### 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/Untyp. 5</td>
<td>A/H3 5</td>
<td>10</td>
</tr>
<tr>
<td>Ft. Jackson</td>
<td>A/Untyp. 5</td>
<td>A/H1 4</td>
<td>19</td>
</tr>
<tr>
<td>Ft. Leonard Wood</td>
<td></td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>NRTC Great Lakes</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Lackland AFB</td>
<td></td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>MCRD Parris Island</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>MCRD San Diego</td>
<td></td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>CGTC Cape May</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>0</td>
<td>5</td>
<td>58</td>
</tr>
</tbody>
</table>

*New cases presented 3-13 Oct. and all were unvaccinated.

- 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.

### Items of Note

- **Elevated FRI rate at Fort Benning**
- **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, 2014-16

<table>
<thead>
<tr>
<th>Week of Illness</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Cases</td>
<td>50</td>
<td>40</td>
<td>30</td>
</tr>
<tr>
<td>Percent Flu Positive</td>
<td>80</td>
<td>70</td>
<td>60</td>
</tr>
</tbody>
</table>

### Other Items of Interest

- 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 2012-16. 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 29 October 2016:
- At or below expected value:
  - Fort Jackson
  - Fort Leonard Wood
  - Naval Recruit Training Command, Great Lakes
  - Marine Corps Recruit Depot, San Diego
  - Marine Corps Recruit Depot, Parris Island
  - Lackland Air Force Base (data through 8 Oct.)
  - Coast Guard Training Center, Cape May

- Moderately elevated:
  - Fort Benning

- Substantially elevated:
  - None
Observed FRI rate (expected rate = dashed line)

- Moderately elevated
- Substantially elevated
- Pneumonia rate (incl. afebrile)
Observation 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 (pH1N1) HA and NA Protein Sequences

- 47 analyzed Influenza A pH1N1 HA sequences were derived from MDCK isolates and 4 belonged to clade 6B while 43 belonged to the subclade 6B.1, defined by mutations S84N, S162T (ADD GLY) and I216T.
- 46 analyzed Influenza A pH1N1 NA sequences were derived from MDCK isolates.
- 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>47</td>
<td>A/California/07/2009</td>
<td>97.0-98.0%</td>
</tr>
<tr>
<td>A/pH1N1 NA</td>
<td>46</td>
<td>A/California/07/2009</td>
<td>96.1-97.3%</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.\(^1\) 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/pH1N1 Segment</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>S162N</td>
</tr>
<tr>
<td>NA</td>
<td>N44S, S70N, N386K</td>
</tr>
</tbody>
</table>

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

- **33** analyzed H3N2 HA sequences were derived from MDCK isolates and **5** were derived from clinical specimen.
- **28** analyzed H3N2 NA sequences were derived from MDCK isolates and **5** 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 to 2015-2016 Vaccine Strain**

<table>
<thead>
<tr>
<th>Segment</th>
<th>No.</th>
<th>2015-2016 Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3N2 HA</td>
<td>38</td>
<td>A/Switzerland/9715293/2013</td>
<td>97.0-99.6%</td>
</tr>
<tr>
<td>H3N2 NA</td>
<td>33</td>
<td>A/Switzerland/9715293/2013</td>
<td>97.9-98.6%</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>S47P N122D T128A N144S N158K N158H T160K T160I</td>
</tr>
<tr>
<td>NA</td>
<td>S245N N329I S331R</td>
<td>S247T N329T</td>
</tr>
</tbody>
</table>

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

- 50 analyzed Influenza B HA sequences were derived from MDCK isolates. 26 (52%) isolates belonged to the V1A clade of the Victoria Lineage and 24 (48%) belonged to the Y3 clade of the Yamagata lineage.
- 50 analyzed Influenza B NA sequences were derived from MDCK isolates. 26 isolates belonged to the V1A clade of the Victoria Lineage and 24 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 strains B/Ohio/01/2005-like virus for B/Victoria specimens and B/Florida/04/2006-like virus for B/Yamagata specimens.

Summary of Influenza B 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>B/Victoria HA</td>
<td>26</td>
<td>B/Brjebane/60/2008</td>
<td>99.1-99.5%</td>
</tr>
<tr>
<td>B/Victoria NA</td>
<td>26</td>
<td>B/Brjebane/60/2008</td>
<td>98.3-98.54%</td>
</tr>
<tr>
<td>B/Yamagata HA</td>
<td>24</td>
<td>B/Phuket/3073/2013</td>
<td>99.1-99.5%</td>
</tr>
<tr>
<td>B/Yamagata NA</td>
<td>24</td>
<td>B/Phuket/3073/2013</td>
<td>98.7-100.0%</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/

<table>
<thead>
<tr>
<th>INF B Segment</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>A198T</td>
<td>N196D T198N</td>
</tr>
<tr>
<td>NA</td>
<td>D463N</td>
<td></td>
</tr>
</tbody>
</table>

Summary of Influenza A/pH1N1, A/H3N2 and Influenza B Hemagglutinin (HA) Genetic Groups

**Influenza A/pH1N1**

- 6B.1, 43, 91%
- 6B, 4, 9%

**Influenza A/H3N2**

- 3C.3a, 25, 66%
- 3C.2a, 13, 34%

**Influenza B**

- B/Vic (1A), 26, 52%
- B/Yam (Y3), 24, 48%
Evolutionary Relationships Among Influenza A (pH1N1) Hemagglutinin (HA) Genes 2015-2016 Influenza Season

Vaccine Strain
Reference Strain
2013-2014 consensus*

December 2015
January 2016
February 2016
March 2016
April 2016
May 2016

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
Ship: Shipboard

*No pH1N1 sequencing data available for 2014-2015 season
Evolutionary Relationships Among Influenza A (pH1N1) Neuraminidase (NA) Genes 2015-2016 Influenza Season

Vaccine Strain
Reference Strain
2013-2014 consensus*

December 2015
January 2016
February 2016
March 2016
April 2016

May 2016

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

*No pH1N1 sequencing data available for 2014-2015 season
Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes 2015-2016 Influenza Season

Vaccine Strain
Reference Strain

December 2015
January 2016
February 2016
March 2016
April 2016
May 2016

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
Ship: Shipboard

A/California/NHRC_BRD21412N/2016 [T265I]
A/California/NHRC_BRD80496N/2016 [M241I]
A/SouthCarolina/NHRC_75444/2016
A/SouthCarolina/NHRC_75450/2016
A/SouthCarolina/NHRC_75458/2016*
A/SouthCarolina/NHRC_75461/2016*
A/SouthCarolina/NHRC_75462/2016*
A/SouthCarolina/NHRC_75472/2016*
A/SouthCarolina/NHRC_75488/2016*
A/California/NHRC_FDX21905/2016
A/California/NHRC_BRD12210N/2016
A/California/NHRC_BRD41334N/2016
A/California/NHRC_BRD80554N/2016
A/California/NHRC_FDX40639/2016
A/California/NHRC_BRD21370N/2016
A/California/NHRC_BRD41318N/2016
A/California/NHRC_BRD41264N/2016
A/California/NHRC_FDX11931/2016
A/California/NHRC_BRD41236N/2016
A/California/NHRC_BRD41189N/2016
A/California/NHRC_SAR41345N/2016
A/California/NHRC_SAR41353N/2016
A/California/NHRC_SAR41380N/2016
A/California/NHRC_CVS0066/2016
A/California/NHRC_SAR41446N/2016
A/Missouri/NHRC_36888/2016
A/California/19/2015
A/California/NHRC_BRD21336N/2016
A/California/NHRC_BRD41174N/2016 [P79S]
A/California/NHRC_BRD27582/2016
A/California/NHRC_BRD27575/2015
A/California/NHRC_SAR20825N/2015
A/NewYork/57/2015
A/California/NHRC_SAR41418N/2016 [E64K]
A/California/NHRC_BRD41207N/2016
A/California/NHRC_BRD41199N/2016
A/Canberra/82/2014
A/Switzerland/9715293/2013
A/Nebraska/04/2014 [P79S]
A/Victoria/361/2011 [E358K, N329T (LOSS GLY)]
A/Texas/50/2012 [R150H]
A/HongKong/146/2013
A/Perth/16/2009
A/Norway/1186/2011

Amino Acid Substitution per 100 residues

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
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