange bar]					

# Working Virus Seed for the Production of Inactivated Influenza Vaccines

- Egg isolated candidate vaccine virus strains are used traditionally
  - Antigenically characterized by WHO CCs
  
- August 31, 2016, the use of MDCK cell isolated candidate vaccine virus strain was approved for the manufacture of Flucelvax monovalent bulk
  - Manufacturer specific
  - Derived from 2 approved WHO CCs
  - Antigenic analysis as for egg isolated vaccine virus strains
  
- Working virus seeds are approved for quality and safety by the National Regulatory Authorities

# Trivalent and Quadrivalent Seasonal Influenza Vaccines

- Two antigenically distinct lineages of influenza B co-circulate
  - Represented by B/Victoria/2/87 and B/Yamagata/16/88
- Both trivalent and quadrivalent influenza vaccines now available
  - 7 quadrivalent vaccines currently licensed in U.S.
- Current process for selecting appropriate B strains for inclusion in trivalent and quadrivalent vaccines similar to procedure for trivalent vaccine recommendation
  - WHO and VRBPAC review and make recommendations for each formulation – trivalent and quadrivalent

# Review of the 2016-2017 NH Seasonal Influenza Vaccine Strain Composition

- VRBPAC strain selection – March 4, 2016
- Committee recommended the following strains for inclusion in U.S. 2016-2017 trivalent influenza vaccines
  - A/California/7/2009 (H1N1)pdm09-like virus
    - *No change from the 2015-2016 NH recommendation*
  - A/Hong Kong/4801/2014 (H3N2)-like virus
    - *Change from the A/Switzerland/9715293/2013 (H3N2)-like virus vaccine, but same as 2016 SH recommendation*
  - B/Brisbane/60/2008-like virus (B/Victoria lineage)
    - *Change from the B/Phuket/3073/2013-like virus (B/Yamagata lineage), but same as 2016 SH recommendation*
- For manufacturers producing a quadrivalent influenza vaccine, the Committee recommended a second B strain
  - B/Phuket/3073/2013-like virus (B/Yamagata lineage), previously recommended for quadrivalent vaccines in 2016 SH



# Recommendations for Influenza Vaccine Composition Southern Hemisphere: 2017

- VRBPAC recommendation – 10/13/2016
- Recommended that the following viruses be used for trivalent influenza vaccines in the 2017 southern hemisphere influenza season:
  - an A/Michigan/45/2015 (H1N1)pdm09-like virus
  - an A/Hong Kong/4801/2014 (H3N2)-like virus
  - a B/Brisbane/60/2008-like virus (B/Victoria lineage)
- It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Phuket/3073/2013-like virus (B/Yamagata lineage)

# WHO Recommendations for Influenza Vaccine Composition Northern Hemisphere: 2017-2018

- WHO recommendation – 3/2/2017
- Recommended that the following viruses be used for trivalent influenza vaccines in the 2017-2018 NH influenza season:
  - an A/Michigan/45/2015 (H1N1)pdm09-like virus
    - *Change from A/California/7/2009 (H1N1)pdm09-like virus, but same as 2017 SH recommendation*
  - an A/Hong Kong/4801/2014 (H3N2)-like virus
    - *No change from 2016-2017 NH recommendation*
  - a B/Brisbane/60/2008-like virus (B/Victoria lineage)
    - *No change from 2016-2017 NH recommendation*
- Recommended that quadrivalent vaccines containing two influenza B viruses contain the above 3 viruses and a B/Phuket/3073/2013-like virus (B/Yamagata)
  - *No change from 2016-2017 NH recommendation*
- As in previous years, national or regional control authorities approve the composition and formulation of vaccines used in each country

## Committee Discussion

- Which influenza strains should be recommended for the antigenic composition of the 2017-2018 influenza virus vaccine in the U.S.?

# Options for Strain Composition for 2017-2018 Trivalent Influenza Vaccines

- Influenza A (H1N1)
  - Recommend an A/Michigan/45/2015 (H1N1)pdm09-like virus
  - Recommend an alternative H1N1 candidate vaccine virus
- Influenza A (H3N2)
  - Recommend an A/Hong Kong/4801/2014 (H3N2)-like virus
  - Recommend an alternative H3N2 candidate vaccine virus
- Influenza B
  - Recommend a B/Brisbane/60/2008-like virus (B/Victoria lineage)
  - Recommend an alternative candidate vaccine virus from the B/Victoria lineage
  - Recommend a candidate vaccine virus from the B/Yamagata lineage

# Options for Strain Selection for the 2<sup>nd</sup> Influenza B Strain in a Quadrivalent Influenza Vaccine

- Influenza B
  - Recommend inclusion of a B/Phuket/3073/2013-like virus (B/Yamagata lineage)
  - Recommend an alternative candidate vaccine virus from the B/Yamagata lineage
  - Recommend a candidate vaccine virus from the B/Victoria lineage

## Voting Questions for the Committee

1. For the composition of the trivalent 2017-2018 influenza virus vaccine in the U.S., does the committee recommend:
  - A. Inclusion of an A/Michigan/45/2015 (H1N1)pdm09-like virus
  - B. Inclusion of an A/Hong Kong/4801/2014 (H3N2)-like virus
  - C. Inclusion of a B/Brisbane/60/2008-like virus (B/Victoria lineage)
  
2. For quadrivalent 2017-2018 influenza vaccines in the U.S., does the committee recommend:
  - A. Inclusion of a B/Phuket/3073/2013-like virus (B/Yamagata lineage) as the 2<sup>nd</sup> influenza B strain in the vaccine