USAF School of Aerospace Medicine & Defense Health Agency

DoD Global Respiratory Pathogen Surveillance Program

2017-2018

Cumulative Results

Locations	98
Collected	11,775
Tested	11,648

Influenza A	**2,616**
A(H1N1)pdm09	537
A(H1N1)pdm09 Coinfection	47
A(H1N1)pdm09 & A(H3N2)	3
A(H1N1)pdm09 & B	8
A(H3N2)	1,800
A(H3N2) Coinfection	190
A(H3N2) & B	9
A/not subtyped	19
A/not subtyped Coinfection	3

Influenza B*	**1,422**
B	1,313
B & Coinfection	109

Other Respiratory Pathogens	**3,731**
Adenovirus	138
Chlamydophila pneumoniae	28
Coronavirus	638
Human Bocavirus	31
Human Metapneumovirus	425
Mycoplasma pneumoniae	44
Parainfluenza	238
RSV	546
Rhinovirus/Enterovirus	1,198
Non-influenza Viral Coinfections	434
Non-influenza Bacterial Coinfections	11
-*C. pneumo* coinfections *(4)*	
-*M. pneumo* coinfections *(7)*	

No Pathogen Detected	**3,879**

Results are preliminary and may change as more results are finalized.
**Influenza B lineages and specimens submitted for sequencing only will be reported in the periodic molecular sequencing reports.*

Respiratory Highlights
8 - 28 July 2018 (Surveillance Weeks 28 - 30)

- During 8 - 28 July 2018, a total of 46 specimens were collected and received from 24 locations. Results were finalized for 42 specimens from 22 locations. During Week 29, there was one influenza A(H1N1)pdm09 virus detected. There were no positive influenza specimens detected during Weeks 28 and 30. The percent influenza positive for Week 29 was 7%. The influenza percent positive for the season is approximately 35%.
- One woman from Shenzhan, China was hospitalized on 23 July for a confirmed case of avian influenza A(H9N2). This is the third human case reported in China this year. There was no recorded exposure to poultry in this case but most cases are a result of human-bird contact. The other two cases occurred in a child from the Guangdong province and a woman from Beijing. Within the past 20 years, only three countries (i.e., China, Pakistan, and Egypt) have reported Influenza A(H9N2) cases (CIDRAP, cited 1 August 2018).
- Scientists have already determined that obesity increases the risk of severe flu complications but a recent epidemiologic study shows that obesity may also increase disease transmission. This investigation monitored two cohorts which included 1,783 individuals from 320 households in Managua, Nicaragua over 3 seasons (1.e., 2015-2017). The study found that symptomatic obese adults shed influenza A virus 42% longer than non-obese adults (adjusted event time ratio [ETR], 1.42; 95% confidence interval [CI], 1.06-1.89) with no association indicated for those with influenza B illness. Among asymptomatic individuals or those with milder infections, obesity increased the shedding duration for influenza A by 104% (adjusted ETR, 2.04; 95% CI, 1.35-3.09). These findings emphasize the impact of obesity in influenza transmission (JID, cited 2 August 2018).
- This report contains the eighth molecular sequence analysis report which includes 65 specimens collected between 19 December 2018 and 27 May 2018.

Table of Contents

DoD Global Respiratory Pathogen Surveillance Program

Table 1. Finalized results by region and location for specimens collected during Weeks 28 - 30

Region*		A(H1N1)pdm09	Adenovirus	hMPV	*M. pneumoniae*	Parainfluenza	Rhinovirus/Enterovirus	Non-Influenza Viral Coinfection	No Pathogen	Total
Deployed	Country 4, Location B	-	-	-	-	-	-	-	1	1
EUCOM	Landstuhl RMC, Germany	-	2	-	-	-	-	-	3	5
	NAS Sigonella, Italy	-	-	-	-	-	-	-	1	1
	NSA Naples, Italy	-	-	-	-	-	-	-	1	1
	RAF Lakenheath, England	-	-	-	-	1	-	-	-	1
	Vilseck AHC, Germany	-	-	-	-	-	-	-	1	1
INDOPACOM	JR Marianas - Andersen AFB, Guam	-	-	-	-	-	-	-	1	1
	Misawa AB, Japan	-	-	-	-	-	-	-	1	1
Region 2	Ft Drum, NY	-	-	-	-	-	-	-	1	1
	USMA - West Point, NY	-	-	-	-	-	1	-	1	2
Region 4	Keesler AFB, MS	-	-	-	-	-	-	1	1	2
	NH Beaufort, SC	-	-	1	-	-	-	-	-	1
	Seymour Johnson AFB, NC	-	-	-	-	-	-	-	1	1
Region 5	Wright-Patterson AFB, OH	1	-	-	-	-	3	-	7	11
Region 6	Cannon AFB, NM	-	-	-	-	1	-	-	-	1
	Kirtland AFB, NM	-	-	-	-	-	-	-	2	2
	Little Rock AFB, AR	-	-	-	-	-	-	-	1	1
Region 8	Hill AFB, UT	-	-	-	-	-	-	-	1	1
	Minot AFB, ND	-	-	-	1	-	-	-	1	2
	USAF Academy, CO	-	-	-	-	-	2	-	-	2
Region 9	Davis-Monthan AFB, AZ	-	-	-	-	-	-	-	1	1
Region 10	Fairchild AFB, WA	-	-	-	-	-	-	-	2	2
Total		1	2	1	1	2	6	1	28	42

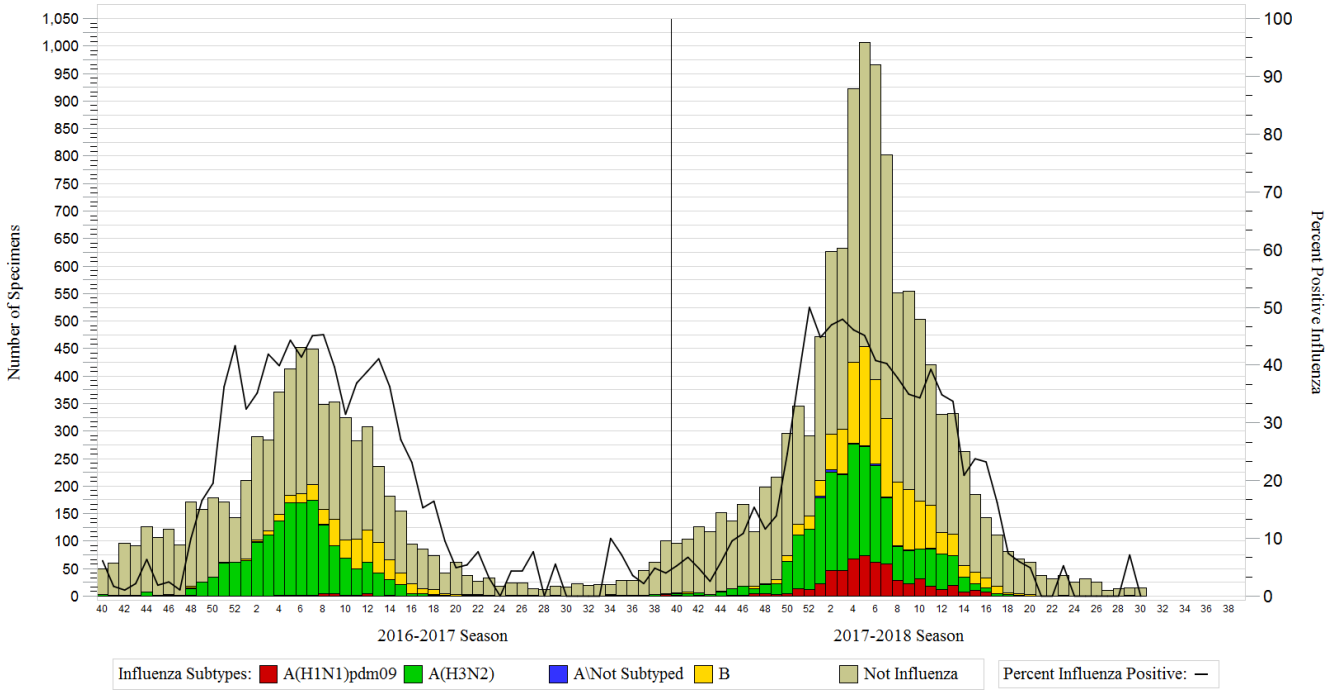
**CONUS locations are based on Health & Human Services regions. Other locations are defined by COCOM.*

DoD Global Respiratory Pathogen Surveillance Program

Cumulative Laboratory Results

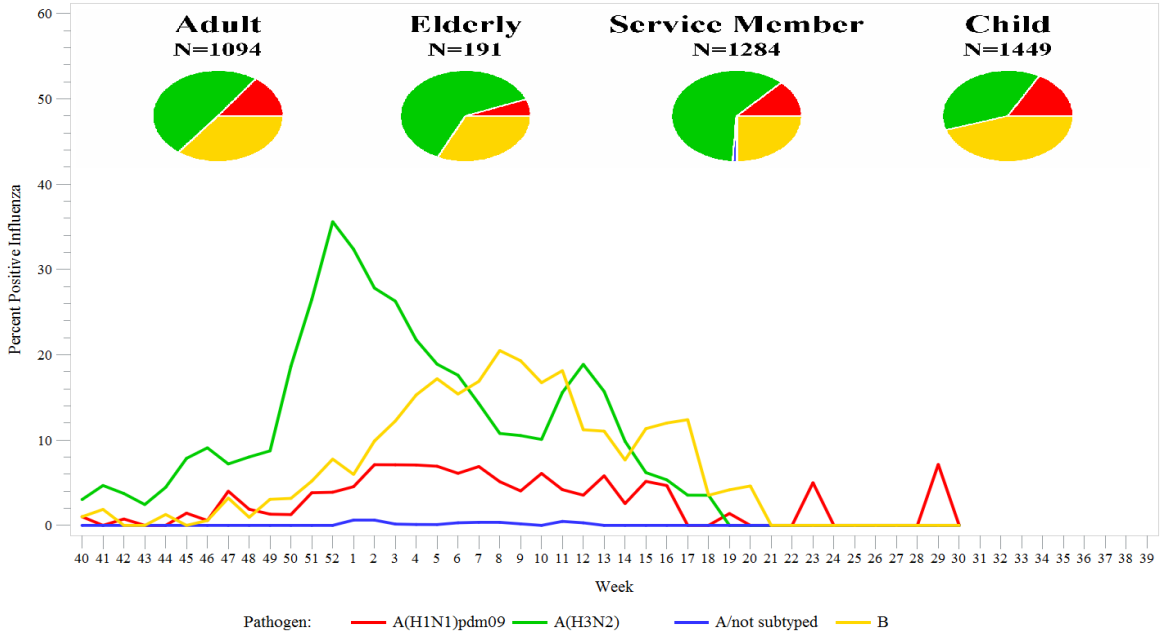
Link to cumulative results by region and location:

Graph 1. Percent influenza positive by week: 2016-2017 surveillance year and through Week 30 of the 2017-2018 surveillance year



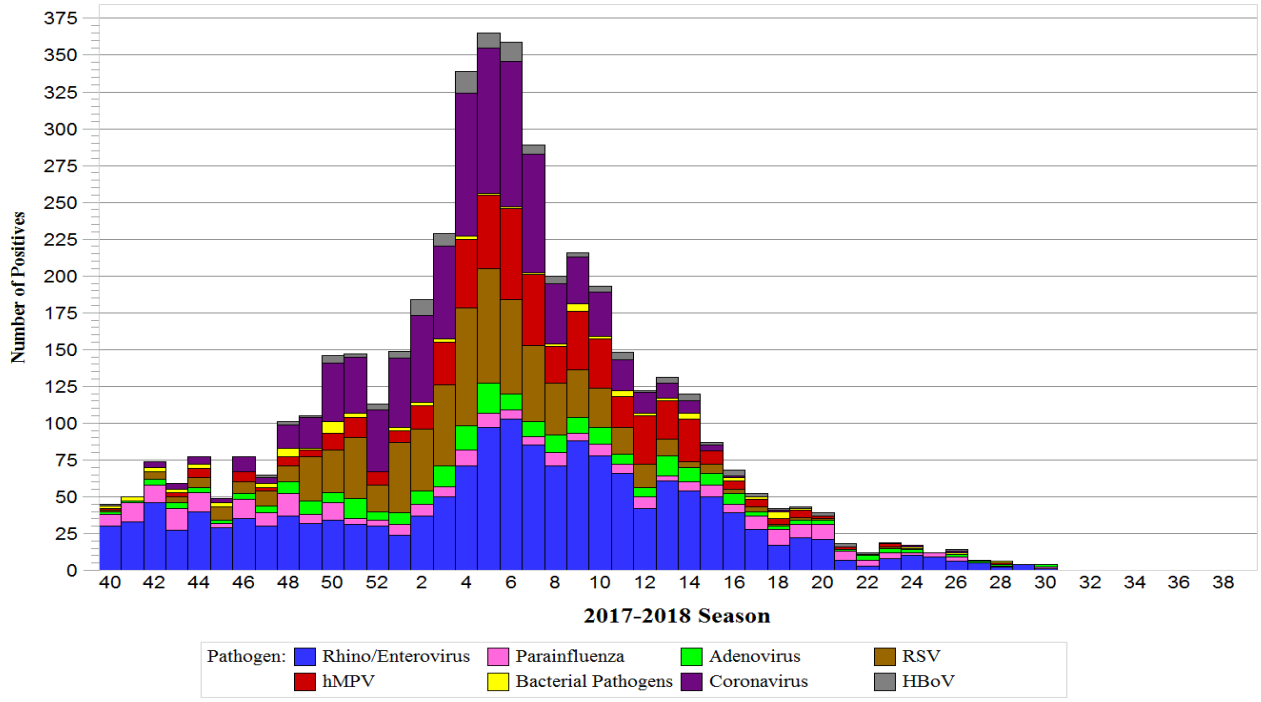
Note: Dual influenza coinfections are excluded from this graph.

Graph 2. Percent positive for influenza through ILI trends by subtype and beneficiary status through Week 30 of the 2017-2018 surveillance year

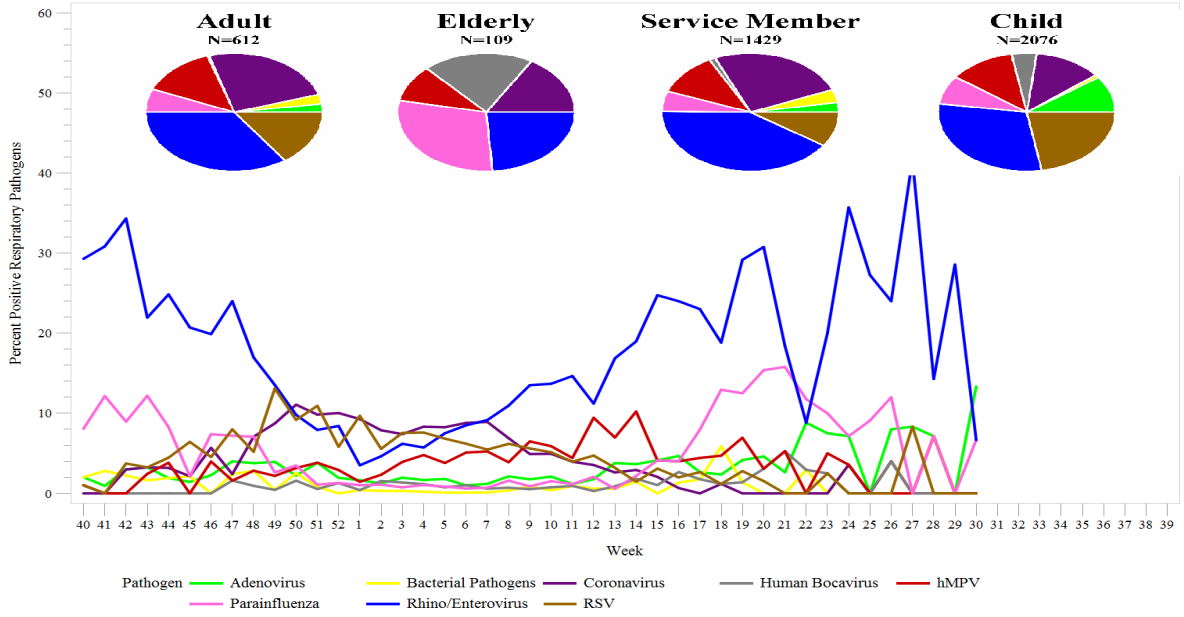


Note: Dual influenza coinfections are excluded from this graph.

Graph 3. Other positive respiratory pathogens through Week 30 of the 2017-2018 surveillance year



Graph 4. Percent positive for respiratory pathogens through ILI trends by week and beneficiary status through Week 30 of the 2017-2018 surveillance year



88ABW-2015-5508 and PA email guidance dated 10 November 2015.

Graph 5. Vaccination status by beneficiary type through Week 30 of the 2017-2018 surveillance year (excluding 'Unknown' beneficiary type)

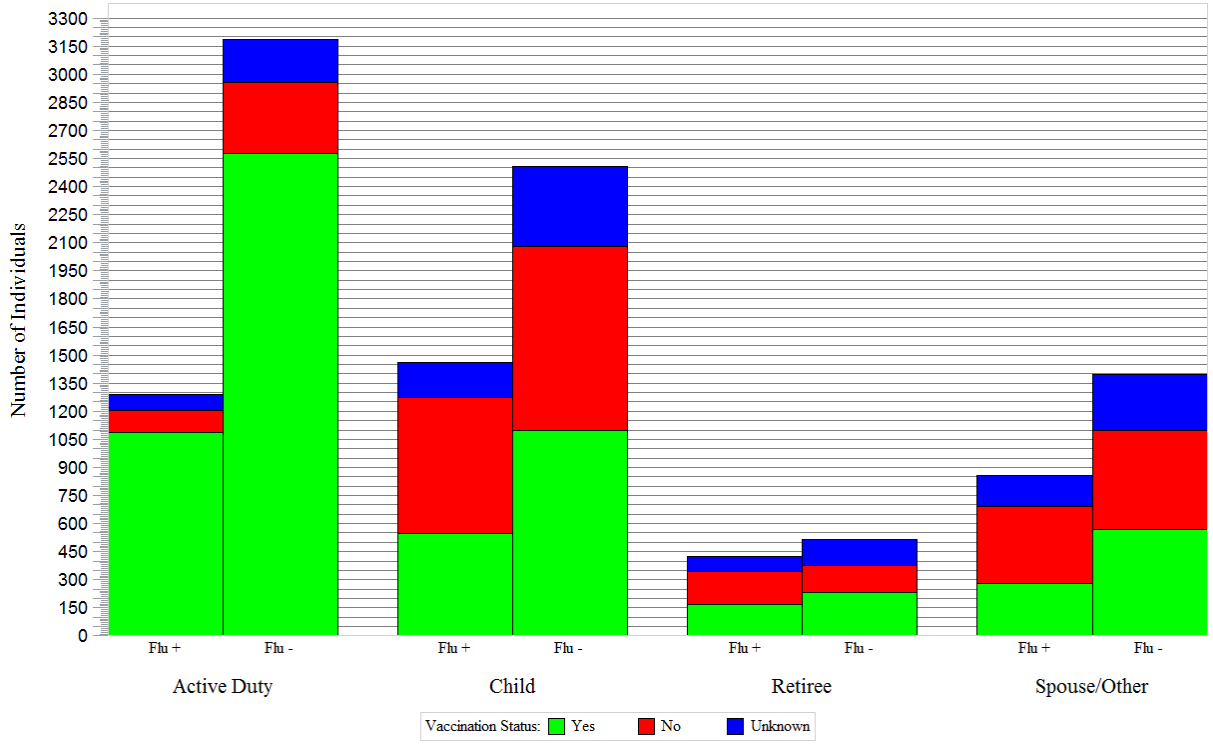
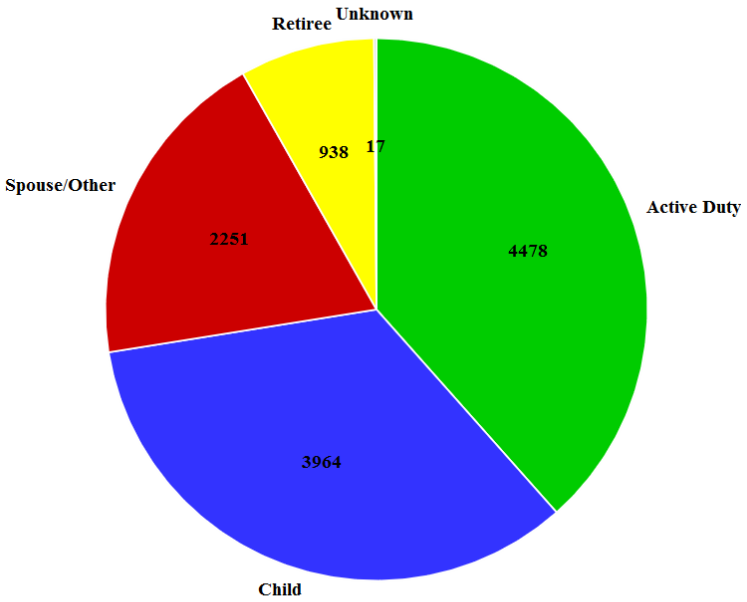


Table 2. ILI by age group through Week 30 of the 2017-2018 surveillance year

Age Group	Frequency	Percent
0-5	2301	19.75
6-9	761	6.53
10-17	974	8.36
18-24	1798	15.44
25-44	3756	32.25
45-64	1499	12.87
65+	559	4.80

Graph 6. ILI by beneficiary status through Week 30 of the 2017-2018 surveillance year

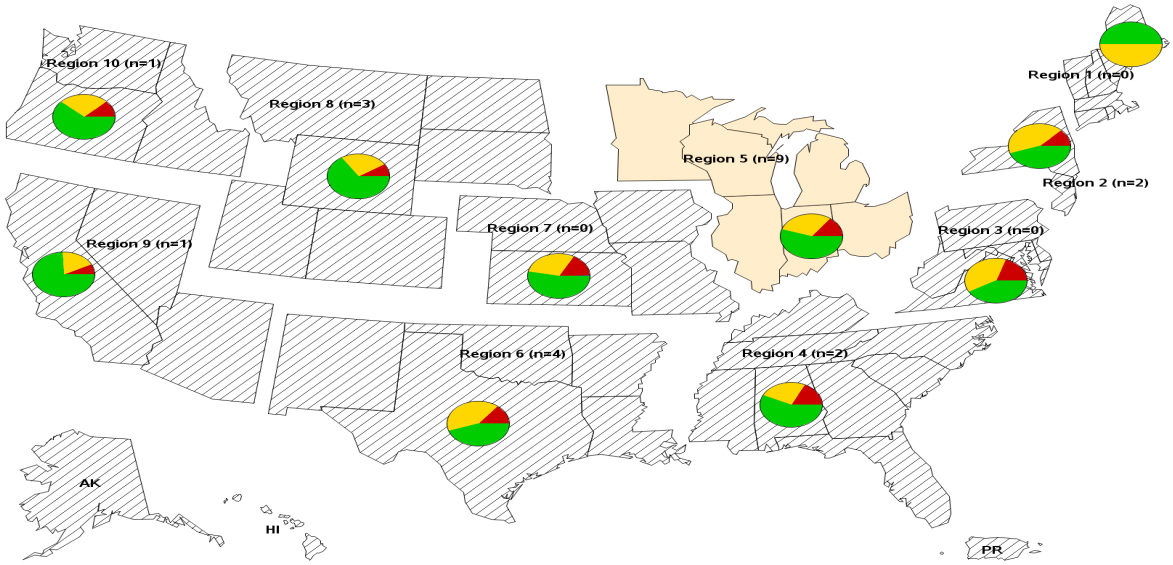


Demographic Summary

Of 11,648 ILI cases, 4,478 are service members (38.4%), 3,964 are children (34.0%), 2,251 are spouse/other beneficiaries (19.3%), 938 are retirees (8.1%), and 17 are unknown (0.2%). The median age of ILI cases with known age (n=11,648) is 24 (range 0, 98).

DoD Global Respiratory Pathogen Surveillance Program

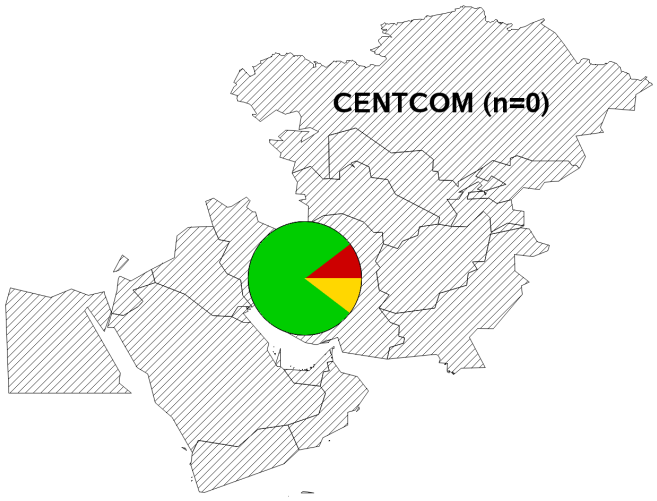
Map 1. Influenza subtypes and activity level by U.S. region through Week 30 of the 2017-2018 surveillance year



HI - Region 9
AK - Region 10

PR - Region 2

Map 2. Influenza subtypes and activity level for CENTCOM through Week 30 of the 2017-2018 surveillance year



Legend

Influenza Activity - Past 2 weeks

(n = # of submissions)

- No activity (0% +) or no submissions
- Low (<25% +)
- Moderate (25-49% +)
- High (>50% +)

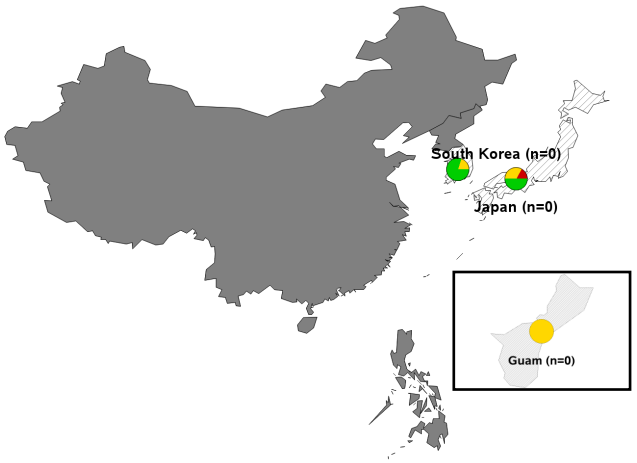
Influenza Results - Cumulative

- Influenza A(H3N2)
- Influenza A(H1N1)pdm09
- Influenza B
- Influenza A/not subtyped

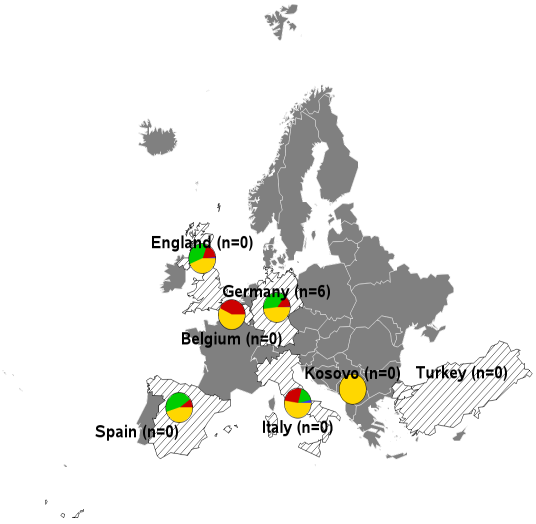
88ABW-2015-5508 and PA email guidance dated 10 November 2015.

DoD Global Respiratory Pathogen Surveillance Program

Map 3. Influenza subtypes and activity level by country through Week 30 of the 2017-2018 surveillance year (Pacific)



Map 4. Influenza subtypes and activity level by country through Week 30 of the 2017-2018 surveillance year (Europe)



Note - Countries shaded in gray do not contain submitting sites and are only displayed for geographical perspective.

Legend

Influenza Activity - Past 2 weeks

(n = # of submissions)

- No activity (0% +) or no submissions
- Low (<25% +)
- Moderate (25-49% +)
- High (>50% +)

Influenza Results - Cumulative

- Influenza A(H3N2)
- Influenza A(H1N1)pdm09
- Influenza B
- Influenza A/not subtyped

Table 3. Cumulative specimens submitted for sequencing only by location through Week 30 of the 2017-2018 surveillance year

Location	Number Received	Number Tested
Al Udeid AB, Qatar	1	0
Aviano AB, Italy	8	1
Brian Allgood ACH, South Korea	184	0
Camp Bondsteel, Kosovo	2	0
Ft Benning, GA	1	1
Ft Bliss, TX	7	1
Ft Bragg, NC	5	4
Ft Hood, TX	6	5
JB Elmendorf-Richardson, AK	2	2
Keesler AFB, MS	318	123
Landstuhl RMC, Germany	184	15
NAS Sigonella, Italy	23	0
NAVSTA Rota, Spain	13	1
NCRM - Walter Reed NMMC, MD	14	3
NMC Portsmouth, VA	11	0
NSA Naples, Italy	54	0
Nellis AFB, NV	1	1
RAF Lakenheath, England	44	8
Ramstein AB, Germany	55	3
SAMMC, TX	856	108
SHAPE, Belgium	12	1
Spangdahlem AB, Germany	3	0
Tripler AMC, HI	39	3
USAG Baumholder, Germany	13	1
USAG Grafenwoehr, Germany	48	0
USAG Hohenfels, Germany	1	0
USAG Kaiserslautern, Germany	32	0
USAG Stuttgart, Germany	61	4
USAG Vicenza, Italy	37	0
USAG Wiesbaden, Germany	41	1
Vilseck AHC, Germany	81	1
Total	**2157**	**287**

2017-2018 Influenza Sequence Analysis Report #8

This is the eighth USAFSAM influenza sequence surveillance report for the 2017-2018 influenza season. Of the specimens sequenced during this reporting period, results were finalized for 65 specimens with collection dates between 19 December 2017 and 27 May 2018. Among those tested, 42 specimens were sequenced at USAFSAM, 14 sequences were contributed by the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Thailand, and nine sequences were contributed by the Navy Medical Research Unit 2 (NAMRU-2) in Cambodia. For the 2017-2018 influenza season, 1,007 sequencing specimens have been reported.

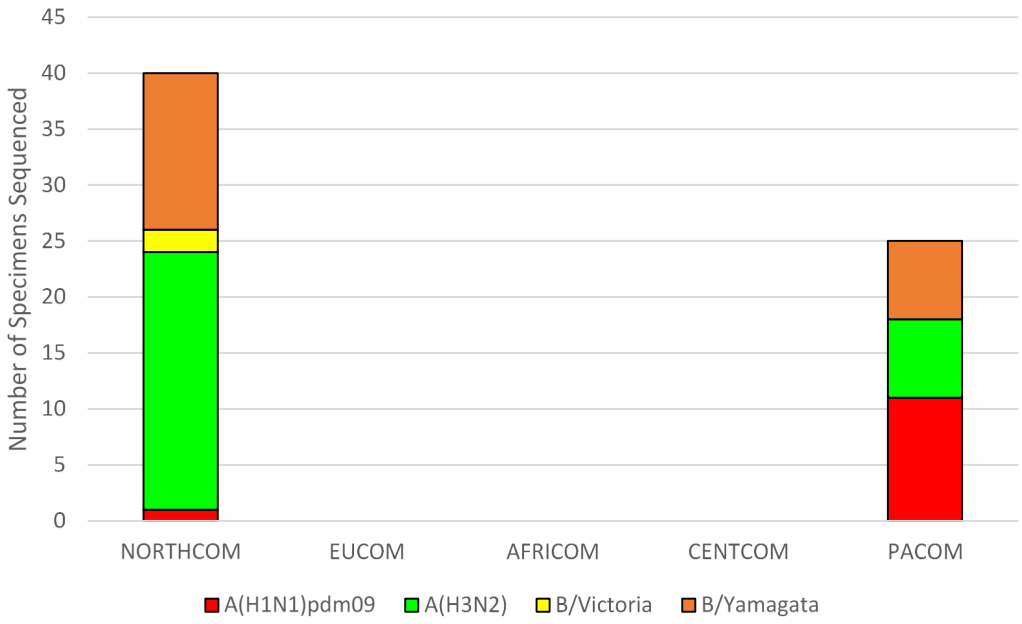


Figure 1: Total influenza sequences from each of the United States Combatant Commands analyzed for this report.

Table 4: Distribution of CONUS and OCONUS sentinel sites that contributed influenza specimens or sequences for this report.

	A(H1N1)pdm09	A(H3N2)	B/Victoria	B/Yamagata
CONUS				
Arkansas				
Little Rock AFB				1
California				
Travis AFB				1
Colorado				
USAF Academy		1		
Delaware				
Dover AFB			1	1
Illinois				
Scott AFB		1		
Maryland				
JB Andrews				1
NCRM - Walter Reed NMMC		1		
New Jersey				
JB McGuire-Dix-Lakehurst				1
New Mexico				
Kirtland AFB				1
New York				
Ft Drum		1		1
USMA - West Point		1		1
North Carolina				
Ft Bragg			1	
Ohio				
Wright-Patterson AFB		3		2
Oklahoma				
Altus AFB				1
Tinker AFB		1		
South Dakota				
Ellsworth AFB	1			1
Texas				
JBSA Lackland		1		1
SAMMC		11		
Utah				
Hill AFB		1		1
Virginia				
JB Langley-Eustis		1		
OCONUS				
Cambodia				
NAMRU-2	4			5
Japan				
Yokota AB		1		
South Korea				
Kunsan AB		1		

	A(H1N1)pdm09	A(H3N2)	B/Victoria	B/Yamagata	Total
Thailand					
AFRIMS	7	5		2	14
Total	**12**	**30**	**2**	**21**	**65**

The Hemagglutinin (HA) gene from select influenza positives was sequenced using dye terminator, Sanger-based methods. Preliminary data are based on the sequence analysis of the hemagglutinin gene. Antigenic sites, receptor binding sites and glycosylation motifs are predicated upon correlations with previously published experimental evidence.[1-3] Sequence data was constructed and analyzed using multiple software programs. Genetic and predicted antigenic information that resulted from this analysis is shared with United States Centers for Disease Control and Prevention (CDC), World Health Organization (WHO) and contribute to the seasonal Northern and Southern Hemisphere vaccine component selections.

Table 5: Cumulative protein homologies (percent amino acid match) of 2017-2018 influenza strains relative to vaccine strains. The influenza A(H1N1)pdm09 vaccine strain was changed from A/California/07/2009-like virus to A/Michigan/45/2015-like virus for the 2017-2018 season. *Quadrivalent only.

Subtype or Lineage	Vaccine Component (clade)	Min	Max	Average
A(H1N1)pdm09	A/Michigan/45/2015-like (6B.1)	98.4%	99.5%	98.9%
A(H3N2)	A/Hong Kong/4801/2014-like (3C.2a)	96.7%	99.1%	98.3%
B/Victoria	B/Brisbane/60/2008-like (V1A)	98.2%	99.5%	98.7%
B/Yamagata	B/Phuket/3073/2013-like (Y3)*	98.8%	99.5%	99.3%

Influenza A(H1N1)pdm09

- Among the 42 influenza A HA sequences, 12 (28.6%) were influenza A(H1N1)pdm09. The influenza A(H1N1)pdm09 sequences are characterized in a neighbor-joining phylogenetic tree with reference strains rooted from the previous vaccine strain, A/California/07/2009 [**Figure 2**].
- The influenza A(H1N1)pdm09 sequences characterized for this report exhibited an overall protein homology of 98.5 – 99.3% (average 99.0%) compared to the 2017-2018 influenza vaccine component, A/Michigan/45/2015-like virus. The cumulative A(H1N1)pmd09 protein homology for the season (N = 165) is 98.4-99.5% (average 98.9%) [**Table 5**].
- All influenza A(H1N1)pdm09 HA sequences contained mutations consistent with the dominating subgroup referred to as clade 6B and could all be further classified as subclade 6B.1.
- Gain or loss of *N*-linked glycosylation sites has been shown to alter HA protein surface topology. A gain in glycosylation could be advantageous to the virus by virtue of a masking effect on important antibody recognition sites, thus potentially modulating viral antigenicity.[4] Observations are based solely on sequence motifs. For the influenza A(H1N1)pdm09 HA sequences characterized in this report, one mutation, S162N (serine to asparagine), was observed that caused a gain of a glycosylation motif.

- Among the 26 influenza A(H1N1)pdm09 amino acid residues that had mutations, nine occurred at antigenic sites (one at site A, one at site B, two at site C, two at site D, and three at site E) and two occurred at the receptor binding site.

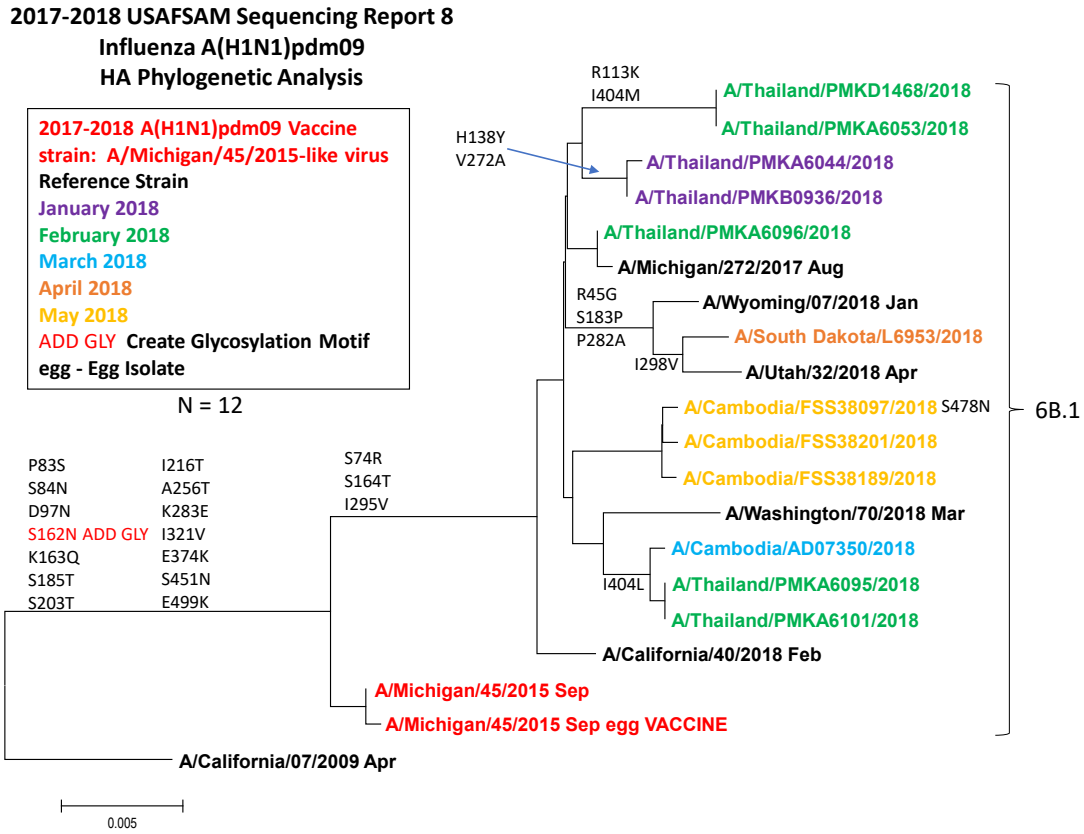


Figure 2: 2017-2018 USAFSAM Report 8 influenza A(H1N1)pdm09 HA phylogenetic analysis. Twelve influenza A(H1N1)pdm09 sequences collected between January 2018 and May 2018 were sequenced and all resided in clade 6B.1, with one shared addition of a glycosylation motif. The vaccine strain A/Michigan/45/2015-like virus was selected again for the 2018-2019 vaccine influenza A(H1N1)pdm09 component.

Influenza A(H3N2)

- Among the 42 influenza A HA sequences, 30 (71.4%) were influenza A(H3N2). The influenza A(H3N2) HA sequences are characterized in a neighbor-joining phylogenetic tree with reference strains rooted from a previous vaccine strain, A/Texas/50/2012 [**Figure 4**].

- The influenza A(H3N2) HA sequences characterized for this report have exhibited an overall protein homology of 97.5 – 98.7% (average 98.1%) compared to the 2017-2018 influenza vaccine component, A/Hong Kong/4801/2014-like virus and 96.9 – 98.5% (average 97.7%) compared to the selected 2018-2019 influenza vaccine A(H3N2) component, A/Singapore/INFIMH-16-0019/2016-like virus. The cumulative protein homology for the season (N = 527) is 96.7 – 99.1% (average 98.3%) as compared to A/Hong Kong/4801/2014-like virus [**Table 5**].

- Twenty-three of the influenza A(H3N2) viruses sequenced for this report were in clade 3C.2a (76.7%) with six (20.0% of total) in clade 3C.2a1b, 16 (53.3% of total) in 3C.2a2, and one (3.3% of total) in 3C.2a3. The remaining seven sequences resided in clade 3C.3a (23.3% of total).

- Among the influenza A(H3N2) HA sequences characterized in this report, four mutations; T135K, N144S, N158S, and T160K, were observed that caused the loss of a glycosylation motif. Four other mutations, A128T, N128T, K160T, and K207N were observed that caused the gain of a glycosylation motif. One additional mutation, T135N, caused a loss of a glycosylation motif at site 133 and the simultaneous gain of a motif at site 135.

- Among the 39 influenza A(H3N2) amino acid residues that had mutations, 14 occurred at antigenic sites (four at site A, four at site B, none at site C, one at site D, and five at site E) and two occurred at the receptor binding site.

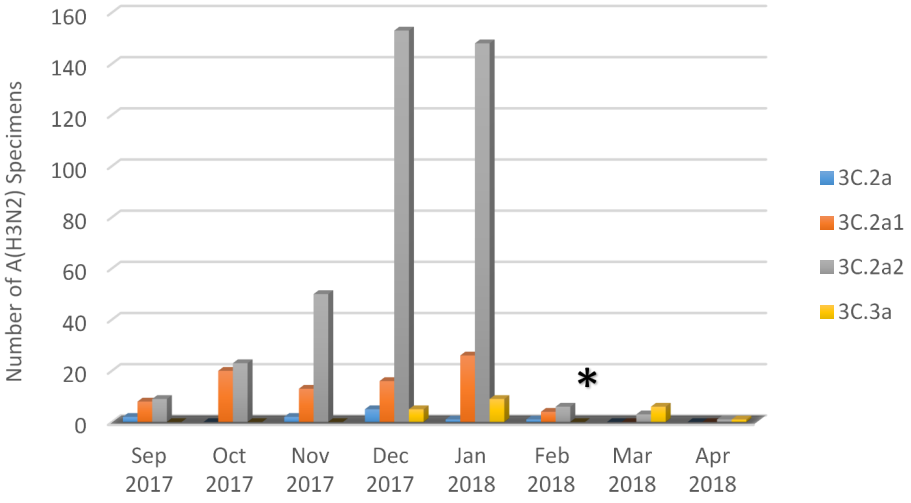


Figure 3: Cumulative proportion of influenza A(H3N2) clades among specimens collected from September 2017 through April 2018 (N = 527). Subclade 3C.2a1 was the dominant A(H3N2) genetic group throughout the 2016-2017 season but declined prior to the start of the 2017-2018 season as clade 3C.2a increased in prevalence. A new subclade of 3C.2a, 3C.2a2, was recently described as well as two new subclades of 3C.2a1, 3C.2a1a and 3C.2a1b (not shown). * - Not all specimens from February-April have been sequenced as of this report, therefore this figure is not indicative of a decline in influenza A(H3N2) in February-March 2018.

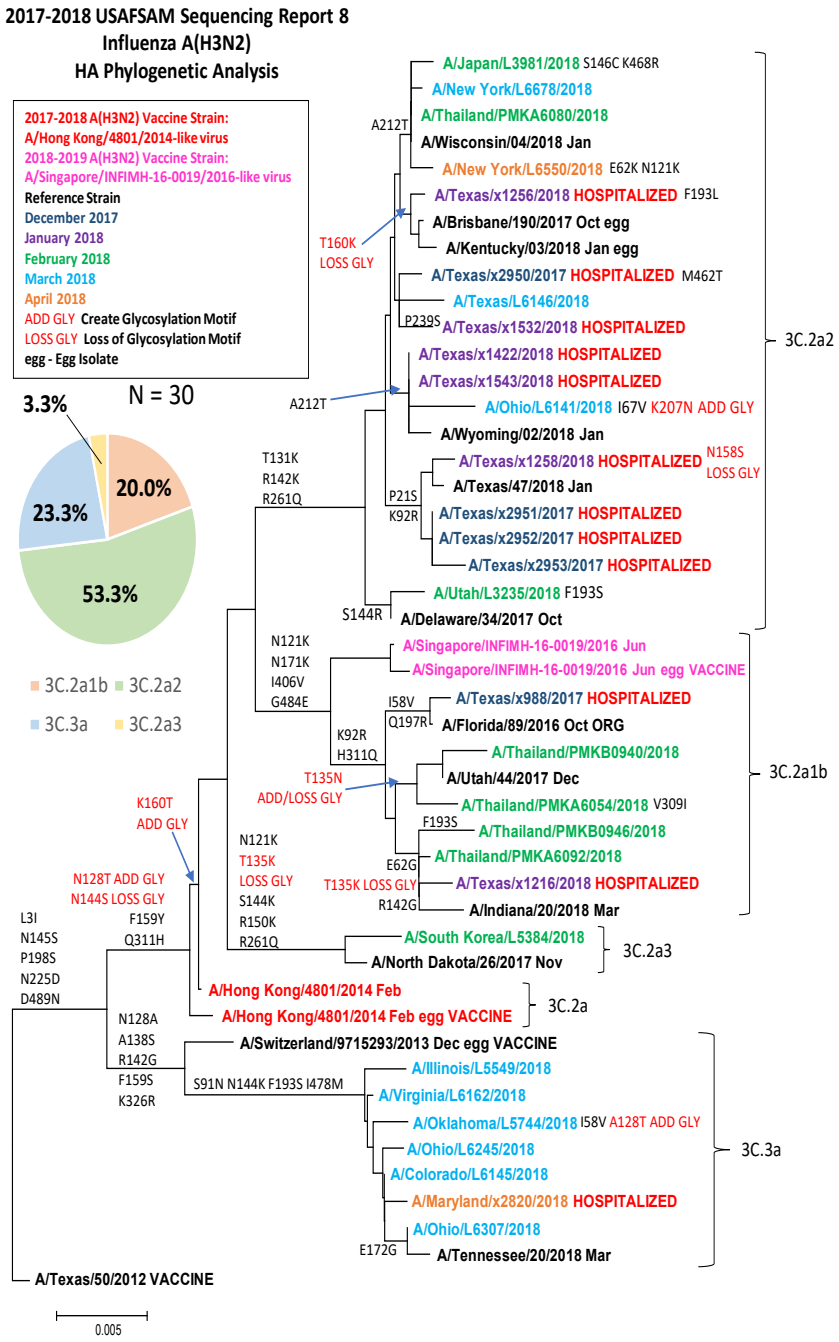


Figure 4: 2017-2018 USAFSAM Report 8 influenza A(H3N2) HA phylogenetic analysis. Thirty influenza A(H3N2) specimens collected between December 2017 and April 2018 were sequenced, of which the majority resided in clade 3C.2a2 (53.3%). Four mutations caused the loss of glycosylation motifs and four mutations caused the gain of glycosylation motifs, while one mutation caused a simultaneous loss and gain at adjacent sites. The selected strain for the influenza A(H3N2) component of the 2018-2019 influenza vaccine is A/Singapore/INFIMH-16-0019/2016-like virus, shown in pink.

Influenza B

- The distinguishing characteristic between the two influenza B lineages is defined by an amino acid deletion in viruses belonging to the B/Yamagata lineage.[1] Twenty-one (91.3%) of the 23 influenza B specimens characterized in this report fell into the B/Yamagata lineage and the remaining two (8.7%) fell into the B/Victoria lineage.

- The influenza B/Victoria HA sequences are characterized in a lineage specific, neighbor-joining phylogenetic tree with reference strains and are rooted from the current vaccine strain B/Brisbane/60/2008-like virus [**Figure 5**].

- The influenza B/Victoria sequences characterized for this report exhibited a protein homology of 98.4% when compared to the 2017-2018 B/Victoria vaccine component, B/Brisbane/60/2008-like virus and 99.1% when compared to the selected 2018-2019 influenza vaccine B/Victoria component, B/Colorado/06/2017-like virus. The cumulative protein homology for the season (N = 75) is 98.2 – 99.5% (average 98.7%) [**Table 5**].

- Both of the influenza B/Victoria sequences displayed a two amino acid deletion at positions 162-163, designated clade V1A.1 and shared the mutations D129G, I180V, and R498K and also the addition of a glycosylation motif resulting from the mutation S/T197N.

- The influenza B/Yamagata HA sequences are characterized in a lineage specific, neighbor-joining phylogenetic tree with reference strains and are rooted from the previous vaccine seed strain B/Massachusetts/02/2012 [**Figure 6**].

- The influenza B/Yamagata sequences characterized for this report exhibited a protein homology of 98.8 – 99.5% (average 99.4%) when compared to the 2017-2018 B/Yamagata vaccine component, B/Phuket/3073/2013-like virus. The cumulative protein homology for the season (N = 240) is 98.8 – 99.5% (average 99.3%) [**Table 5**].

- All of the B/Yamagata sequences fell into clade Y3 and there was one mutation, D232N that resulted in the addition of a glycosylation motif.

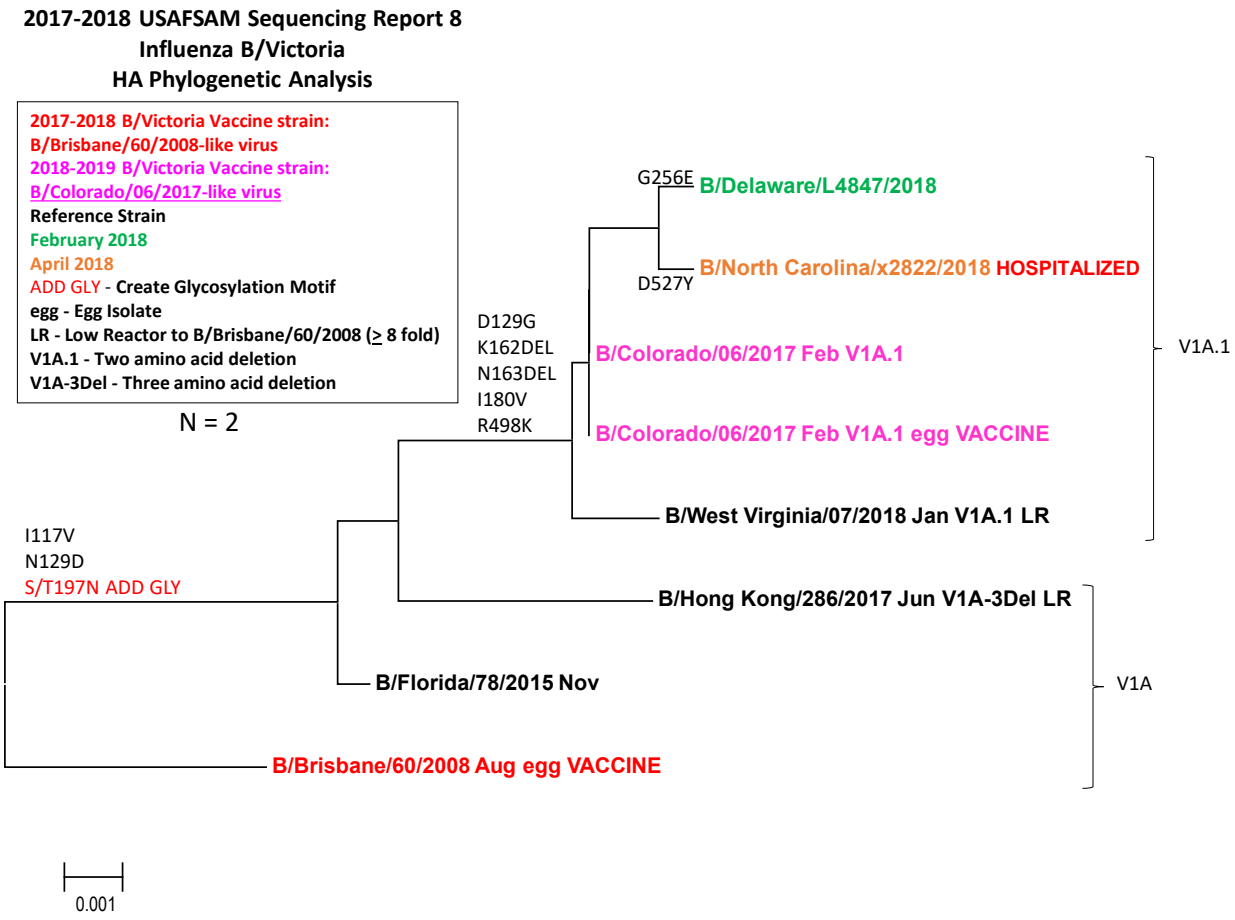


Figure 5: 2017-2018 USAFSAM Report 8 influenza B/Victoria phylogenetic analysis. Two influenza B/Victoria specimens were collected in February 2018 and April 2018 and resided in clade V1A.1, with deletions of amino acid positions 162-163 and the mutations N129G, I180V, and R498K. The selected strain for the B/Victoria component of the 2018-2019 influenza vaccine is B/Colorado/06/2017-like virus, colored in pink.

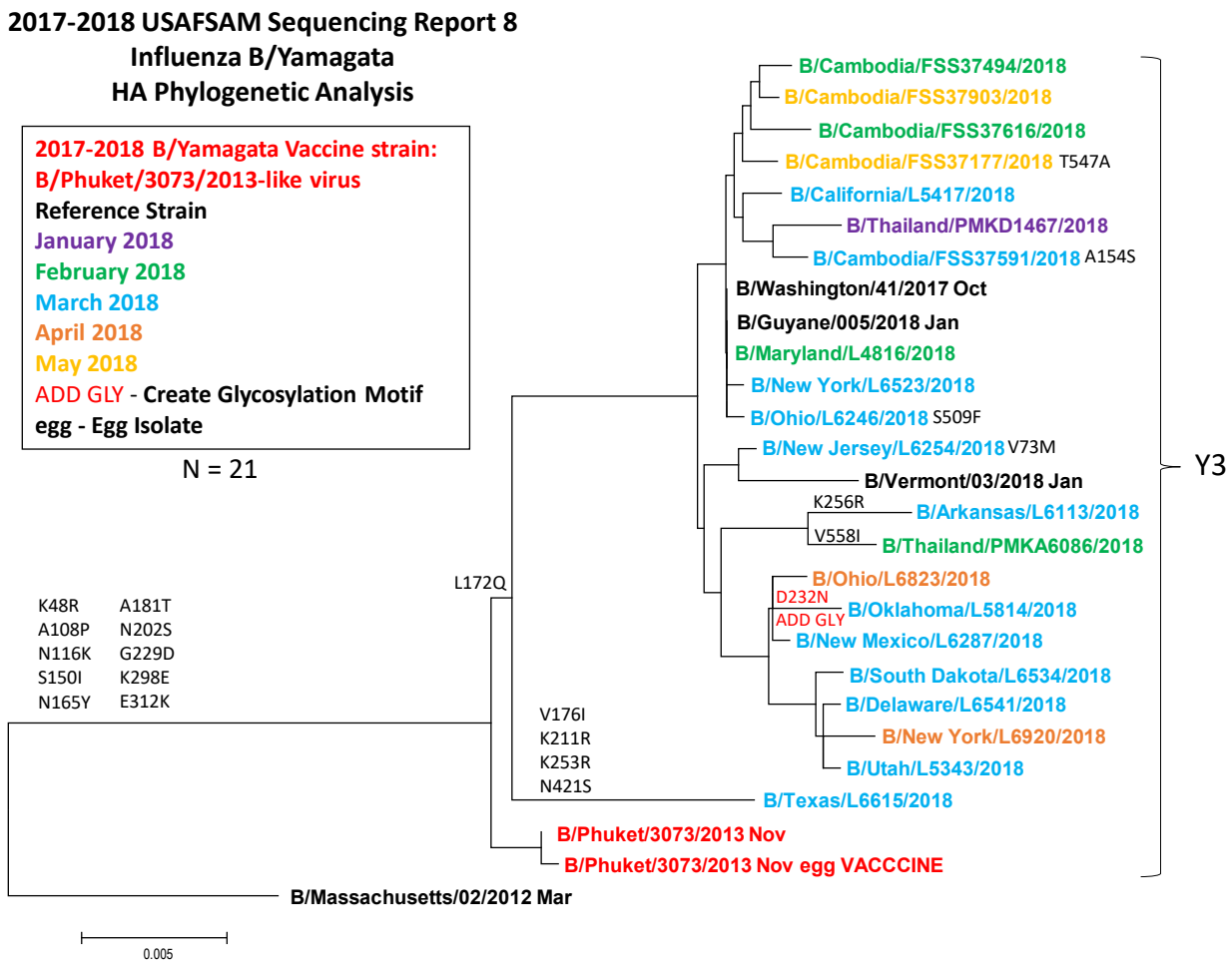


Figure 6: 2017-2018 USAFSAM Report 8 influenza B/Yamagata phylogenetic analysis. Twenty-one influenza B/Yamagata specimens collected between January 2018 and May 2018 were sequenced and all resided in clade Y3, with one addition of a glycosylation motif. The vaccine strain B/Phuket/3073/2013-like virus was selected again as the B/Yamagata component of the 2018-2019 influenza vaccine, to be included in the quadrivalent formulation only, colored in pink.

References:

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USAF School of Aerospace Medicine & Defense Health Agency

DoD Global Respiratory Pathogen Surveillance Program

Background

The DoD-wide program was established by the Global Emerging Infections Surveillance and Response System (GEIS) in 1997. The surveillance network includes the Defense Health Agency/Armed Forces Health Surveillance Branch—Air Force Satellite Cell (DHA/AFHSB-AF) and U.S. Air Force School of Aerospace Medicine (USAFSAM) (sentinel site respiratory surveillance), the Naval Health Research Center (recruit and shipboard population-based respiratory surveillance), the Naval Medical Research Unit (NAMRU-3) in Cairo, Egypt, the Naval Medical Research Unit (NAMRU-2) in Phnom Penh, Cambodia, the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok, Thailand, the Naval Medical Research Unit (NAMRU-6) in Lima, Peru, and the United States Army Medical Research Unit-Kenya (USAMRU-K) located in Nairobi, Kenya. This work is supported by the Air Force and GEIS Operations, a Division of the Armed Forces Health Surveillance Branch (AFHSB).

Sentinel Site Surveillance

In 1976, the U.S. Air Force Medical Service began conducting routine, global, laboratory-based, influenza surveillance. Air Force efforts expanded to DoD-wide in 1997. DHA/AFHSB-AF and USAFSAM manages the surveillance program that includes global surveillance among DoD beneficiaries at 79 sentinel sites (including deployed locations) and many non-sentinel sites (please see map below). Collaborating partner laboratories include five DoD overseas medical research laboratories (AFRIMS, NAMRU-2, NAMRU-3, NAMRU-6, USAMRD-K) who collect specimens from local residents in surrounding countries that may not otherwise be covered in existing surveillance efforts. Additionally, the Naval Health Research Center (NHRC) in San Diego, CA collects specimens from DoD recruit training centers and conducts surveillance along the Mexico border.

Landstuhl Regional Medical Center (LRMC) and Tripler Army Medical Center (TAMC) assist the program by processing DoD specimens for the EUCOM region and the State of Hawaii, respectively. EUCOM respiratory data is obtained from LRMC and incorporated into our weekly report. This process seeks to provide more timely results and efficient transport of specimens.

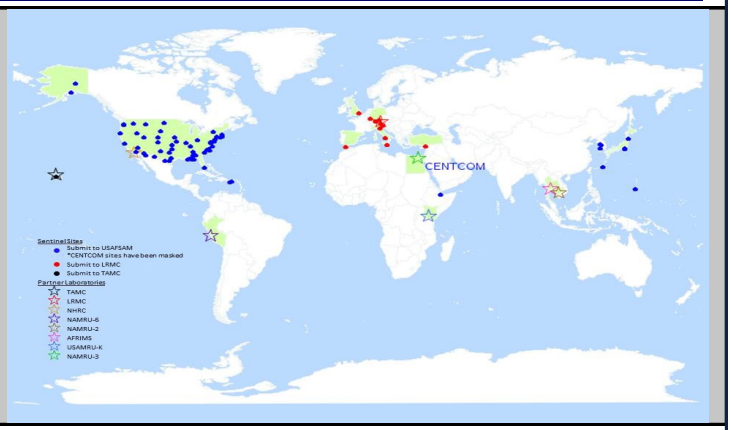
Available on our website (listed below) is a list of previous weekly surveillance reports, program information (including an educational briefing and instruction pamphlets for clinic staff), and a dashboard containing respiratory data for our sentinel sites.

Errata:

For Public Health Services
937-938-3196; DSN 798-3196

For Laboratory Services
937-938-4140; DSN 798-4140

USAFSAM.PHRFlu@us.af.mil



Collaborating Partners

In addition to all participating DoD military sentinel sites, collaborating laboratories and medical centers (described above) may be further understood by reviewing the sites' website. Click on the sites' icon to be directed to their webpage.

88ABW-2015-5508 and PA email guidance dated 10 November 2015.