### Influenza

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

<table>
<thead>
<tr>
<th>Site</th>
<th>Since last report*</th>
<th>Since Sept. 25, 2017</th>
<th>No. Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A/ Untyp.</td>
<td>A/H3</td>
<td>A/H1</td>
</tr>
<tr>
<td>Ft. Benning</td>
<td>1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Ft. Jackson</td>
<td></td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>Ft. Leonard Wood</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRTC Great Lakes</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lackland AFB</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>MCRD Parris Island</td>
<td>2</td>
<td>29</td>
<td>2</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><strong>Total</strong></td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>

*Cases presented 11-30 March. Three A/H3 cases and one B case had been vaccinated more than 14 days prior to illness.

- 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 Leonard Wood
- Small number of A/H3 cases at 3 basic training centers in late March

### Vaccination Status of Confirmed Influenza Cases Among US Military Basic Trainees, 2014-2018

**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 2012-18. 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 14 April 2018:
- At or below expected value:
  Fort Benning
  Fort Jackson
  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 24 March)
  Coast Guard Training Center, Cape May
  - Moderately elevated:
    None
  - Substantially elevated:
    Fort Leonard Wood
Observed FRI rate (expected rate = dashed line)  
- Moderately elevated  
- Substantially elevated  
- Pneumonia rate (incl. afebrile)
NHRC Respiratory Illness Update

Back to FRI Report

− Observed FRI rate (expected rate = dashed line)  ● Moderately elevated  ● Substantially elevated  — Pneumonia rate (incl. afebrile)
NHRC Respiratory Illness Update

Week Ending: 14 April 2018

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)

Samples Received

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenovirus</td>
<td>13%</td>
<td>9%</td>
<td>8%</td>
</tr>
<tr>
<td>Influenza</td>
<td>38%</td>
<td>27%</td>
<td>5%</td>
</tr>
<tr>
<td>RSV</td>
<td></td>
<td>10%</td>
<td>29%</td>
</tr>
<tr>
<td>C. pneumo</td>
<td></td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>M. pneumo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhinovirus</td>
<td></td>
<td>55%</td>
<td>13%</td>
</tr>
</tbody>
</table>

Influenza Subtype

<table>
<thead>
<tr>
<th>Subtype</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1</td>
<td>9%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>A/H3</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>B invent</td>
<td>19%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Back to FRI Report
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.
Phylogenetic Comparison of Influenza A(H1N1)pdm09 HA and NA Protein Sequences

- 18 analyzed H3N2 HA and 19 NA sequences were derived from whole genome sequencing.
- This sequence belonged to the subclade 6B.1, defined by mutations S84N, S162T (ADD GLY) and I216T.
- 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>18</td>
<td>A/Michigan/45/2015 (2017-18)</td>
<td>98.5-99.3%</td>
</tr>
<tr>
<td>A(H1N1)pdm09 NA</td>
<td>19</td>
<td>A/Michigan/45/2015 (2017-18)</td>
<td>98.1-99.1%</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.\(^1\) Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server
  \[\text{http://www.cbs.dtu.dk/services/NetNGlyc/}\]

<table>
<thead>
<tr>
<th>A/A(H1N1)pdm09 Segment</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ADD GLY</td>
</tr>
<tr>
<td>HA</td>
<td>S164T</td>
</tr>
<tr>
<td>NA</td>
<td>N44S, S70N</td>
</tr>
</tbody>
</table>

Evolutionary Relationships Among Influenza (H1N1)pdm09 Hemagglutinin (HA) Genes 2017-2018 Influenza Season

Vaccine Strain
Reference Strain
2016-2017 Consensus (1 strain)
Nov 2017 (1 strain)
Dec 2017 (7 strains)
Jan 2018 (7 strains)
February 2018 (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
SEA: US Special Forces

A/California/NHRC_BRD41866N/2018 (3 strains)
A/California/NHRC_BRD41808N/2018 (2 strains)
A/SouthCarolina/NHRC_75742/2018
A/Arizona/NHRC_MAP6094A/2017
A/California/NHRC_28352/2017
A/California/NHRC_QV853/2018 [H273Y]
A/California/NHRC_28351/2017
A/California/NHRC_QV10858/2017
A/Japan_NHRC_FDX70322/2018
A/Japan/NHRC_FDX70303/2017
A/Japan/NHRC_FDX70298/2017
A/California/NHRC_BRD41800N/2018
A/California/NHRC_BRD41771N/2017
A/California/NHRC_SAR41891N/2017
A/California/NHRC_BRD80970N/2018

A/North Dakota/03/2016 [R205K]
A/Michigan/45/2015 [Q233R]
2016-2017 Group 6B.1 (1 whole genome strain)
A/Minnesota/32/2015
A/Darwin/11/2015
A/Norway/2417/2013 (Group 6B)
A/California/07/2009

Amino Acid Substitution per 100 residues
Evolutionary Relationships Among Influenza (H1N1)pdm09 Nauraminidase (NA) Genes 2017-2018 Influenza Season

Vaccine Strain
Reference Strain
2016-2017 Consensus (1 strain)

Nov 2017 (1 strain)
Dec 2017 (8 strains)
Jan 2018 (7 strains)
February 2018 (3 strains)

A/California/NHRC_28351/2017
A/California/NHRC_QV10858/2017
A/California/NHRC_28352/2017
A/California/NHRC_BRD41808N/2018 (2 strains)
A/California/NHRC_BRD41800N/2018
A/California/NHRC_BRD41771N/2017
A/California/NHRC_SAR41891N/2017
A/Arizona/NHRC_MAP6094A/2017 [V338I]
A/California/NHRC_QV853/2018
A/California/NHRC_BRD80970N/2018 [F351Y]
A/California/NHRC_BRD41866N/2018 (3 strains)
A/California/NHRC_QV11073/2017
A/SouthCarolina/NHRC_75742/2018
A/Japan_NHRC_FDX70322/2018 [I46V, A75V]
A/Japan/NHRC_FDX70303/2017
A/Japan/NHRC_FDX70298/2017

A/Delaware/39/2015 [V394I, I443M]
2016-2017 Group 6B.1 (1 whole genome strain)

A/Michigan/45/2015

A/California/80/2015 [I13V, I32V, V67I, S79L]
A/California/07/2009 [I241V, D248N K369N]

Amino Acid Substitution per 100 residues
Phylogenetic Comparison of Influenza A (H3N2) HA and NA Protein Sequences

- 110 analyzed H3N2 HA and 111 NA sequences were derived from whole genome sequencing.
- All sequences were in subclone 3C.2a. Of those 3C.2a sequences, 17 were further classified as 3C.2a1, defined by the mutations N171K, I406V (HA2: I77V), and G484E (HA2: G155E).
- 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/Texas/50/2012 for HA and A/Perth/16/2009 for NA sequences.

Summary of Influenza A (H3N2) Protein Homology When Compared with 2017-2018 Vaccine Strain

<table>
<thead>
<tr>
<th>Segment</th>
<th>No.</th>
<th>Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>H3N2 HA</td>
<td>110</td>
<td>A/HongKong/4801/2014</td>
<td>97.3-98.9%</td>
</tr>
<tr>
<td>H3N2 NA</td>
<td>111</td>
<td>A/HongKong/4801/2014</td>
<td>97.0-98.7%</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/](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>D93N, S245N, S329N</td>
<td>N70K, D329S, I331G</td>
</tr>
</tbody>
</table>

Evolutionary Relationships Among Influenza A (H3N2) Hemagglutinin (HA) Genes
2017-2018 Influenza Season

Vaccine Strain
WHO Recommended 2018-19 Vaccine Strain

Reference Strain
2016-2017 Consensus (75 strains)
Sept 2017 (2 strains)
Oct 2017 (8 strains)
Nov 2017 (21 strains)
Dec 2017 (42 strains)
Jan 2018 (36 strains)
Feb 2018 (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

3C.2a

1, 77,
15%

3C.3a

1, 77,
15%

3C.2a

1, 77,
15%

3C.3a

1, 77,
15%

3C.2a

1, 77,
15%

3C.3a

1, 77,
15%
Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes 2017-2018 Influenza Season

**WHO Recommended 2018-19 Vaccine Strain**

Reference Strain

**2016-2017 Consensus** (9 whole genome strains)
- Sept 2017 (2 strains)
- Oct 2017 (8 strains)
- Nov 2017 (21 strains)
- Dec 2017 (42 strains)
- Jan 2018 (37 strains)
- Feb 2018 (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
JR or no prefix: US Recruit
SEA: US Special Forces
Shipboard Surveillance
Phylogenetic Comparison of Influenza B (Yamagata and Victoria) HA and NA Protein Sequences

- 28 HA sequence belonged to the Y3 clade of the Yamagata lineage and 57 HA sequences belonged to the V1A clade of the Victoria lineage.
- 27 NA sequence belonged to the Yamagata lineage and 57 NA sequences belonged to the Victoria lineage. All sequences were derived from whole genome sequencing.
- Of note, 46 Victoria sequences contained the double amino acid deletion at positions 162 and 163.
- 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, and B/Brisbane/60/2008 for both HA and NA Victoria 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>Vaccine Strain</th>
<th>Protein Homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>B/Yamagata HA</td>
<td>28</td>
<td>B/Phuket/3073/2013</td>
<td>99.1-99.3%</td>
</tr>
<tr>
<td>B/Yamagata NA</td>
<td>27</td>
<td>B/Phuket/3073/2013</td>
<td>98.5-98.9%</td>
</tr>
<tr>
<td>B/Victoria HA</td>
<td>57</td>
<td>B/Brisbane/60/2008</td>
<td>98.1-99.1%</td>
</tr>
<tr>
<td>B/Victoria NA</td>
<td>57</td>
<td>B/Brisbane/60/2008</td>
<td>98.1-98.5%</td>
</tr>
</tbody>
</table>
Evolutionary Relationships Among Influenza B Hemagglutinin (HA) Genes 2017-2018 Influenza Season

**Yamagata Lineage**
- B/California/NHRC_BRD41863N/2018
- B/NewJersey/NHRC_03800/2018
- B/California/NHRC_SAR41921N/2018
- B/California/NHRC_MAP4172A/2018
- B/California/NHRC_BRD412459N/2017
- B/California/NHRC_BRD21633N/2017
- B/California/NHRC_BRD12451N/2017
- B/Colorado/6/2017
- B/Washington/63/2016
- B/Texas/02/2013
- B/Brisbane/60/2008

**Victoria Lineage**
- B/California/NHRC_BRD41863N/2018
- B/NewJersey/NHRC_03800/2018
- B/California/NHRC_SAR41921N/2018
- B/California/NHRC_MAP4172A/2018
- B/California/NHRC_BRD412459N/2017
- B/California/NHRC_BRD21633N/2017
- B/California/NHRC_SAR10524N/2018
- B/California/NHRC_BRD12453N/2017
- B/California/NHRC_BRD12452N/2017
- B/California/NHRC_BRD12451N/2017
- B/California/NHRC_BRD41863N/2018
- B/NewJersey/NHRC_03800/2018
- B/California/NHRC_SAR41921N/2018
- B/California/NHRC_MAP4172A/2018
- B/California/NHRC_BRD412459N/2017
- B/California/NHRC_BRD21633N/2017
- B/California/NHRC_SAR10524N/2018
- B/California/NHRC_BRD12453N/2017
- B/California/NHRC_BRD12452N/2017
- B/California/NHRC_BRD12451N/2017
- B/Colorado/6/2017
- B/Washington/63/2016
- B/Texas/02/2013
- B/Brisbane/60/2008

**Vaccination Strain**

**Reference Strain**
- B/Sydney/7/2014
- B/Phuket/3073/2013

**2016-2017 Consensus**
- (16 whole genome strains)

**2017-2018 Consensus**
- Oct 2017 (1 strain)
- Nov 2017 (7 strains)
- Dec 2017 (30 strains)
- Jan 2018 (43 strains)
- Feb 2018 (9 strains)

LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of glycosylation
NHRC: Naval Health Research Center
BRD: U.S./Mexico Border outpatient
SAR: U.S./Mexico Border inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit
SEA: US Special Forces
Shipboard Surveillance

**Amino Acid Substitution per 100 residues**
Evolutionary Relationships Among Influenza B Neuraminidase (NA) Genes 2017-2018 Influenza Season

Vaccine Strain
Reference Strain

2016-2017 Consensus (28 whole genome strains)
Oct 2017 (1 strain)
Nov 2017 (7 strains)
Dec 2017 (30 strains)
Jan 2018 (42 strains)
Feb 2018 (9 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
SEA: US Special Forces
Shipboard Surveillance

- 17 -