Influenza

NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

<table>
<thead>
<tr>
<th>Site</th>
<th>Current Week*</th>
<th>Since Oct.1, 2016</th>
<th>No. Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ft. Benning</td>
<td>A/Un typ.</td>
<td>A/H3</td>
<td>A/H1</td>
</tr>
<tr>
<td>Ft. Jackson</td>
<td>2</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Ft. Leonard Wood</td>
<td>2</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>NRTC Great Lakes</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Lackland AFB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCRD Parris Island</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCRD San Diego</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CGTC Cape May</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

*New cases presented for care in mid-December and had been vaccinated in mid-October

- NHRC also conducts shipboard FRI surveillance that includes large-deck ships of the US Fleet Forces (Atlantic), 3rd (Pacific), and 7th (Far East) Fleets.
- NHRC conducts FRI surveillance among (non-active duty) DoD beneficiaries in Illinois and San Diego (details on page 7).
- NHRC-CDC-BIDS collaborative border FRI/SARI surveillance program is ongoing at 7 US-Mexico border sites in San Diego (2) and Imperial (5) counties in California. Details on page 8.
- For more information about NHRC FRI surveillance programs, please contact NHRC.

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, view the Quarterly Meningococcal Report.
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 2012-16. 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 21 January 2017:
- At or below expected value:
  - Fort Benning
  - Fort Jackson
  - Fort Leonard Wood
  - Marine Corps Recruit Depot, San Diego
  - Lackland Air Force Base (data through 14 Jan.)
  - Coast Guard Training Center, Cape May

- Moderately elevated:
  - Marine Corps Recruit Depot, Parris Island

- Substantially elevated:
  - Naval Recruit Training Command, Great Lakes
- Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)
Lackland AFB FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

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

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

- NHRC conducts FRI surveillance among (non-active duty) DoD beneficiaries at Lovell FHCC (Great Lakes, IL) and in 4 NMC San Diego facilities: the Emergency Department, Pediatric Department, Naval Branch Health Clinic Kearny Mesa, and NH Camp Pendleton.

- For questions regarding surveillance in this population, please contact the principal investigators at NHRC-FRI_Ben@med.navy.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.
Phylogenetic Comparison of Influenza A-pandemic 2009 H1N1 A(H1N1)pdm09 HA and NA Protein Sequences

- 2 analyzed Influenza A pH1N1 HA sequences were derived from clinical specimens and belonged to the subclade 6B.1, defined by mutations S84N, S162T (ADD GLY) and I216T.
- 1 analyzed Influenza A pH1N1 NA sequence was 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 (both HA and NA sequences) are with respect to A/California/07/2009-like virus.

Summary of Influenza A (pH1N1) Protein Homology When Compared to 2015-2016 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No. Isolates</th>
<th>2015-2016 Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/pH1N1 HA</td>
<td>2</td>
<td>A/California/07/2009</td>
<td>97.0-97.3%</td>
</tr>
<tr>
<td>A/pH1N1 NA</td>
<td>1</td>
<td>A/California/07/2009</td>
<td>96.6%</td>
</tr>
</tbody>
</table>

Summary of Influenza A (pH1N1) 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/](http://www.cbs.dtu.dk/services/NetNGlyc/)

<table>
<thead>
<tr>
<th>A/pH1N1 Segment</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>

Phylogenetic Comparison of Influenza A (H3N2) HA and NA Protein Sequences

- 3 analyzed H3N2 HA sequences were derived from MDCK isolates and 21 were derived from clinical specimen and belonged to the subclade 3C.2a1, defined by the mutations: 171K, 406V, and 484E.
- 2 analyzed H3N2 NA sequences were derived from MDCK isolates and 17 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 2010 vaccine strain A/Perth/16/2009-like virus for HA sequences and A/Norway/1186/2011 for 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>24</td>
<td>A/HongKong/4801/2014</td>
<td>97.8-98.6%</td>
</tr>
<tr>
<td>H3N2 NA</td>
<td>19</td>
<td>A/HongKong/4801/2014</td>
<td>97.0-98.2%</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>HA</td>
<td>K160T</td>
<td>S124G, T135K</td>
</tr>
<tr>
<td>NA</td>
<td>S245N</td>
<td>D329S</td>
</tr>
</tbody>
</table>

Phylogenetic Comparison of Influenza B (Yamagata) HA and NA Protein Sequences

- 1 analyzed Influenza B HA sequence was derived from MDCK isolate and belonged to the Y3 clade of the Yamagata lineage.
- 1 analyzed Influenza B NA sequence was derived from MDCK isolate and another was derived from clinical specimen. Both belonged to the Y3 clade of the Yamagata lineage.
- 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 previous vaccine strain, B/Florida/04/2006-like virus.

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>1</td>
<td>B/Phuket/3073/2013</td>
<td>99.3%</td>
</tr>
<tr>
<td>B/Yamagata NA</td>
<td>2</td>
<td>B/Phuket/3073/2013</td>
<td>98.8%</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. 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>
</tr>
</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 A (H1N1)pdm09
Hemagglutinin (HA) Genes
2016-2017 Influenza Season

Vaccine Strain
Reference Strain

2015-16 Consensus (47 strains)
Dec 2016 (2 strains)

A/Michigan/45/2015
- A/Fiji/3/2016 [Q223R]
- A/California/NHRC_NMCSD0076/2016*

2015-16 6B.1 Consensus (43 strains)
- A/California/NHRC_NMCSD0075/2016*
- A/North Dakota/03/2016
- A/Singapore/GP1911/2015 [D127E]

A/Minnesota/32/2015
- A/Darwin/11/2015

2015-16 6B Consensus (4 strains)
- A/Norway/2417/2013
- A/Estonia/76677/2013

- A/California/04/2009 [S183P, A197T]

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 (1 strain)

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

*: clinical specimen

A/Delaware/39/2015 [V394I, I443M]
A/California/NHRC_NMCSD0076/2016*
A/Michigan/45/2015

2015-16 6B.1 Consensus (46 strains)

A/India/5964/2014 [G147R]
A/Stockholm/15/2013 [S70N ADD GLY]
A/California/07/2009 [I241V, D248N K369N]
A/Astrakhan/1/2011 [V106I]

Amino Acid Substitution per 100 Residues
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 (8 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: 00D beneficiaries
JX or no prefix: US Recruit

*: clinical specimen
*: shipboard surveillance

A/Philippines/NHRC_MCY0116/2016*
A/Illinois/NHRC_18495/2016* [T135K (LOSS GLY)]
A/New.Jersey/NHRC_93422/2016* (10 strains)
A/California/NHRC_SAR41594N/2016*
A/California/NHRC_FDX90142/2016*
A/Georgia/NHRC_68549/2016*
A/Pennsylvania/50/2015
A/SouthCarolina/NHRC_JX41626/2016
A/SouthCarolina/NHRC_JX41638/2016
A/SouthCarolina/NHRC_JX41610/2016*
A/SouthCarolina/NHRC_JX41611/2016*
A/SouthCarolina/NHRC_JX41620/2016
A/California/NHRC_FDX90131/2016* [IS8, A106T]
A/California/NHRC_BRD12267N/2016* [K2R]
A/SouthCarolina/NHRC_75576/2016*
A/Alaska/232/2015
A/HongKong/5738/2014
A/HongKong/4801/2014 [N96S, L194P]
A/HongKong/146/2013 [S312N] (3C.2)
A/Switzerland/9715293/2013
A/NewYork/39/2012 (3C.3)
A/Stockholm/28/2014 (3C.3b)
A/Texas/50/2012 [T128N], [S198P] (3C.1)
A/Victoria/361/2011 (3C)
A/Perth/16/2009

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 (13 strains)

Oct-Dec 2016 (6 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

= shipboard surveillance

- A/Philippines/NHRC_MCY0116/2016*
- A/Philippines/NHRC_MCY0131/2016*
- A/South Carolina/NHRC_75576/2016*[L140V]
- A/California/NHRC_SAR41594N/2016*
- A/California/NHRC_FDX90142/2016*
- A/California/NHRC_BRD12267N/2016*[I62V]
- A/Alaska/232/2015
- A/New Jersey/NHRC_93422/2016*[9 strains]
- A/South Carolina/NHRC_JX41626/2016
- A/South Carolina/NHRC_JX41638/2016
- A/South Carolina/NHRC_JX41610/2016*
- A/South Carolina/NHRC_JX41611/2016*
- A/Alaska/240/2015
- A/New York/57/2015[S335G]
- A/Canberra/82/2014

2015-16 H3NA Consensus (37 strains)

- A/California/19/2015
- A/Switzerland/9715293/2013
- A/Hong Kong/4801/2014
- A/Victoria/361/2011[E358K, N329T (LOSS GLY)]
- A/Texas/50/2012[R150H]

Amino Acid Substitution per 100 Residues

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

**Vaccine Strain**
Reference Strain
**2015-16 Consensus (25 strains)**

**Oct 2016 (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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Amino Acid Substitution per 100 Residues
Evolutionary Relationships
Among Influenza B
(Yamagata Lineage)
Neuraminidase (NA) Genes
2016-2017 Influenza Season

Vaccine Strain
Reference Strain

2015-16 Consensus (26 strains)
June 2016 (1 strain)
Oct 2016 (1 strain)

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

*clinical specimen

shipboard surveillance

A/Philippines/NHRC_MCY0103/2016*
B/Illinois/NHRC_18462/2016
B/Wisconsin/05/2015

2015-16 B/YAM Consensus (26 strains)
B/Sydney/7/2014 [T46I, G70E]

B/Phuket/3073/2013
B/Wisconsin/01/2010 [D340N]
B/Brasilia/3/2007
B/Florida/4/2006

Amino Acid Substitution per 100 Residues