



# **Influenza Virus Vaccine 2016-2017 Strain Selection**

**Vaccines and Related Biological Products  
Advisory Committee (3/4/2016)**

*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 2016-2017 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/CBER*)
  - 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 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

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]					

# 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
  - 4 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 2015-2016 Seasonal Influenza Vaccine Strain Composition

- VRBPAC strain selection – March 4, 2015
- Committee recommended the following strains for inclusion in U.S. 2015-2016 trivalent influenza vaccines
  - A/California/7/2009 (H1N1)pdm09-like virus
    - *No change from the 2014-2015 vaccine recommendation*
  - A/Switzerland/9715293/2013 (H3N2)-like virus
    - *Change from the A/Texas/50/2012 (H3N2)-like virus vaccine recommendation*
  - B/Phuket/3073/2013-like virus (B/Yamagata lineage)
    - *Change from the B/Massachusetts/2/2012-like virus vaccine recommendation*
- For manufacturers producing a quadrivalent influenza vaccine, the Committee recommended a second B strain
  - B/Brisbane/60/2008-like virus (B/Victoria lineage), previously recommended for quadrivalent vaccines in 2014-2015

# WHO Recommendations for Influenza Vaccine Composition Southern Hemisphere: 2016

- WHO recommendation – 9/24/2015
- Recommended that the following viruses be used for trivalent influenza vaccines in the 2016 influenza season (SH winter):
  - an A/California/7/2009 (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 vaccine virus)



# WHO Recommendations for Influenza Vaccine Composition Northern Hemisphere: 2016-2017

- WHO recommendation – 2/25/2016
- Recommended that the following viruses be used for trivalent influenza vaccines in the 2016-2017 influenza season (NH winter):
  - an A/California/7/2009 (H1N1)pdm09-like virus
    - *No change from 2015-2016 NH*
  - an A/Hong Kong/4801/2014 (H3N2)-like virus
    - *Change from 2015-2016 NH, but same as 2016 SH recommendation*
  - a B/Brisbane/60/2008-like virus (B/Victoria lineage)
    - *Change from 2015-2016 NH recommendation, previously recommended for quadrivalent vaccines*
- Recommended that quadrivalent vaccines containing two influenza B viruses contain the above 3 viruses and a B/Phuket/3073/2013-like virus (B/Yamagata)
  - *Previously recommended for trivalent vaccines*
- 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 2016-2017 influenza virus vaccine in the U.S.?

# Options for Strain Composition for 2016-2017 Trivalent Influenza Vaccines

- Influenza A (H1N1)
  - Recommend an A/California/7/2009 (H1N1)pdm09-like virus (current vaccine strain)
  - 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

# Voting Questions for the Committee

1. For the composition of the trivalent 2016-2017 influenza virus vaccine in the U.S., does the committee recommend:
  - A. Inclusion of an A/California/7/2009 (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 2016-2017 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