

# Febrile Respiratory Illness (FRI) Surveillance Update

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



**2016 Week 40 (through 8 October 2016)**

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### Influenza

NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

Site	Current Week*				Since Oct.1, 2015				No. Tested
	A/ Untyp.	A/H3	A/H1	B	A/ Untyp.	A/H3	A/H1	B	
Ft. Benning		1				1	1	5	223
Ft. Jackson		10				10	3		237
Ft. Leonard Wood						1	7	4	172
NRTC Great Lakes							3	1	166
Lackland AFB							1	1	26
MCRD Parris Island						30	6		189
MCRD San Diego						18	1	4	474
CGTC Cape May					2	47	3	9	195
<b>Total</b>	<b>0</b>	<b>11</b>	<b>0</b>	<b>0</b>	<b>2</b>	<b>107</b>	<b>25</b>	<b>24</b>	<b>1682</b>

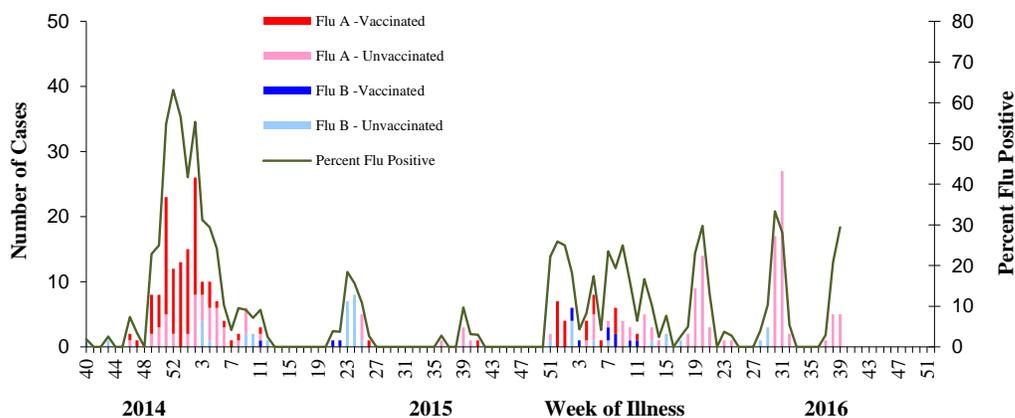
\*New cases presented for care 13-30 Sept. and all were unvaccinated

- NHRC also conducts shipboard FRI surveillance that includes large-deck ships of the US Fleet Forces (Atlantic), 3<sup>rd</sup> (Pacific), and 7<sup>th</sup> (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 CGTC Cape May
- Cluster of influenza A/H3 at Fort Jackson in late September; seems to have slowed by early Oct.
- 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**

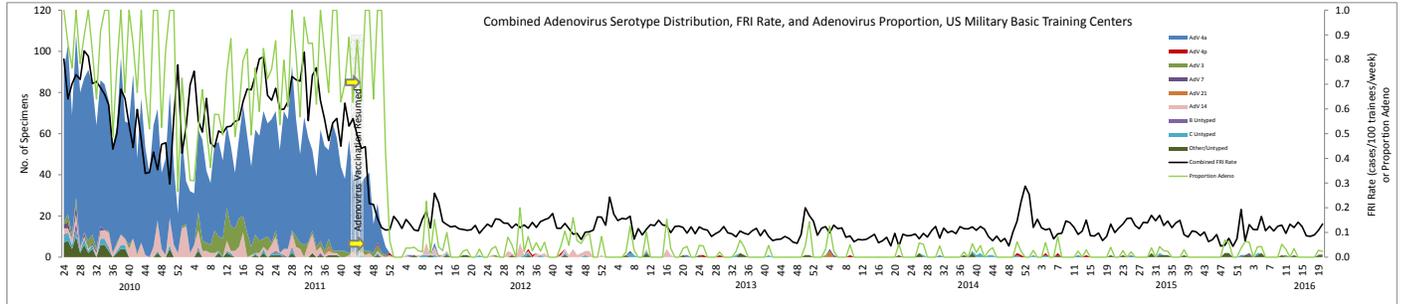


### Other Items of Interest

- 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 8 October 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](#)

[Marine Corps Recruit Depot, Parris Island](#) (data through 24 Sept.)

[Lackland Air Force Base](#) (data through 10 Sept.)

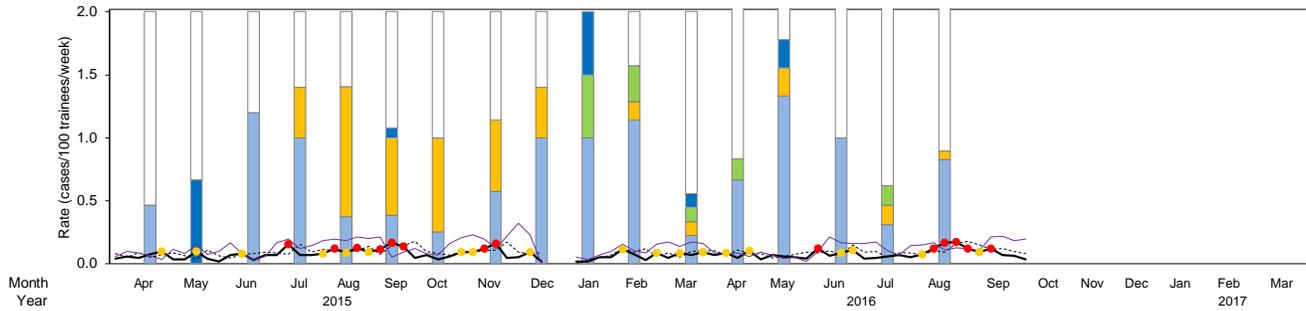
• **Moderately elevated:**

[Coast Guard Training Center, Cape May](#)

• **Substantially elevated:**

None

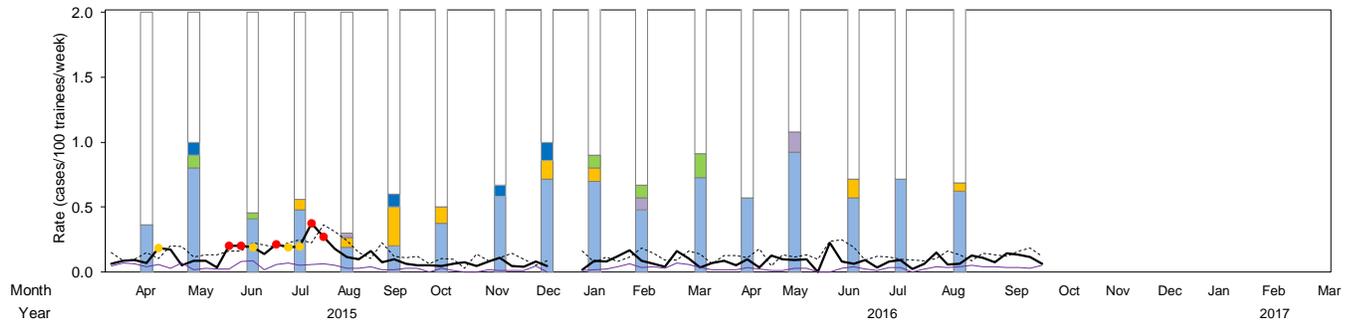
Ft. Benning FRI Rates and Diagnostic Test Results  
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	13	6	10	20	27	26	24	35	10	4	14	18	12	9	26	13	29
Adenovirus		33%				4%				25%	14%	6%	8%	11%			
Influenza																8%	
RSV																	
C. pneumo																	
M. pneumo				20%	52%	31%	38%	29%	20%		7%	6%		11%		8%	3%
Rhinovirus	23%		60%	50%	19%	19%	13%	29%	50%	50%	57%	11%	33%	67%	50%	15%	41%
Influenza Subtype											0%	100%	100%	100%		100%	
A/H3											0%	0%	0%	0%		0%	
A/pH1											100%	0%	0%	0%		0%	
Untyped											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)

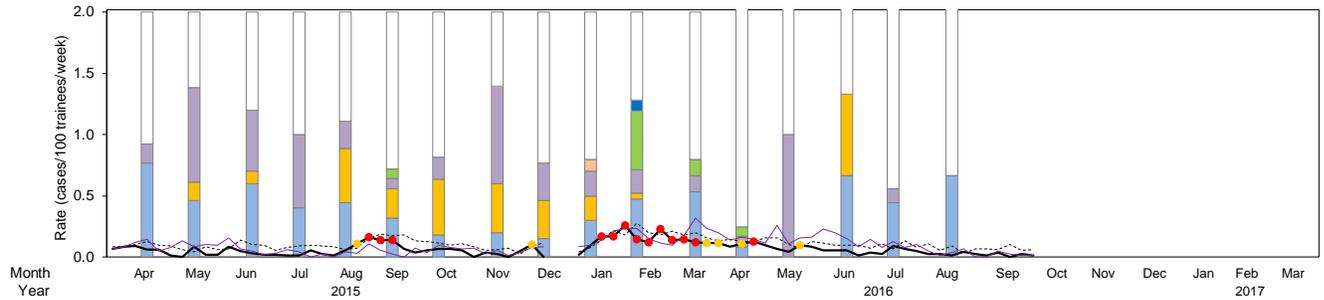


Samples Received	33	20	44	50	53	20	16	24	14	20	21	11	21	13	14	14	32
Adenovirus		5%				5%		4%	7%								
Influenza		5%	2%							5%	5%	9%					
RSV																	
C. pneumo					2%						5%			8%			
M. pneumo				4%	4%	15%	6%		7%	5%					7%		3%
Rhinovirus	18%	40%	20%	24%	9%	10%	19%	29%	36%	35%	24%	36%	29%	46%	29%	36%	31%
Influenza Subtype											100%	100%		0%	0%	0%	
A/H3											0%	0%		0%	0%	0%	
A/pH1											0%	0%		100%	100%	100%	
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)

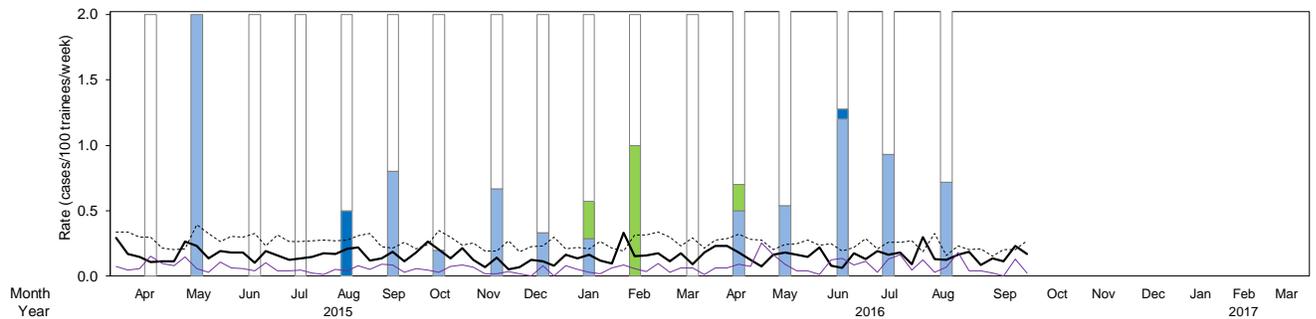
Ft. Leonard Wood FRI Rates and Diagnostic Test Results  
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received		26	13	20	10	9	25	22	10	13	20	42	15	24	6	3	18	3	
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%		
Rhinovirus		38%	23%	30%	20%	22%	16%	9%	10%	8%	15%	24%	27%	4%			33%	22%	33%
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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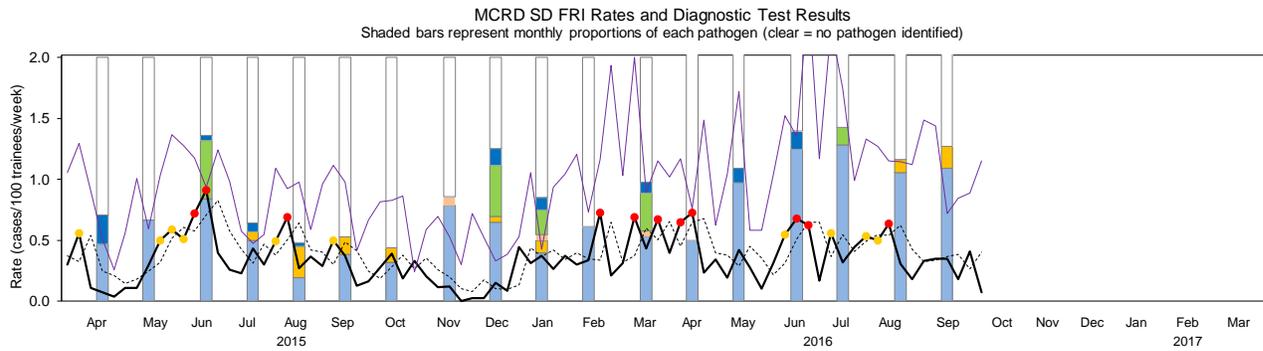
Great Lakes FRI Rates and Diagnostic Test Results  
 Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received		1	1	1	3	4	5	10	3	6	7	2	3	20	26	25	30	25	
Adenovirus						25%													
Influenza											14%	50%		10%					
RSV																			
C. pneumo																			
M. pneumo																			
Rhinovirus		100%				40%	10%	33%	17%	14%				25%	27%	60%	47%	36%	
Influenza Subtype	B										0%	0%	50%						
	A/H3										0%	0%	0%						
	A/pH1										100%	100%	50%						
	Untyped										0%	0%	0%						

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

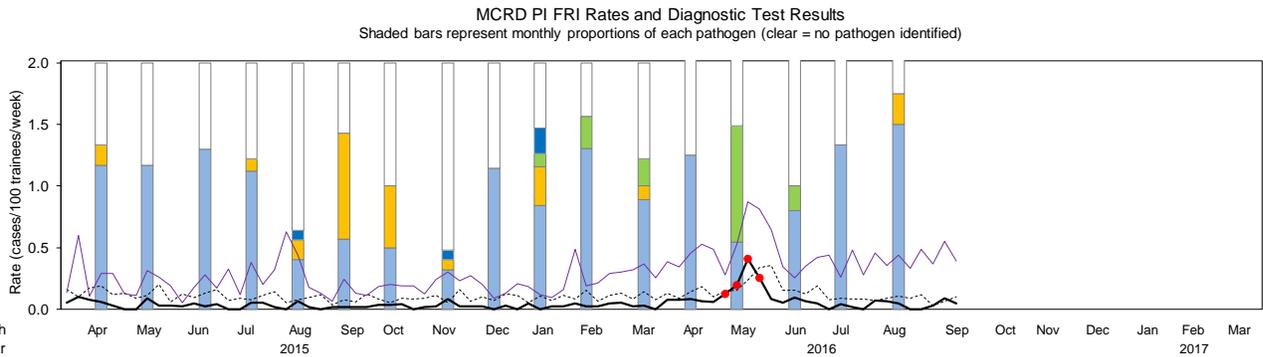


Samples Received		34	42	88	56	62	57	50	28	43	40	13	45	48	33	53	42	55	11
Adenovirus		12%		2%	4%	2%				7%	5%		4%		6%	8%			
Influenza			24%							21%	10%		16%				7%		
RSV									4%		3%	2%							
C. pneumo																			
M. pneumo					4%	13%	7%	6%		2%	5%							5%	9%
Rhinovirus		24%	33%	42%	25%	10%	19%	16%	39%	33%	20%	31%	27%	25%	48%	62%	64%	53%	55%

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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Samples Received		12	12	20	41	25	14	4	25	7	19	23	18	8	59	20	6	8
Adenovirus						4%			4%		11%							
Influenza											5%	13%	11%		47%	10%		
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%

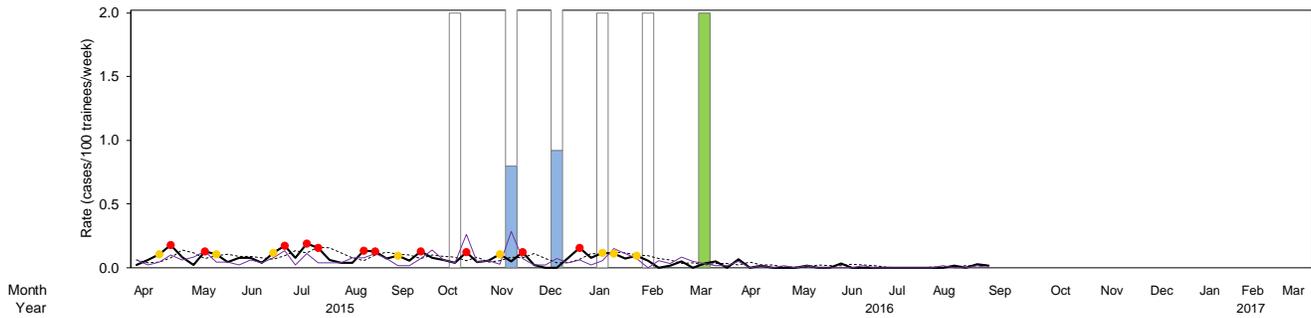
  

Influenza Subtype	B										0%	0%	0%		0%	0%		
	A/H3										0%	0%	0%		100%	100%		
	A/pH1										100%	100%	100%		0%	0%		
	Untyped										0%	0%	0%		0%	0%		

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

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



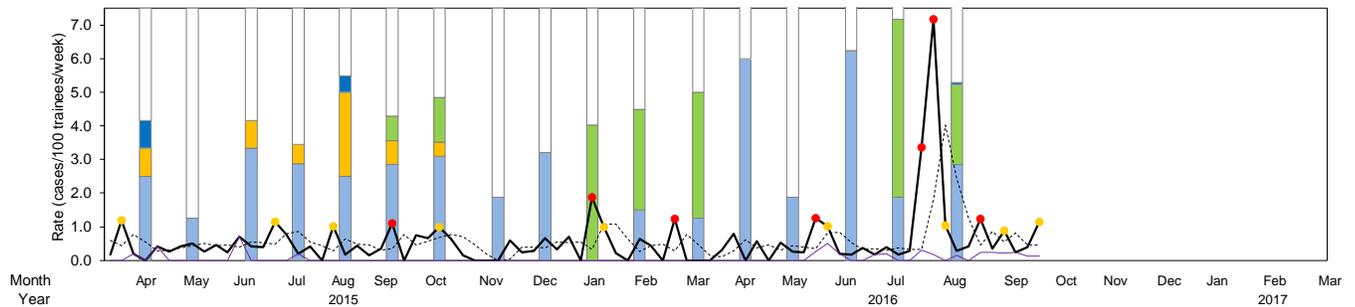
Samples Received	0	0	0	0	0	0	0	1	5	13	3	2	2
Adenovirus													
Influenza													100%
RSV													
C. pneumo													
M. pneumo													
Rhinovirus								40%	46%				

Influenza Subtype	B	A/H3	A/pH1	Untyped
	50%	0%	50%	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	92
Adenovirus	11%				7%												
Influenza						10%	18%			54%	40%	50%				71%	32%
RSV																	
C. pneumo																	
M. pneumo	11%	11%	8%	33%	10%	6%											
Rhinovirus	33%	17%	44%	38%	33%	38%	41%	25%	43%		20%	17%	80%	25%	83%	25%	38%

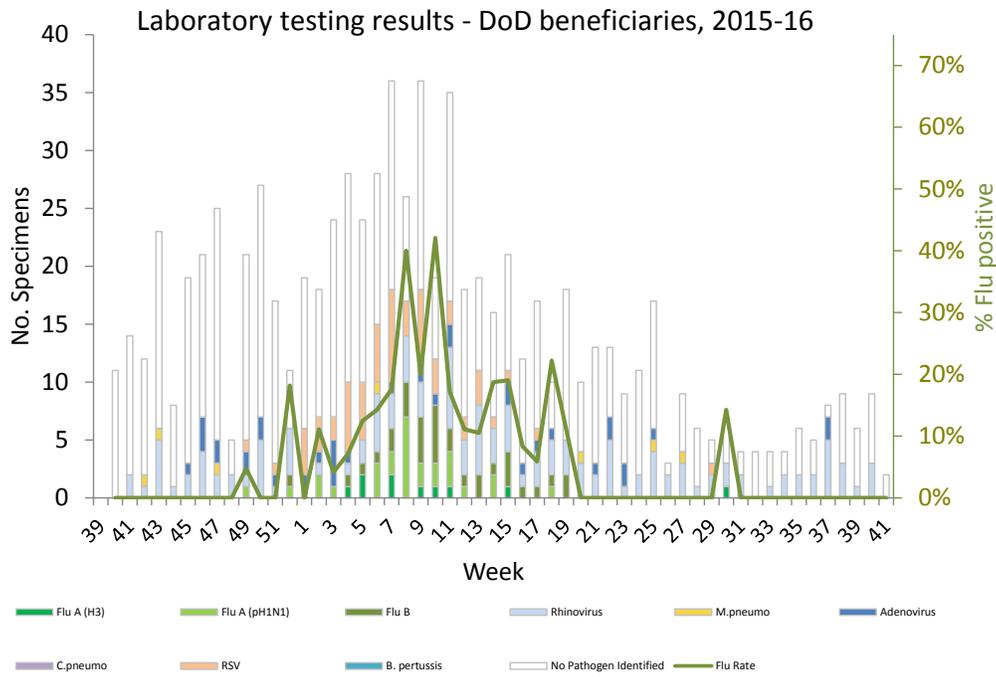
Influenza Subtype	B	A/H3	A/pH1	Untyped
	0%	0%	100%	0%
	100%	100%	0%	0%
	0%	0%	0%	100%
	0%	0%	0%	0%
	0%	0%	0%	7%

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

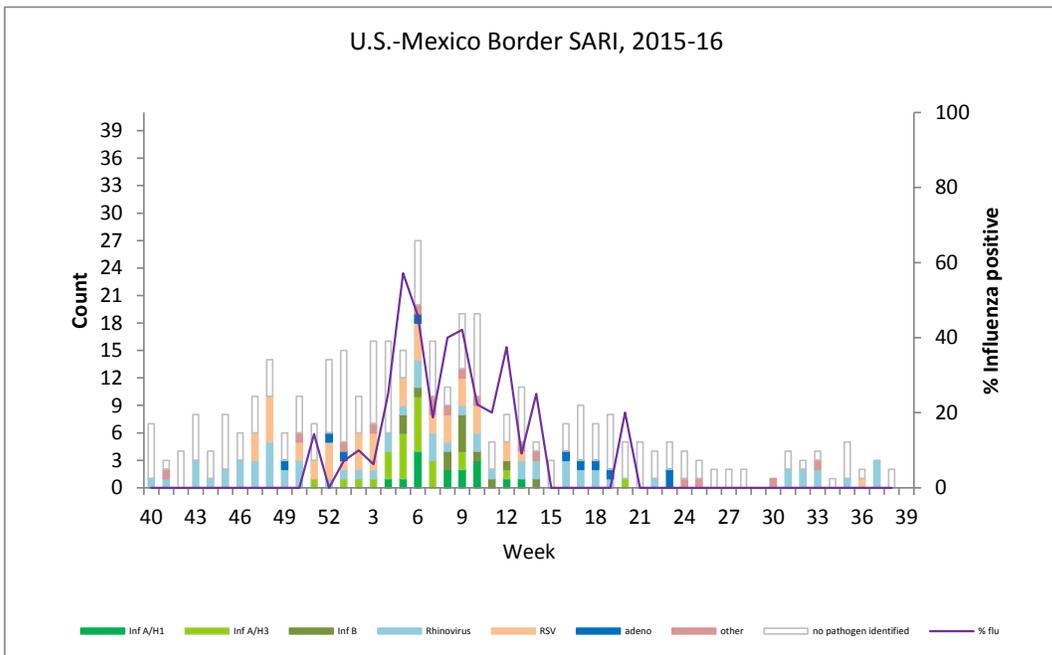
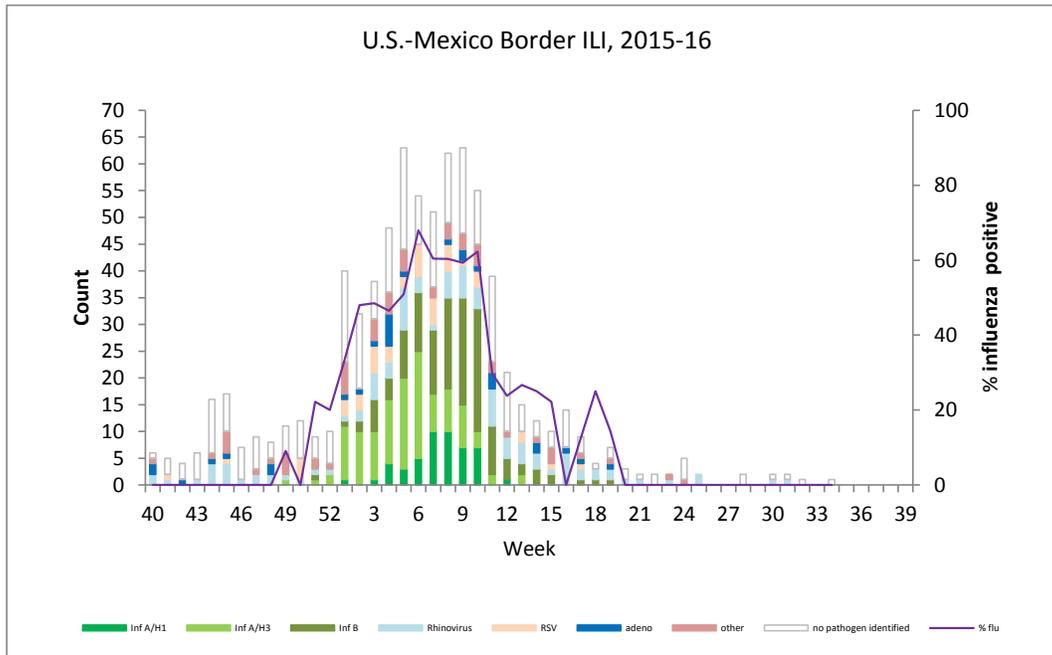
**DoD Beneficiary Surveillance**

- 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 (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

Segment	No. Isolates	2015-2016 Vaccine Strain	Protein Homology
A/pH1N1 HA	47	A/California/07/2009	97.0-98.0%
A/pH1N1 NA	46	A/California/07/2009	96.1-97.3%

## 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.<sup>1</sup> 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
<b>HA</b>	S162N	
<b>NA</b>	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* 8756-8766.

2. Lee H, Tang J, Kong D, Loh T, Chiang D, Lam T, Koay E. (2013). Comparison of Mutation Patterns in Full-Genome A/H3N2 Influenza Sequences Obtained Directly from Clinical Samples and the Same Samples after a Single MDCK Passage. *PLoS One*.

## 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

Segment	No.	2015-2016 Vaccine Strain	Protein Homology
H3N2 HA	38	A/Switzerland/9715293/2013	<b>97.0-99.6%</b>
H3N2 NA	33	A/Switzerland/9715293/2013	<b>97.9-98.6%</b>

## 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.<sup>1</sup> 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
<b>HA</b>	K160T	S47P N122D T128A N144S N158K N158H T160K T160I
<b>NA</b>	S245N N329I S331R	S247T N329T

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 (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

Segment	No. Isolates	2015-2016 Vaccine Strain	Protein Homology
B/Victoria HA	26	B/Brisbane/60/2008	<b>99.1-99.5%</b>
B/Victoria NA	26	B/Brisbane/60/2008	<b>98.3-98.54%</b>
B/Yamagata HA	24	B/Phuket/3073/2013	<b>99.1-99.5%</b>
B/Yamagata NA	24	B/Phuket/3073/2013	<b>98.7-100.0%</b>

## Summary of Influenza B N-Linked Glycosylation Mutations

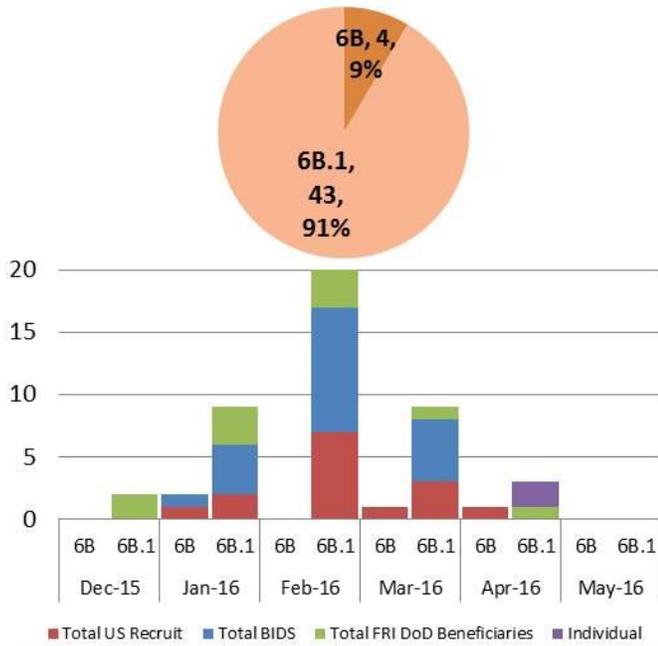
- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity.<sup>1</sup> Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server <http://www.cbs.dtu.dk/services/NetNGlyc/>

INF B Segment	Mutation	
	ADD GLY	LOSS GLY
<b>HA</b>	A198T	N196D T198N
<b>NA</b>	D463N	

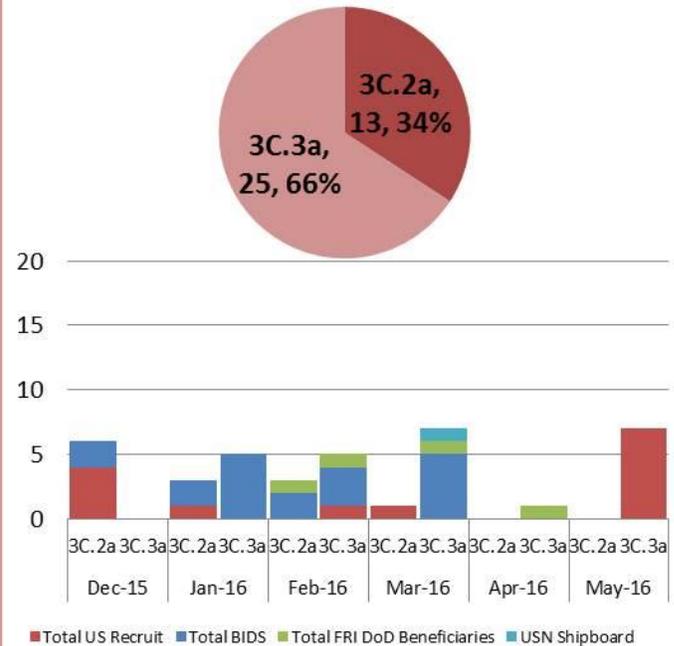
1. Sun X, Jayaraman A, Mainprasad P, Raman R, Houser K, Pappas C, ...Tumpey T. (2013). N-Linked Glycosylation of the Hemagglutinin Protein Influences Virulence and Antigenicity of the 1918 Pandemic and Seasonal H1N1 Influenza A Viruses. *Journal of Virology* 8756-8766.
2. Lee H, Tang J, Kong D, Loh T, Chiang D, Lam T, Koay E. (2013). Comparison of Mutation Patterns in Full-Genome A/H3N2 Influenza Sequences Obtained Directly from Clinical Samples and the Same Samples after a Single MDCK Passage. *PLoS One*.

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

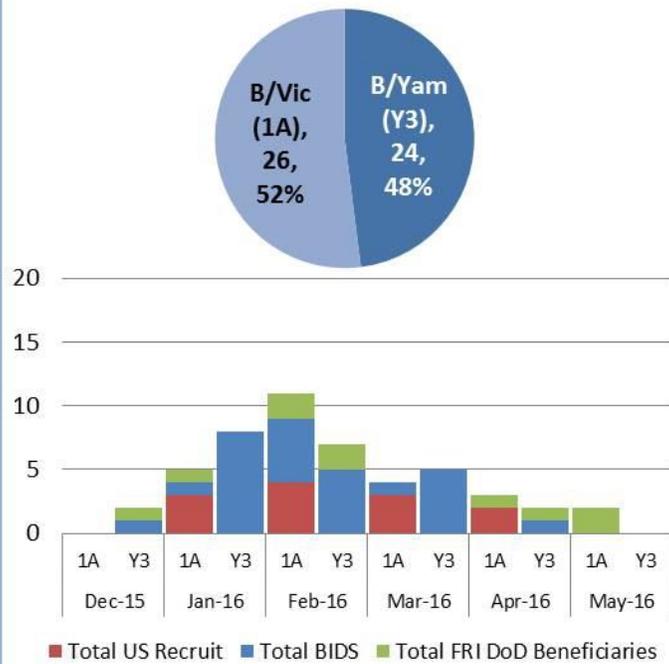
#### Influenza A/pH1N1



#### Influenza A/H3N2



#### Influenza B



# 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**

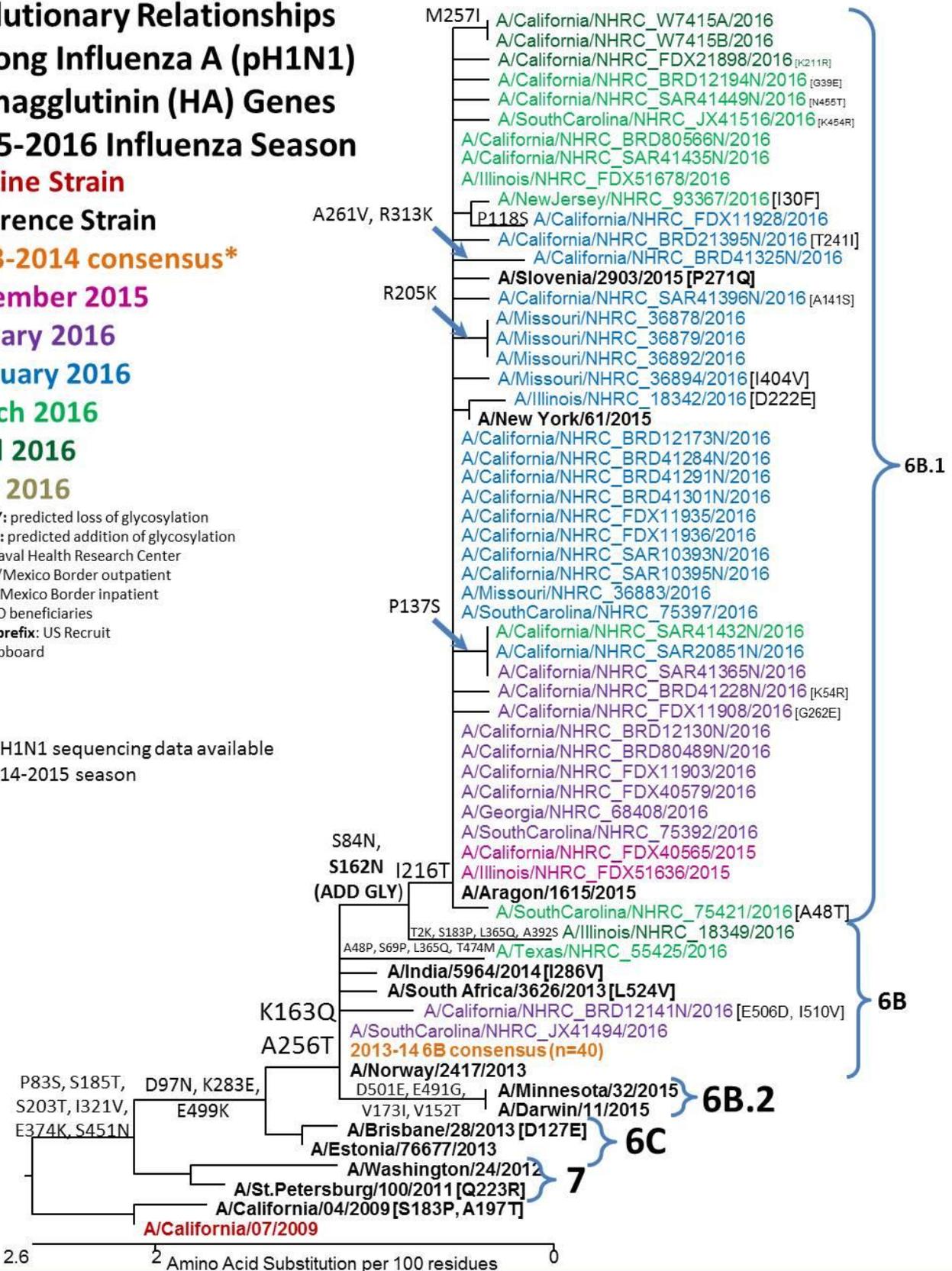
**March 2016**

**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

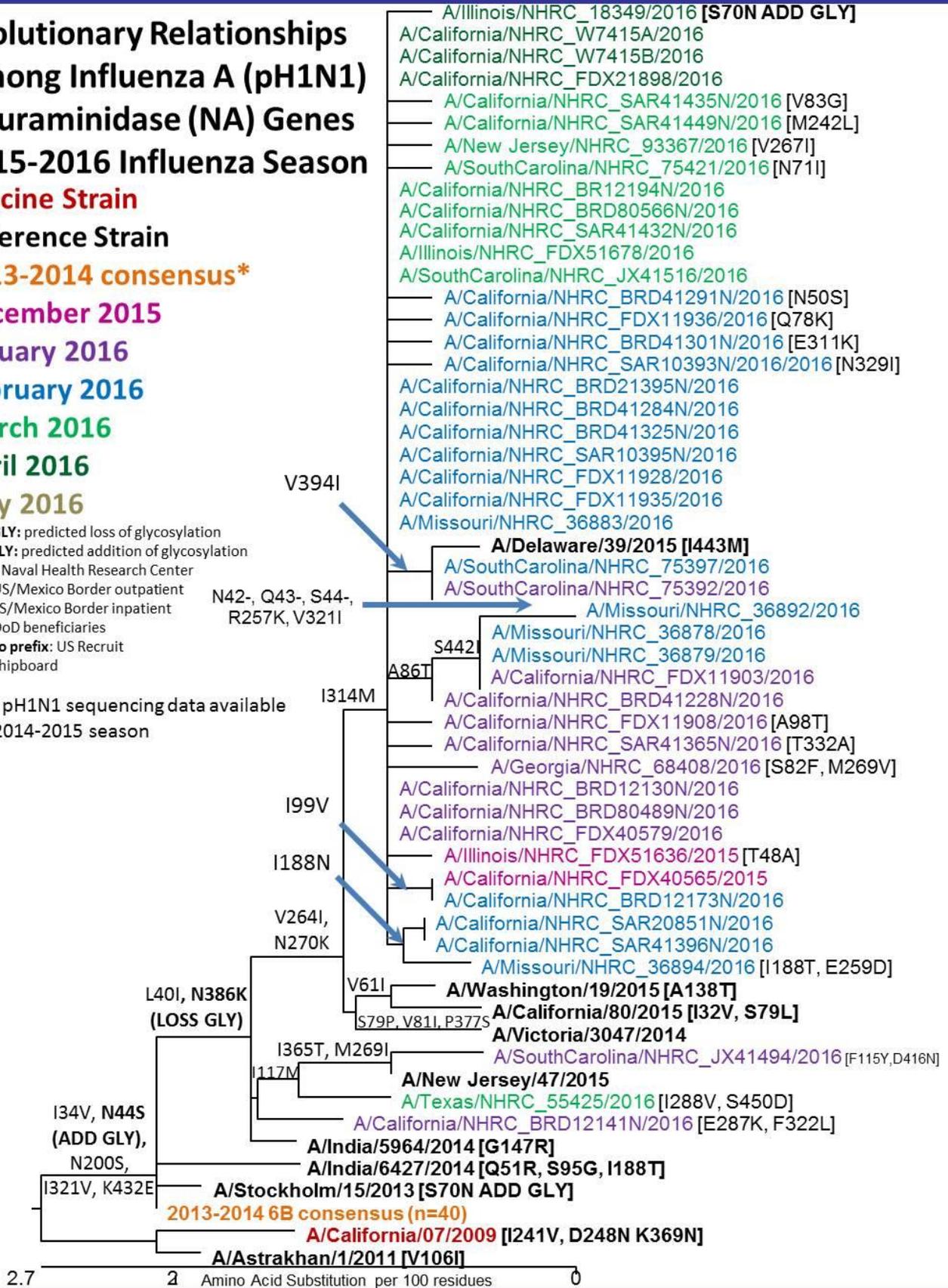
March 2016

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**

**Reference Strain**

**2013-2014 consensus**

**December 2015**

**January 2016**

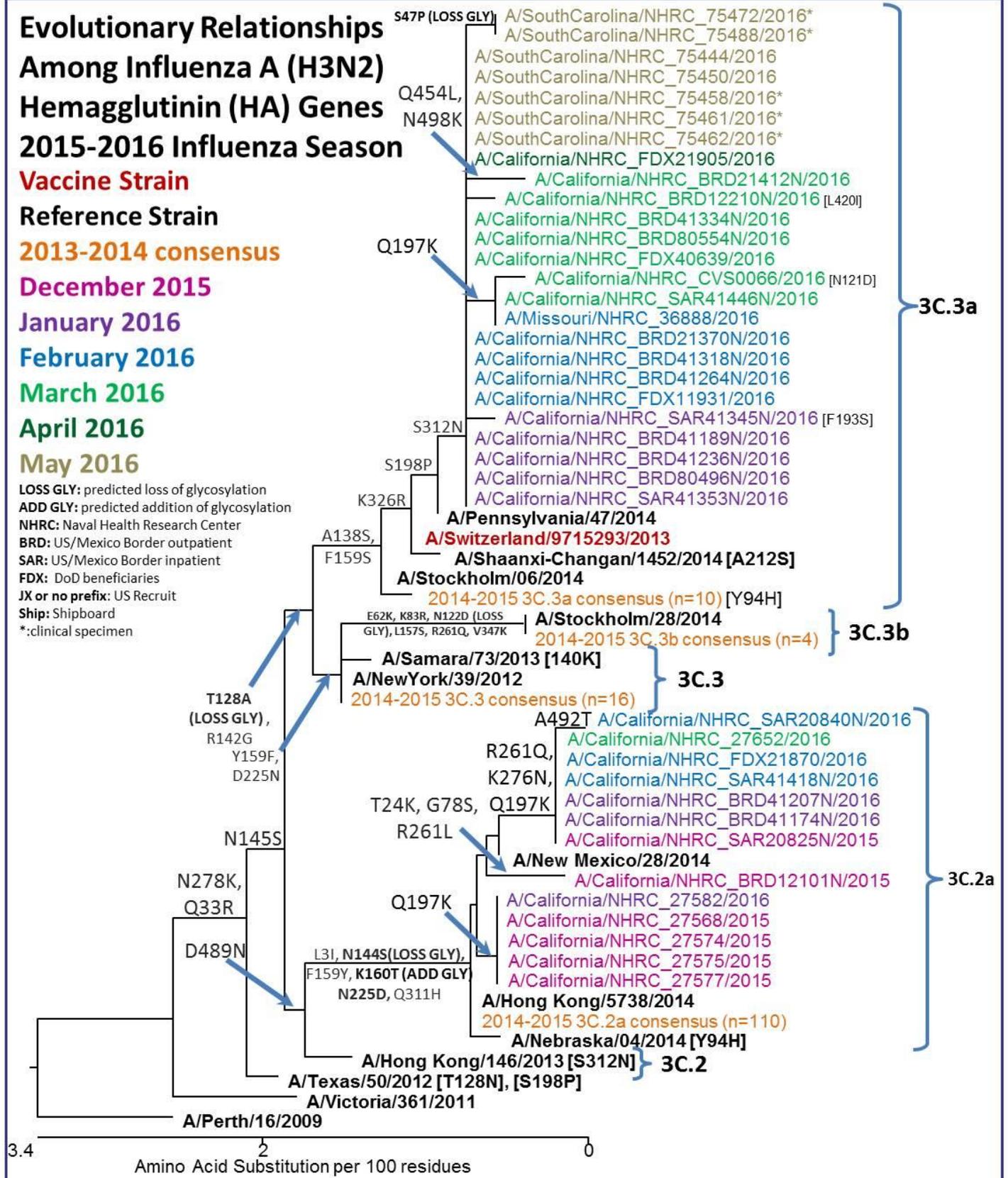
**February 2016**

**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  
 \*:clinical specimen



# Evolutionary Relationships Among Influenza A (H3N2) Neuraminidase (NA) Genes 2015-2016 Influenza Season

**Vaccine Strain**

**Reference Strain**

**December 2015**

**January 2016**

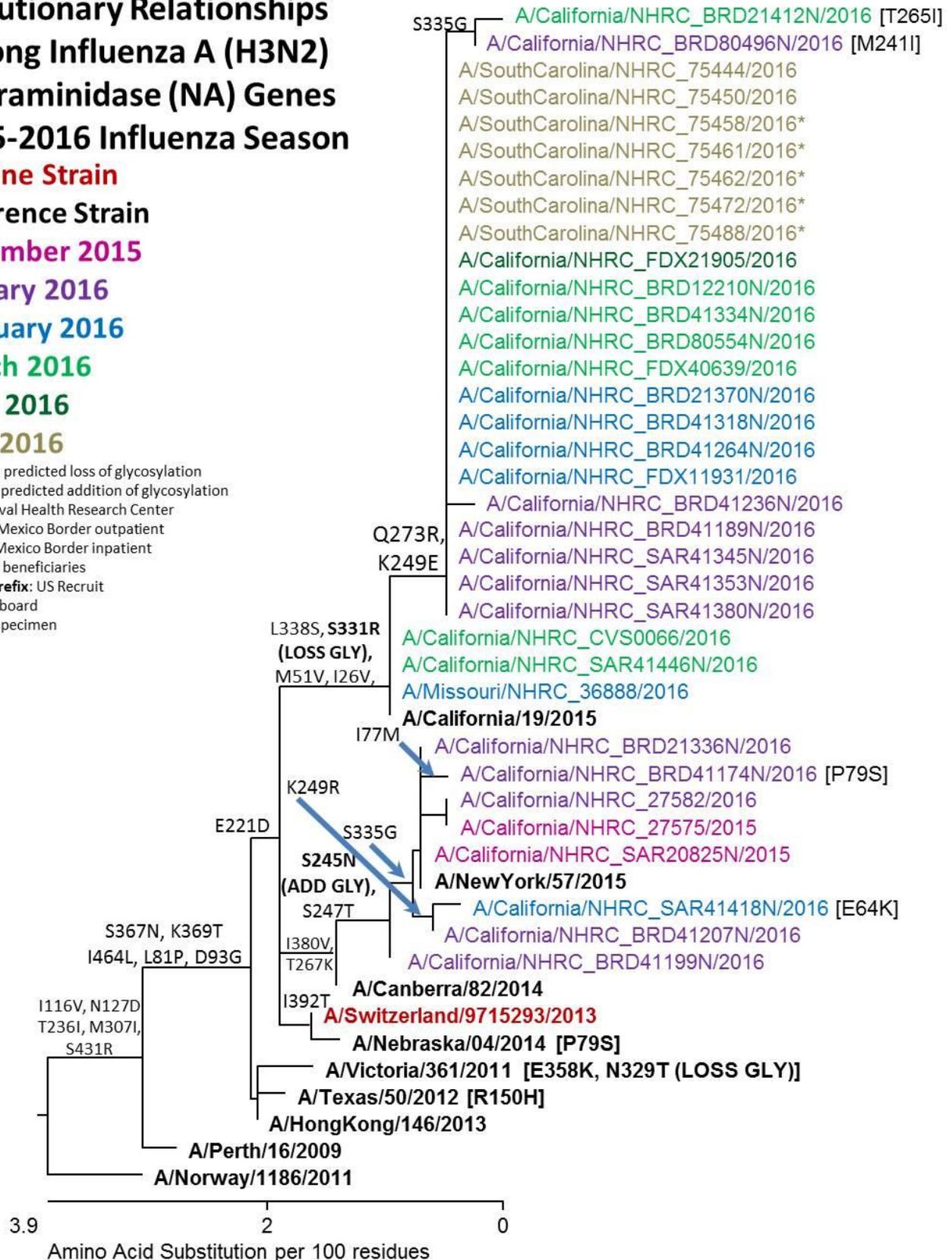
**February 2016**

**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  
 \*:clinical specimen



# Evolutionary Relationships Among Influenza B Hemagglutinin (HA) Genes 2015-2016 Influenza Season

**Vaccine Strain**

**Reference Strain**

**2013-2014 consensus**

**December 2015**

**January 2016**

**February 2016**

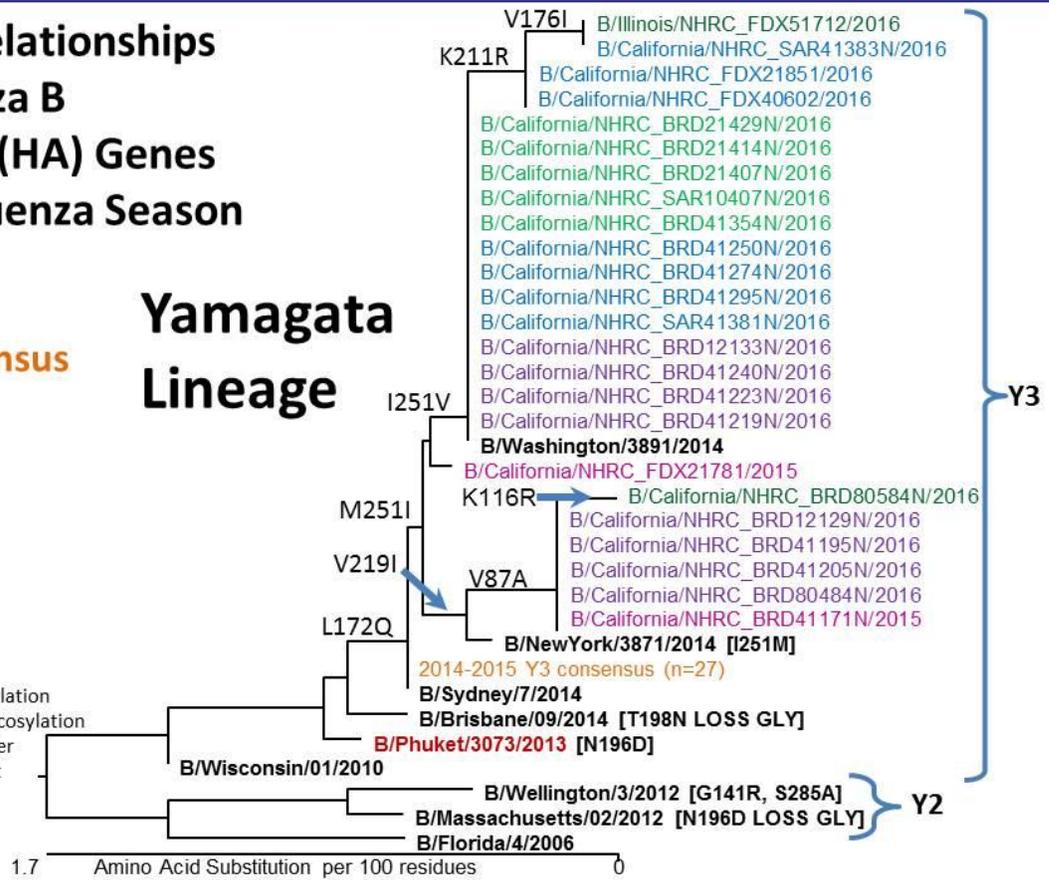
**March 2016**

**April 2016**

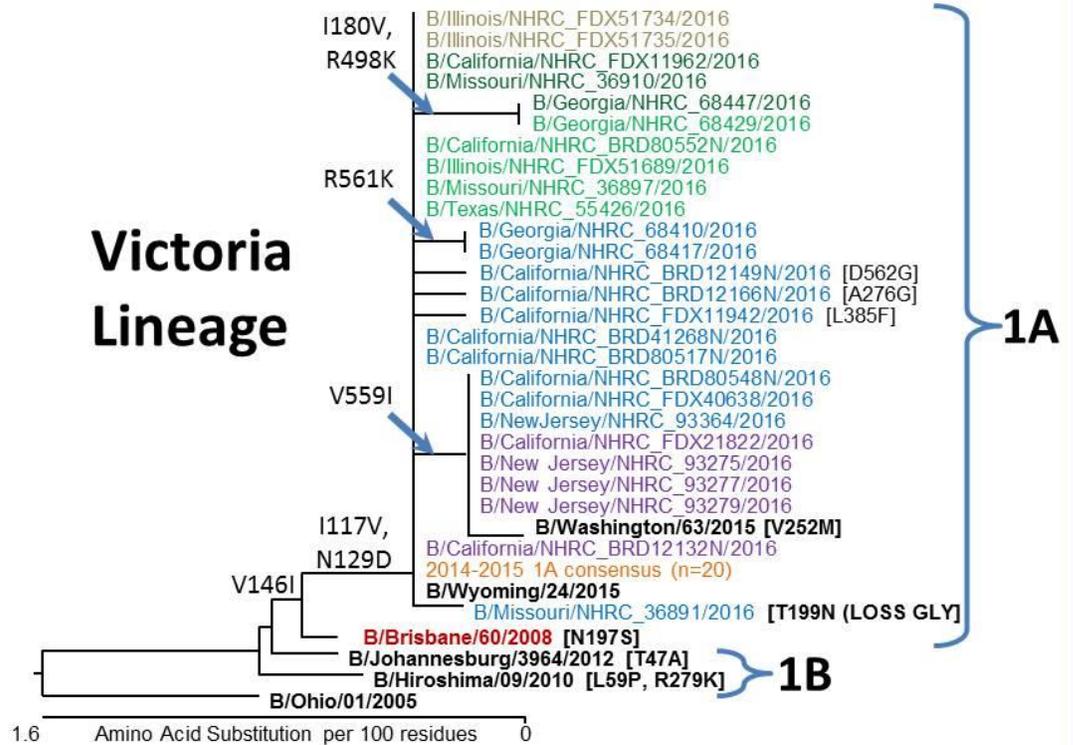
**May 2016**

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## Yamagata Lineage



## Victoria Lineage



# Evolutionary Relationships Among Influenza B Neuraminidase (NA) Genes 2015-2016 Influenza Season

**Vaccine Strain**

**Reference Strain**

**2013-2014 consensus**

**December 2015**

**January 2016**

**February 2016**

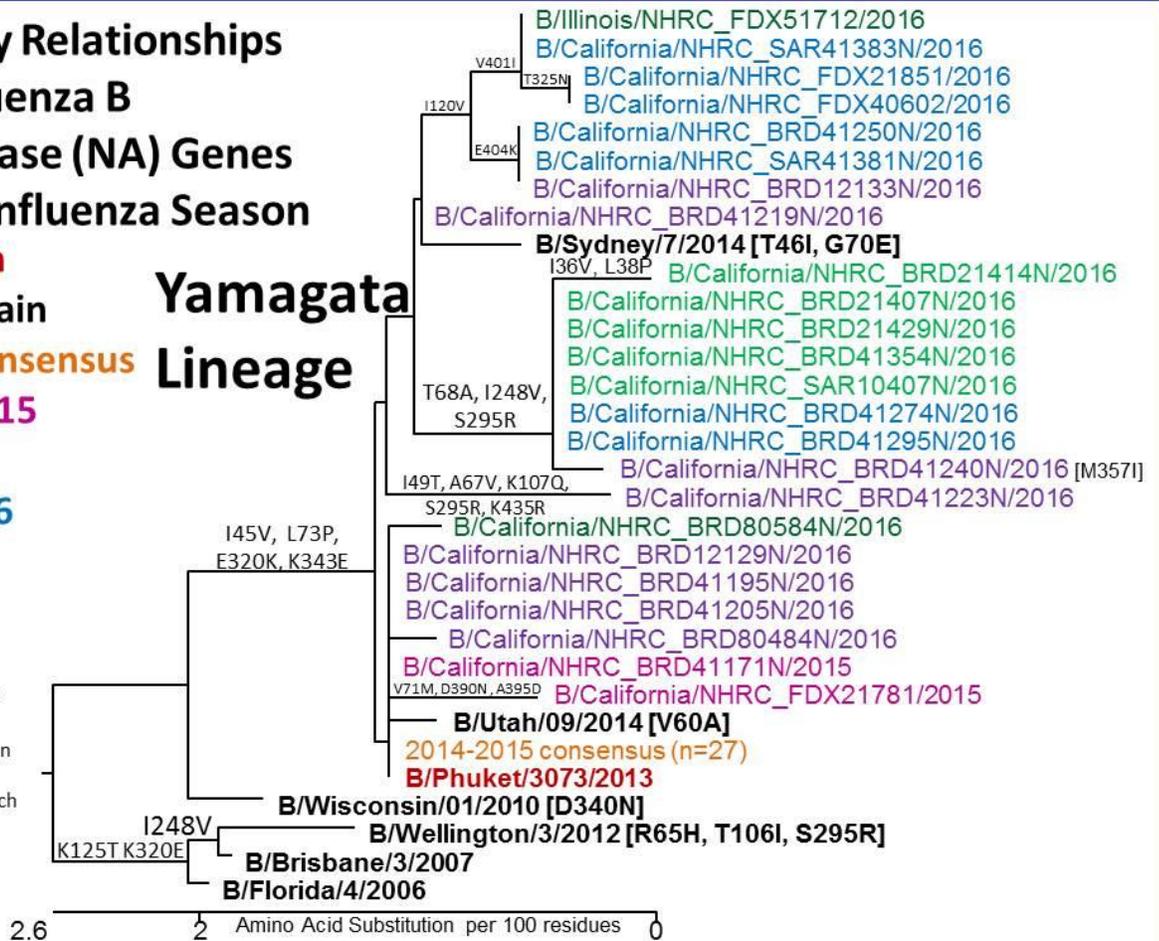
**March 2016**

**April 2016**

**May 2016**

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## Yamagata Lineage



## Victoria Lineage

