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>
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<tbody>
<tr>
<td></td>
<td>A/ Untyp.</td>
<td>A/H3</td>
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<tr>
<td>Ft. Benning</td>
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<tr>
<td>Ft. Jackson</td>
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<td>Ft. Leonard Wood</td>
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<tr>
<td>NRTC Great Lakes</td>
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<td>Lackland AFB</td>
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<td>MCRD Parris Island</td>
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<tr>
<td>MCRD San Diego</td>
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<td>CGTC Cape May</td>
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- 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, 2014-16

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 17 December 2016:
- **At or below expected value:**
  - Fort Benning
  - Fort Jackson
  - Fort Leonard Wood
  - Naval Recruit Training Command, Great Lakes
  - Marine Corps Recruit Depot, San Diego (data through 10 Dec.)
  - Lackland Air Force Base (data through 29 Oct.)
  - Coast Guard Training Center, Cape May

- **Moderately elevated:**
  - None

- **Substantially elevated:**
  - Marine Corps Recruit Depot, Parris Island
**NHRC Respiratory Illness Update**

**Week Ending: 17 December 2016**

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**Ft. Benning FRI Rates and Diagnostic Test Results**

Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

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**Ft. Jackson FRI Rates and Diagnostic Test Results**

Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

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**Back to FRI Report**

- Observed FRI rate (expected rate = dashed line)
- Moderately elevated
- Substantially elevated
- Pneumonia rate (incl. afebrile)

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**Back to FRI Report**
Ft. Leonard Wood FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

Great Lakes FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)
### Fort Benning FRI Rate Status

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#### FRI Rate (cases/100 trainees/week)
- **At/ Below Expected**
- **Moderately Elevated**
- **Substantially Elevated**
- **Expected Rate**

### Fort Jackson FRI Rate Status

<table>
<thead>
<tr>
<th>Month</th>
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</table>

### Observed FRI rate (expected rate = dashed line)
- **Moderately elevated**
- **Substantially elevated**
- **Pneumonia rate (incl. afebrile)**

---

**MCRD SD FRI Rates and Diagnostic Test Results**

Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)

**MCRD PI FRI Rates and Diagnostic Test Results**

Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)
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)

Influenza Subtype
- A/H3
- A/PhH1
- Untyped

Back to FRI Report

- 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 (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>
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<tbody>
<tr>
<td>A/pH1N1 HA</td>
<td>47</td>
<td>A/California/07/2009</td>
<td>97.0-98.0%</td>
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<tr>
<td>A/pH1N1 NA</td>
<td>46</td>
<td>A/California/07/2009</td>
<td>96.1-97.3%</td>
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</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/

<table>
<thead>
<tr>
<th>A/pH1N1 Segment</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
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<tbody>
<tr>
<td>HA</td>
<td>S162N</td>
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</tr>
<tr>
<td>NA</td>
<td>N44S, S70N</td>
<td>N386K</td>
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Phylogenetic Comparison of Influenza A (H3N2) HA and NA Protein Sequences

- 33 analyzed H3N2 HA sequences were derived from MDCK isolates and 17 were derived from clinical specimen.
- 28 analyzed H3N2 NA sequences were derived from MDCK isolates and 9 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

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<th>Segment</th>
<th>No.</th>
<th>2015-2016 Vaccine Strain</th>
<th>Protein Homology</th>
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<td>H3N2 HA</td>
<td>50</td>
<td>A/Switzerland/9715293/2013</td>
<td>96.8-99.6%</td>
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<td>H3N2 NA</td>
<td>37</td>
<td>A/Switzerland/9715293/2013</td>
<td>97.9-98.6%</td>
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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/

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<th>Mutation</th>
<th>ADD GLY</th>
<th>LOSS GLY</th>
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<tr>
<td>HA</td>
<td>K160T</td>
<td>S47P N122D T128A N144S N158K</td>
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<td>N158H T160K T160I</td>
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<tr>
<td>NA</td>
<td>S245N</td>
<td>S247T N329S N329T</td>
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<td>S329R</td>
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Phylogenetic Comparison of Influenza B (Victoria and Yamagata) HA and NA Protein Sequences

- 52 analyzed Influenza B HA sequences were derived from MDCK isolates. 27 isolates belonged to the V1A clade of the Victoria Lineage and 25 belonged to the Y3 clade of the Yamagata lineage.
- 53 analyzed Influenza B NA sequences were derived from MDCK isolates. 27 isolates belonged to the V1A clade of the Victoria Lineage and 26 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>
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<tbody>
<tr>
<td>B/Victoria HA</td>
<td>27</td>
<td>B/Brisbane/60/2008</td>
<td>99.1-99.5%</td>
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<tr>
<td>B/Victoria NA</td>
<td>27</td>
<td>B/Brisbane/60/2008</td>
<td>98.3-98.54%</td>
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<tr>
<td>B/Yamagata HA</td>
<td>25</td>
<td>B/Phuket/3073/2013</td>
<td>99.1-99.5%</td>
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<tr>
<td>B/Yamagata NA</td>
<td>26</td>
<td>B/Phuket/3073/2013</td>
<td>98.7-100.0%</td>
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</tbody>
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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/

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<th>INF B Segment</th>
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<td>HA</td>
<td>A198T</td>
<td>N196D T198N</td>
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<tr>
<td>NA</td>
<td>D463N, S295N</td>
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</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

- H3N2 3C.3a 50%
- H3N2 3C.2a 50%

Influenza B

- B/Vic (1A), 27, 52%
- B/Yam (Y3), 25, 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 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 (H3N2) Hemagglutinin (HA) Genes 2015-2016 Influenza Season Vaccine Strain (season) Reference Strain
2013-2014 consensus
December 2015
January 2016
February 2016
March 2016
April 2016
May 2016
July-Sept 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
*clinical specimen

Amino Acid Substitution per 100 residues
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
July 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
*: clinical specimen

Amino Acid Substitution per 100 residues
Evolutionary Relationships Among Influenza B Hemagglutinin (HA) Genes 2015-2016 Influenza Season Vaccine Strain

Reference Strain
2013-2014 consensus

January 2016
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March 2016
April 2016
May 2016

July 2016

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

Yamagata Lineage

Victoria Lineage

Amino Acid Substitution per 100 residues