



OFFLU Swine Influenza Virus technical meeting

27 – 28 February 2019

OIE Headquarters, Paris, France

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Influenza Division,

Centers for Disease Control and Prevention

Updated surveillance data and research activities since April 2018

- Human cases of H1 and H3 variant influenza A viruses in the USA
- Human cases internationally
- Emerging swine influenza virus lineages
- Population immunity

Updated surveillance data and research activities since April 2018

Strains of concern:

- H3N2v

H3N2v

Summary of human infections with influenza A(H3N2)v

Country	Subtype	State	Age (yrs)	Sex	Onset date	Outcome	Exposure	Confirmed/ Reported	Isolate available	HI test date	Strain name
USA	H3N2v (human-like)	IN	9y	F	6/19/2018	Recovered	Exposure to swine	CDC, USA	yes	07/12/2018	A/Indiana/27/2018

Genome Comparisons of H3N2v 2005-2018



Evolutionary Relationships Among Influenza A(H3N2)v HA, 2018

H3N2v vaccine candidate in red

CDC H1 reference viruses in blue

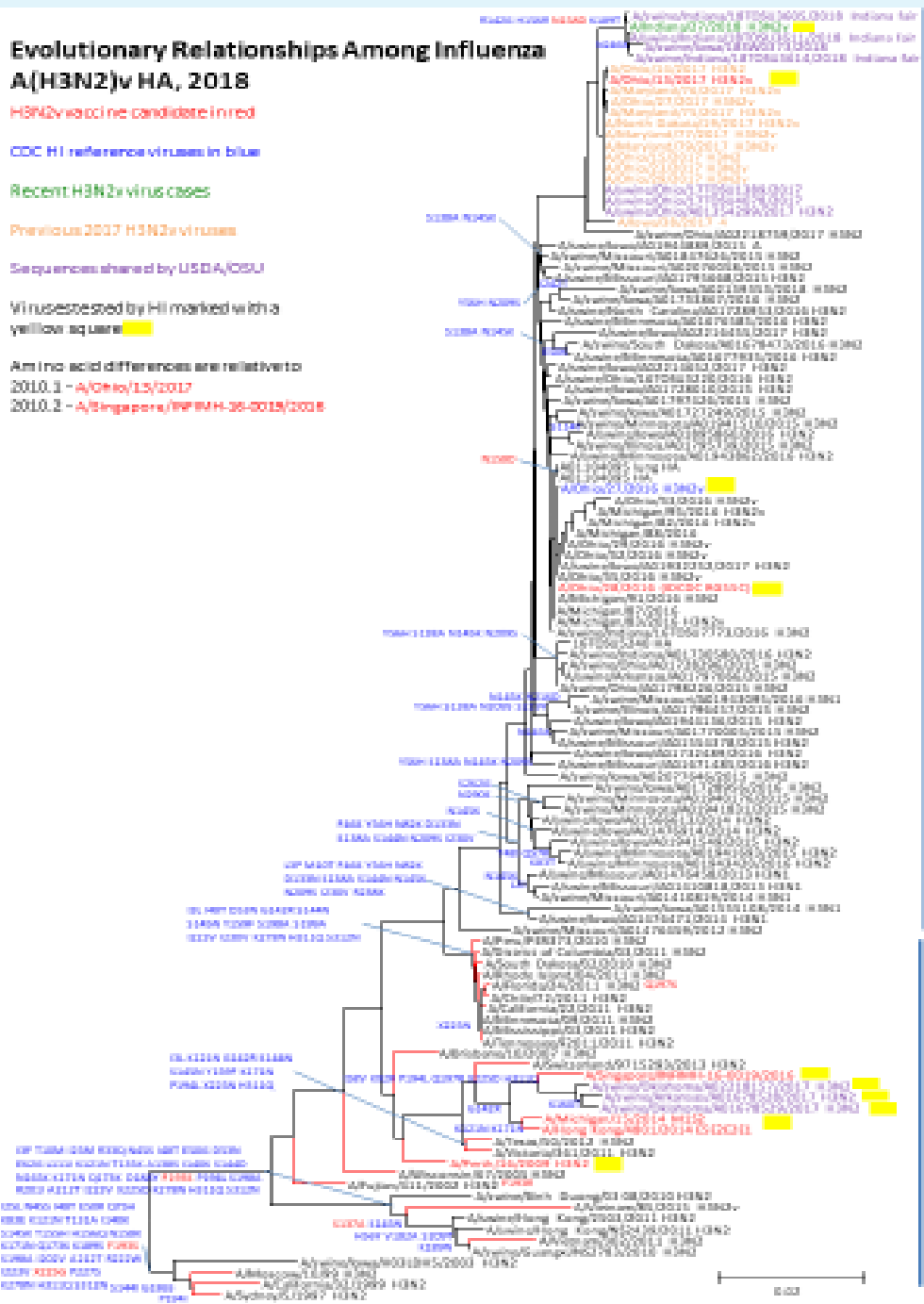
Recent H3N2v virus cases

Previous 2007 H3N2v viruses

Sequences shared by USDA/USU

Viruses tested by HI marked with a yellow square

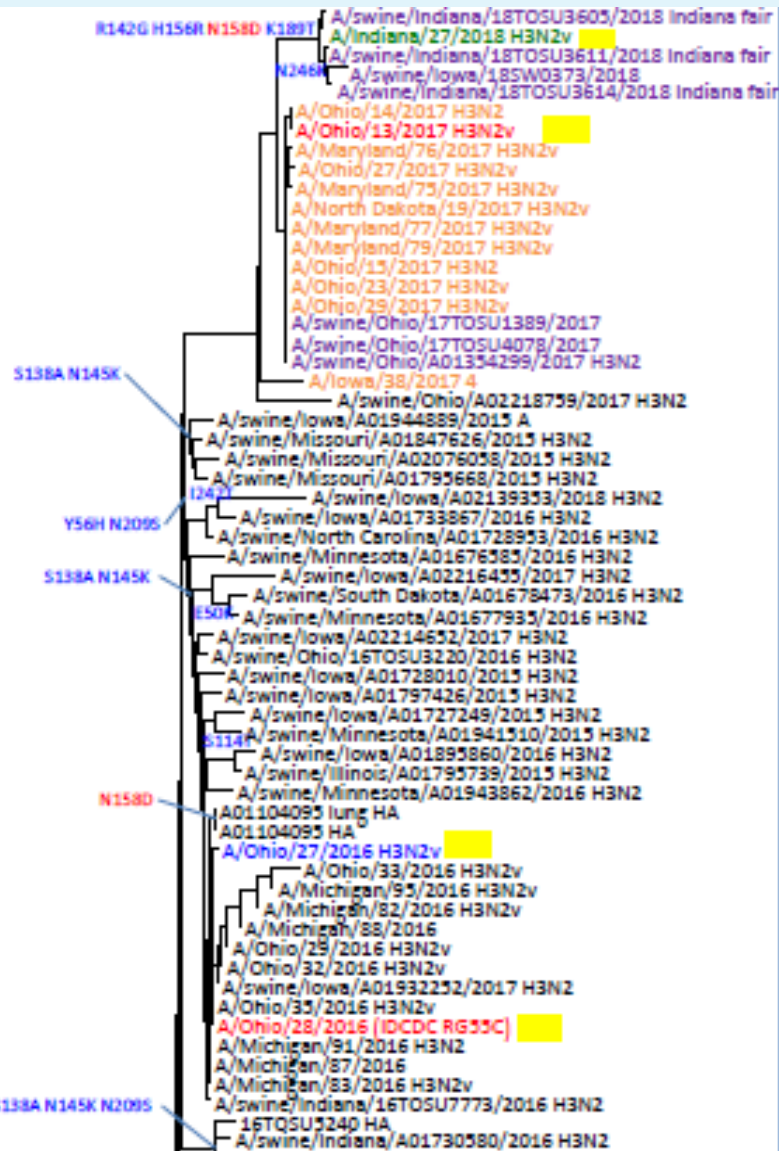
Amino acid differences are relative to 2010.1 - A/Ohio/15/2017
 2010.2 - A/Syngenta/99/04H-30-0018/2008



Seasonal human-like H3 (2010.1)

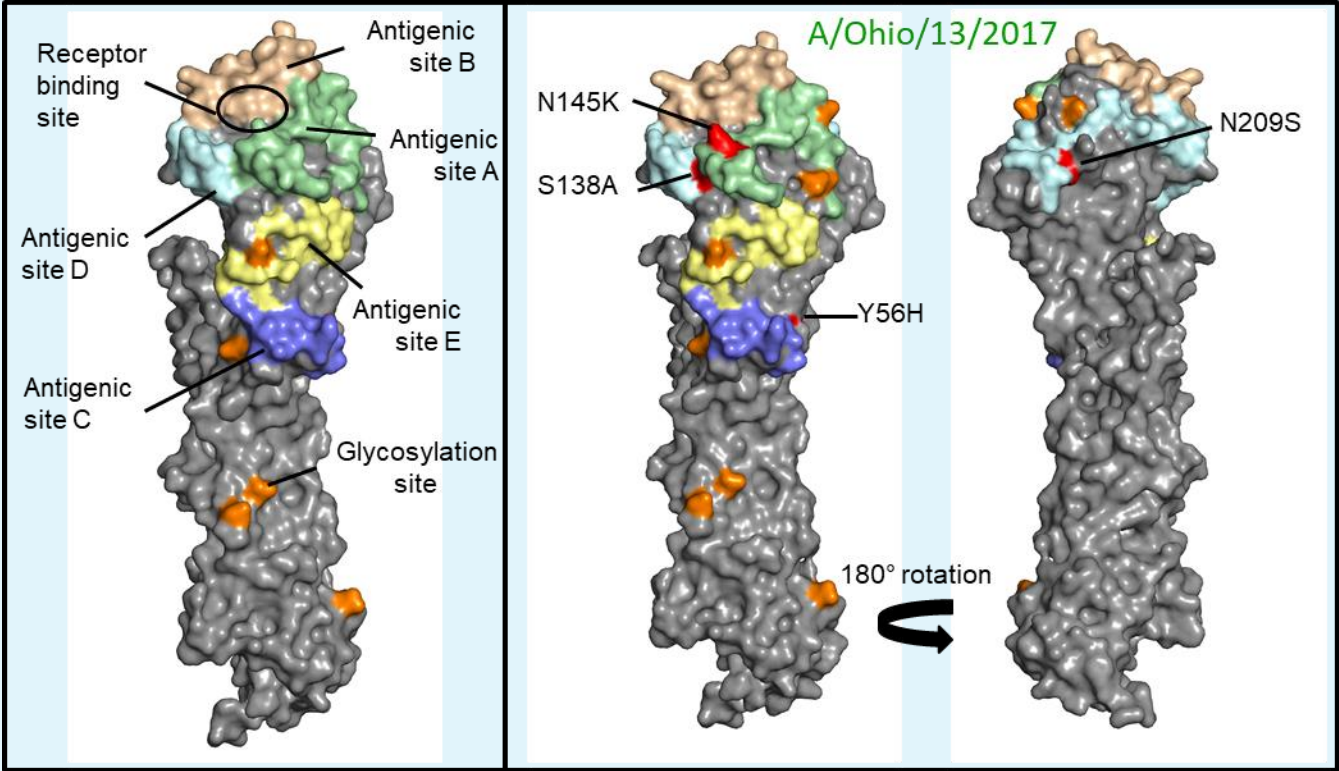
Seasonal human H3 (2010.2)





Seasonal human-like H3 (2010.1)

2017 H3N2v '2010 human-like' hemagglutinin changes compared to A/Ohio/28/2016 CVV



		Reference Antisera													
		Seas	Seas	Seas	IV-A	IV-A	2010.1	2010.1	2010.1						
		59414852	2015-032	2018-012	2017-034	2017-032	2016-115	2017-047	2017-117	17/18	17/18				
REFERENCE ANTIGENS		Perth/16	MI/15	Sing	MN/11	MN/11	OH/27	RG55C	OH/13	Child pool#	Adult Pool*	MN/11	MN/11	PASSAGE	
						X203						Adult ^	Elderly &		
1	A/Perth/16/2009	Seas	<u>80</u>	320	80	<20	<20	80	20	80	1280	640	320	640	E3/E3 (2/29/2016)
2	A/Michigan/15/2014	Seas	80	<u>640</u>	320	<20	<20	20	<20	80	1280	320	320	640	M1/S2(10/19/17)
3	A/Singapore/INFIMH-16-0019/2016	Seas	40	160	<u>640</u>	<20	<20	<20	<20	<20	1280	80	80	160	E5/E2(8/1/18)
4	A/Minnesota/11/2010	IV-A	80	<20	<20	<u>2560</u>	2560	40	20	<20	80	80	1280	1280	E2(7/22/13)
5	A/Minnesota/11/2010 X-203	IV-A	160	40	40	2560	<u>2560</u>	<20	20	<20	80	80	1280	1280	EX/E1 (2/25/11)
6	A/Ohio/27/2016	2010.1	640	20	20	<20	<20	<u>5120</u>	2560	1280	80	160	320	640	C1S2 (10/3/16)
7	A/Ohio/28/2016 IDCDC RG55C	2010.1	80	<20	<20	<20	<20	2560	<u>1280</u>	320	40	160	160	320	V1E3 (5/25/17)
8	A/Ohio/13/2017	2010.1	1280	40	20	40	<20	640	160	<u>2560</u>	80	320	320	640	C1(2/13/18)
TEST ANTIGENS															
9	A/Indiana/27/2018	2010.1	160	40	<20	40	20	80	80	1280	40	160	640	320	S1(7/1/18)
10	VPT 18-v68.1 (A/Ohio/13/2017-like)	2010.1	640	80	160	80	<20	320	160	1280	80	160	320	320	p1E3(8/17/18)
12	A/swine/Oklahoma/A02218157/2017	2010.2	640	640	<u>640</u>	80	<20	640	80	1280	1280	640	1280	1280	C1/C1(6/28/18)
13	A/swine/Arkansas/A01678528/2017	2010.2	80	80	<u>160</u>	<20	<20	80	20	160	1280	320	320	320	C1
14	A/swine/Oklahoma/A01678529/2017	2010.2	ND	ND	<u>160</u>	ND	ND	ND	ND	ND	ND	ND	ND	ND	C1
#2017-2018 post-vaccine immune serum pool from child (0-3 yrs) vaccinees (A/Hong Kong/4801/2014 vaccine)															
*2017-2018 post-vaccine immune serum pool from adult (19-49 yrs) vaccinees (A/Hong Kong/4801/2014 vaccine)															
^post-vaccine immune serum pool from adult (19-49 yrs) vaccinees (A/Minnesota/11/2010 vaccine)															
&post-vaccine immune serum pool from elderly vaccinees (A/Minnesota/11/2010 vaccine)															

									NEW	NEW	NEW	NEW
			Seas	Seas	Seas	2010.1	2010.1	2010.1		2010.2		
			59414852	2018-012	2019-001	2017-047	2017-117	2019-011	2019-012	2018-105	2018-106	
REFERENCE ANTIGENS			Perth/2009	Sing/2016	Switz/2017	RG55C	OH/2017	IN/2018	IN/2018	SW/OK/2017	SW/OK/2017	
1	A/Perth/16/2009	Seas	<u>2560</u>	160	80	<20	40	20	20	80	160	
2	A/Singapore/INFIMH-16-0019/2016	Seas	80	<u>640</u>	160	<20	<20	<20	<20	160	320	
3	A/Switzerland/8060/2017	Seas	80	1280	<u>5120</u>	<20	<20	80	<20	160	640	
4	A/Ohio/28/2016 IDCDC RG55C	2010.1	80	80	20	<u>2560</u>	320	80	80	80	160	
5	A/Ohio/13/2017	2010.1	80	40	40	80	<u>1280</u>	640	640	80	320	
6	A/Indiana/27/2018	2010.1	<20	<20	40	640	640	<u>5120</u>	<u>5120</u>	ND	2560	
7	A/swine/Oklahoma/A02218157/2017	2010.2	320	2560	1280	40	320	40	40	<u>1280</u>	<u>2560</u>	
TEST ANTIGENS												
8	A/Ohio/13/2017-like CVV VPT 18-v68.1 1.5b1 non GLP		160	160	40	80	1280	160	40	40	160	
9	A/Ohio/13/2017-like CVV VPT 18-v68.1 1.5b3 non GLP		320	320	80	160	5120	320	160	160	320	
10	A/Ohio/13/2017-like CVV VPT 18-v68.1 non GLP		80	40	40	160	2560	640	640	80	320	
11	A/swine/Iowa/18Tosu0373/2018	2010.1	<20	<20	<20	<20	<20	5120	2560	<20	80	
12	A/swine/Iowa/18Tosu0394/2018	2010.1	<20	<20	<20	<20	20	2560	640	<20	80	

Genetic characterization

- The 2010.1 lineage swine viruses had 4 conserved amino acid changes in putative antigenic sites A and B in HA1 relative to A/Ohio/13/2017, the wt strain of the recommended CVV.
- 2010.2 lineage swine viruses from Oklahoma and Arkansas were closely related to human, seasonal A/Singapore/INFIMH-16-0019/2016-like viruses. These viruses had six conserved amino acid differences in HA1 compared to this seasonal vaccine virus. Glycosylation in 2010.2 viruses change inhibition of seasonal viruses.

Antigenic characterization

- Ferret antiserum raised to the closest wt strain of the recommended CVV (A/Ohio/13/2017) reacted with the variant virus , A/Indiana/27/2018, with a heterologous titer within 2-fold of the homologous virus titer.
- Ferret antisera raised to A/Indiana/27/2018 well inhibited the 2010.1 lineage swine viruses.
- Ferret antisera raised to seasonal A/Singapore/INFIMH-16-0019/2016 and A/Switzerland/8060/2017 viruses well inhibited the 2010.2 lineage swine virus, but not the opposite.
- Adult vaccinees have higher titers than children vaccinees.
- MN/11 CVV vaccine recipients are cross-reactive with 2010.1 and 2010.2 viruses

Candidate vaccine viruses

- Non-GLP A/Ohio/13/2017-like CVVs were tested by one-way analysis and were well inhibited by antisera raised to A/Ohio/13/2017.
- Two-way analysis of one or more of these CVVs is pending.

- NYMC X-203, A/Minnesota/11/2010
- NYMC X-213, A/Indiana/10/2011
- IDCDC-RG55C, A/Ohio/28/2016-like
- IDCDC-RG, A/Ohio/13/2017-like

North American; cluster IV-A
North American; cluster IV-A
2010.1 human-like
2010.1 human-like (Pending)

Updated surveillance data and research activities since April 2018

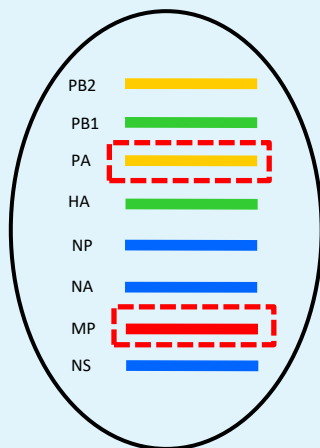
Strains of concern:

- H1N2v

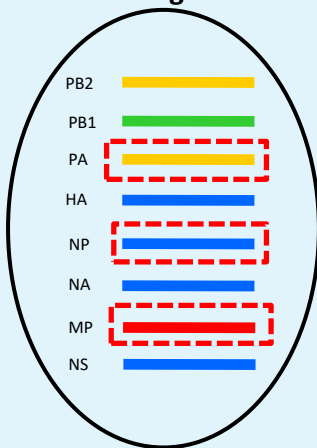
Summary of human infections with influenza A(H1N2)v virus

Country	Subtype	State	Age	Sex	Onset Date	Exposure	Confirmed/ reported	Isolate available	HI test (date)	Strain Designation
USA	H1N2v (delta 2; 1B.2)	CA	12 y	M	7/26/18	Exposure to swine	CDC, USA	not attempted		A/California/58/2018
USA	H1N2v (delta 2; 1B.2)	CA	12 y	M	7/30/18	Exposure to swine	CDC, USA	not attempted		A/California/59/2018
USA	H1N2v (delta 2; 1B.2)	CA	11 y	M	7/27/18	Exposure to swine	CDC, USA	VNR		A/California/60/2018
USA	H1N2v (delta 2; 1B.2)	CA	12 y	M	unk	Exposure to swine	CDC, USA	VNR		A/California/61/2018
USA	H1N2v (delta 2; 1B.2)	CA	9 y	M	8/03/18	Did not attend fair; no exposure to swine	CDC, USA	C1 (8-17-18)		A/California/62/2018
USA	H1N2v (delta 2; 1B.2)	CA	2 y	F	8/03/18	Exposure to swine	CDC, USA	C1 (8-17-18)		A/California/63/2018
USA	H1N2v (delta 2; 1B.2)	MI	14 y	M	7/27/18	Exposure to swine	CDC, USA	C1 (8-10-18)	8/16/18	A/Michigan/382/2018
USA	H1N2v (delta 2; 1B.2)	MI	5 y	M	7/29/18	Exposure to swine	CDC, USA	C1 (8-10-18)	8/16/18	A/Michigan/383/2018
USA	H1N2v (delta 2; 1B.2)	MI	21 y	F	7/27/18	Exposure to swine	CDC, USA	C1 (8-12-18)	8/16/18	A/Michigan/384/2018
USA	H1N2v (delta 2; 1B.2)	OH	3 y	F	8/06/18	Attended fair, no exposure to swine	CDC, USA	C1 (8-12-18)	8/16/18	A/Ohio/24/2018
USA	H1N2v (delta 2; 1B.2)	OH	9 y	F	8/08/18	Exposure to swine	CDC, USA	C1 (8-17-18)		A/Ohio/25/2018
USA	H1N2v (delta 2; 1B.2)	OH	16 y	M	8/06/18	Exposure to swine	CDC, USA	VNR		
USA	H1N2v (delta 2; 1B.2)	OH	14 y	M	8/18/18	Exposure to swine	CDC, USA	C1 (8/25/2018)		A/Ohio/28/2018

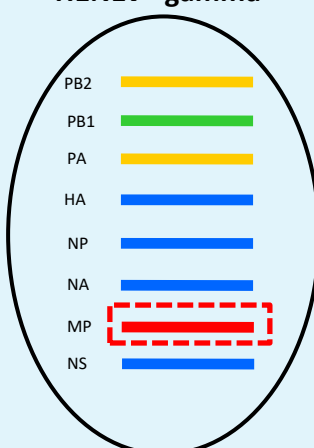
**A/Missouri/12/2012
H1N1v - delta**



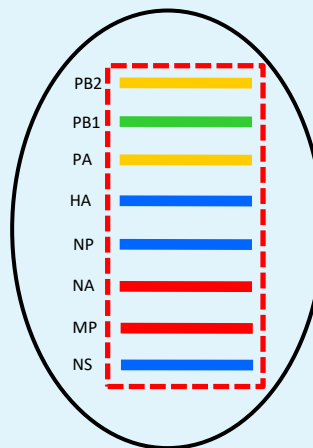
**A/Arkansas/14/2013
A/Iowa/39/2015
A/Minnesota/46/2015
H1N1v - gamma**



**A/Minnesota/33/2014
A/Ohio/09/2015
H1N1v - gamma**

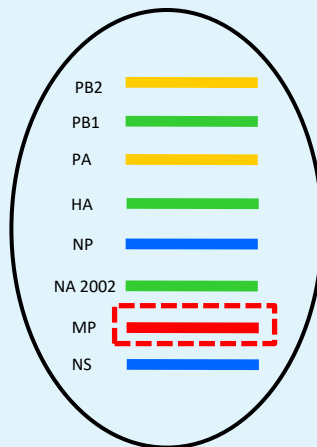


2009 Pandemic H1N1

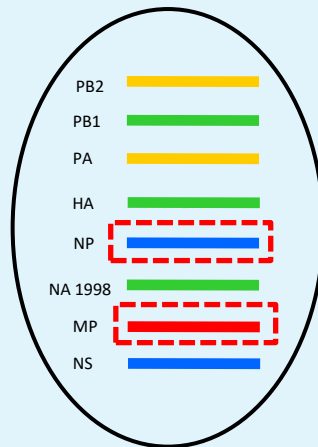


**A/Wisconsin/71/2016
A/Minnesota/70/2016**

**A/Iowa/32/2016 (H1N2v - delta 1)
A/Ohio/35/2017 (H1N2v - delta 2)**



**California, Michigan, Ohio
2018 cases (H1N2v - delta 2)**



-  Classical Swine H1N1
-  Avian – North American Lineage
-  Human Seasonal Lineage
-  Eurasian Swine Lineage
-  Genes derived from H1N1 pdm09 virus

Evolutionary Relationships Among Influenza A(H1)v HA, 2018

H1v candidate vaccine virus

CDC reference viruses in blue

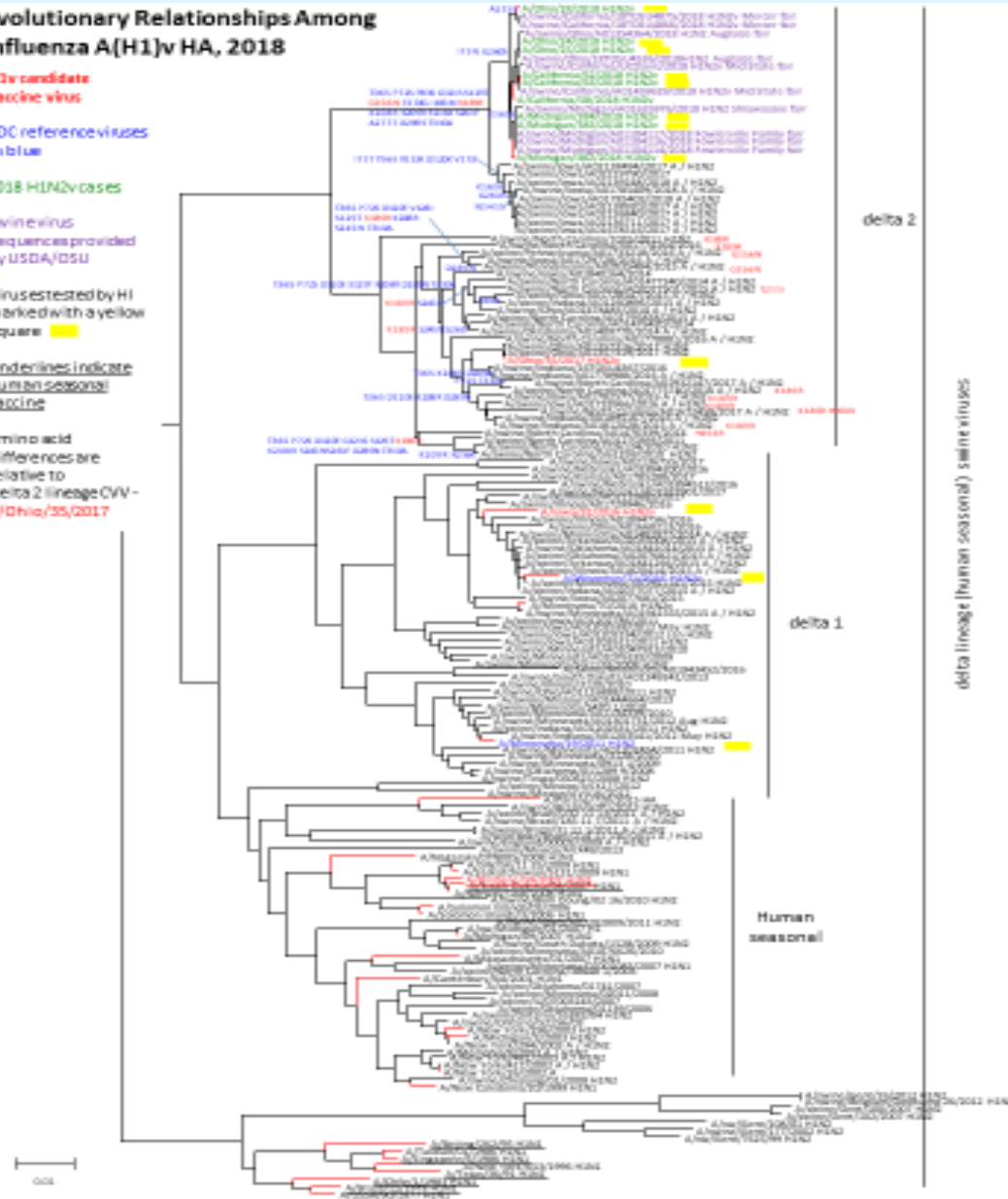
2018 H1N1v cases

Swine virus sequences provided by USDA/ISU

Virus tested by HI marked with a yellow square

Underlines indicate human seasonal lineage

Amino acid differences are relative to Delta 2 lineage CVV-A/DHic/25/2017



Evolutionary Relationships Among Influenza A Variant (H1N2)v HA, 2018 Delta2

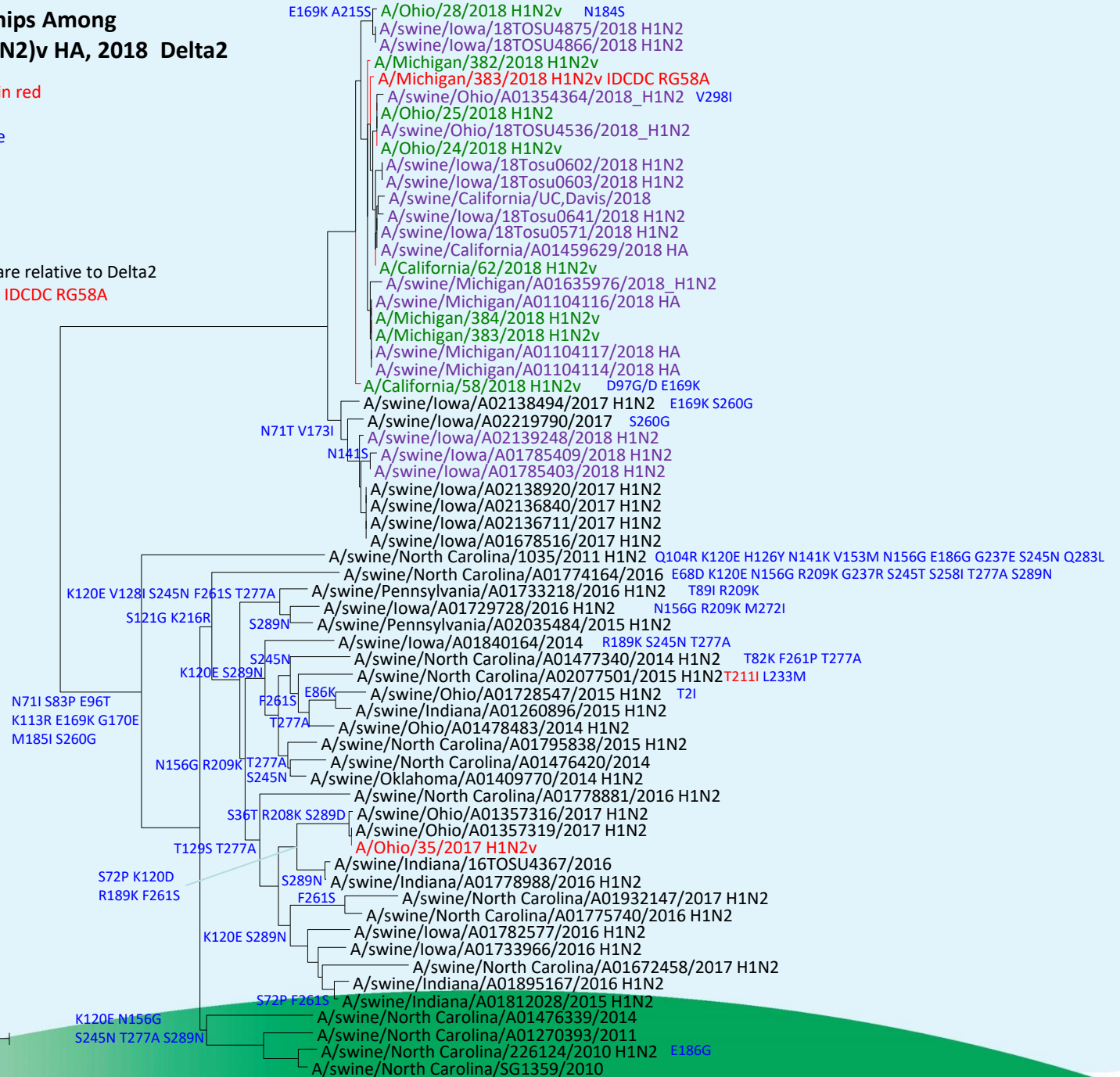
Reassortant vaccine candidate in red

CDC HI reference viruses in blue

2018 US H1v viruses

2018 Swine viruses

Amino acid differences shown are relative to Delta2 lineage - A/Michigan/383/2018 IDCCD RG58A



0.01

		Reference Antisera										
		pdm09	H1N1v (gamma)	H1N1v (gamma)	H1N2v (delta 1)	H1N2v (delta 1)	H1N2v (delta 2)					
		2017-094	2015-158	2016-010 (B)	2015-168 (B)	2016-016 (B)	2017-129	2017/2018	2017/2018			
REFERENCE ANTIGENS		Lineage	MI/45	Ohio/9	RG48A	MN/19	WI/71	OH/35	Child pool#	Adult pool*	Passage	Date collected
1	A/Michigan/45/2015	pdm09	<u>5120</u>	80	<10	<10	<10	<10	80	1280	M1/C3(1/18/17)	9/7/2015
2	A/Ohio/9/2015	H1N1v (gamma)	40	<u>2560</u>	640	<10	<10	<10	<10	40	E2(11/23/15)	4/21/2015
3	A/Ohio/9/2015 CVV RG48A	H1N1v (gamma)	80	5120	<u>1280</u>	<10	<10	<10	<10	160	V1E3 (11/27/15)	Reassortant
4	A/Minnesota/19/2011	H1N2v (delta 1)	<10	<10	<10	<u>2560</u>	1280	10	<10	20	C2(12/19/11)	11/4/2011
5	A/Wisconsin/71/2016	H1N2v (delta 1)	<10	<10	<10	160	<u>2560</u>	10	<10	10	C1(6/20/16)	6/9/2016
6	A/Ohio/35/2017	H1N2v (delta 2)	<10	<10	<10	<10	80	<u>1280</u>	<10	<10	C1(8/25/17)	8/17/2017
TEST ANTIGENS												
7	A/Michigan/382/2018	H1N2v (delta 2)	<10	<10	<10	<10	40	160	<10	<10	C1(8/10/18)	7/28/2018
8	A/Michigan/383/2018	H1N2v (delta 2)	<10	<10	<10	<10	40	320	<10	<10	C1(8/10/18)	7/31/2018
9	A/Michigan/383/2018	H1N2v (delta 2)	<10	40	<10	<10	40	640	<10	<10	E1(8/16/18)	7/31/2018
10	A/Ohio/24/2018	H1N2v (delta 2)	<10	<10	<10	<10	20	160	<10	<10	C1(8/12/18)	8/7/2018
11	A/Michigan/384/2018	H1N2v (delta 2)	<10	<10	<10	<10	20	160	<10	<10	C1(8/12/18)	7/31/2018
#2017-2018 post-vaccine immune serum pool from child (0-3 yrs) vaccinees (A/Michigan/45/2015 vaccine)										TEST DATE: 8/16/2018		
*2017-2018 post-vaccine immune serum pool from adult (19-49 yrs) vaccinees (A/Michigan/45/2015 vaccine)												
(B) Ferrets were boosted 2 weeks post-infection												

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA A(H1)v

				NEW	NEW	NEW	NEW			
				2019-015	2019-016	2019-017	2019-018			
REFERENCE ANTIGENS	Lineage	RG48A	OH/35	MI 383 wt	MI 383 wt	RG58A GLP	RG58A GLP	Passage	Date collected	
1	A/Ohio/9/2015 CVV RG48A	H1N1v (gamma)	<u>5120</u>	10	80	80	40	40	V1E3 (11/27/15)	Reassortant
2	A/Ohio/35/2017	H1N2v (delta2)	<10	<u>1280</u>	160	160	80	40	C1 (8/25/17)	8/17/2017
3	A/Michigan/383/2018	H1N2v (delta2)	40	320	<u>1280</u>	<u>320</u>	320	320	C1 (8/10/18)	7/31/2018
4	A/Michigan/383/2018-like IDCCD-RG58A	H1N2v (delta2)	160	640	1280	640	<u>640</u>	<u>640</u>	V1E2 (9/7/18)	Reassortant
TEST ANTIGENS										
5	A/Ohio/25/2018	H1N2v (delta2)	40	160	320	320	320	320	C1 (8/10/18)	8/9/2018
6	A/Michigan/382/2018	H1N2v (delta2)	40	160	640	640	320	320	C1 (8/17/18)	7/28/2018
7	A/California/62/2018	H1N2v (delta2)	40	320	1280	640	320	640	C1 (8/17/18)	8/6/2018
8	A/swine/Iowa/18Tosu0641/2018	H1N2v (delta2)	40	320	640	640	320	320	C1/C1 (11/13/18)	6/7/2018
9	A/swine/Iowa/18Tosu0571/2018	H1N2v (delta2)	40	320	640	320	320	320	C1/C1 (11/13/18)	6/7/2018
10	A/swine/Iowa/18Tosu0602/2018	H1N2v (delta2)	40	320	640	320	320	320	C1/C1 (11/13/18)	6/7/2018
11	A/swine/Iowa/18Tosu0603/2018	H1N2v (delta2)	80	320	1280	320	320	320	C1/C1 (11/13/18)	6/7/2018

Antigenic characterization

- Ferret antiserum raised to the wt strain of a recommended delta 2 lineage CVV, A/Ohio/35/2017, inhibited the A(H1N2) swine and 2018 variant viruses, but with titers that were reduced 4 to 8-fold compared to the homologous virus titer
- Ferret antisera raised to either the delta 2 lineage wt A/Michigan/383/2018 or the IDCDC-RG58A CVV viruses, inhibited both variant and swine viruses with heterologous titers that were within 2-fold of homologous virus titers.
- new A(H1N2)v CVV (IDCDC-RG58A) passed two-way HI testing and is available for distribution.

Candidate vaccine viruses

- | | |
|---|-------------------------------|
| • IDCDC-RG48A, A/Ohio/09/2015-like | Classical gamma lineage |
| • CNIC-42443, A/Hunan/42443/2015 | Eurasian avian-like |
| • IDCDC-RG, A/Iowa/32/2016-like | Delta 1 lineage (pending) |
| • NIBRG, A/Netherlands/3315/2016 | Eurasian avian-like (pending) |
| • NIBRG, A/Ohio/35/2017-like | Delta 2 lineage (pending) |
| • IDCDC-RG, A/Ohio/24/2017-like | Alpha lineage (pending) |
| • IDCDC-RG58A, A/Michigan/383/2018-like | Delta 2 lineage |

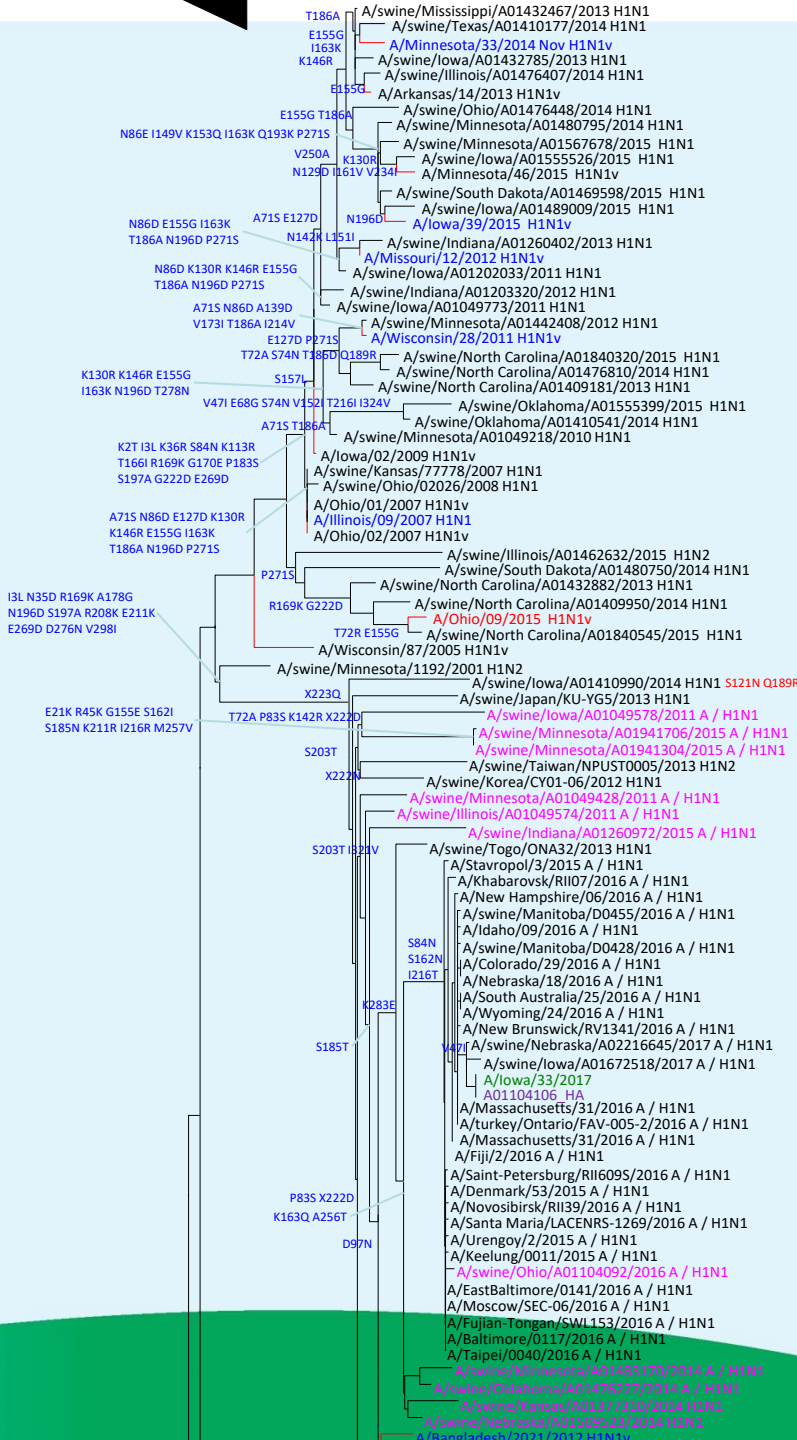
Updated surveillance data and research activities since April 2018

Strains of concern:

- H1N1v

Country	Subtype	State	Age (yrs)	Sex	Onset date	Outcome	Exposure	Confirmed/ Reported	Isolate available	HI test date	Strain name
USA	H1N1v (pdm09)	IA	33y	F	10/21/2017	Recovered	Exposure to swine	CDC, USA	yes	11/17/2017	A/Iowa/33/2017
Switzerland	H1N1v (EA avian-like)		48y	M	12/20/2017	Recovered	Exposure to swine	WHO	unknown	N/A	unknown

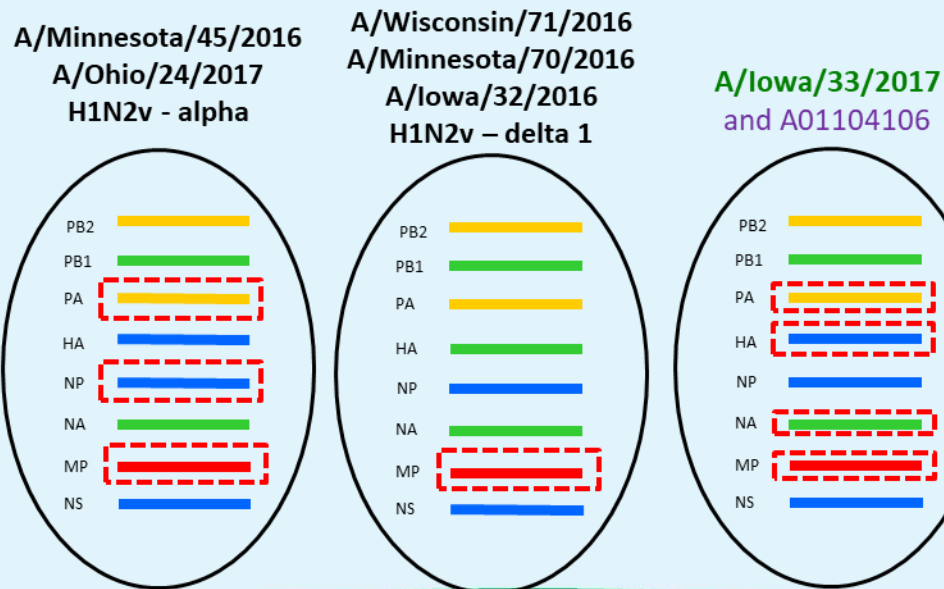
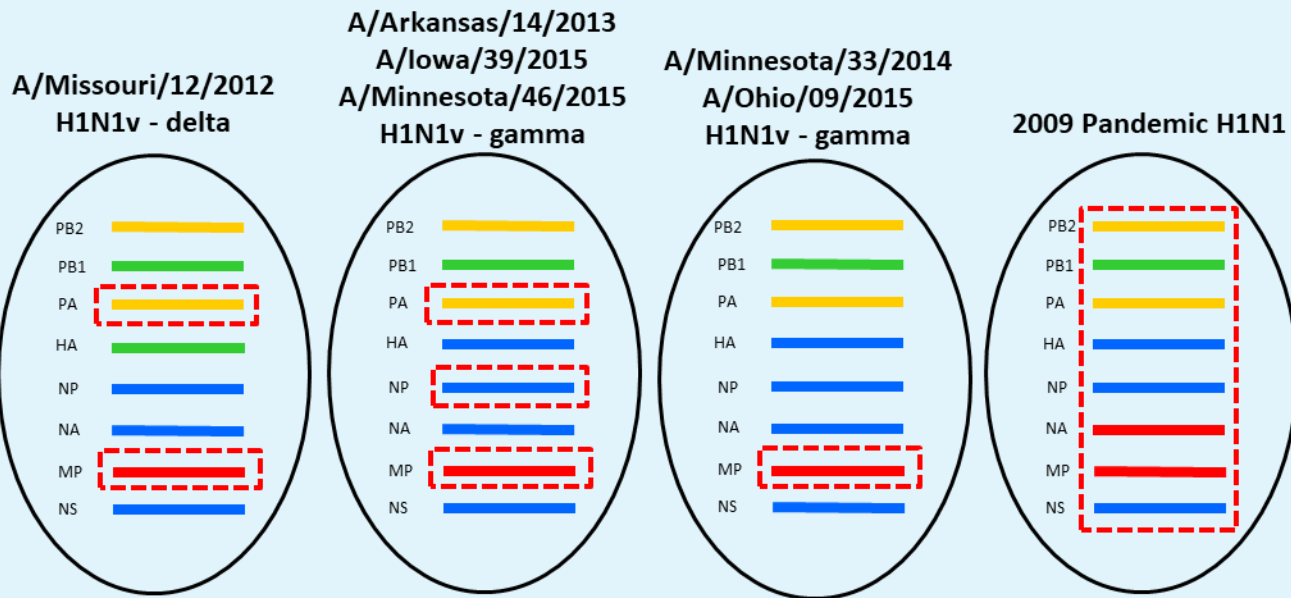
- The patient from Iowa with A(H1N1)v reported direct exposure to swine at a swine premises in the week preceding illness onset. The patient was not hospitalized and fully recovered.
- On 20 December 2017, a case of influenza A(H1N1)v virus was detected in Switzerland in a farm worker with mild acute respiratory symptoms.



gamma

pdm09





REFERENCE ANTIGENS	Lineage	STRAIN DESIGNATION	CDC ID#	Date of collection	seasonal H1N1	pdm09 H1N1	pdm09 H1N1	H1N1v (gamma)	H1N2v (delta1)	H1N2v (delta1)	2016/2017 vaccinees	2016/2017 vaccinees	
					2009-165	2009-172	2017-094	2010-132	2015-168	2016-106	Child pool	Adult pool	
					Bris/07	CA/179	MI/45	Ohio/9	MN/19	Wis/71			
1	AU	seasonal H1N1	A/Brisbane/59/2007	2008704388	7/1/2007	<u>320</u>	<10	<10	320	320	320	320	80
2	NY	pdm09	A/California/7/09 X-179	2009713113	Reassortant	<10	<u>160</u>	160	160	<10	20	320	320
3	MI	pdm09	A/Michigan/45/2015 A/Ohio/9/2015 CVV RG48A	3000413713	9/7/2015	<10	1280	<u>5120</u>	80	<10	80	80	640
4	GA	H1N1v (gamma)	(155E)	3000411138	Reassortant	<10	<10	<10	<u>5120</u>	<10	<10	10	320
5	MN	H1N2v (delta1)	A/Minnesota/19/2011	2012701623	11/4/2011	40	<10	<10	10	<u>640</u>	640	20	80
6	WI	H1N2v (delta1)	A/Wisconsin/71/2016	3000414182	6/9/2016	<10	<10	<10	20	320	<u>5120</u>	80	80
TEST ANTIGENS													
7	IA	H1N1v(gamma pdm09)	A/Iowa/33/2017	3025631276	10/22/2017	<10	640	5120	160	<10	10	40	640



Acknowledgements

Influenza Division,
Centers for Disease Control and Prevention

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