

Febrile Respiratory Illness (FRI) Surveillance Update

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



2017 Week 3 (through 21 January 2017)

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Influenza

NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

Site	Current Week*				Since Oct.1, 2016				No. Tested
	A/ Untyp.	A/H3	A/H1	B	A/ Untyp.	A/H3	A/H1	B	
Ft. Benning									69
Ft. Jackson					6				67
Ft. Leonard Wood		2			2				15
NRTC Great Lakes					1			1	43
Lackland AFB									8
MCRD Parris Island					3				22
MCRD San Diego									70
CGTC Cape May									30
Total	0	2	0	0	0	12	0	1	324

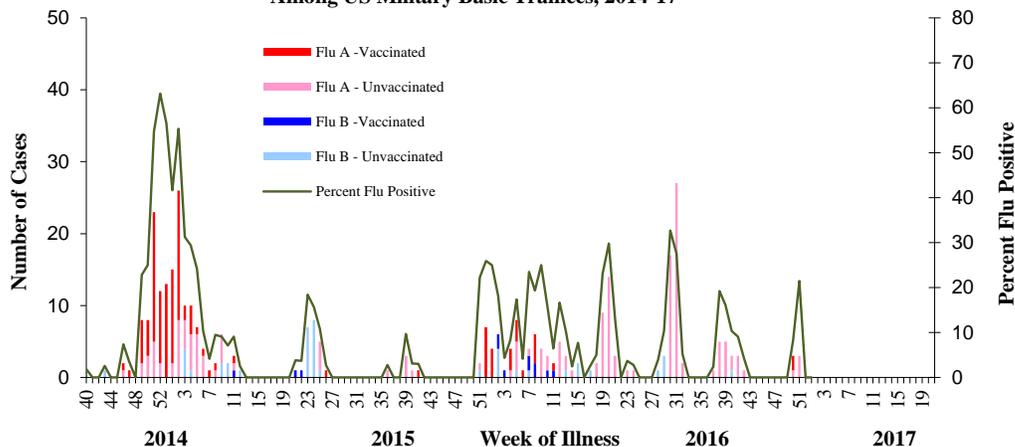
*New cases presented for care in mid-December and had been vaccinated in mid-October

- 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](#).

Items of Note

- Elevated FRI rates at NRTC Great Lakes and MCRD Parris Island
- 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, 2014-17

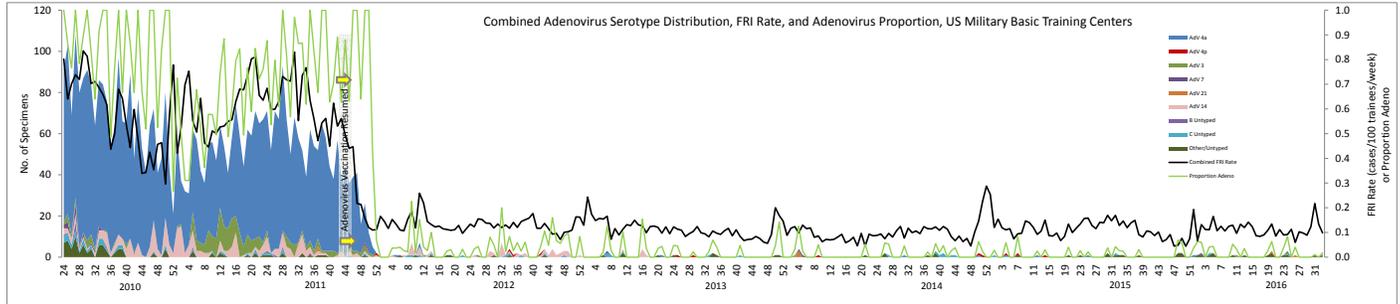


Other Items of Interest

- 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](#).

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](#)

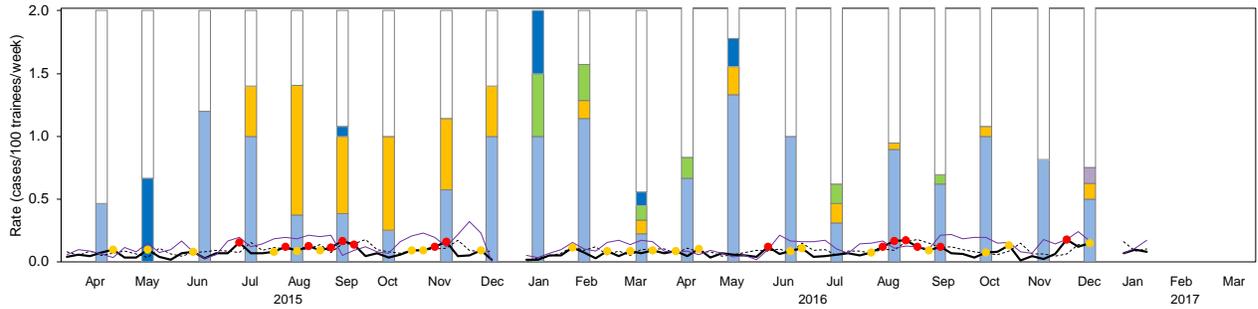
• **Moderately elevated:**

[Marine Corps Recruit Depot, Parris Island](#)

• **Substantially elevated:**

[Naval Recruit Training Command, Great Lakes](#)

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

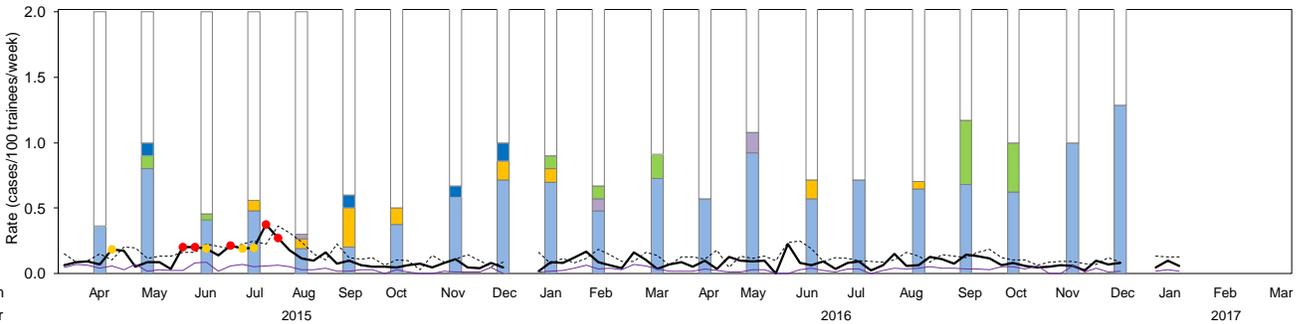


Month	Year	Samples Received	Adenovirus	Influenza	RSV	C. pneumo	M. pneumo	Rhinovirus
Apr	2015	13						23%
May	2015	6	33%					60%
Jun	2015	10						50%
Jul	2015	20					20%	19%
Aug	2015	27					52%	19%
Sep	2015	26					31%	13%
Oct	2015	24					38%	29%
Nov	2015	35					29%	50%
Dec	2015	10					20%	50%
Jan	2016	4	25%				7%	57%
Feb	2016	14	6%				6%	11%
Mar	2016	18						33%
Apr	2016	12						67%
May	2016	9	11%					50%
Jun	2016	26					8%	45%
Jul	2016	13					3%	31%
Aug	2016	38						50%
Sep	2016	26					4%	41%
Oct	2016	26						25%
Nov	2016	27						
Dec	2016	16						
Jan	2017							
Feb	2017							
Mar	2017							

Influenza Subtype	Apr 2015	May 2015	Jun 2015	Jul 2015	Aug 2015	Sep 2015	Oct 2015	Nov 2015	Dec 2015	Jan 2016	Feb 2016	Mar 2016	Apr 2016	May 2016	Jun 2016	Jul 2016	Aug 2016	Sep 2016	Oct 2016	Nov 2016	Dec 2016	Jan 2017	
B										0%	100%	100%	100%		100%								
A/H3										0%	0%	0%	0%		0%						100%	100%	
A/pH1										100%	0%	0%	0%		0%						0%	0%	
Untyped										0%	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)



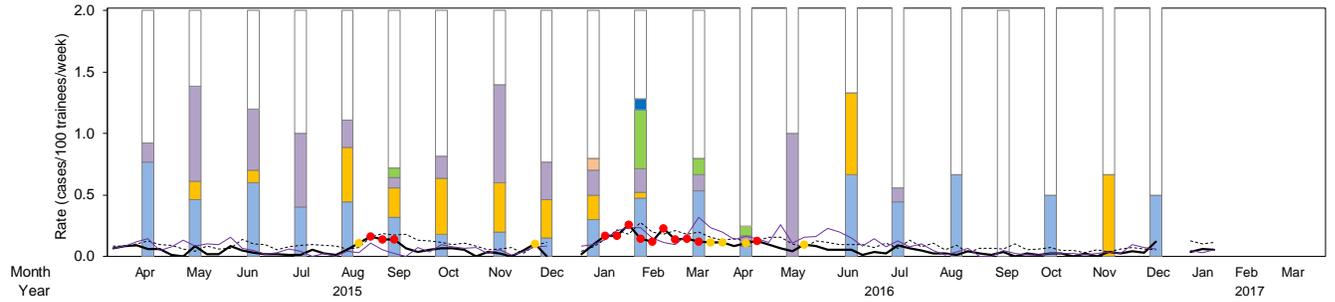
Month	Year	Samples Received	Adenovirus	Influenza	RSV	C. pneumo	M. pneumo	Rhinovirus
Apr	2015	33						18%
May	2015	20	5%					40%
Jun	2015	44		2%				20%
Jul	2015	50					4%	24%
Aug	2015	53					4%	9%
Sep	2015	20					15%	10%
Oct	2015	16					6%	19%
Nov	2015	24						29%
Dec	2015	14					7%	36%
Jan	2016	20					5%	35%
Feb	2016	21					5%	24%
Mar	2016	11						36%
Apr	2016	21						29%
May	2016	13						46%
Jun	2016	14					7%	29%
Jul	2016	14					3%	36%
Aug	2016	34						32%
Sep	2016	41						34%
Oct	2016	32						31%
Nov	2016	22						50%
Dec	2016	14						64%
Jan	2017							
Feb	2017							
Mar	2017							

Influenza Subtype	Apr 2015	May 2015	Jun 2015	Jul 2015	Aug 2015	Sep 2015	Oct 2015	Nov 2015	Dec 2015	Jan 2016	Feb 2016	Mar 2016	Apr 2016	May 2016	Jun 2016	Jul 2016	Aug 2016	Sep 2016	Oct 2016	Nov 2016	Dec 2016	Jan 2017	
B	100%	100%								0%	0%	0%	0%		0%								
A/H3	0%	0%								0%	0%	0%	0%		0%						100%	100%	
A/pH1	0%	0%								100%	100%	100%			0%						0%	0%	
Untyped	0%	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)

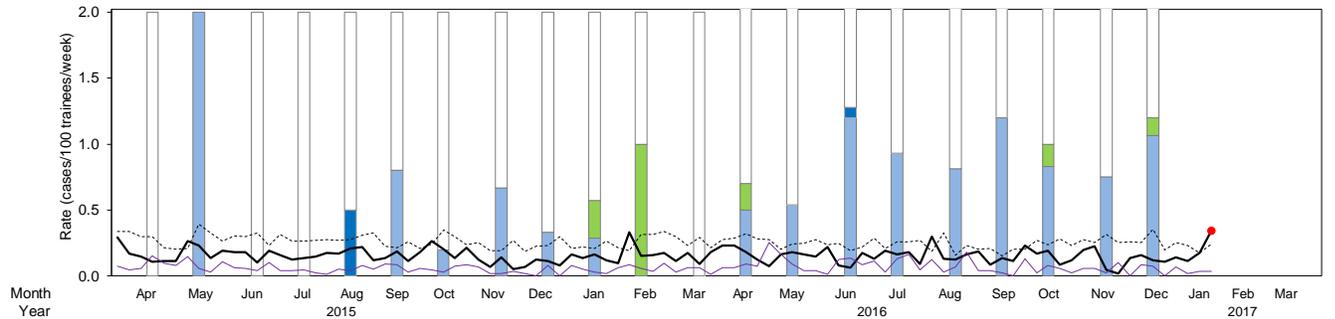
Ft. Leonard Wood FRI Rates and Diagnostic Test Results
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



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%						
					A/H3					100%				10%	0%	0%						
					A/pH1					0%				70%	0%	0%						
					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)

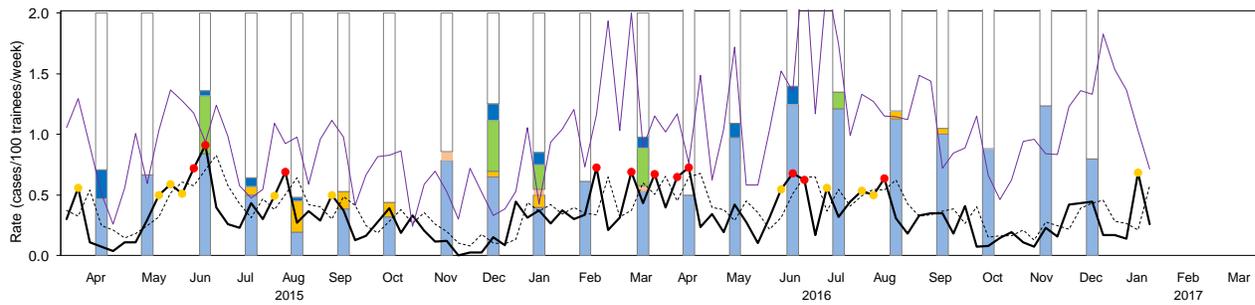


Samples Received	1	1	1	3	4	5	10	3	6	7	2	3	20	26	25	30	32	15	12	8	15		
Adenovirus					25%										4%								
Influenza										14%	50%		10%						8%			7%	
RSV																							
C. pneumo																							
M. pneumo																							
Rhinovirus	100%				40%	10%	33%	17%	14%				25%	27%	60%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

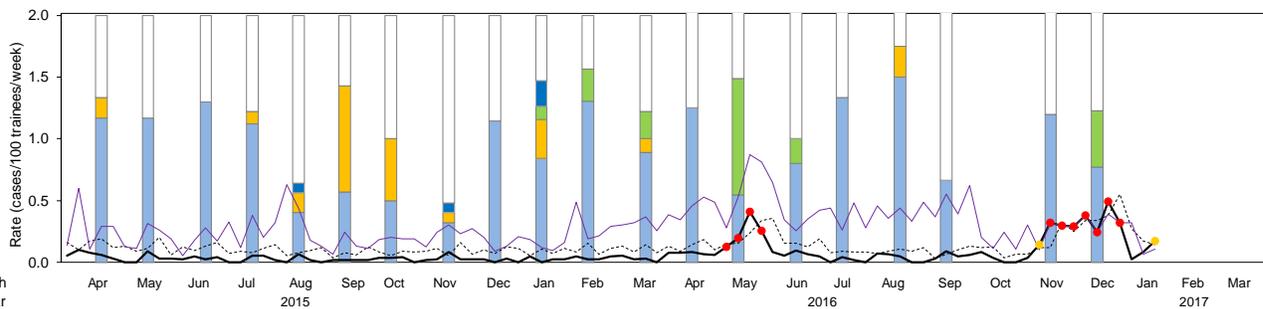


Samples Received	34	42	88	56	62	57	50	28	43	40	13	45	48	33	53	43	62	40	25	21	5	
Adenovirus	12%		2%	4%	2%				7%	5%		4%		6%	8%							
Influenza			24%						21%	10%		16%				7%						
RSV								4%		3%	2%											
C. pneumo																						
M. pneumo				4%	13%	7%	6%		2%	5%							3%	3%				
Rhinovirus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



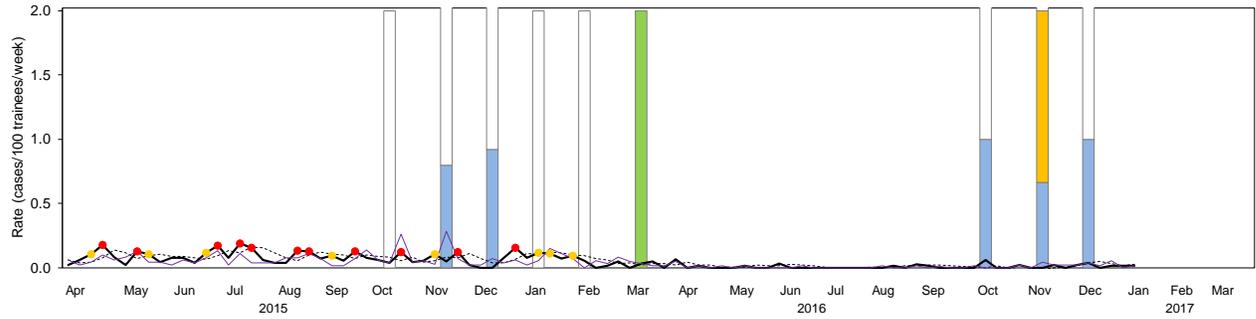
Samples Received	12	12	20	41	25	14	4	25	7	19	23	18	8	59	20	6	8	3	0	5	13	
Adenovirus					4%			4%		11%												
Influenza										5%	13%	11%		47%	10%							23%
RSV																						
C. pneumo																						
M. pneumo	8%			5%	8%	43%	25%	4%		16%	6%											13%
Rhinovirus	58%	58%	65%	56%	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)

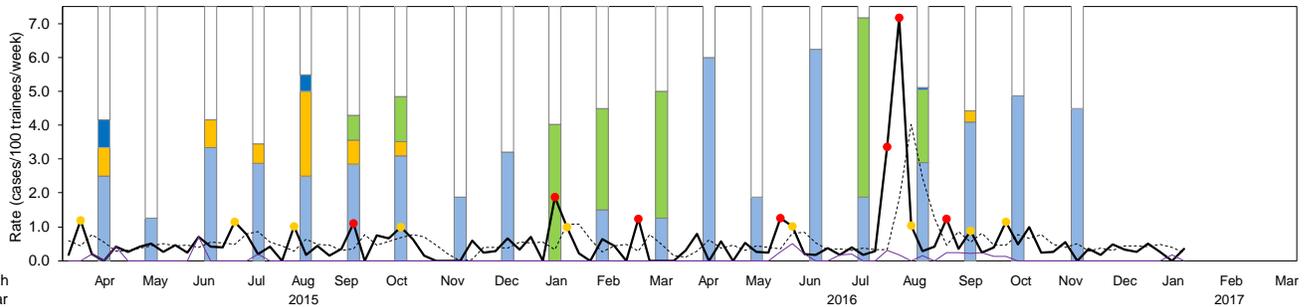


Samples Received	0	0	0	0	0	0	0	1	5	13	3	2	2					2	3	4	
Adenovirus																					
Influenza													100%								
RSV																					
C. pneumo																					
M. pneumo																					67%
Rhinovirus									40%	46%								50%	33%	50%	

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

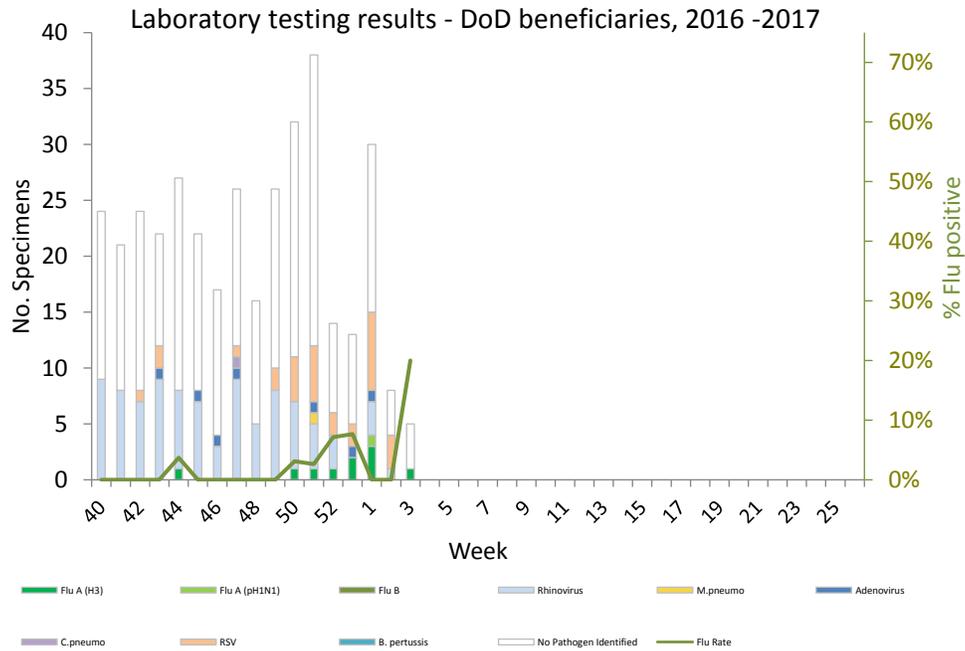
Influenza Subtype	B	A/H3	A/pH1	Untyped
		0%	0%	100%
		100%	100%	0%
		0%	0%	100%
		0%	0%	0%
		0%	0%	7%

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

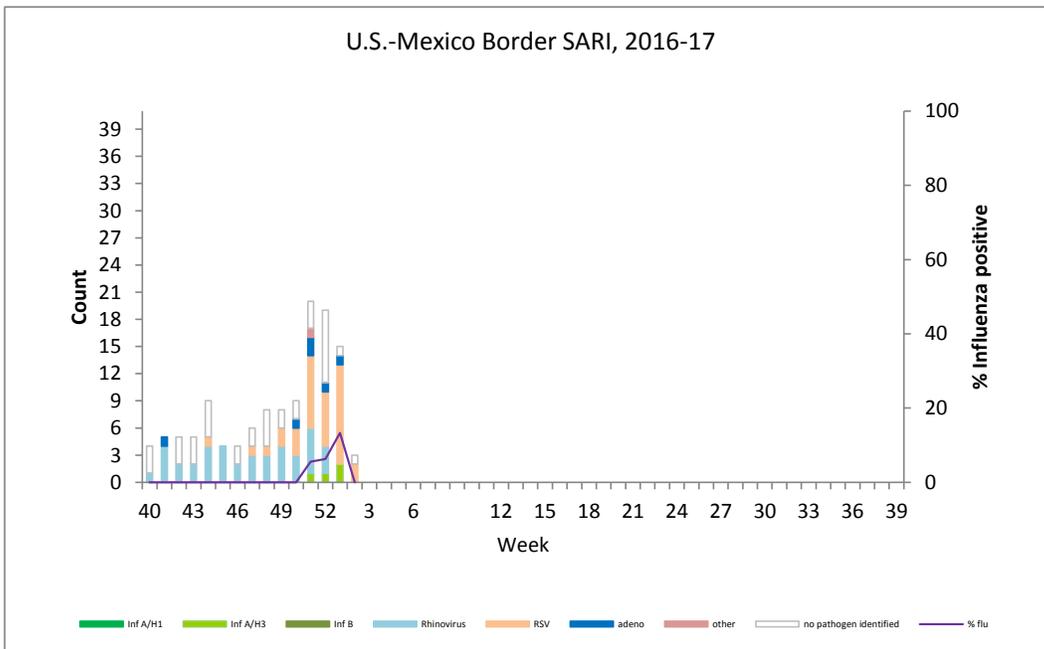
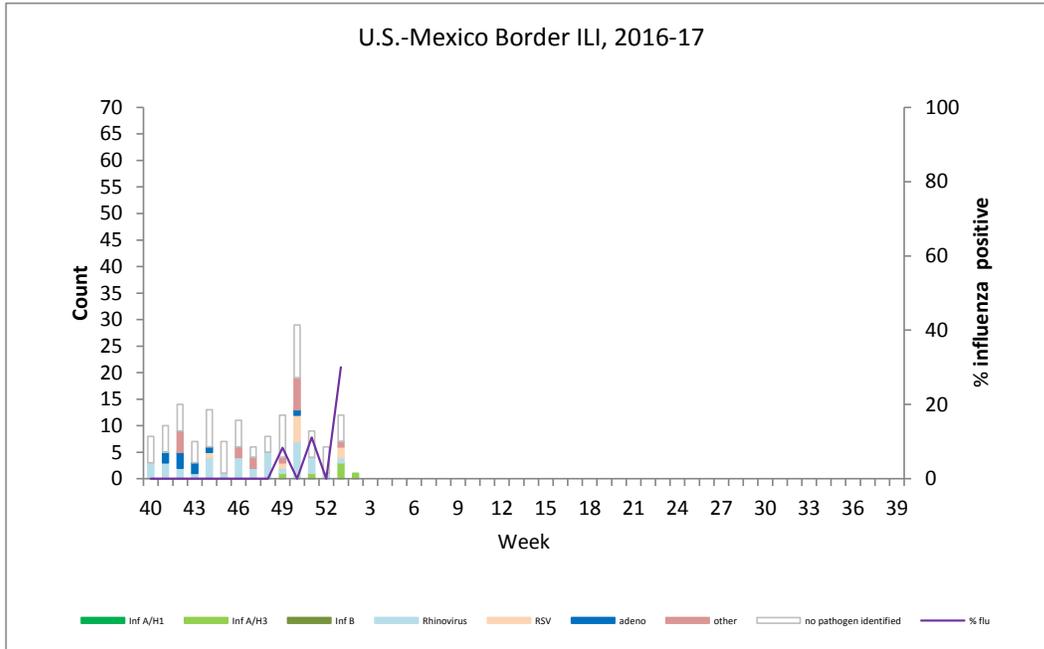
DoD Beneficiary Surveillance

- 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-like virus.

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/>

A/pH1N1 Segment	Mutation	
	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 Hemagglutinin Protein Influences Virulence and Antigenicity of the 1918 Pandemic and Seasonal H1N1 Influenza A Viruses. *Journal of Virology* 87:56-8766.

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 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

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/>

A/H3N2 Segment	Mutation	
	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 Hemagglutinin 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 previous vaccine strain, B/Florida/04/2006-like virus.

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/>

INF B Segment	Mutation	
	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 Hemagglutinin Protein Influences Virulence and Antigenicity of the 1918 Pandemic and Seasonal H1N1 Influenza A Viruses. *Journal of Virology* 87:56-8766.

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

Vaccine Strain

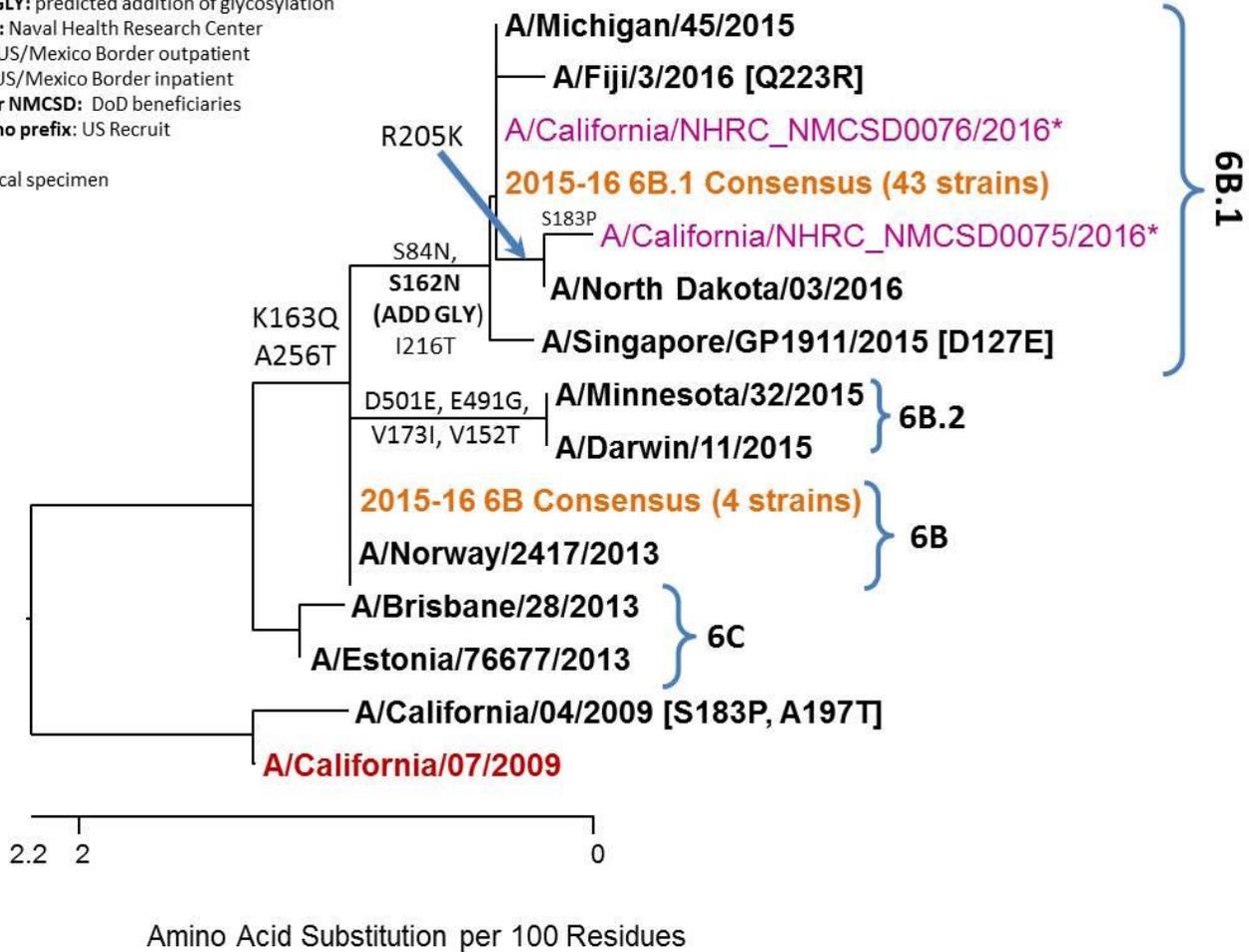
Reference Strain

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 NMCS D: DoD beneficiaries
 JX or no prefix: US Recruit

*:clinical specimen



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

Vaccine Strain

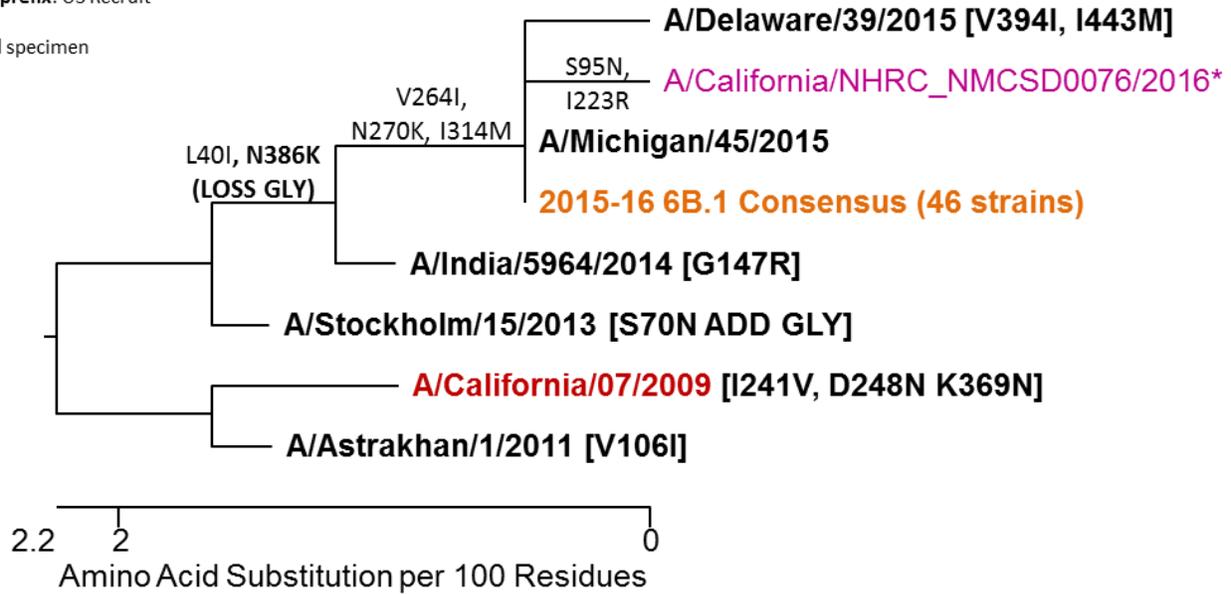
Reference Strain

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 NMCS D: DoD beneficiaries
JX or no prefix: US Recruit

*:clinical specimen



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

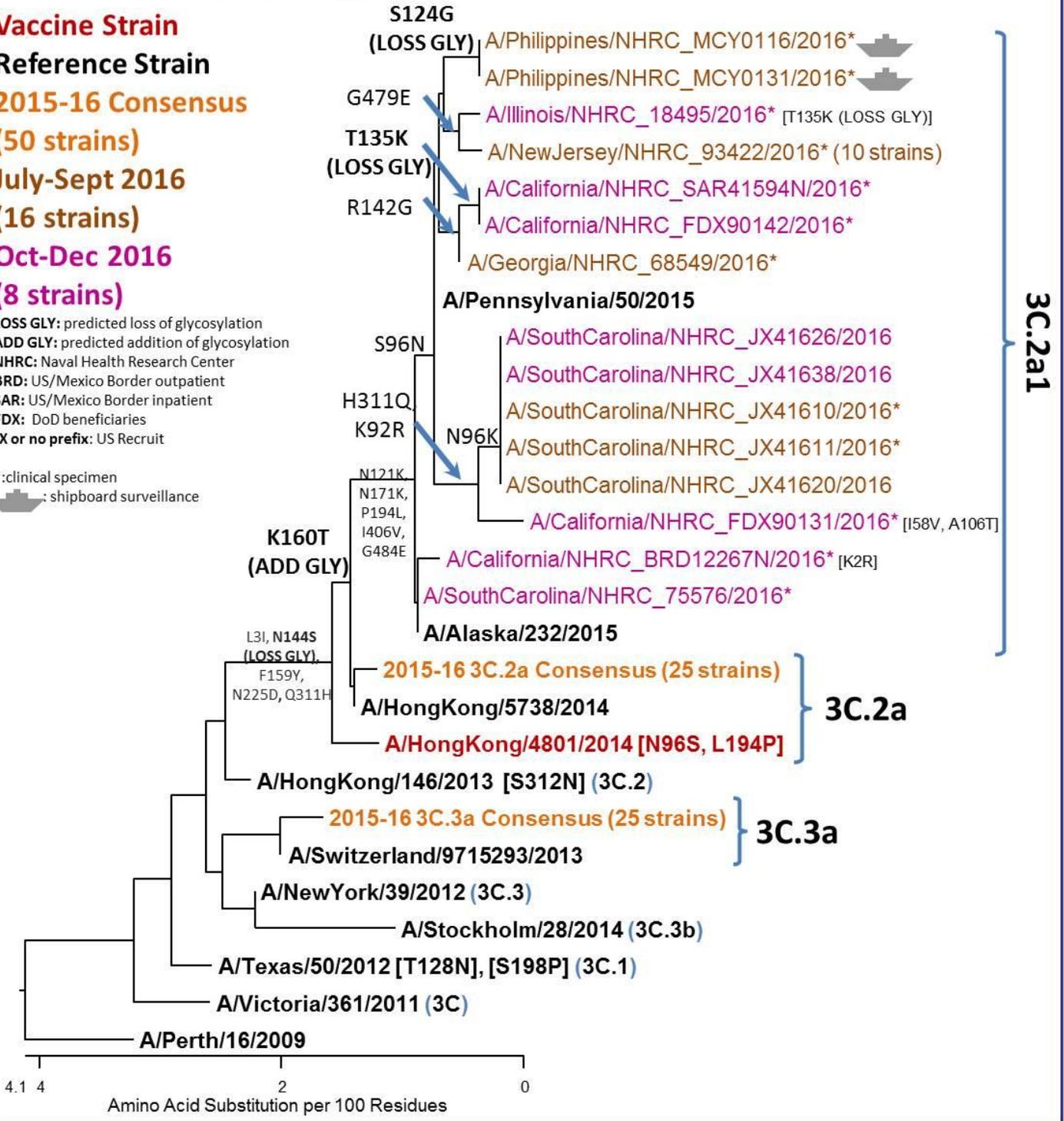
(16 strains)

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: DoD beneficiaries
 JX or no prefix: US Recruit

*:clinical specimen
 : shipboard surveillance



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

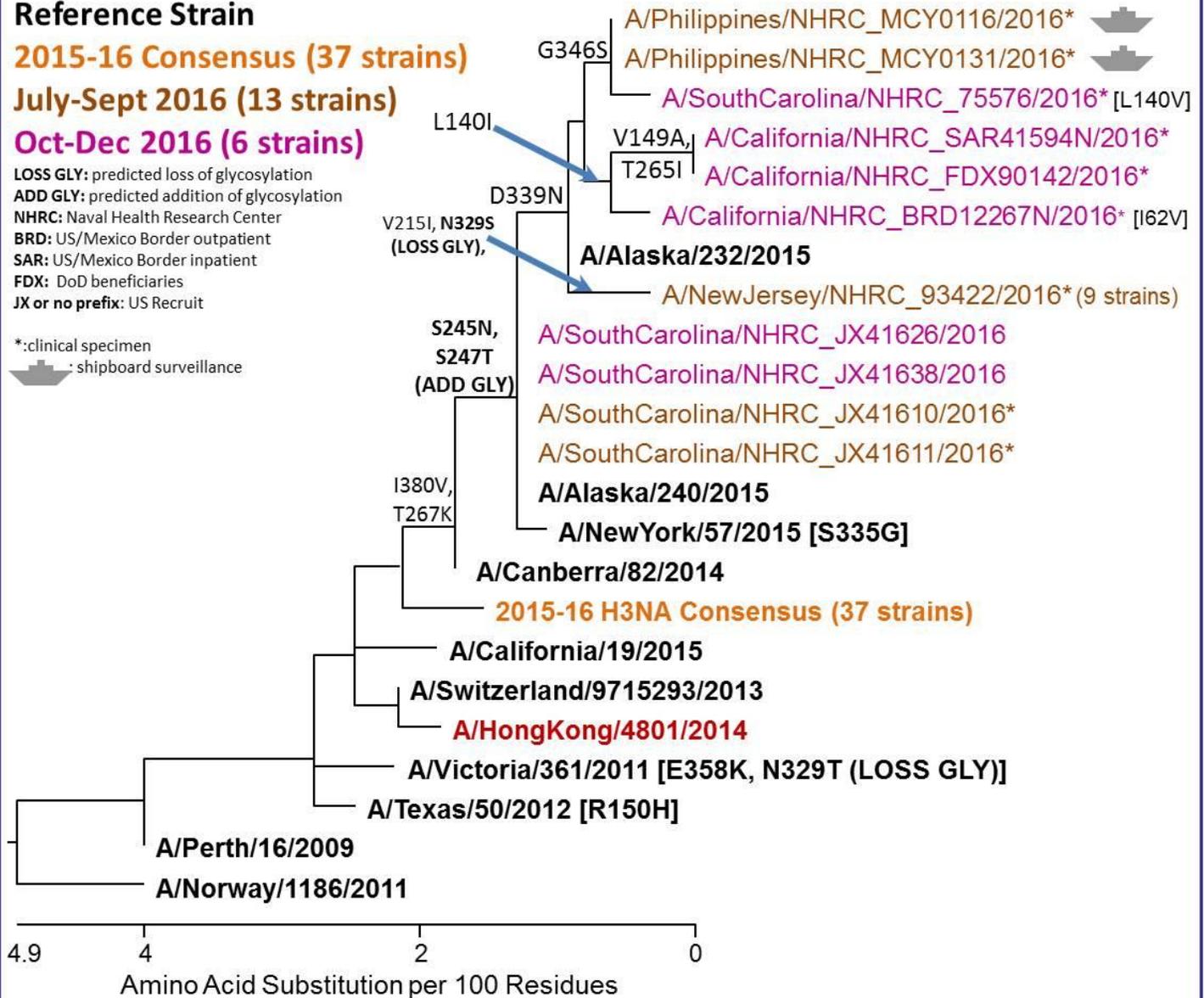
SAR: US/Mexico Border inpatient

FDX: DoD beneficiaries

JX or no prefix: US Recruit

*:clinical specimen

shipboard surveillance



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

Vaccine Strain

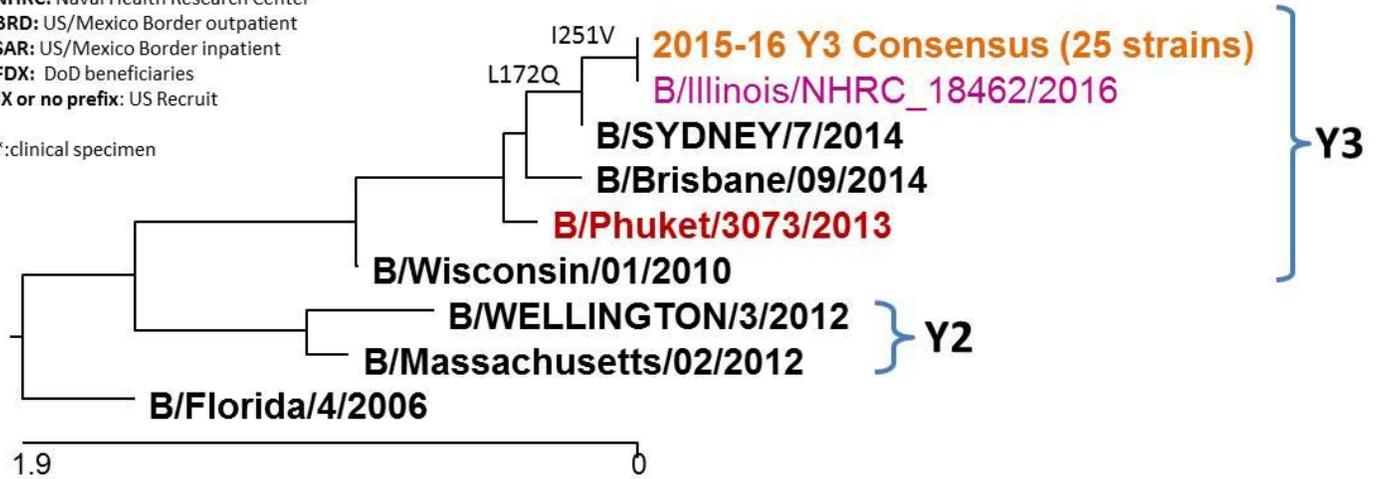
Reference Strain

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

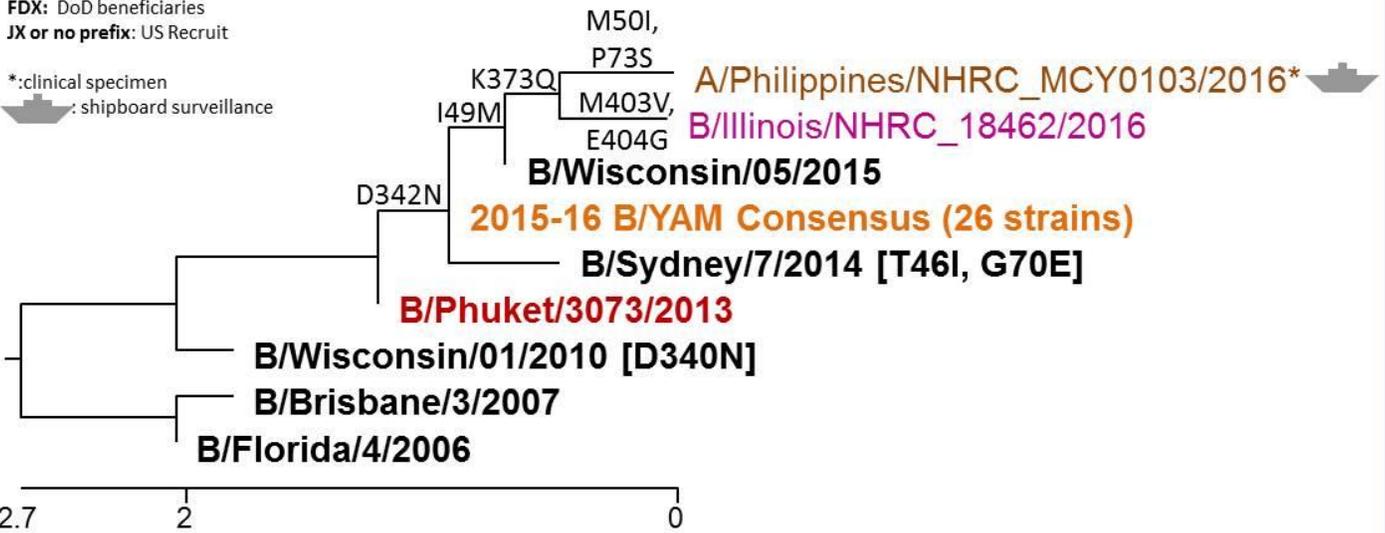
2015-16 Consensus (26 strains)

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