Febrile Respiratory Illness (FRI) Surveillance Update

Operational Infectious Diseases, Naval Health Research Center, San Diego, CA

2017 Week 4 (through 28 January 2017)

Contact Information

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NHRC FRI Surveillance Program

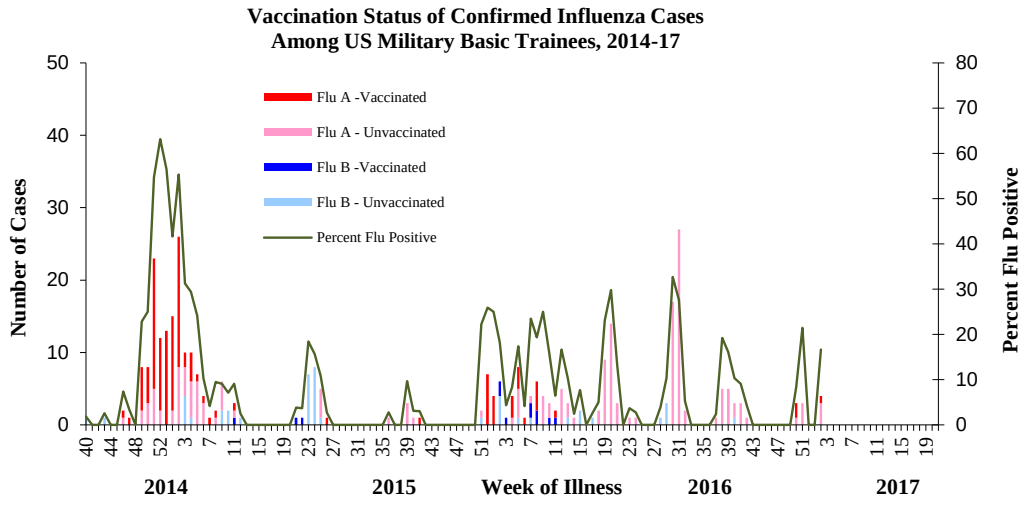
Influenza

NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

	Current Week*				Since Oct.1, 2016				
Site	A/ Untyp.	A/H3	A/H1	B	A/ Untyp.	A/H3	A/H1	B	No. Tested
Ft. Benning		1				1			79
Ft. Jackson						6			67
Ft. Leonard Wood						2			15
NRTC Great Lakes		1				2		1	47
Lackland AFB									8
MCRD Parris Island						3			22
MCRD San Diego		1	1			1	1		88
CGTC Cape May									30
Total	0	3	1	0	0	15	1	1	356

*New cases presented for care 11-12 January. One case had been vaccinated > 14 days prior.

- 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.



Other Items of Interest

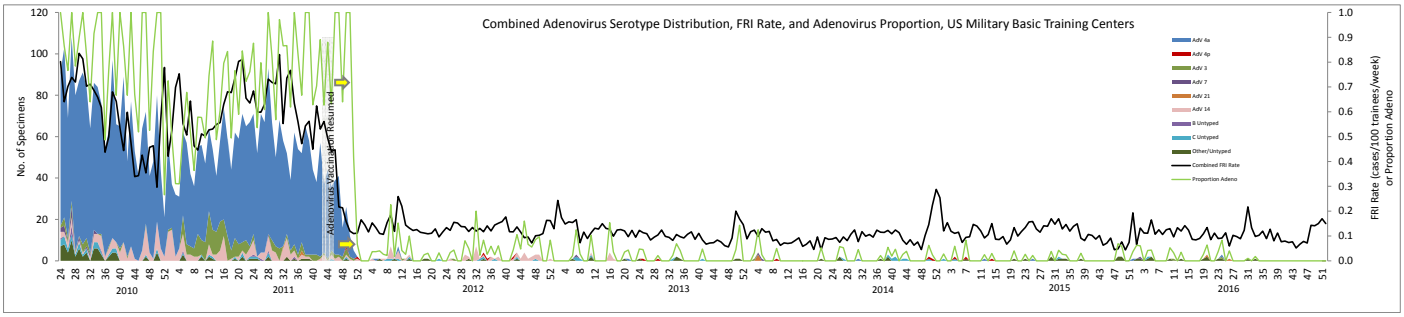
- NHRC is conducting laboratory-based surveillance for meningococcal disease. The program's purpose is to track and characterize meningococcal cases among DoD medical beneficiaries. For more information and the most recent data, view the Quarterly Meningococcal Report.

Items of Note

- *Elevated FRI rates at Fort Benning and MCRD Parris Island*
- *NHRC is able to test for novel influenza strains, MERS coronavirus, enterovirus EV-68, Ebola virus, and Zika virus*

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 28 January 2017:

- **At or below expected value:**

Fort Benning
Fort Jackson
Fort Leonard Wood
Naval Recruit Training Command, Great Lakes
Marine Corps Recruit Depot, San Diego
Lackland Air Force Base (data through 14 Jan.)
Coast Guard Training Center, Cape May

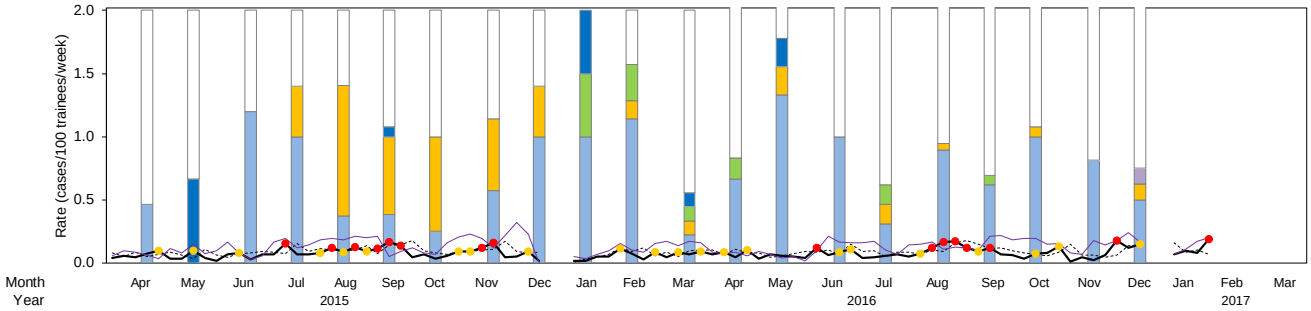
- **Moderately elevated:**

None

- **Substantially elevated:**

Fort Benning
Marine Corps Recruit Depot, Parris Island

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



Samples Received	13	6	10	20	27	26	24	35	10	4	14	18	12	9	26	13	38	26	26	27	16
Adenovirus		33%				4%				25%		6%		11%							
Influenza										25%	14%	6%	8%			8%		4%			
RSV																					
C. pneumo																					6%
M. pneumo				20%	52%	31%	38%	29%	20%		7%	6%		11%		8%	3%		4%		6%
Rhinovirus	23%		60%	50%	19%	19%	13%	29%	50%	50%	57%	11%	33%	67%	50%	15%	45%	31%	50%	41%	25%

Influenza Subtype																					
B										0%	100%	100%	100%			100%		0%			
A/H3										0%	0%	0%	0%			0%		100%			
A/pH1										100%	0%	0%	0%			0%		0%			
Untyped										0%	0%	0%	0%			0%		0%			

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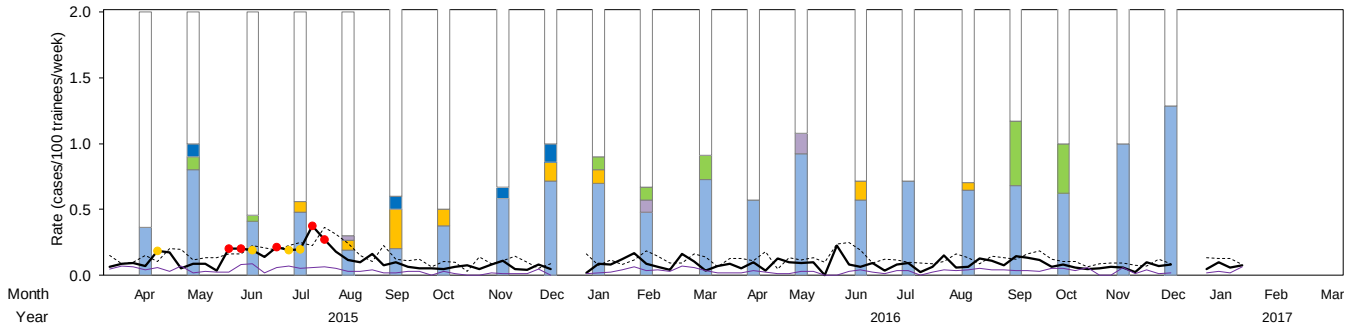
Ft. Jackson FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	33	20	44	50	53	20	16	24	14	20	21	11	21	13	14	14	34	41	32	22	14
Adenovirus		5%				5%		4%	7%												
Influenza		5%	2%							5%	5%	9%						24%	19%		
RSV																					
C. pneumo					2%						5%			8%							
M. pneumo				4%	4%	15%	6%		7%	5%					7%		3%				
Rhinovirus	18%	40%	20%	24%	9%	10%	19%	29%	36%	35%	24%	36%	29%	46%	29%	36%	32%	34%	31%	50%	64%

Influenza Subtype																					
B		100%	100%							0%	0%	0%						0%	0%		
A/H3		0%	0%							0%	0%	0%						100%	100%		
A/pH1		0%	0%							100%	100%	100%						0%	0%		
Untyped		0%	0%							0%	0%	0%						0%	0%		

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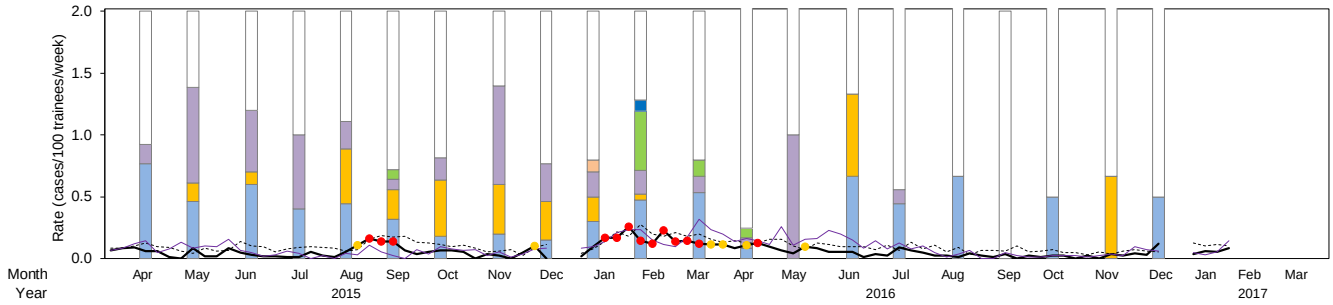
– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated —— Pneumonia rate (incl. afebrile)

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



Samples Received	**26**	**13**	**20**	**10**	**9**	**25**	**22**	**10**	**13**	**20**	**42**	**15**	**24**	**6**	**3**	**18**	**3**	**1**	**4**	**3**	**4**
Adenovirus											5%										
Influenza						4%					24%	7%	4%								
RSV										5%											
C. pneumo	8%	38%	25%	30%	11%	4%	9%	40%	15%	10%	10%	7%	4%	50%		6%					
M. pneumo		8%	5%		22%	12%	23%	20%	15%	10%	2%				33%					33%	
Rhinovirus	38%	23%	30%	20%	22%	16%	9%	10%	8%	15%	24%	27%	4%		33%	22%	33%		25%		25%
Influenza Subtype: B						0%					20%	100%	100%								
Influenza Subtype: A/H3						100%					10%	0%	0%								
Influenza Subtype: A/pH1						0%					70%	0%	0%								
Influenza Subtype: Untyped						0%					0%	0%	0%								

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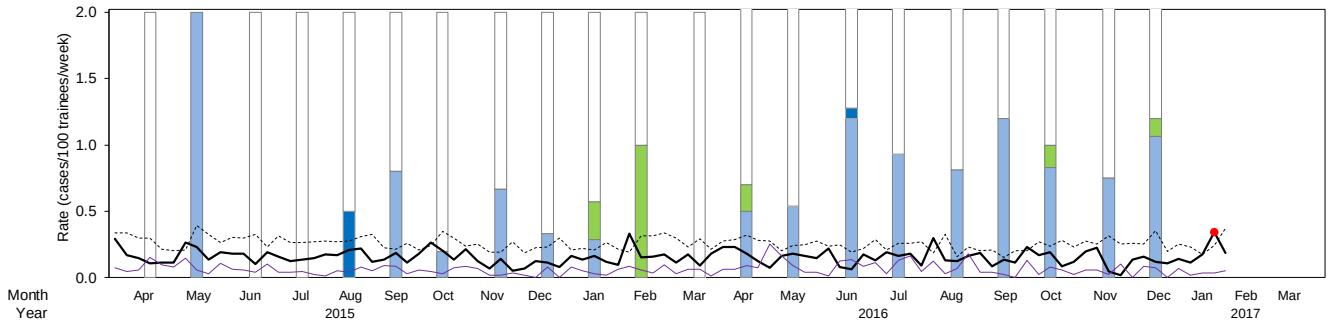
Great Lakes FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	**1**	**1**	**1**	**3**	**4**	**5**	**10**	**3**	**6**	**7**	**2**	**3**	**20**	**26**	**25**	**30**	**32**	**15**	**12**	**8**	**15**
Adenovirus					25%										4%						
Influenza										14%	50%		10%						8%		7%
RSV																					
C. pneumo																					
M. pneumo																					
Rhinovirus		100%				40%	10%	33%	17%	14%			25%	27%	60%	47%	41%	60%	42%	38%	53%
Influenza Subtype: B										0%	0%		50%						100%		0%
Influenza Subtype: A/H3										0%	0%		0%						0%		100%
Influenza Subtype: A/pH1										100%	100%		50%						0%		0%
Influenza Subtype: Untyped										0%	0%		0%						0%		0%

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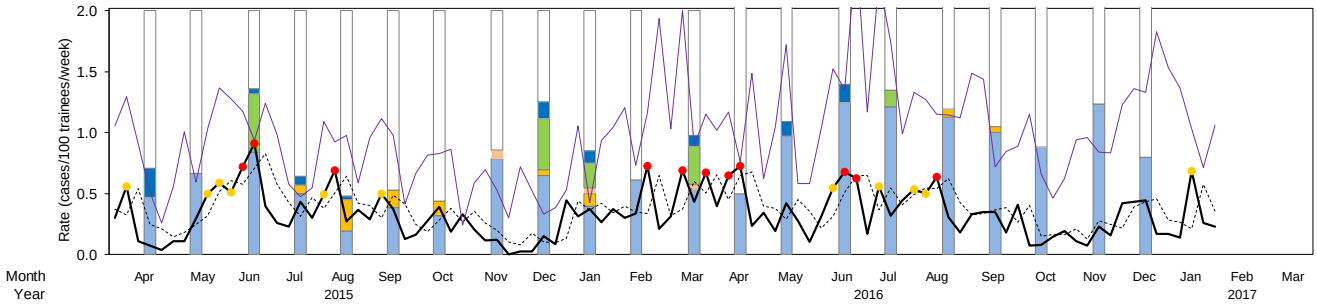
– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)

MCRD SD FRI Rates and Diagnostic Test Results

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



Samples Received	**34**	**42**	**88**	**56**	**62**	**57**	**50**	**28**	**43**	**40**	**13**	**45**	**48**	**33**	**53**	**43**	**62**	**40**	**25**	**21**	**5**
Adenovirus	12%		2%	4%	2%				7%	5%		4%		6%	8%						
Influenza			24%						21%	10%		16%				7%					
RSV								4%		3%		2%									
C. pneumo																					
M. pneumo				4%	13%	7%	6%		2%	5%							3%	3%			
Rhinovirus	24%	33%	42%	25%	10%	19%	16%	39%	33%	20%	31%	27%	25%	48%	62%	60%	56%	50%	44%	62%	40%

Influenza Subtype																					
B			76%						11%	0%		0%				100%					
A/H3			24%						89%	100%		86%				0%					
A/pH1			0%						0%	0%		14%				0%					
Untyped			0%						0%	0%		0%				0%					

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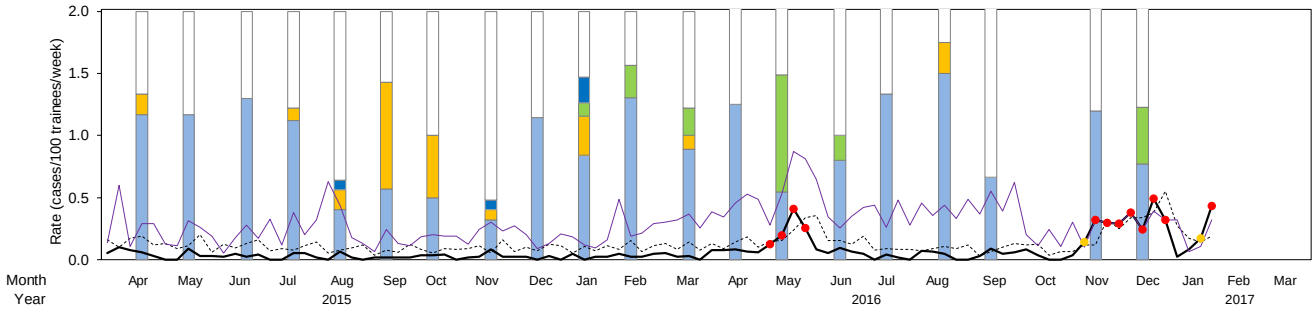
MCRD PI FRI Rates and Diagnostic Test Results

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



Samples Received	**12**	**12**	**20**	**41**	**25**	**14**	**4**	**25**	**7**	**19**	**23**	**18**	**8**	**59**	**20**	**6**	**8**	**3**	**0**	**5**	**13**
Adenovirus					4%			4%		11%											
Influenza										5%	13%	11%		47%	10%						23%
RSV																					
C. pneumo																					
M. pneumo	8%			5%	8%	43%	25%	4%		16%		6%					13%				
Rhinovirus	58%	58%	65%	56%	20%	29%	25%	16%	57%	42%	65%	44%	63%	27%	40%	67%	75%	33%		60%	38%

Influenza Subtype																					
B										0%	0%	0%		0%	0%						0%
A/H3										0%	0%	0%		100%	100%						100%
A/pH1										100%	100%	100%		0%	0%						0%
Untyped										0%	0%	0%		0%	0%						0%

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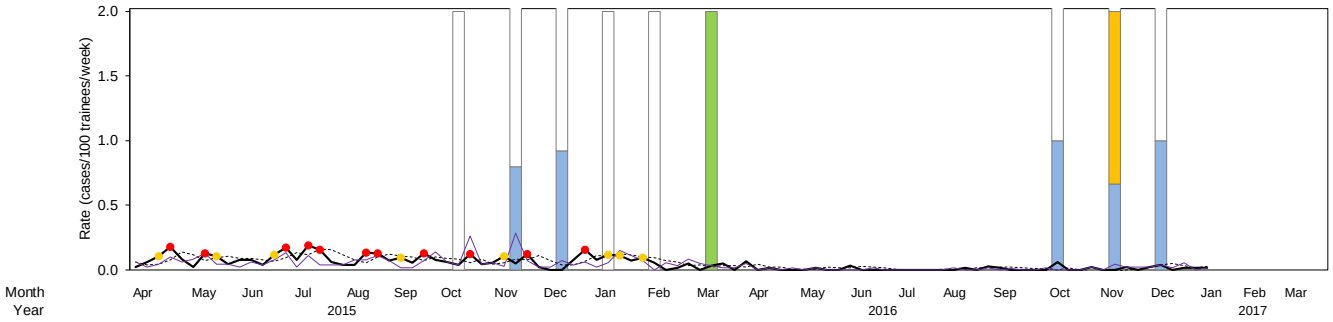
– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)

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



Samples Received	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**5**	**13**	**3**	**2**	**2**						**2**	**3**	**4**		
Adenovirus																						
Influenza												100%										
RSV																						
C. pneumo																						
M. pneumo																			67%			
Rhinovirus								40%	46%									50%	33%	50%		

Influenza Subtype																						
B												50%										
A/H3												0%										
A/pH1												50%										
Untyped												0%										

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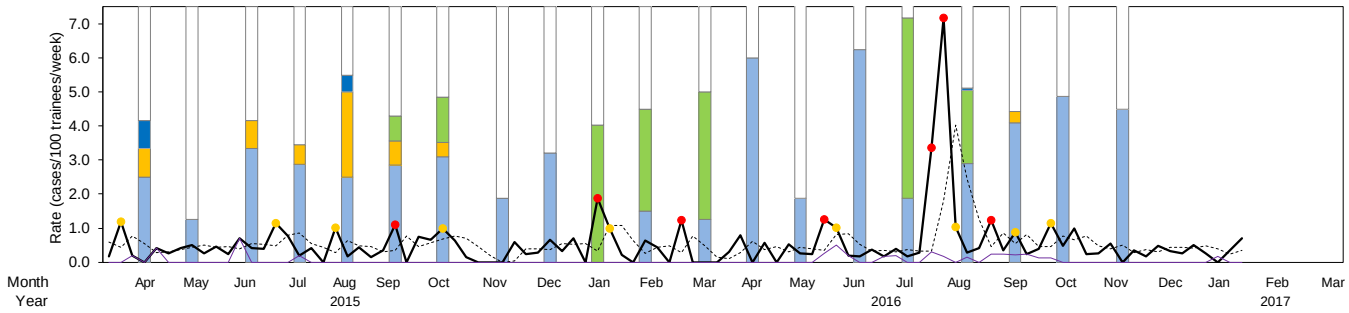
Cape May FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	**9**	**6**	**9**	**13**	**15**	**21**	**17**	**4**	**7**	**13**	**5**	**6**	**5**	**12**	**6**	**24**	**101**	**22**	**20**	**10**		
Adenovirus	11%				7%												1%					
Influenza						10%	18%			54%	40%	50%				71%	29%					
RSV																						
C. pneumo																						
M. pneumo	11%		11%	8%	33%	10%	6%											5%				
Rhinovirus	33%	17%	44%	38%	33%	38%	41%	25%	43%		20%	17%	80%	25%	83%	25%	39%	55%	65%	60%		

Influenza Subtype																						
B						0%	0%			100%	100%	0%				0%	0%					
A/H3						100%	100%			0%	0%	0%				100%	93%					
A/pH1						0%	0%			0%	0%	100%				0%	0%					
Untyped						0%	0%			0%	0%	0%				0%	7%					

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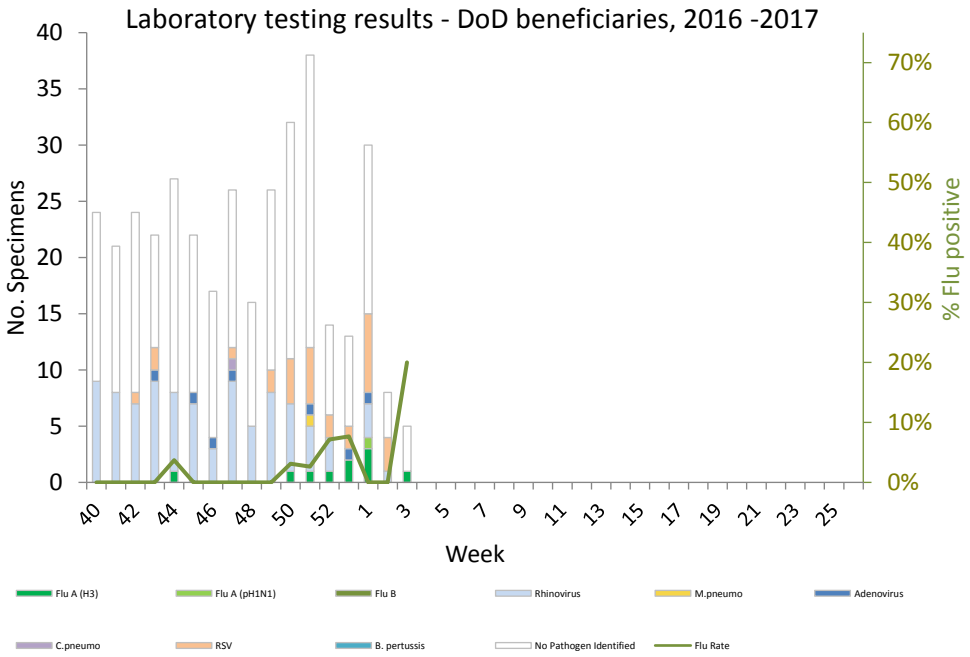
– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)

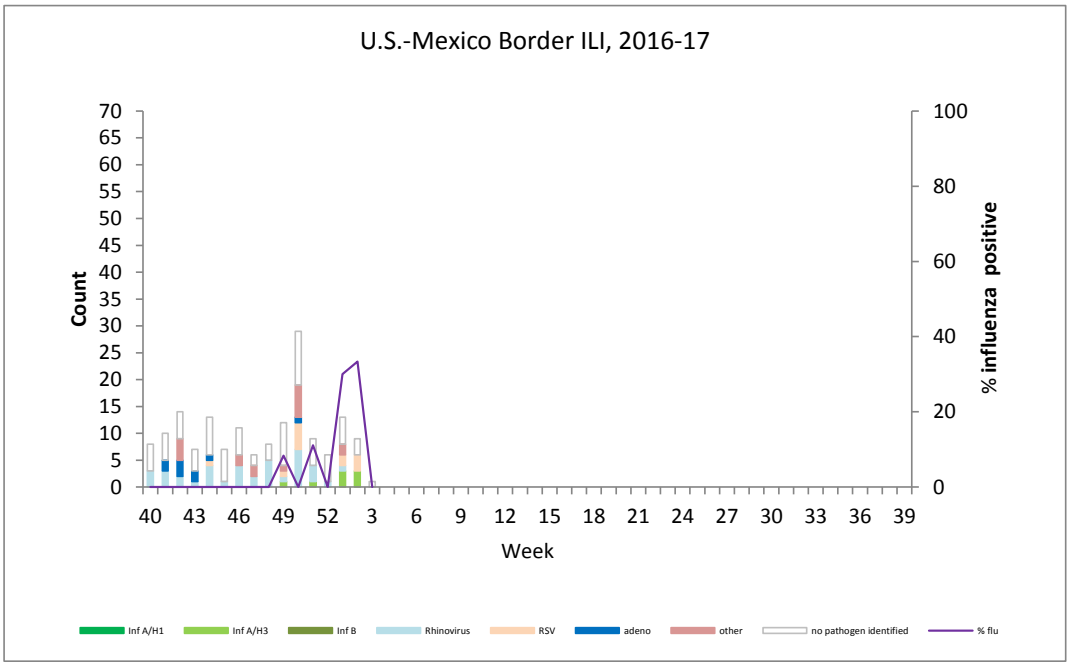
DoD Beneficiary Surveillance

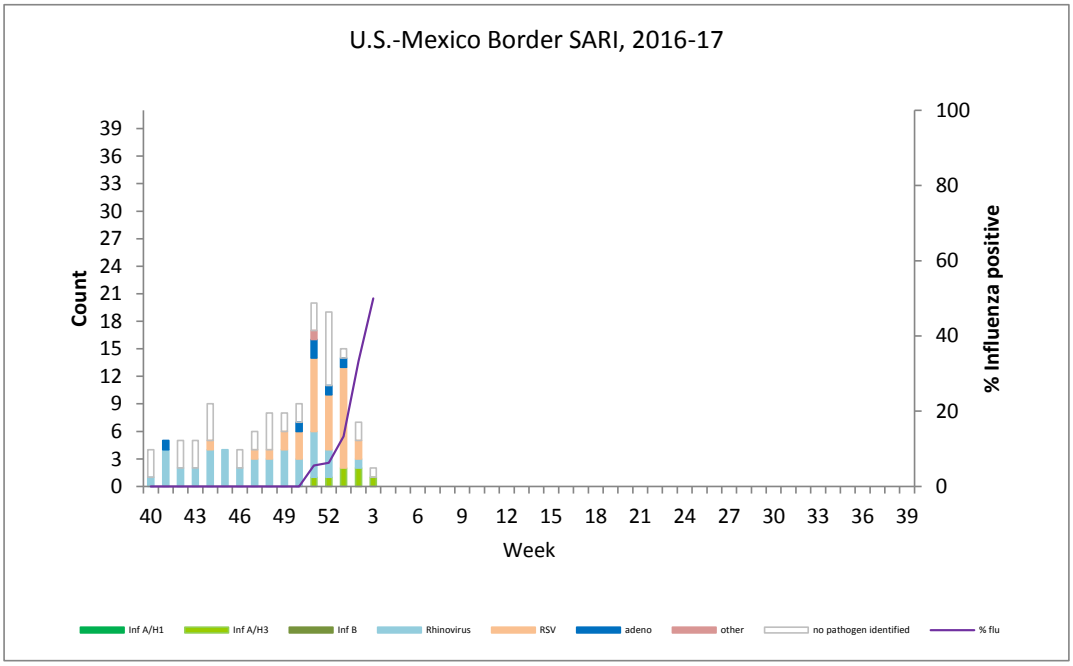
- NHRC conducts FRI surveillance among (non-active duty) DoD beneficiaries at Lovell FHCC (Great Lakes, IL) and in 4 NMC San Diego facilities: the Emergency Department, Pediatric Department, Naval Branch Health Clinic Kearny Mesa, and NH Camp Pendleton.
    - For questions regarding surveillance in this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

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

Segment	No. Isolates	2015-2016 Vaccine Strain	Protein Homology
A/pH1N1 HA	2	A/California/07/2009	97.0-97.3%
A/pH1N1 NA	1	A/California/07/2009	96.6%

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/

	Mutation	
A/pH1N1 Segment	ADD GLY	LOSS GLY
HA	S162N	N/A
NA	N44S, S70N	N386K

1. Sun X. Jayaraman A. Mainprasad P. Raman R. Houser K. Pappas C. ...Tumpey T. (2013).
N-Linked Glycosylation of the Hemagglutin Protein Influences Virulence and Antigenicity of the 1918 Pandemic and Seasonal H1N1 Influenza A Viruses.
Journal of Virology 8756-8766.

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 **A/Perth/16/2009** 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

Segment	No.	2016-2017 Vaccine Strain	Protein Homology
H3N2 HA	24	A/HongKong/4801/2014	**97.8-98.6%**
H3N2 NA	19	A/HongKong/4801/2014	**97.0-98.2%**

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.[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/

	Mutation	
A/H3N2 Segment	ADD GLY	LOSS GLY
HA	K160T	S124G, T135K
NA	S245N	D329S

1. Sun X. Jayaraman A. Mainprasad P. Raman R. Houser K. Pappas C. ...Tumpey T. (2013).
N-Linked Glycosylation of the Hemagglutin Protein Influences Virulence and Antigenicity of the 1918 Pandemic and Seasonal H1N1 Influenza A Viruses. *Journal of Virology* 8756-8766.

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 **B/Florida/04/2006.**

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

Segment	No. Isolates	2016-2017 Vaccine Strain	Protein Homology
B/Yamagata HA	1	B/Phuket/3073/2013	**99.3%**
B/Yamagata NA	2	B/Phuket/3073/2013	**98.8%**

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.[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/

	Mutation	
INF B Segment	ADD GLY	LOSS GLY
HA	N/A	N/A
NA	N/A	N/A

1. Sun X. Jayaraman A. Mainprasad P. Raman R. Houser K. Pappas C. ...Tumpey T. (2013).
N-Linked Glycosylation of the Hemagglutin Protein Influences Virulence and Antigenicity of the 1918 Pandemic and Seasonal H1N1 Influenza A Viruses.
Journal of Virology 8756-8766.

Evolutionary Relationships Among Influenza A (H1N1)pdm09 Hemagglutinin (HA) Genes 2016-2017 Influenza Season

Vaccine Strain

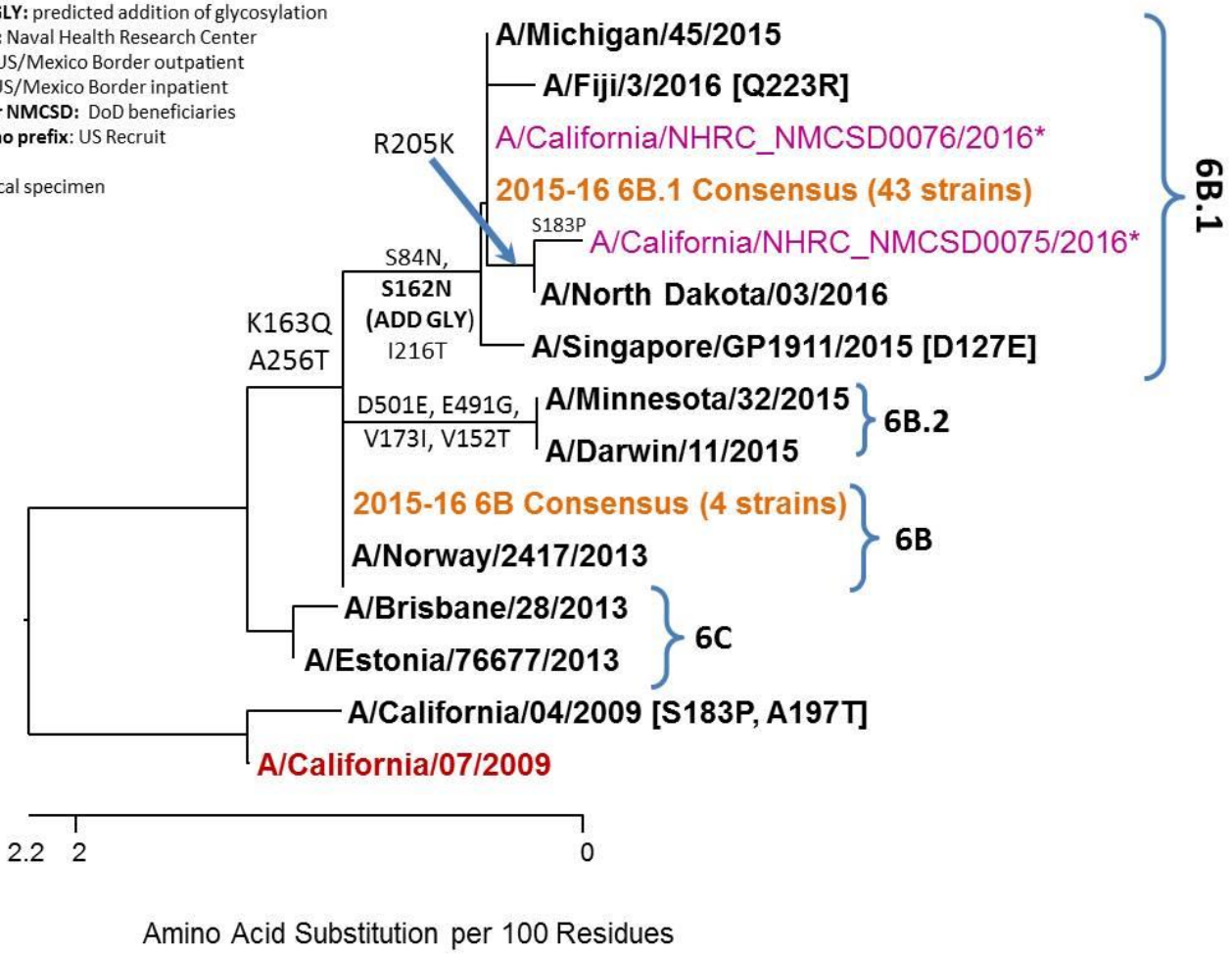
Reference Strain

2015-16 Consensus (47 strains)

Dec 2016 (2 strains)

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 or NMCSD: DoD beneficiaries
JX or no prefix: US Recruit

*:clinical specimen



Amino Acid Substitution per 100 Residues

Evolutionary Relationships Among Influenza A (H1N1)pdm09 Neuraminidase (NA) 2016-2017 Influenza Season

Vaccine Strain

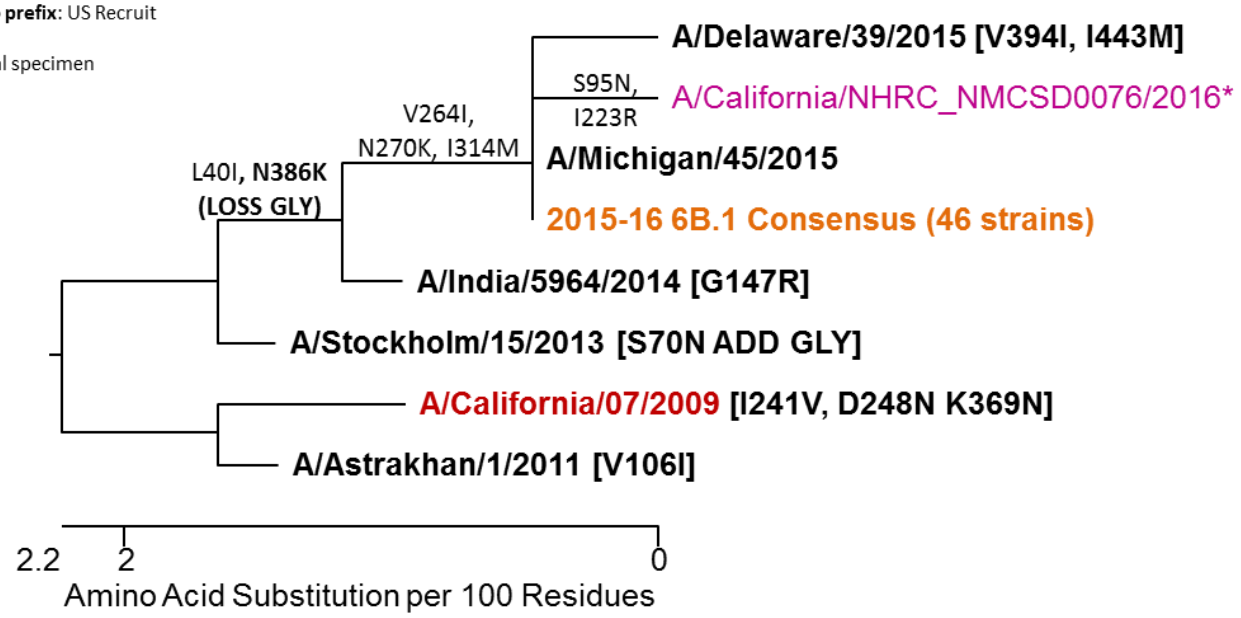
Reference Strain

2015-16 Consensus (46 strains)

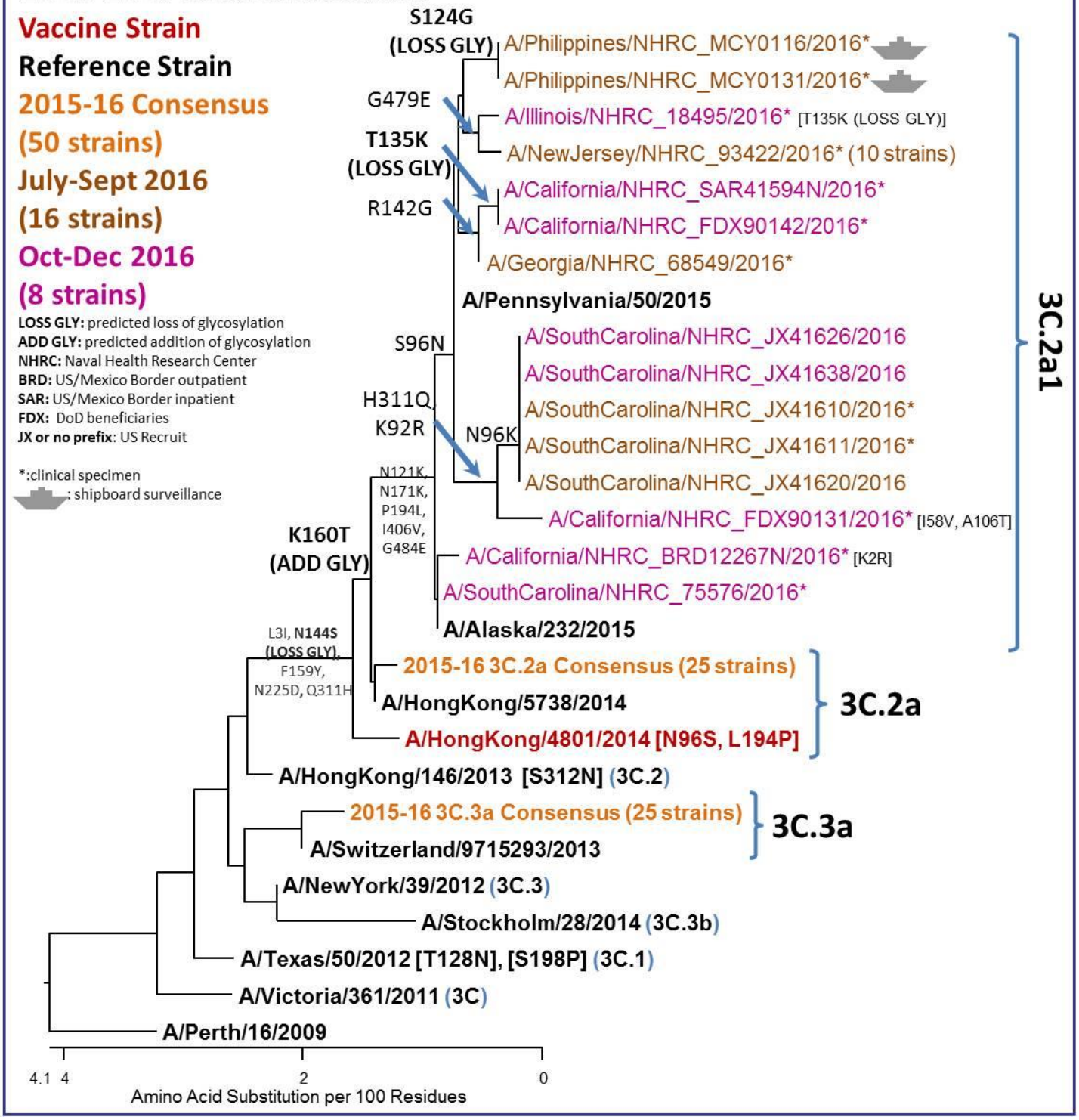
Dec 2016 (1 strain)

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

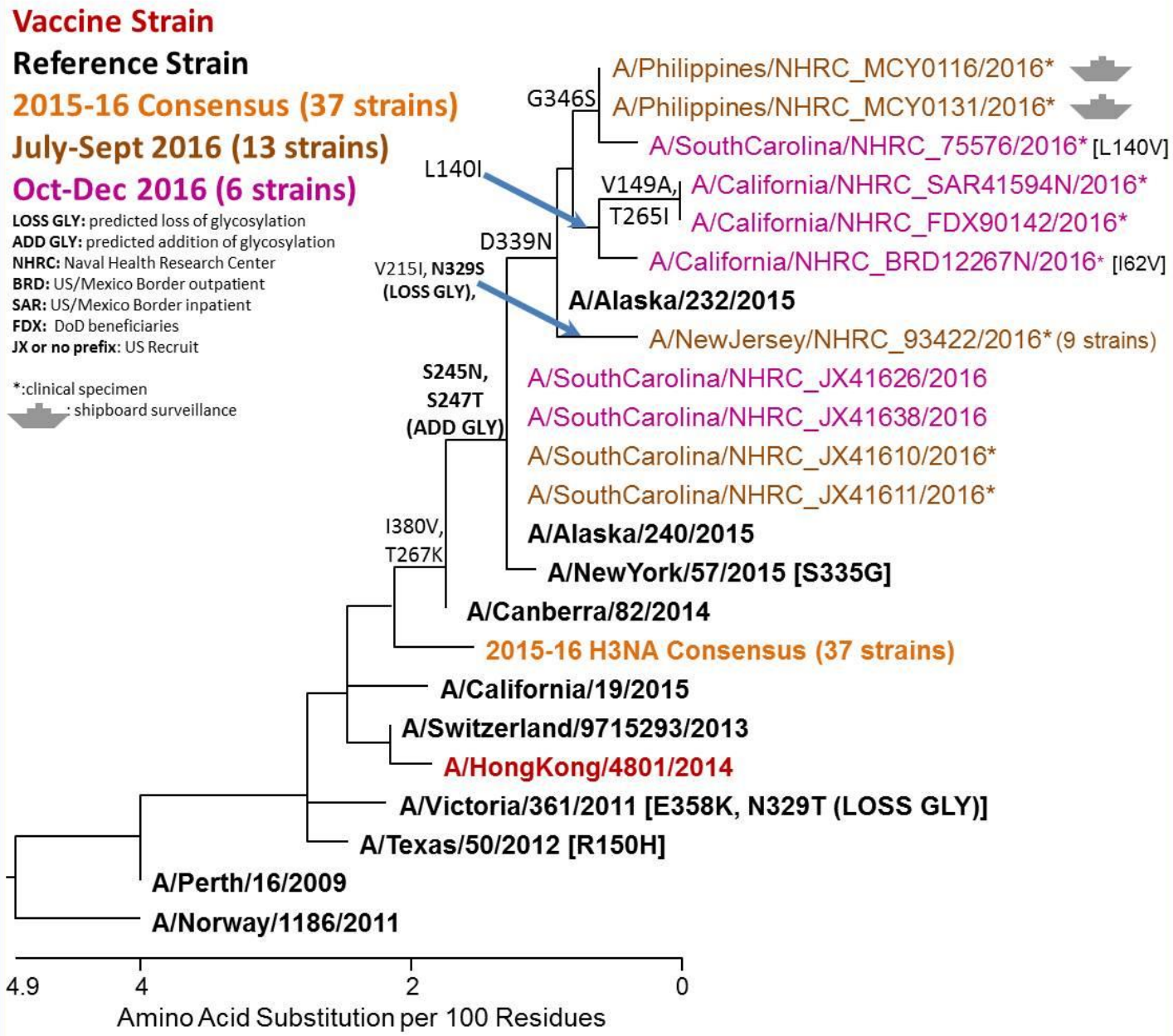
*:clinical specimen



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



Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes 2016-2017 Influenza Season



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

Vaccine Strain

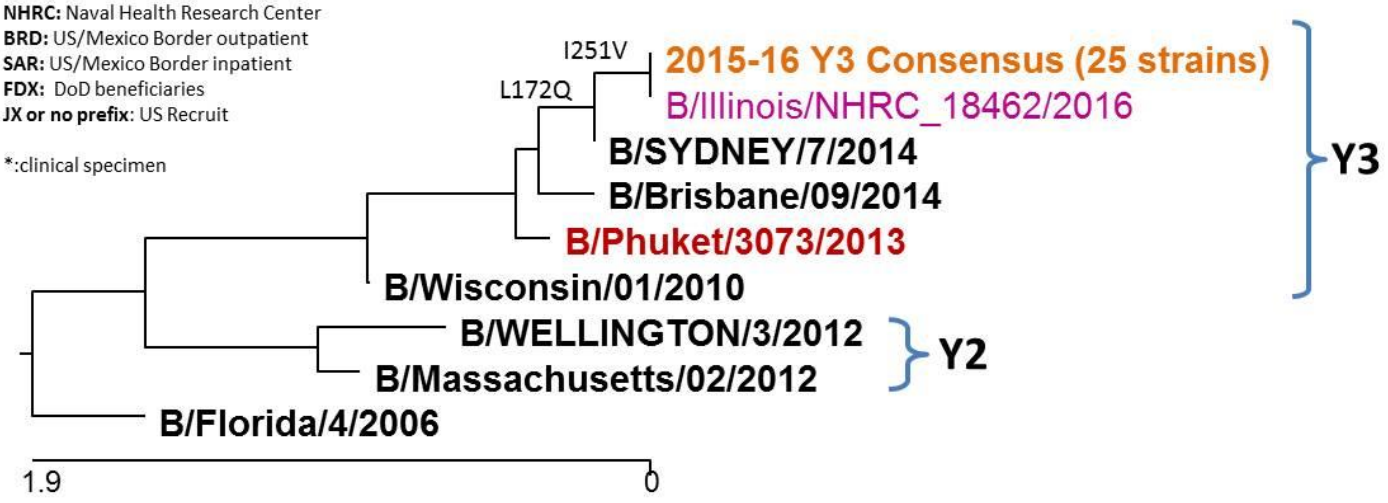
Reference Strain

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



Amino Acid Substitution per 100 Residues

Evolutionary Relationships Among Influenza B (Yamagata Lineage) Neuraminidase (NA) Genes 2016-2017 Influenza Season

Vaccine Strain

Reference Strain

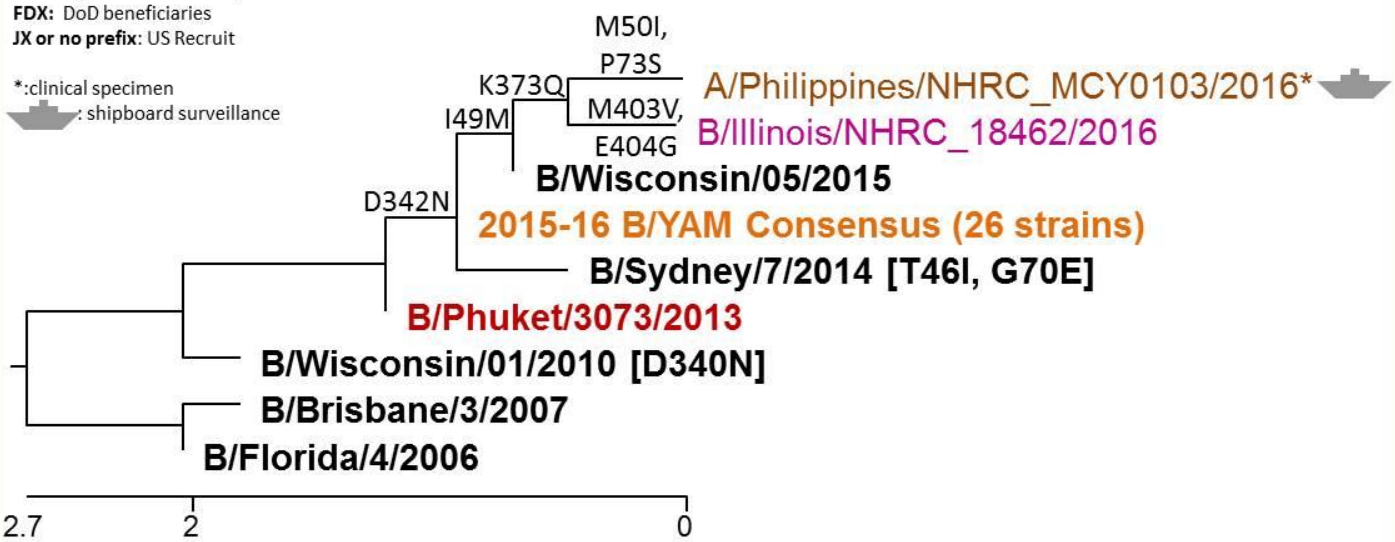
2015-16 Consensus (26 strains)

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
BRD: US/Mexico Border outpatient
SAR: US/Mexico Border inpatient
FDX: DoD beneficiaries
JX or no prefix: US Recruit

*:clinical specimen
: shipboard surveillance



Amino Acid Substitution per 100 Residues