Influenza Virus Vaccine
2015-2016 Strain Selection

Vaccines and Related Biological Products
Advisory Committee (3/4/2015)

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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 2015-2016 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 necessary for availability of vaccine for subsequent northern hemisphere winter (influenza season)
  - Manufacturers typically begin production of one monovalent 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

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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 2014-2015 Seasonal Influenza Vaccine Strain Composition

- VRBPAC strain selection – 2/28/2014
- Committee recommended the following strains for inclusion in U.S. 2014-2015 trivalent influenza vaccines
  - A/California/7/2009 (H1N1)-like virus
    - No change from the 2013-2014 vaccine recommendation
  - A/Texas/50/2012 (H3N2)-like virus
    - No change from the 2013-2014 vaccine recommendation
  - B/Massachusetts/2/2012-like virus (B/Yamagata lineage)
    - No change from the 2013-2014 vaccine recommendation
- For manufacturers producing a quadrivalent influenza vaccine, the Committee recommended a second B strain
  - B/Brisbane/60/2008 (B/Victoria lineage), previously recommended for quadrivalent vaccines in 2013-2014
WHO Recommendations for Influenza Vaccine Composition
Southern Hemisphere: 2015

- WHO recommendation – 9/25/2014

- Recommended that the following viruses be used for influenza vaccines in the 2015 influenza season (SH winter):
  - an A/California/7/2009 (H1N1) pdm09-like virus
  - an A/Switzerland/9715293/2013 (H3N2)-like virus
  - a B/Phuket/3073/2013-like virus (B/Yamagata lineage)

- It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus (B/Victoria lineage vaccine virus)
WHO Recommendations for Influenza Vaccine Composition
Northern Hemisphere: 2015-2016

WHO recommendation – 2/26/2015

Recommended that the following viruses be used for influenza vaccines in the 2015-2016 influenza season (NH winter):
- an A/California/7/2009 (H1N1) pdm09-like virus
- an A/Switzerland/9715293/2013 (H3N2)-like virus
- a B/Phuket/3073/2013-like virus (B/Yamagata lineage)

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus (B/Victoria lineage vaccine virus)

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 2015-2016 influenza virus vaccine in the U.S.?
Options for Strain Composition for 2015-2016 Trivalent Influenza Vaccines

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

- Influenza A (H3N2)
  - Recommend an A/Switzerland/9715293/2013 (H3N2)-like virus
  - Recommend an alternative H3N2 candidate vaccine virus

- Influenza B
  - Recommend 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
Options for Strain Selection for the 2nd Influenza B Strain in a Quadrivalent Influenza Vaccine

- **Influenza B**
  - Recommend inclusion of a B/Brisbane/60/2008-like virus (B/Victoria lineage) (current quadrivalent vaccine recommended strain)
  - Recommend an alternative candidate vaccine virus from the B/Victoria lineage
Voting Questions for the Committee

1. For the composition of the trivalent 2015-2016 influenza virus vaccine in the U.S., does the committee recommend:
   A. Inclusion of an A/California/7/2009 (H1N1)-like virus
   B. Inclusion of an A/Switzerland/9715293/2013 (H3N2)-like virus
   C. Inclusion of a B/Phuket/3073/2013-like virus (B/Yamagata lineage)

2. For quadrivalent 2015-2016 influenza vaccines in the U.S., does the committee recommend:
   A. Inclusion of a B/Brisbane/60/2008-like virus (B/Victoria lineage) as the 2nd influenza B strain in the vaccine