Influenza
NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

<table>
<thead>
<tr>
<th>Site</th>
<th>A/Un typ</th>
<th>A/H3</th>
<th>A/H1</th>
<th>B</th>
<th>A/Un typ</th>
<th>A/H3</th>
<th>A/H1</th>
<th>B</th>
<th>No. Tested</th>
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</thead>
<tbody>
<tr>
<td>Ft. Benning</td>
<td></td>
<td>9</td>
<td>1</td>
<td>197</td>
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<td>1</td>
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<td>Ft. Jackson</td>
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<td>16</td>
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<td>335</td>
<td></td>
<td>1</td>
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<tr>
<td>Ft. Leonard Wood</td>
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<td>6</td>
<td>1</td>
<td>119</td>
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<td>3</td>
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<td>NRTC Great Lakes</td>
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<td>Lackland AFB</td>
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<td>4</td>
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<tr>
<td>MCRD Parris Island</td>
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<td>21</td>
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<tr>
<td>MCRD San Diego</td>
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<td>343</td>
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<td>CGTC Cape May</td>
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<td>Total</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>121</td>
<td>2</td>
<td>18</td>
<td>1626</td>
</tr>
</tbody>
</table>

*Case presented 1Sept. and had not been vaccinated.

- FRI rates at all basic training centers are at or below expected values
- Twelve confirmed cases of adenovirus serotype 14 at MCRD Parris Island, June-Sept 2017
- NHRC is able to test for novel influenza strains, MERS coronavirus, enterovirus EV-68, Ebola virus, and Zika virus

Vaccination Status of Confirmed Influenza Cases Among US Military Basic Trainees, 2014-17

- NHRC is conducting laboratory-based surveillance for meningococcal disease. The program’s purpose is to track and characterize meningococcal cases among DoD medical beneficiaries. For more information and the most recent data, click here.
Adenovirus

- Vaccination against types 4 and 7 adenovirus was instituted at all basic training centers by mid-November 2011.
- FRI rates and the proportion of FRI cases positive for adenovirus have decreased markedly since vaccine was reintroduced.
- Sporadic adenovirus cases at basic training centers 2012-17. FRI rates remain low in general.

FRI Rates

- FRI surveillance is ongoing at 8 U.S. military basic training centers, representing all service branches. As each week’s FRI count is reported, FRI Rate Status is classified into one of 3 categories:
  - At or below expected value (expected value shown as dashed line)
    - Moderately elevated
    - Substantially elevated

Week ending 23 September 2017:
- At or below expected value:
  - Fort Benning
  - Fort Jackson
  - Fort Leonard Wood
  - Naval Recruit Training Command, Great Lakes (data through 16 September)
  - Marine Corps Recruit Depot, San Diego
  - Marine Corps Recruit Depot, Parris Island
  - Lackland Air Force Base (data through 2 September)
  - Coast Guard Training Center, Cape May

- Moderately elevated:
  None

- Substantially elevated:
  None
NHRC Respiratory Illness Update  
Week Ending: 23 September 2017

Ft. Benning FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

Ft. Jackson FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

Back to FRI Report

- Observed FRI rate (expected rate = dashed line)
- Moderately elevated
- Substantially elevated
- Pneumonia rate (incl. afebrile)
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified).

Back to FRI Report
Back to FRI Report

- Observed FRI rate (expected rate = dashed line)  
  - Moderately elevated  
  - Substantially elevated  
  — Pneumonia rate (incl. afebrile)
Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)
DoD Beneficiary Surveillance

- NHRC conducts FRI surveillance among DoD beneficiaries at 12 military facilities including Naval Medical Center San Diego (NMCSD), Naval Branch Health Clinic Kearny Mesa (NBHCKM), Naval Branch Health Clinic, Naval Training Center (NTC), Naval Hospital Camp Pendleton (NHCP), Branch Health Clinic Yuma (BHCY), James A. Lovell Federal Health Care Center (JALFHCC), United States Naval Hospital, Japan (PRSH), Naval Medical Center Portsmouth (NMCP), Boone Branch Health Clinic (BBHC), Oceana Branch Health Clinic (OBHC), Naval Hospital Lemoore (NHL), and Robert E. Bush Naval Hospital (RBNH).

- For questions regarding surveillance in this population, please contact the principal investigator (Chris Myers, christopher.a.myers48.civ@mail.mil) or the study coordinator (Michelle Ricketts, michelle.n.ricketts.ctr@mail.mil).
US-Mexico Border Surveillance

- In collaboration with the CDC Border Infectious Disease Surveillance program and San Diego/Imperial Counties, NHRC performs laboratory testing for FRI cases among civilians near the US-Mexico border. Both outpatient (FRI) and inpatient (Severe Acute Respiratory Illness; SARI) cases are included in the program. Current sites are located in San Diego (2) and Imperial (5) counties in California.
Summary of Influenza A(H1N1)pdm09, A(H3N2) and Influenza B Hemagglutinin (HA) Genetic Groups

**Influenza A(H1N1)pdm09**

- 68.1, 8, 100%
- Jul-Sept 2016 | Oct-Dec 16 | Jan-17 | Feb-17 | Mar-17 | Apr-17 | May-17

**Influenza A(H3N2)**

- 3C.3a 1, 1%
- 3C.2a 17, 21%
- 3C.2a 1, 68, 78%
- July-Sept 2016 | Oct-Dec 2016 | Jan-17 | Feb-17 | Mar-17 | Apr-17 | May-17

**Influenza B**

- B/Yam Y3, 9, 56%
- B/Vic 1A, 7, 44%
- Jul-Sept 2016 | Oct-Dec 2016 | Jan-17 | Feb-17 | Mar-17 | Apr-17 | May-17

- Individual
- USN Shipboard
- US Recruit
- US Special Forces
- Japan – NH Yokosuka
- DoD Beneficiaries
- Border Surveillance
Phylogenetic Comparison of Influenza A(H1N1)pdm09 HA and NA Protein Sequences

- 2 analyzed Influenza A(H1N1)pdm09 HA sequences were derived from MDCK-SIAT1 isolates and 6 were derived by clinical specimens.
- All sequences belonged to the subclade 6B.1, defined by mutations S84N, S162T (ADD GLY) and I216T.
- 4 analyzed Influenza A(H1N1)pdm09 NA sequence was derived from MDCK-SIAT1 isolates and 7 were from clinical specimen.
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown (both HA and NA sequences) are with respect to A/California/07/2009.

Summary of Influenza A(H1N1)pdm09 Protein Homology When Compared with 2016-2017 Vaccine Strain and upcoming 2017-2018 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No. Isolates</th>
<th>Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(H1N1)pdm09 HA</td>
<td>8</td>
<td>A/California/07/2009 (2016-17)</td>
<td>96.4-97.2%</td>
</tr>
<tr>
<td>A(H1N1)pdm09 HA</td>
<td>8</td>
<td>A/Michigan/45/2015 (2017-18)</td>
<td><strong>99.0-100%</strong></td>
</tr>
<tr>
<td>A(H1N1)pdm09 NA</td>
<td>11</td>
<td>A/California/07/2009 (2016-17)</td>
<td>96.5-97.3%</td>
</tr>
<tr>
<td>A(H1N1)pdm09 NA</td>
<td>11</td>
<td>A/Michigan/45/2015 (2017-18)</td>
<td><strong>99.3-100%</strong></td>
</tr>
</tbody>
</table>

Summary of Influenza A(H1N1)pdm09 N-Linked Glycosylation Mutations

- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity. Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server

<table>
<thead>
<tr>
<th>Mutation</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>S162N</td>
<td>N/A</td>
</tr>
<tr>
<td>NA</td>
<td>N44S, S70N</td>
<td>N386K</td>
</tr>
</tbody>
</table>

Evolutionary Relationships Among Influenza A(H1N1)pdm09 Hemagglutinin (HA) Genes

2016-2017 Influenza Season

Vaccine Strain

Reference Strain

2015-16 Consensus (47 strains)

Dec 2016 (2 strains)

Jan 2017 (1 strain)

Feb 2017 (4 strains)

Mar 2017 (1 strain)

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SARI: US/Mexico Border inpatient
FDX or NMCSO: DoD beneficiaries
JX or no prefix: US Recruit

*: clinical specimen

A/California/NHC/BRD4/2016
A/California/NHC/NOS/2089/2017
A/Cold/03/2016
A/California/NHC/BRD4140N/2017
A/California/NHC/NMCSD0075/2016
A/California/NHC/BRD1209N/2017
A/California/NHC/27982/2017
A/California/NHC/NMCSD0076/2016
2015-16 6B.1 Consensus (43 strains)
A/Michigan/45/2015 (2017-18 season)

6B.1

2015-16 6B Consensus (4 strains)

6B

A/Norway/2417/2013
A/California/07/2009

Amino Acid Substitution per 100 residues
Evolutionary Relationships
Among Influenza A(H1N1)pdm09
Neuraminidase (NA) 2016-2017
Influenza Season
Vaccine Strain
Reference Strain
2015-16 Consensus (46 strains)

Dec 2016 (2 strains)
A/Missouri/NHRC_36962/2017* [A75V, K260R]
A/California/NHRC_BRD41523N/2017

Jan 2017 (1 strain)
A/California/NHRC_BRD41511N/2017
A/California/NHRC_BRD41503N/2017*
A/California/NHRC_BRD41506N/2017*
A/California/NHRC_SAR20891N/2017* [R173K]
A/Delaware/39/2015 [V394I, I443M]
A/California/NHRC_BRD12309N/2017 [V81I]
A/California/NHRC_BRD41490N/2017*
A/California/NHRC_27982/2017
A/California/NHRC_NMCSD0076/2016* [S95N, I223R']
A/California/NHRC_NMCSD0075/2016 [N68S]

Feb 2017 (5 strains)
2015-16 6B.1 Consensus (46 strains)
A/Michigan/45/2015 (2017-18 season)
A/California/80/2015 [I32V, V67I, S79L]
A/Astrakhan/1/2011 [V106I]

Mar 2017 (3 strains)
1.9
A/California/07/2009 [I241V, D248N K369N]

0
Amino Acid Substitution per 100 residues

1. Known marker for Neuraminidase inhibitor (NAI) resistance. NAI inhibition assay (NA Star) was performed using MDCK-SIAT1 isolate. With respect to the wild type NAI susceptible virus (A/CA,12/2012), IC50 fold change was 11.03 for Zanamivir and 19.02 for Oseltamivir. These fold changes both fall in the reduced inhibition range (RI).
http://www.who.int/influenza/gisrs_laboratory/antiviral_susceptibility/nai_overview/en/
Phylogenetic Comparison of Influenza A (H3N2) HA and NA Protein Sequences

- 5 analyzed H3N2 HA sequences were derived from MDCK isolates and 78 were derived from clinical specimen.
- 1 sequence belonged to 3C.3a and 82 were in subclade 3C.2a. Of those 3C.2a sequences, 49 were further classified as 3C.2a1, defined by the mutations N171K, I406V (HA2: I77V), and G484E (HA2: G155E).
- 2 analyzed H3N2 NA sequences were derived from MDCK isolates and 24 were derived from clinical specimen.
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown are with respect to A/Perth/16/2009 for HA and NA sequences.

Summary of Influenza A (H3N2) Protein Homology When Compared with 2016-2017 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No.</th>
<th>2016-2017 Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3N2 HA</td>
<td>83</td>
<td>A/HongKong/4801/2014</td>
<td>97.2-98.9%</td>
</tr>
<tr>
<td>H3N2 NA</td>
<td>26</td>
<td>A/HongKong/4801/2014</td>
<td>97.0-98.9%</td>
</tr>
</tbody>
</table>

Summary of Influenza A (H3N2) N-Linked Glycosylation Mutations

- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity. Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server http://www.cbs.dtu.dk/services/NetNGlyc/.

<table>
<thead>
<tr>
<th>A/H3N2 Segment</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td>S245N</td>
<td>D329S</td>
</tr>
</tbody>
</table>

Evolutionary Relationships Among Influenza A (H3N2) Hemagglutinin (HA) Genes 2016-2017 Influenza Season

Vaccine Strain

Reference Strain

2015-16 Consensus (50 strains)

July-Sept 2016 (16 strains)

Oct-Dec 2016 (13 strains)

Jan 2017 (20 strains)

Feb 2017 (16 strains)

Mar 2017 (10 strains)

April 2017 (7 strains)

May 2017 (1 strain)

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit
SEA: US Special Forces
* Clinical specimen
$ shipboard surveillance

3C.2a1

3C.2a

3C.3a

Amino Acid Substitution per 100 residues
Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes 2016-2017 Influenza Season

**Vaccine Strain**

**Reference Strain**

2015-16 Consensus (37 strains)

July-Sept 2016 (14 strains)

Oct-Dec 2016 (5 strains)

January 2017 (1 strain)

March 2017 (4 strains)

April 2017 (3 strains)

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit

*: clinical specimen

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A/Alaska/232/2015

A/Illinois/NHRC_18564/2017* [F205I]

A/Georgia/NHRC_68549/2016* [K220N]

A/Philippines/NHRC_MCY0131/2016* (2 strains)

A/NewJersey/NHRC_93692/2017*

A/SouthCarolina/NHRC_JX41822/2017*

A/NewJersey/NHRC_93675/2017*

A/California/NHRC_BRD12386N/2017*

A/NewJersey/NHRC_93422/2016* (9 strains) [V215I]

A/Japan/NHRC_FDX70127/2017* [K296R]

A/California/NHRC(CG)5904/2017*

A/SouthCarolina/NHRC_JX41626/2016

A/SouthCarolina/NHRC_JX41638/2016

A/SouthCarolina/NHRC_JX41610/2016*

A/SouthCarolina/NHRC_JX41611/2016*

A/Alaska/240/2015

A/NewYork/57/2015 [S335G]

2015-16 H3NA Consensus (37 strains)

A/Canberra/82/2014

A/HongKong/4801/2014 [V231I]

A/Switzerland/9715293/2013

A/Texas/50/2012

A/Perth/16/2009

3.6

Amino Acid Substitution per 100 residues
Phylogenetic Comparison of Influenza B (Yamagata and Victoria) HA and NA Protein Sequences

- 9 sequences belonged to the Y3 clade of the Yamagata lineage and 7 sequence belonged to the V1A clade of the Victoria lineage.
- Two B/Victoria HA sequences contained the double amino acid deletion at positions 162 and 163. Viruses with these deletions are currently referred to as the “B/Victoria deletion variant subgroup” and are antigenically distinct from the vaccine strain.1
- Phylogenetic trees for both HA and NA protein sequences were generated by Clustal V method using DNASTAR® Lasergene Megalign software.
- Amino acid changes shown with respect to B/Phuket/3073/2013 for B/Yamagata HA sequences, B/Wisconsin/01/2010 for B/Yamagata NA sequences, B/Ohio/01/2005 for B/Victoria HA sequences, and B/Brisbane/60/2008 for B/Victoria NA sequences.

Summary of Influenza B Protein Homology When Compared with 2016-2017 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No. Isolates</th>
<th>2016-2017 Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>B/Yamagata HA</td>
<td>9</td>
<td>B/Phuket/3073/2013</td>
<td>99.3-99.5%</td>
</tr>
<tr>
<td>B/Yamagata NA</td>
<td>12</td>
<td>B/Phuket/3073/2013</td>
<td>98.9-99.3%</td>
</tr>
<tr>
<td>B/Victoria HA</td>
<td>7</td>
<td>B/Brisbane/60/2008</td>
<td>98.4-99.5%</td>
</tr>
<tr>
<td>B/Victoria NA</td>
<td>15</td>
<td>B/Brisbane/60/2008</td>
<td>98.0-98.7%</td>
</tr>
</tbody>
</table>

Summary of Influenza B N-Linked Glycosylation Mutations

- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity.2 Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server [http://www.cbs.dtu.dk/services/NetNGlyc/](http://www.cbs.dtu.dk/services/NetNGlyc/)

<table>
<thead>
<tr>
<th>INF B Segment</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
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</thead>
<tbody>
<tr>
<td>HA</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>NA</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Evolutionary Relationships
Among Influenza B
Hemagglutinin (HA) Genes
2016-2017 Influenza Season

**Vaccine Strain**

**Reference Strain**

- **2015-16 Y3 Consensus (25 strains)**
- **2015-16 1A Consensus (27 strains)**

**Oct 2016 (1 strain)**

**Jan 2017 (2 strains)**

**Feb 2017 (3 strains)**

**Mar 2017 (3 strains)**

**April 2017 (6 strains)**

**May 2017 (1 strain)**

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border Inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit

*: clinical specimen

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**Yamagata Lineage**

- B/SouthCarolina/NHRC_JX41701/2017*
- B/Illinois/NHRC_FDX51909/2017
- B/California/NHRC_BRD80728N/2017*
- B/California/NHRC_SAR10492N/2017*
- B/California/NHRC_BRD12374N/2017*
- B/SouthCarolina/NHRC_75620/2017
- B/California/NHRC_BRD12337N/2017*
- B/Illinois/NHRC_FDX51839/2017*
- B/Illinois/NHRC_18462/2016

**2015-16 Y3 Consensus (25 strains)**

**Victoria Lineage**

- B/Illinois/NHRC_FDX51841/2017*[S510F]
- B/Illinois/NHRC_FDX51878/2017*
- B/Illinois/NHRC_18512/2017*
- B/California/NHRC_BRD41581N/2017*
- B/Washington/63/2015 [V252M, I559V]
- B/Illinois/NHRC_18545/2017*

**2015-16 V1A Consensus (27 strains)**

**B/Wyoming/24/2015**

- B/California/NHRC_MAP2003A/2017*[T121I]
- B/Illinois/NHRC_FDX51883/2017[A154V]

**B/Texas/02/2013**

**B/Ohio/01/2005**

1.8 Amino Acid Substitution per 100 residues

☆B/Victoria deletion variant subgroup
Evolutionary Relationships Among Influenza B Neuraminidase (NA) Genes 2016-2017 Influenza Season

**Vaccine Strain**

**Reference Strain**

2015-16 Consensus (26 strains)

June 2016 (1 strain)

Oct 2016 (1 strain)

Jan 2017 (4 strains)

Feb 2017 (8 strains)

March 2017 (3 strains)

April-June 2017 (8 strains)

**Yamagata Lineage**

B/California/NHRC_SAR10463N/2017* [I262V]

B/California/NHRC_BRD12420N/2017*

B/California/NHRC_BRD80728N/2017*

B/California/NHRC_SAR10492N/2017*

B/SouthCarolina/NHRC_75620/2017*

B/California/NHRC_BRD12337N/2017*

B/Illinois/NHRC_FDX51839/2017*

B/SouthCarolina/NHRC_JX41701/2017*

B/California/NHRC_BRD12301N/2017*

B/Illinois/NHRC_18462/2016 [M403V, E404G]

A/Philippines/NHRC_MCY0103/2016*

B/Illinois/NHRC_FDX51909/2017*

B/Wisconsin/05/2015 [I49M]

B/Sydney/7/2014 [T46I, G70E]

2015-16 B/YAM Consensus (26 strains)

B/Phuket/3073/2013

B/Wisconsin/01/2010 [D340N]

1.6 Amino Acid Substitution per 100 residues 0

**Victoria Lineage**

B/California/NHRC_BRD41581N/2017*

B/Illinois/NHRC_FDX51883/2017*

B/California/NHRC_BRD12417N/2017* [S397R]

B/Illinois/NHRC_FDX51851/2017* [K107R, D392G]

B/Illinois/NHRC_18545/2017* [F12V]

B/California/NHRC_28039/2017*

B/NewJersey/NHRC_93612/2017*

B/NewJersey/NHRC_93621/2017*

B/Texas/NHRC_55449/2017*

B/Illinois/NHRC_FDX51878/2017*

B/Illinois/NHRC_FDX51841/2017* [N235S]

B/Illinois/NHRC_18512/2017*

B/Virginia/NHRC_BAT0112/2017* [A67T]

2015-16 B/VIC Consensus (27 strains)

B/Wyoming/24/2015

B/SouthAustralia/81/2012 [S99N]

B/Brisbane/60/2008 [A358V]

1.0 Amino Acid Substitution per 100 residues 0