Global Influenza Virus Surveillance and WHO Influenza Vaccine Virus Recommendations for the Northern Hemisphere 2015-16 Influenza Season

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WHO Surveillance Network (GISRS) and Vaccine Virus Selection

- Year around surveillance conducted by the Global Influenza Surveillance and Response System (GISRS)
  - 142 National Influenza Centers (NICs) in 112 countries, 6 WHOCCs, WHO Essential Regulatory Labs, H5 Reference Labs
  - WHO Vaccine Consultation Meeting, 23-25 Feb 2015:
    - Review and analysis of global data on viruses collected since Sept 1, 2014
    - Data presented at VRBPAC Meeting March 4, 2015
    - Full slide set available on FDA website

Considerations for new vaccine virus recommendations

- Are there new antigenic variants with signature genetic changes?
  - Antigenic characterization (HI and VN assays) using ferret or human serum
  - Genetic characterization: sequence analysis of HA and NA genes
- Are new variants spreading?
  - Monitoring influenza disease activity and virus isolation
- Are current vaccines able to induce antibodies to the new variants?
- Are candidate vaccine viruses representing new variants available?
Summary of A(H1N1)pdm09 Viruses

- A(H1N1)pdm09 activity was generally sporadic in Asia, Africa, the Americas, Europe, and was variable in Oceania.
  - Local to widespread outbreaks occurred in Australia, New Caledonia, and New Zealand in September and October, 2014.

- The majority of circulating A(H1N1)pdm09 viruses belonged to genetic clade 6B.

- All of the A(H1N1)pdm09 viruses remained antigenically similar to the recommended vaccine virus A/California/7/2009.
<table>
<thead>
<tr>
<th>WHO CC</th>
<th>A/Cal/07/09</th>
<th>Low (≥ 8 fold)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC</td>
<td>33 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>CNIC</td>
<td>36 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>NIID</td>
<td>2 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>NIMR</td>
<td>85 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>VIDRL</td>
<td>213 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>369 (100%)</strong></td>
<td><strong>0</strong></td>
</tr>
</tbody>
</table>
Antigenic cartography of A(H1N1)pdm09 viruses

From Derek Smith and Colin Russell, University of Cambridge, UK
**A(H3N2) Summary**

- Influenza A(H3N2) activity was generally sporadic in Africa and Oceania, but was regional to widespread in the Americas, Asia and Europe.

- A(H3N2) viruses collected from September 2014 to January 2015 fell into the phylogenetic clades 3C.2 and 3C.3.

- Antigenic characterization of A(H3N2) viruses has become technically difficult – Many 3C.2a viruses had low or undetectable hemagglutination activity.

- The majority of recent A(H3N2) viruses were poorly inhibited by ferret antisera raised against egg- and cell-propagated reference A/Texas/50/2012 (clade 3C.1) viruses.

- Most viruses were well inhibited by ferret antisera raised against cell-propagated A/Switzerland/9715293/2013 (3C.3a) virus and representative cell-propagated 3C.2a viruses – 3C.2a and 3C.3a viruses were antigenically related, but distinguishable in some cases

- Ferret antisera raised against egg-propagated A/Switzerland/9715293/2013 reacted well with most recently circulating viruses.
Global Distribution of H3 HA Clades

HAGroup
- 3C.2
- 3C.2a
- 3C.2b
- 3C.3
- 3C.3a
- 3C.3b
- 6

Location
- Africa
- Asia
- Europe
- North America
- Oceania
- South America

Total Number of Countries with 3C.2a = 47
Total Number of Countries with 3C.3a = 29
### H3 low reactors in HI assays conducted by WHO CCs

<table>
<thead>
<tr>
<th>WHO CC</th>
<th>A/Texas/50/2012 -like</th>
<th>Low (≥ 8 fold)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC</td>
<td>243 (37%)</td>
<td>413 (63%)</td>
</tr>
<tr>
<td>CNIC</td>
<td>22 (4%)</td>
<td>532 (96%)</td>
</tr>
<tr>
<td>NIID</td>
<td>7 (28%)</td>
<td>18 (72%)</td>
</tr>
<tr>
<td>NIMR</td>
<td>84 (62%)</td>
<td>51 (38%)</td>
</tr>
<tr>
<td>VIDRL</td>
<td>30 (17%)</td>
<td>143 (83%)</td>
</tr>
<tr>
<td>Total</td>
<td>386 (27%)</td>
<td>1055 (73%)</td>
</tr>
</tbody>
</table>
Cartography of HI Data from CDC

From Derek Smith and Colin Russell, University of Cambridge, UK
Influenza B Summary

- Influenza B activity was generally low world-wide

- B/Victoria and B/Yamagata lineage viruses co-circulated, with B/Yamagata viruses continuing to predominate.

- **B/Yamagata lineage viruses:**
  - HA genes fell into genetic clades 2 and 3.
  - The great majority of tested viruses belonged to clade 3.
  - Recently circulating viruses were well inhibited by antisera raised against egg-propagated B/Phuket/3073/2013, the virus recommended for use in the 2015 southern hemisphere vaccine.

- **B/Victoria lineage viruses:**
  - Of the low number of viruses tested, most were antigenically and genetically similar to B/Brisbane/60/2008 and belonged to genetic group 1A
    - B/Texas/02/2013 is a B/Brisbane/60/2008-like genetic 1A group virus
# Influenza B low reactors by lineage in HI assays in WHO CCs

<table>
<thead>
<tr>
<th>WHO CC</th>
<th>Victoria (B/Brisbane/60/2008)</th>
<th>Yamagata (B/Phuket/3073/2013)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Reactors</td>
<td></td>
</tr>
<tr>
<td>CDC</td>
<td>55 (90%)</td>
<td>170 (92%)</td>
</tr>
<tr>
<td></td>
<td>6 (10%)</td>
<td>13 (8%)</td>
</tr>
<tr>
<td>CNIC</td>
<td>3 (15%)</td>
<td>201 (100%)</td>
</tr>
<tr>
<td>NIID</td>
<td>1 (100%)</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>NIMR</td>
<td>10 (70%)</td>
<td>107 (100%)</td>
</tr>
<tr>
<td>VIDRL</td>
<td>16 (100%)</td>
<td>36 (100%)</td>
</tr>
<tr>
<td>Total (%)</td>
<td>112 (81%)</td>
<td>519 (98%)</td>
</tr>
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</table>
From Derek Smith and Colin Russell, University of Cambridge, UK
Recommendation

- It is recommended that the following viruses be used for influenza vaccines in the 2015-2016 influenza season (northern hemisphere):
  - an A/California/7/2009 (H1N1)pdm09-like virus;
  - an A/Switzerland/9715293/2013 (H3N2)-like virus;
  - a B/Phuket/3073/2013-like virus.

- For quadrivalent vaccines containing 2 B components:
  - Above 3, plus
  - A B/Brisbane/60/2008-like virus.
Acknowledgements

- WHO Collaborating Centers in Beijing, Melbourne, London and Tokyo and WHO Geneva staff
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  - University of Cambridge partners

- Essential Regulatory Laboratories

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