Febrile Respiratory Illness (FRI) Surveillance Update

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

2016 Week 42 (through 22 October 2016)

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NHRC FRI Surveillance Program

Influenza

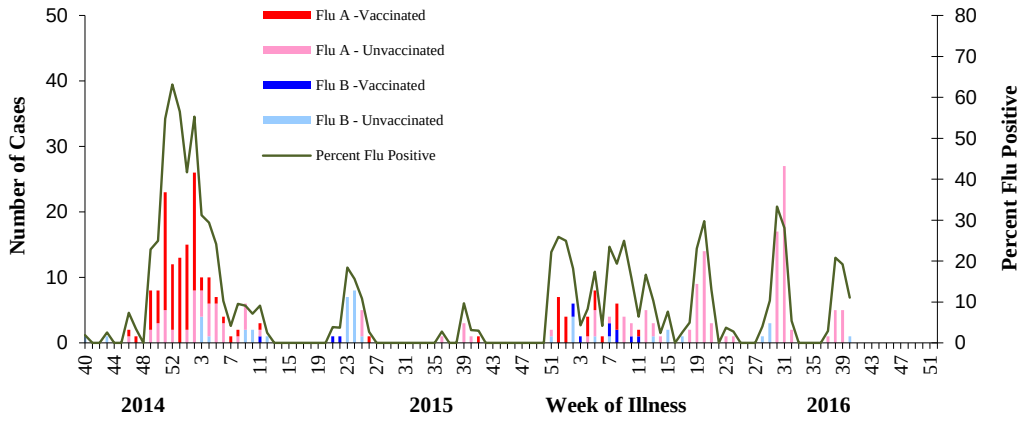
NHRC Laboratory-Confirmed Influenza Cases, US Military Basic Trainees

	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									10
Ft. Jackson									
Ft. Leonard Wood									1
NRTC Great Lakes				1				1	4
Lackland AFB									
MCRD Parris Island									
MCRD San Diego									15
CGTC Cape May									
Total	0	0	0	1	0	0	0	1	30

*Case presented 3 Oct. and was unvaccinated.

- 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

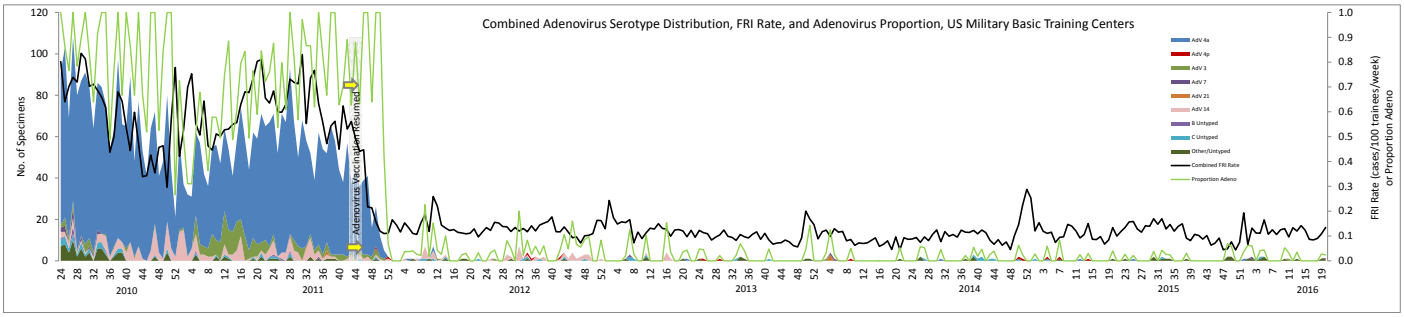
- NHRC is conducting laboratory-based surveillance for meningococcal disease. The program's purpose is to track and characterize meningococcal cases among DoD medical beneficiaries. For more information and the most recent data, click here.

Items of Note

- *FRI rates at all basic training centers are at or below expected values*
- *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 22 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
Lackland Air Force Base (data through 8 Oct.)
Coast Guard Training Center, Cape May

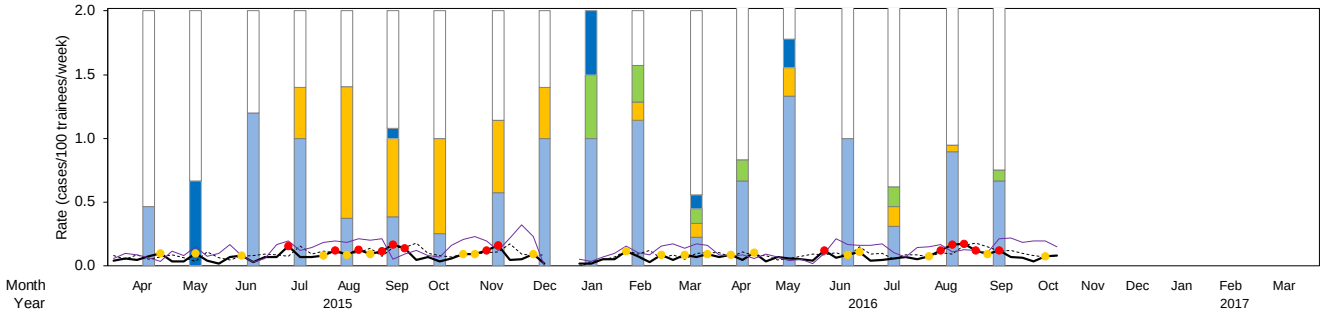
- **Moderately elevated:**

None

- **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**	**38**	**24**
Adenovirus		33%				4%				25%		6%		11%				
Influenza										25%	14%	6%	8%			8%		4%
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%	45%	33%

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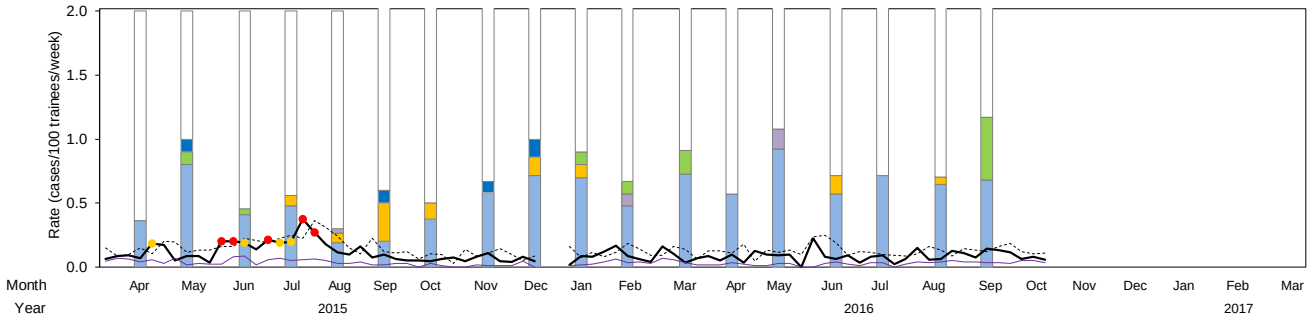
Ft. Jackson FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	**33**	**20**	**44**	**50**	**53**	**20**	**16**	**24**	**14**	**20**	**21**	**11**	**21**	**13**	**14**	**14**	**34**	**41**
Adenovirus		5%				5%		4%	7%									
Influenza		5%	2%							5%	5%	9%						24%
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%

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

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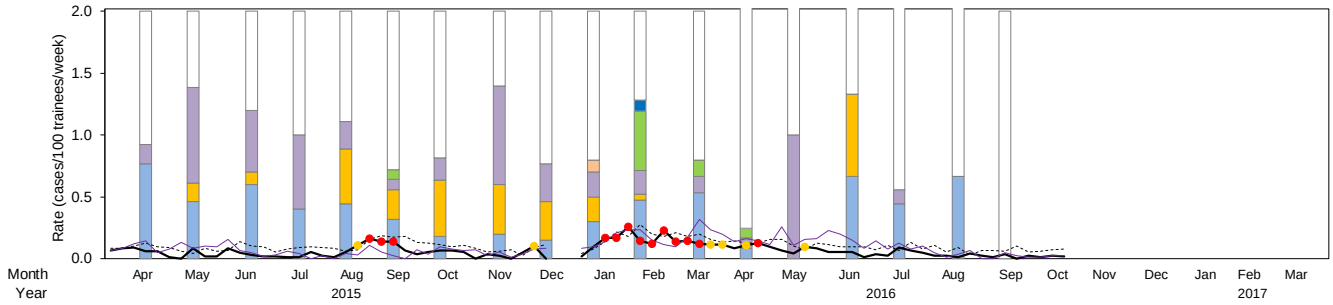
– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated —— Pneumonia rate (incl. afebrile)

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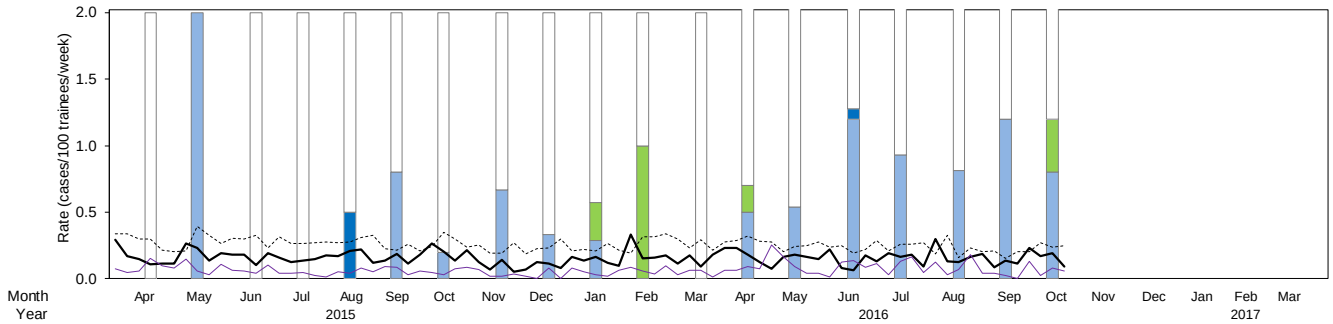
Great Lakes FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	**1**	**1**	**1**	**3**	**4**	**5**	**10**	**3**	**6**	**7**	**2**	**3**	**20**	**26**	**25**	**30**	**32**	**15**	**5**
Adenovirus					25%										4%				
Influenza										14%	50%		10%						20%
RSV																			
C. pneumo																			
M. pneumo																			
Rhinovirus		100%				40%	10%	33%	17%	14%			25%	27%	60%	47%	41%	60%	40%

Influenza Subtype																			
B										0%	0%		50%						100%
A/H3										0%	0%		0%						0%
A/pH1										100%	100%		50%						0%
Untyped										0%	0%		0%						0%

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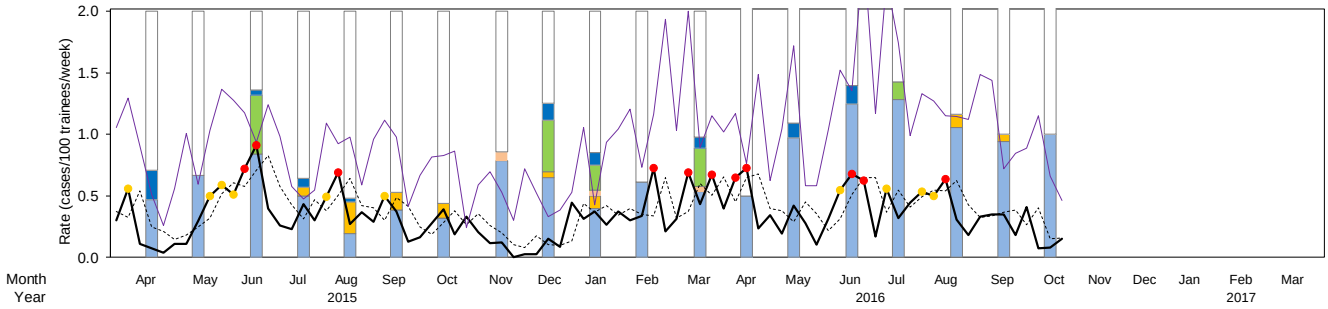
– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)

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**	**42**	**55**	**36**	**4**
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%	3%	
Rhinovirus	24%	33%	42%	25%	10%	19%	16%	39%	33%	20%	31%	27%	25%	48%	62%	64%	53%	47%	50%

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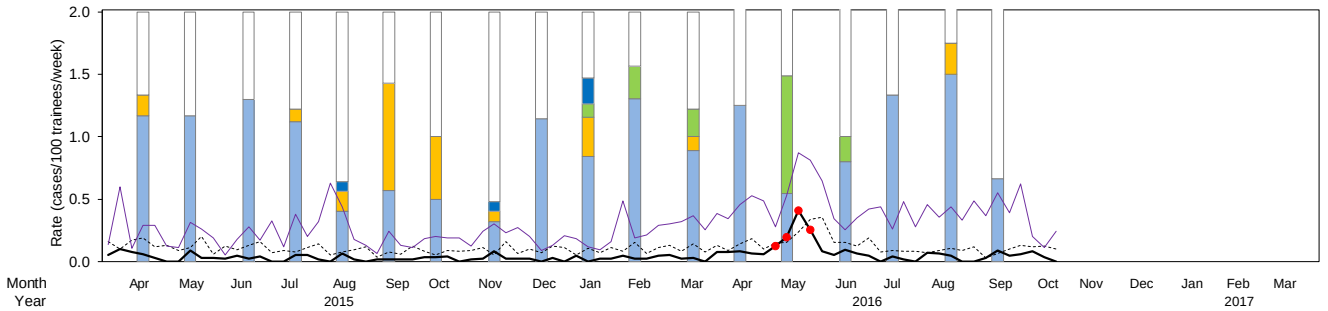
MCRD PI FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	**12**	**12**	**20**	**41**	**25**	**14**	**4**	**25**	**7**	**19**	**23**	**18**	**8**	**59**	**20**	**6**	**8**	**3**	
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%	33%	

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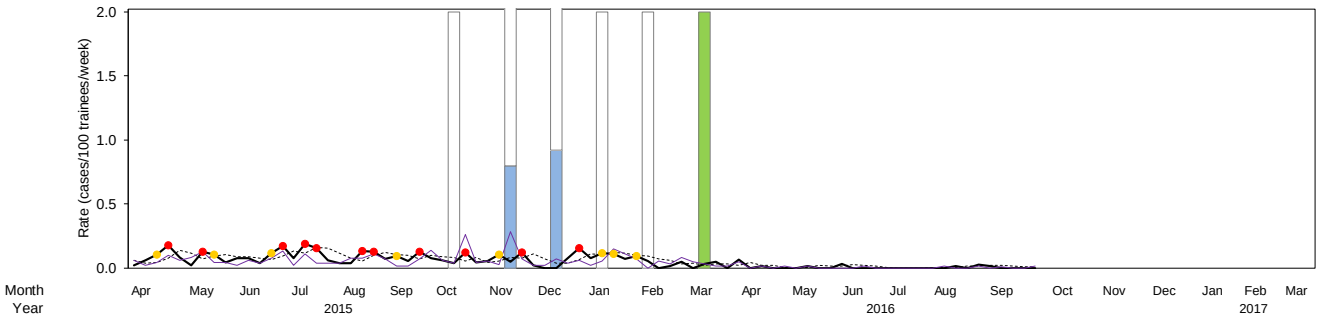
– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)

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**	**1**	**5**	**13**	**3**	**2**	**2**
Adenovirus												
Influenza												100%
RSV												
C. pneumo												
M. pneumo												
Rhinovirus								40%	46%			
Influenza Subtype: B												50%
Influenza Subtype: A/H3												0%
Influenza Subtype: A/pH1												50%
Influenza Subtype: Untyped												0%

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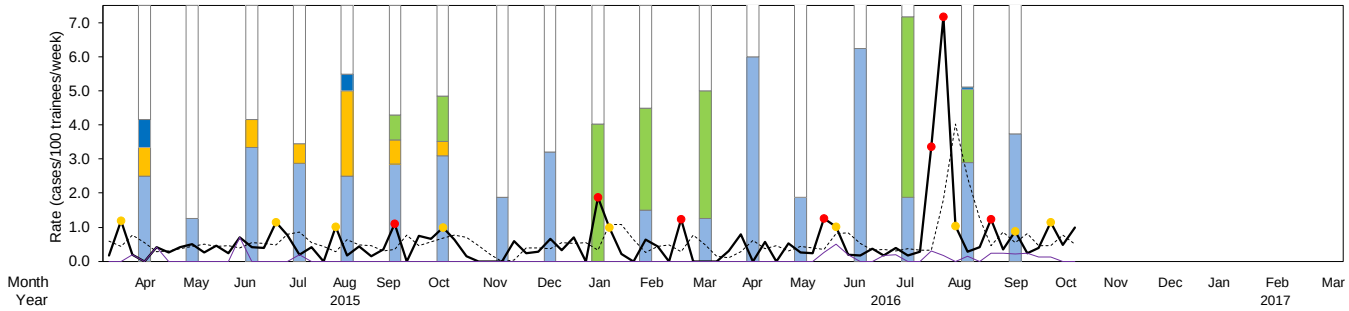
Cape May FRI Rates and Diagnostic Test Results
Shaded bars represent monthly proportions of each pathogen (clear = no pathogen identified)



Samples Received	**9**	**6**	**9**	**13**	**15**	**21**	**17**	**4**	**7**	**13**	**5**	**6**	**5**	**12**	**6**	**24**	**101**	**10**
Adenovirus	11%				7%												1%	
Influenza						10%	18%			54%	40%	50%				71%	29%	
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%	39%	50%
Influenza Subtype: B						0%	0%			100%	100%	0%				0%	0%	
Influenza Subtype: A/H3						100%	100%			0%	0%	0%				100%	93%	
Influenza Subtype: A/pH1						0%	0%			0%	0%	100%				0%	0%	
Influenza Subtype: Untyped						0%	0%			0%	0%	0%				0%	7%	

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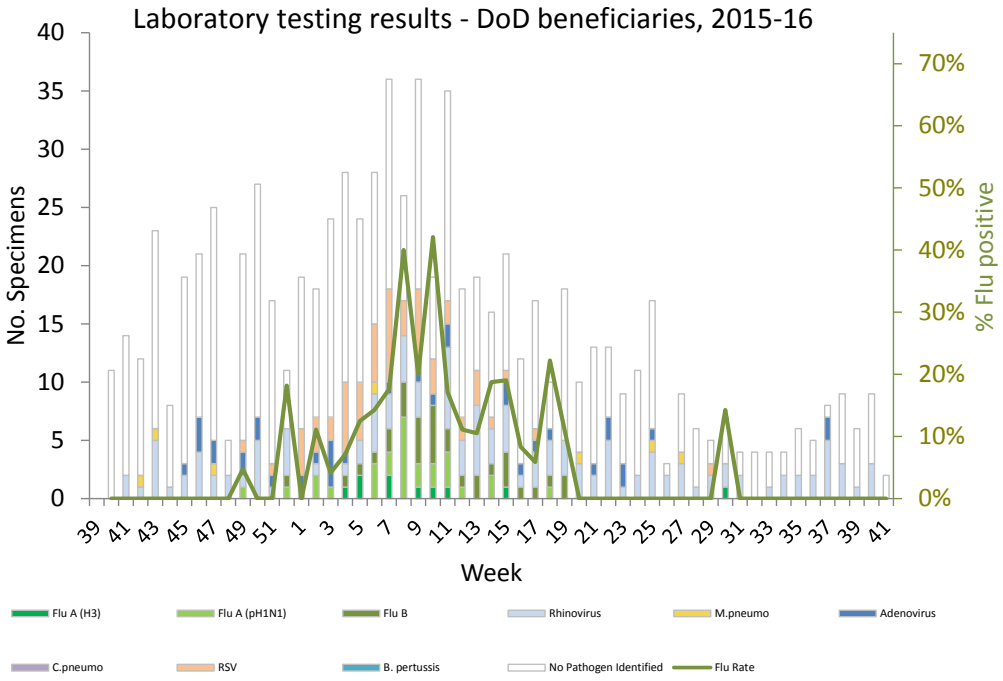
– Observed FRI rate (expected rate = dashed line) • Moderately elevated • Substantially elevated — Pneumonia rate (incl. afebrile)

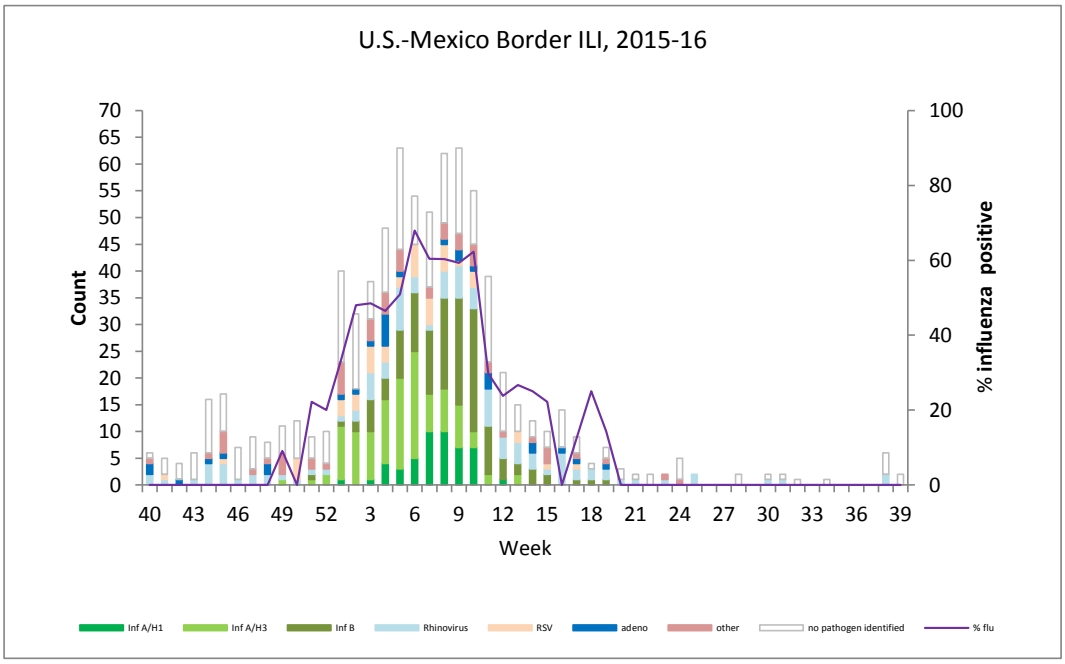
DoD Beneficiary Surveillance

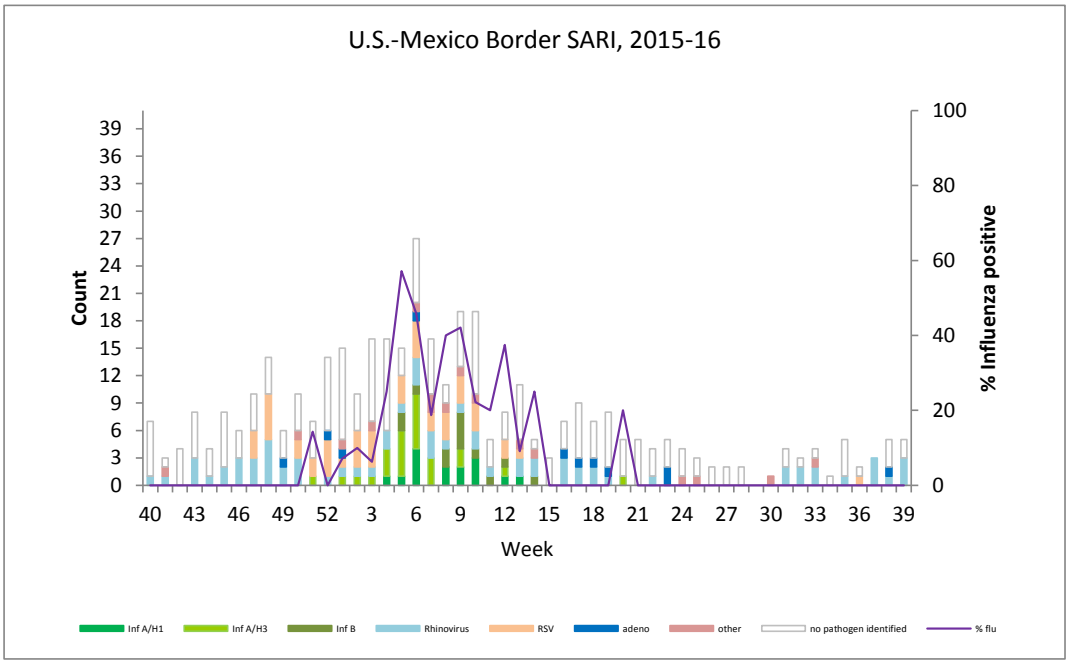
- NHRC conducts FRI surveillance among (non-active duty) DoD beneficiaries at Lovell FHCC (Great Lakes, IL) and in 4 NMC San Diego facilities: the Emergency Department, Pediatric Department, Naval Branch Health Clinic Kearny Mesa, and NH Camp Pendleton.
    - For questions regarding surveillance in this 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 (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.[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	
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.
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	**97.0-99.6%**
H3N2 NA	33	A/Switzerland/9715293/2013	**97.9-98.6%**

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	S47P N122D T128A N144S N158K N158H T160K T160I
NA	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 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 (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	**99.1-99.5%**
B/Victoria NA	26	B/Brisbane/60/2008	**98.3-98.54%**
B/Yamagata HA	24	B/Phuket/3073/2013	**99.1-99.5%**
B/Yamagata NA	24	B/Phuket/3073/2013	**98.7-100.0%**

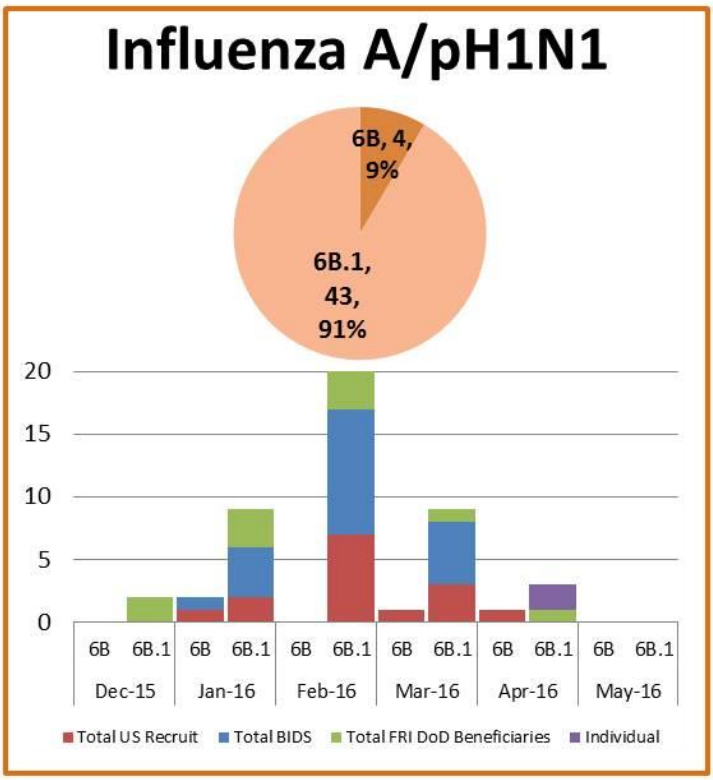
Summary of Influenza B N-Linked Glycosylation Mutations

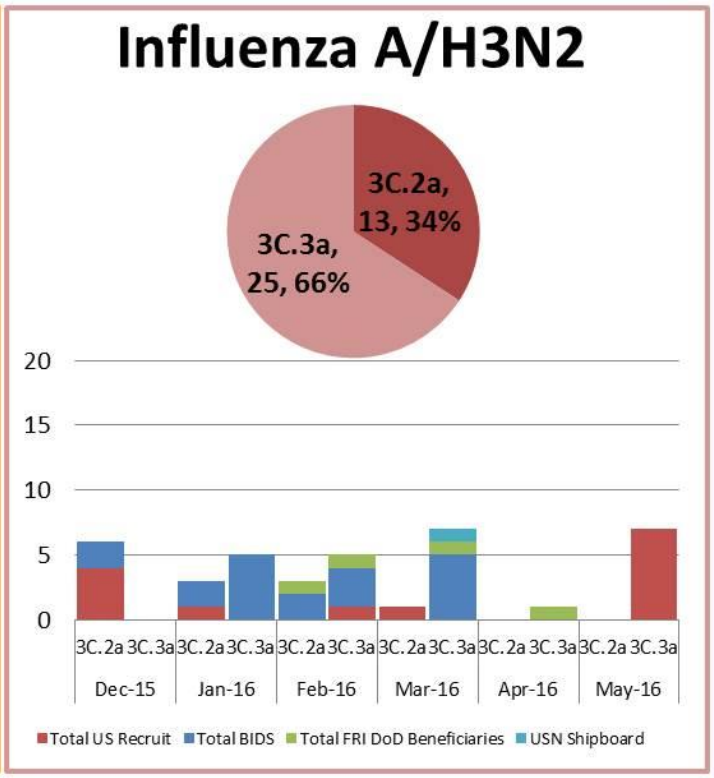
- Loss or gain of N-linked glycosylation sites affect host innate immune system recognition and the ability to induce adaptive immune response thus altering its viral antigenicity.[1] Predicted loss or gain of N-linked glycosylation of protein sequences were calculated using CBS NetNGlyc 1.0 Server http://www.cbs.dtu.dk/services/NetNGlyc/

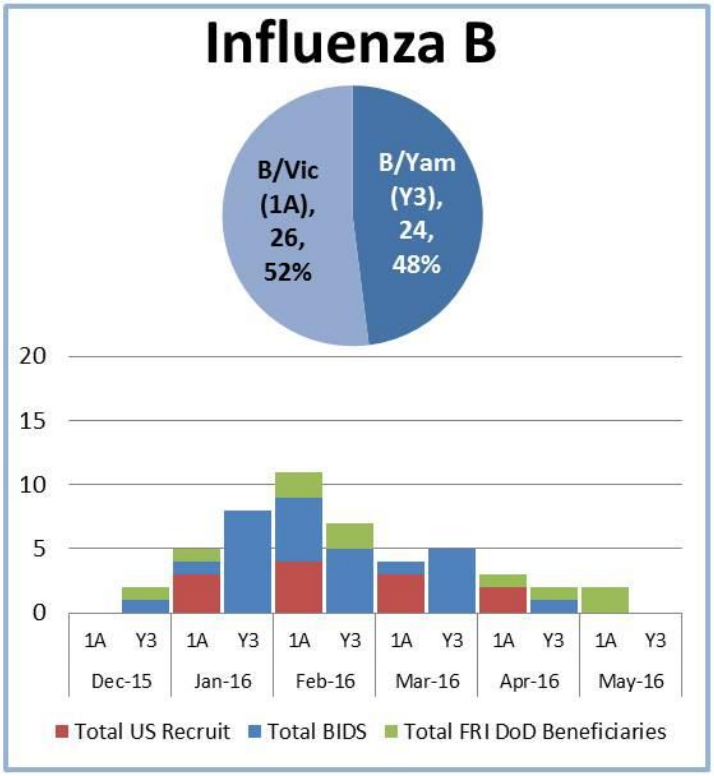
	Mutation	
INF B Segment	ADD GLY	LOSS GLY
HA	A198T	N196D T198N
NA	D463N	

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.
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







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

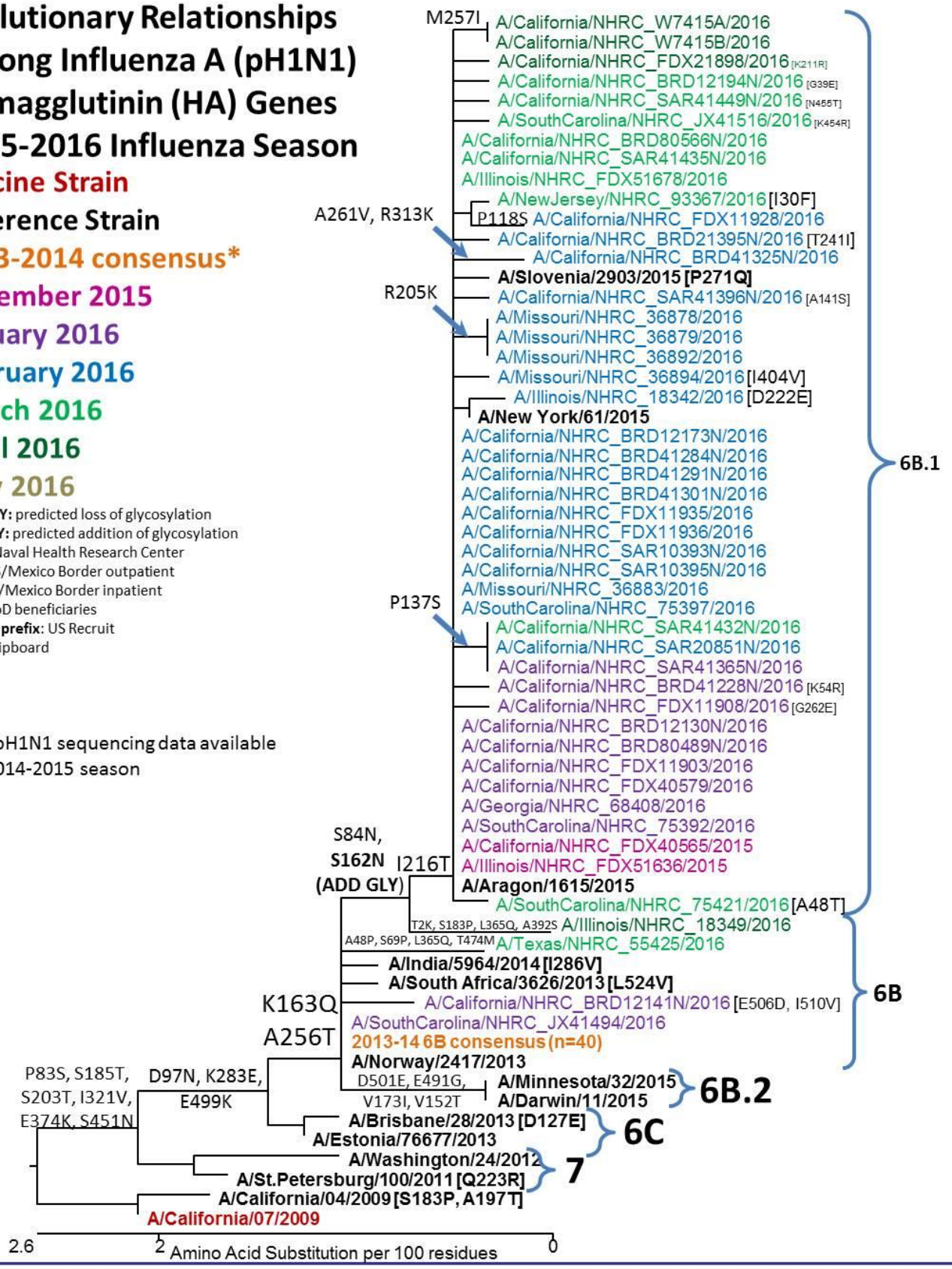
March 2016

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

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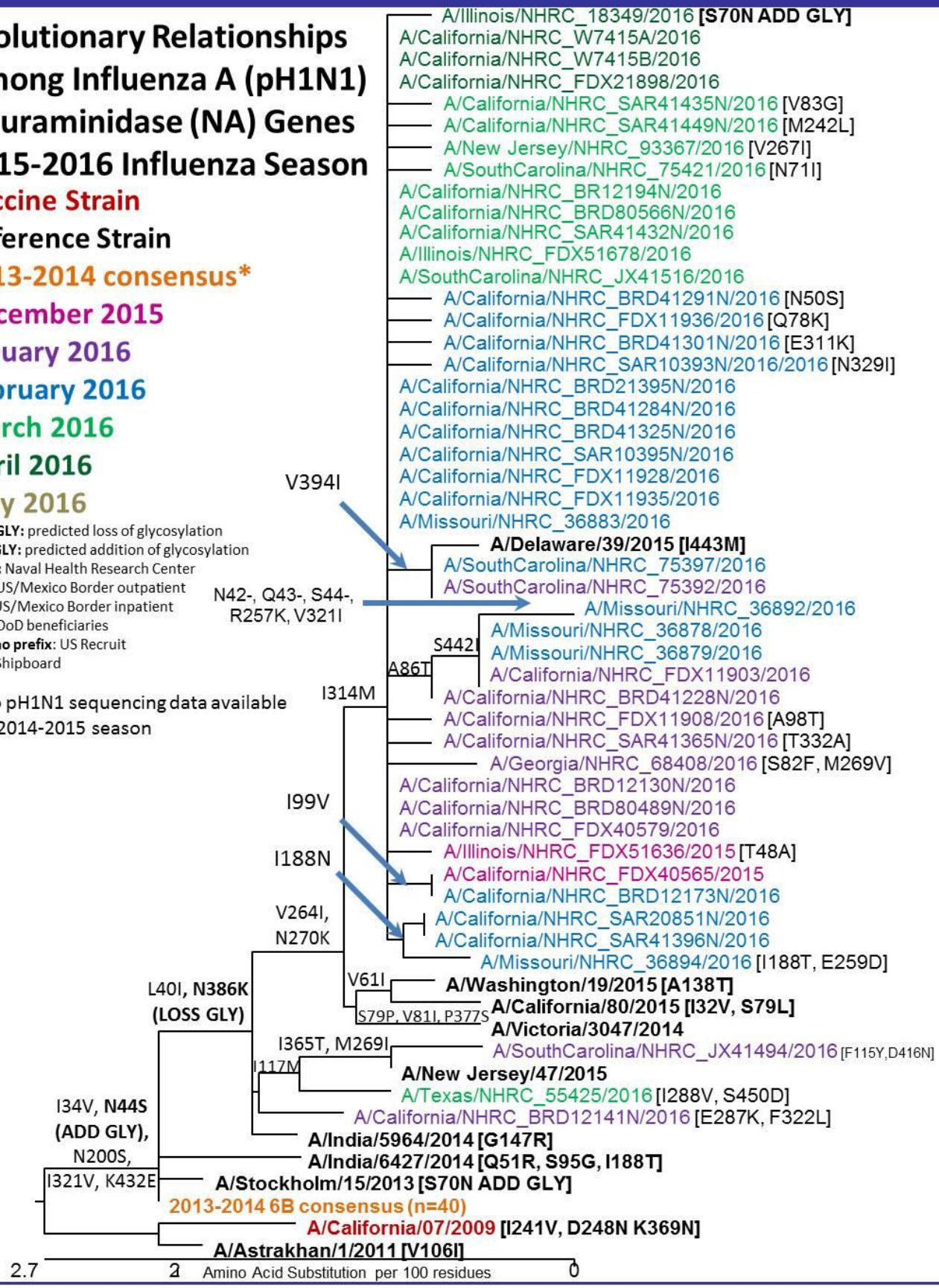

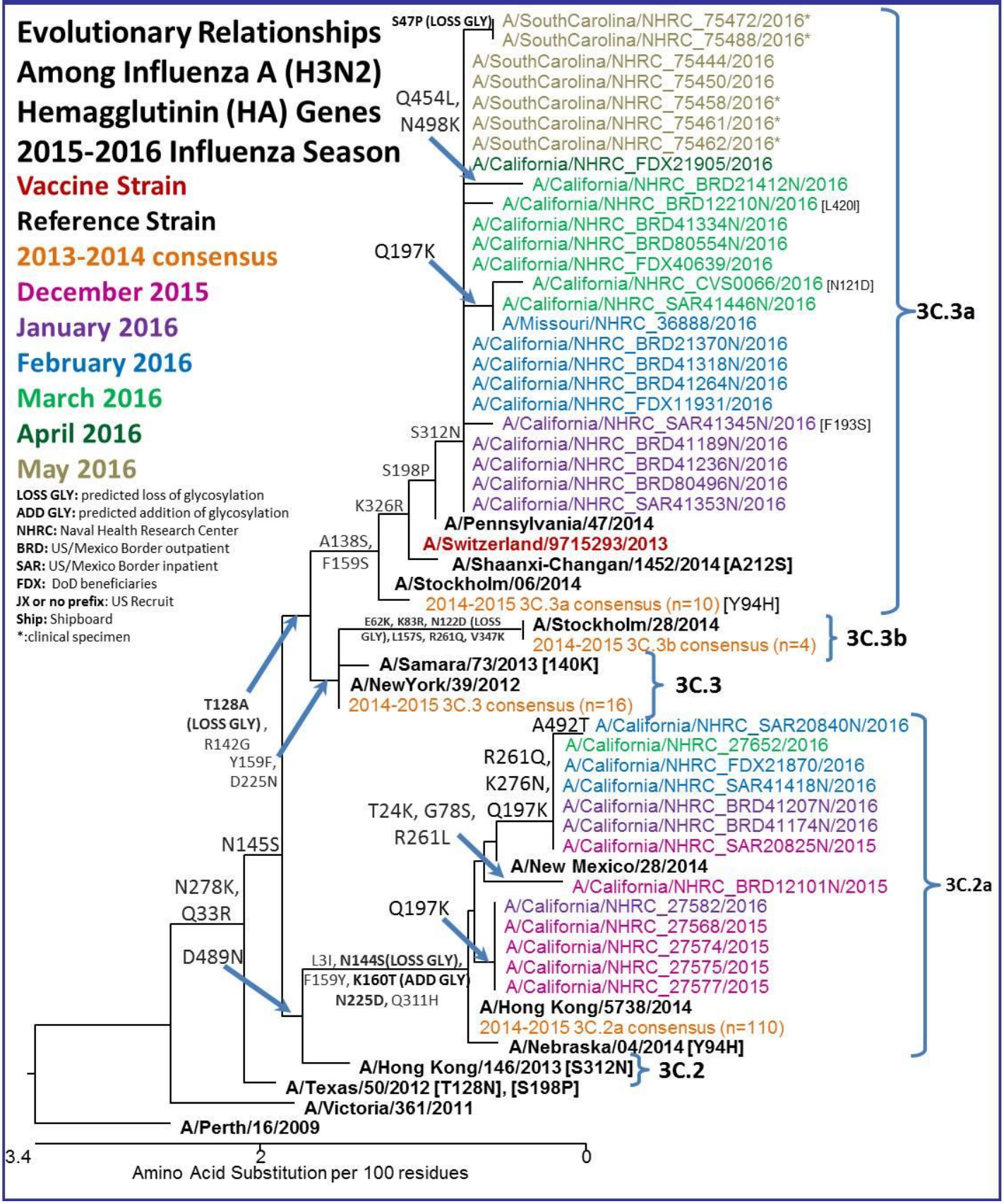
Evolutionary Relationships Among Influenza A (H3N2) Hemagglutinin (HA) Genes 2015-2016 Influenza Season
Vaccine Strain
Reference Strain
2013-2014 consensus
December 2015
January 2016
February 2016
March 2016
April 2016
May 2016
LOSS GLY: predicted loss of glycosylation
ADD GLY: predicted addition of 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
S47P (LOSS GLY)
A/SouthCarolina/NHRC_75472/2016*
A/SouthCarolina/NHRC_75488/2016*
A/SouthCarolina/NHRC_75444/2016
A/SouthCarolina/NHRC_75450/2016
A/SouthCarolina/NHRC_75458/2016*
A/SouthCarolina/NHRC_75461/2016*
A/SouthCarolina/NHRC_75462/2016*
Q454L, N498K
A/California/NHRC_FDX21905/2016
A/California/NHRC_BRD21412N/2016
A/California/NHRC_BRD12210N/2016 [L420I]
A/California/NHRC_BRD41334N/2016
A/California/NHRC_BRD80554N/2016
Q197K
A/California/NHRC_FDX40639/2016
A/California/NHRC_CVS0066/2016 [N121D]
A/California/NHRC_SAR41446N/2016
A/Missouri/NHRC_36888/2016
A/California/NHRC_BRD21370N/2016
A/California/NHRC_BRD41318N/2016
A/California/NHRC_BRD41264N/2016
A/California/NHRC_FDX11931/2016
S312N
A/California/NHRC_SAR41345N/2016 [F193S]
A/California/NHRC_BRD41189N/2016
S198P
A/California/NHRC_BRD41236N/2016
A/California/NHRC_BRD80496N/2016
K326R
A/California/NHRC_SAR41353N/2016
A/Pennsylvania/47/2014
A138S, F159S
A/Switzerland/9715293/2013
A/Shaanxi-Changan/1452/2014 [A212S]
A/Stockholm/06/2014
2014-2015 3C.3a consensus (n=10) [Y94H]
3C.3a
E62K, K83R, N122D (LOSS GLY), L157S, R261Q, V347K
A/Stockholm/28/2014
2014-2015 3C.3b consensus (n=4)
3C.3b
A/Samara/73/2013 [140K]
A/NewYork/39/2012
2014-2015 3C.3 consensus (n=16)
3C.3
T128A (LOSS GLY), R142G Y159F, D225N
A492T
A/California/NHRC_SAR20840N/2016
A/California/NHRC_27652/2016
R261Q, K276N, Q197K
A/California/NHRC_FDX21870/2016
A/California/NHRC_SAR41418N/2016
A/California/NHRC_BRD41207N/2016
A/California/NHRC_BRD41174N/2016
A/California/NHRC_SAR20825N/2015
T24K, G78S, R261L
A/New Mexico/28/2014
A/California/NHRC_BRD12101N/2015
3C.2a
N145S
N278K, Q33R
Q197K
A/California/NHRC_27582/2016
A/California/NHRC_27568/2015
A/California/NHRC_27574/2015
A/California/NHRC_27575/2015
A/California/NHRC_27577/2015
D489N
L3I, N144S(LOSS GLY), F159Y, K160T (ADD GLY) N225D, Q311H
A/Hong Kong/5738/2014
2014-2015 3C.2a consensus (n=110)
A/Nebraska/04/2014 [Y94H]
A/Hong Kong/146/2013 [S312N]
3C.2
A/Texas/50/2012 [T128N], [S198P]
A/Victoria/361/2011
A/Perth/16/2009
3.4
2
0
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

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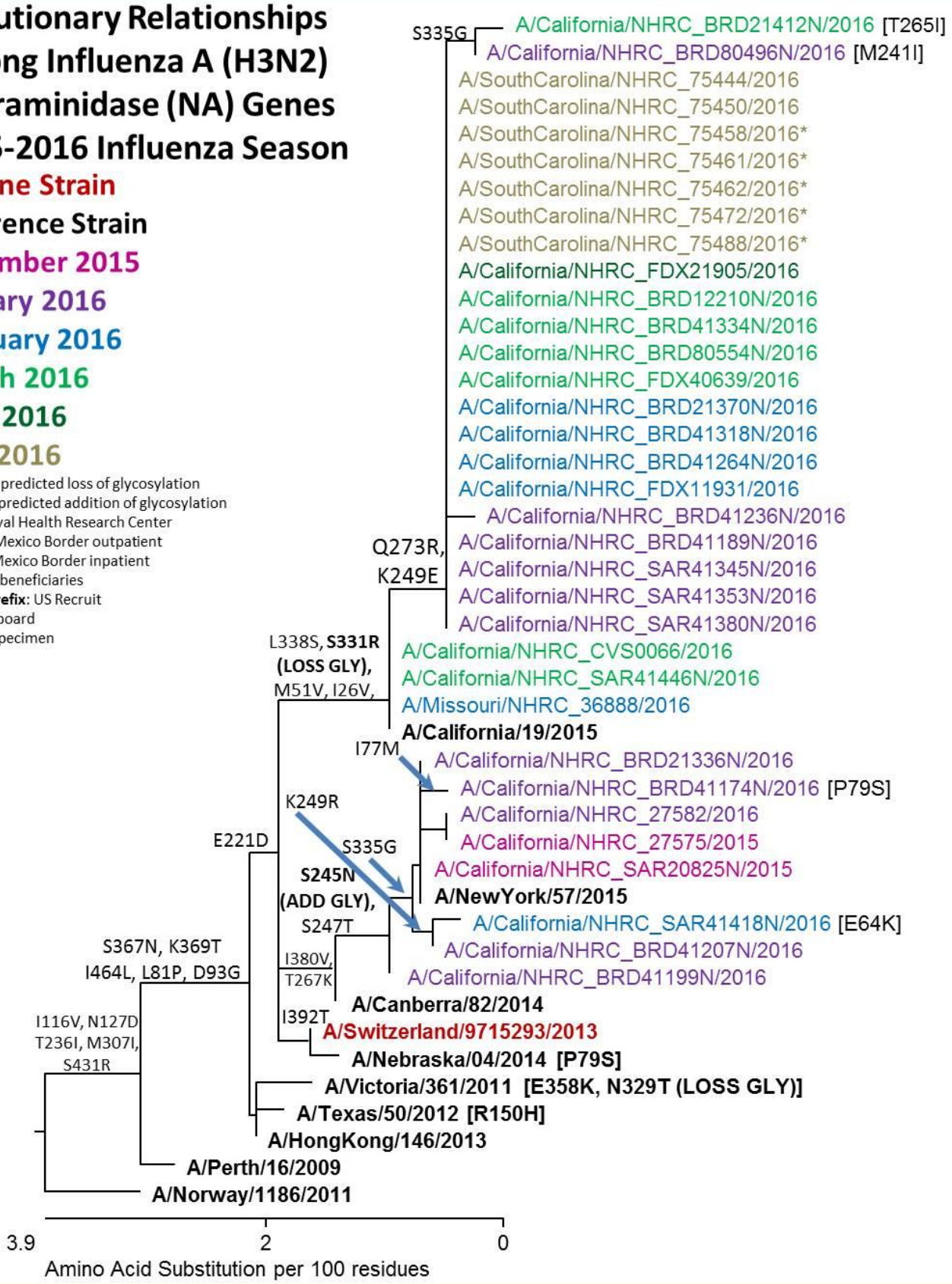
JX or no prefix: US Recruit
Ship: Shipboard
*:clinical specimen



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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BRD: US/Mexico Border outpatient
SAR: US/Mexico Border inpatient
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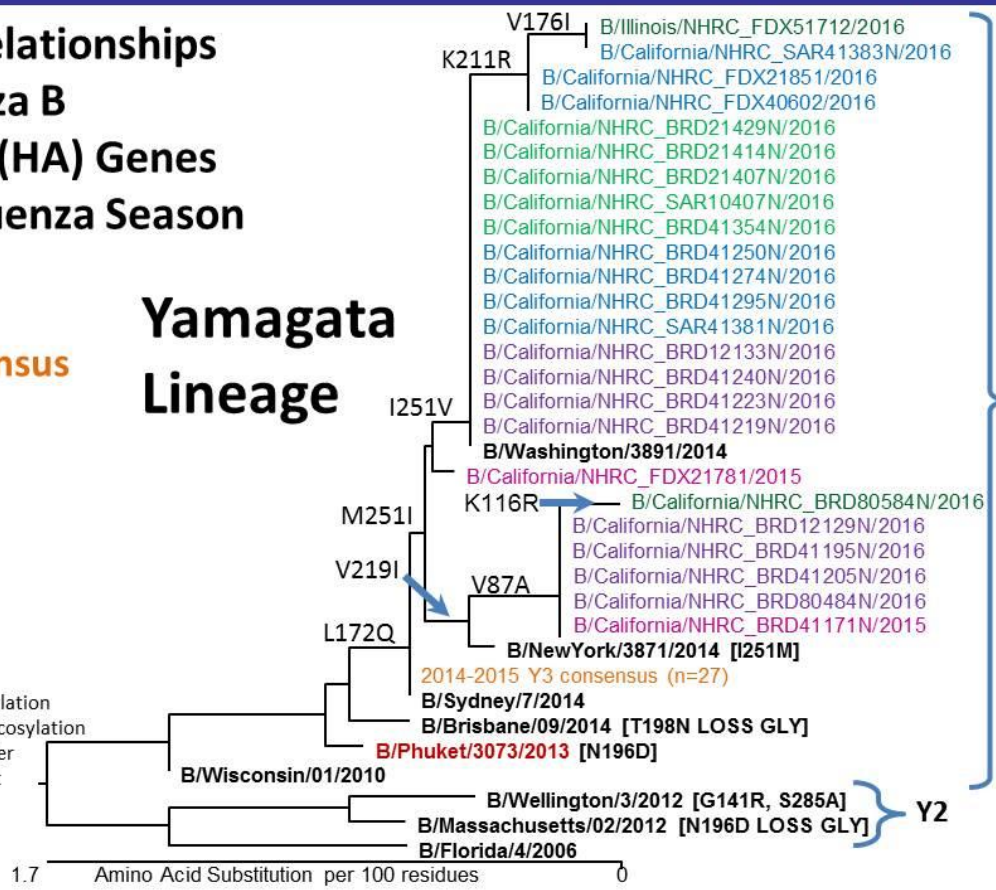
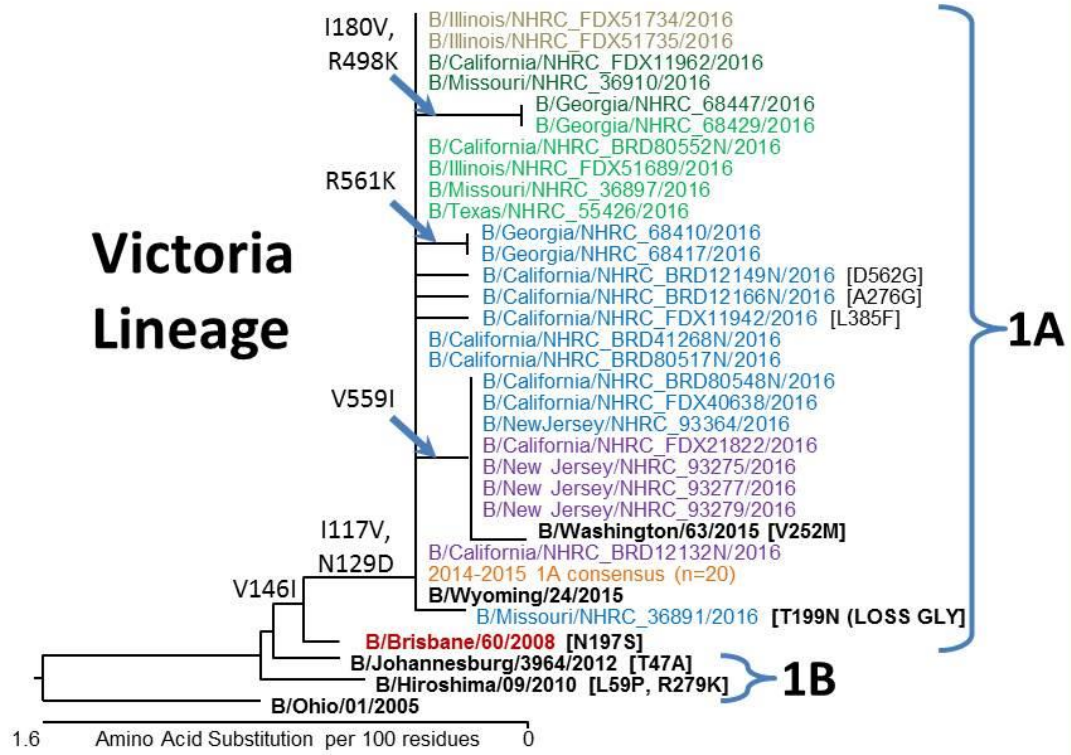
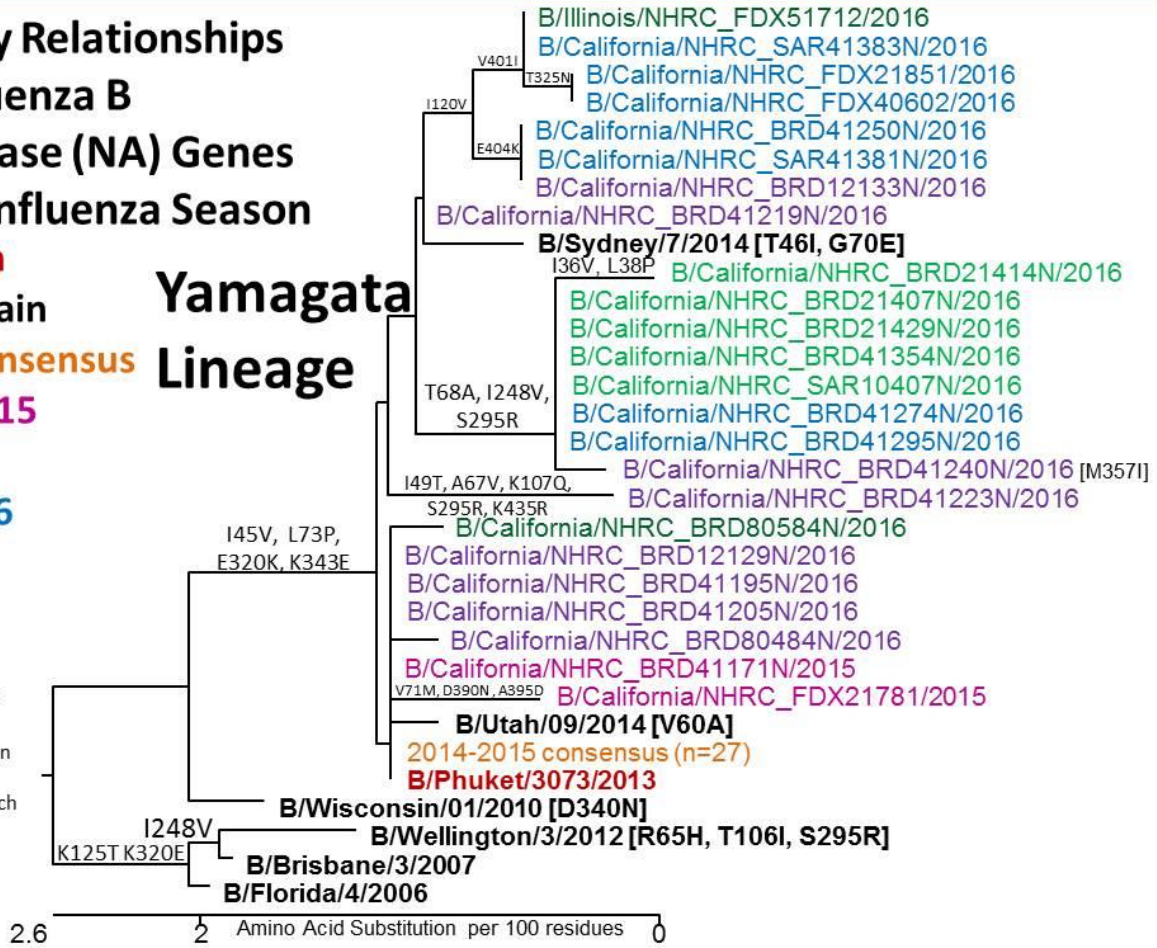
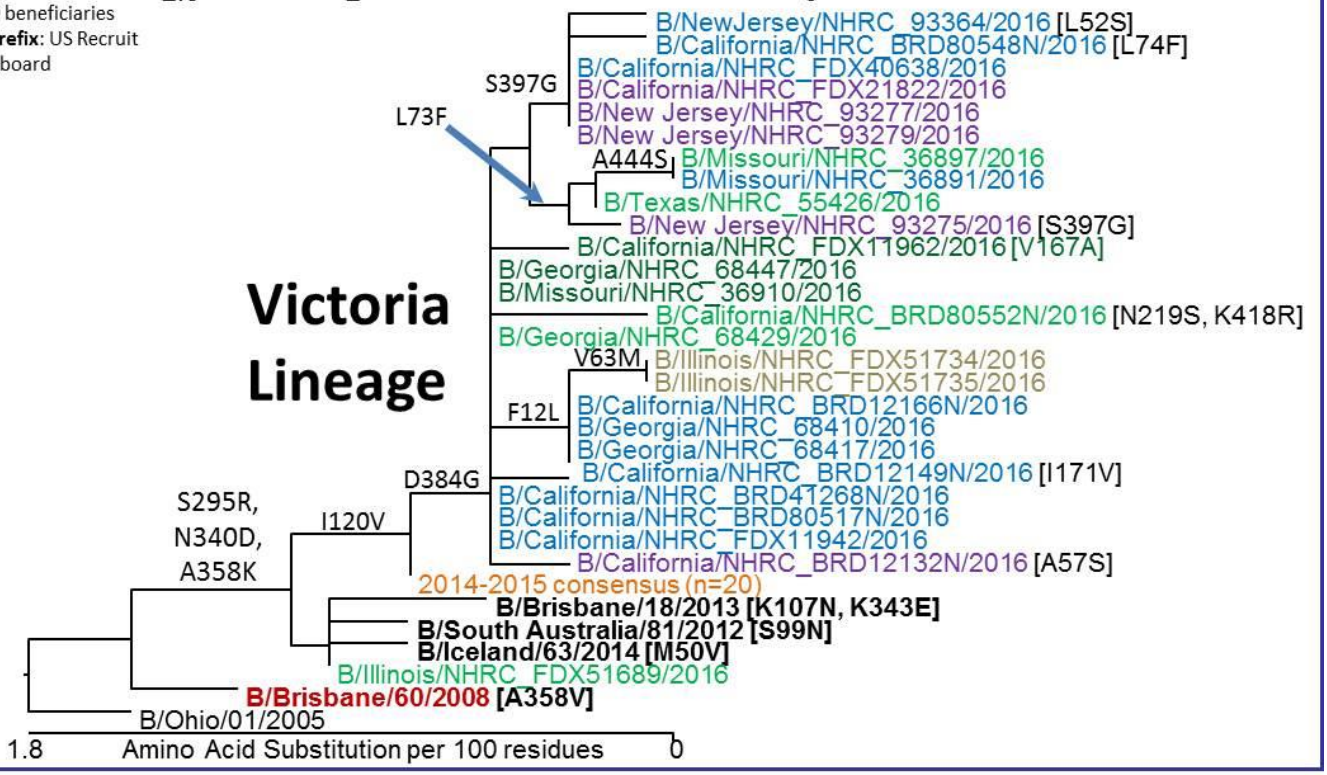
JX or no prefix: US Recruit
Ship: Shipboard





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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JX or no prefix: US Recruit
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