OFFLU swine influenza virus meeting
27 – 28 March 2017
FAO Headquarters, Rome, Italy

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Strains of concerns

Influenza A(H3N2)v activity in 2016/2017

Human infections

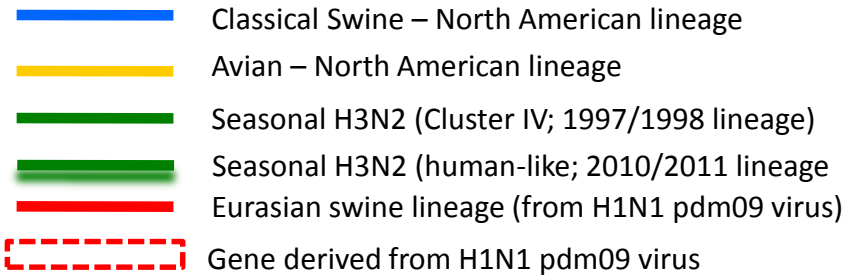
- 18 cases of A(H3N2)v were identified in the United States
  - All cases reported exposure to swine while at one or more of seven agricultural fairs in Michigan and Ohio
  - no human-to-human transmission was identified
  - Sixteen viruses had a seasonal human-like influenza A(H3) HA gene that was likely introduced from humans into swine in 2010 or 2011.
  - Swine specimens from all seven fairs tested positive for swine influenza A(H3N2) virus, and genetic sequencing showed the viruses were very closely related to the human viruses.

- One case of A(H3N2)v was identified in Canada
  - The case developed respiratory infection symptoms in Oct 2016, was hospitalized with the diagnosis of pneumonia, and recovered
  - The case has confirmed exposure to ill swine on a farm.

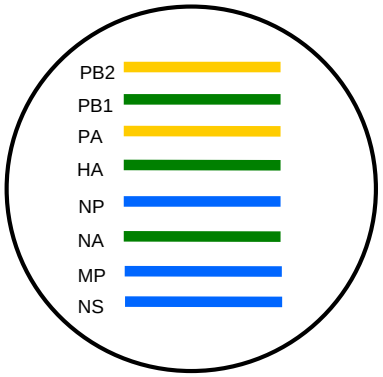
Influenza A(H3N2)v activity in 2016/2017

Country	subtype	Age	Sex	Location	Onset date	Outcome	Exposure	Confirmed/ Reported	Isolate	CDC ID	CDC HI test	HA sequence	Virus name
USA	H3N2v (human-like)	13	M	OH	7/28/2016	Recovered	Fair attendee	CDC	Yes	3000478486	9/8/2016	Yes	A/Ohio/28/2016
	H3N2v (human-like)	2	F	OH	7/29/2016	Recovered	Fair attendee	CDC	Yes	3000480507	9/8/2016	Yes	A/Ohio/27/2016
	H3N2v (human-like)	9	M	MI	7/29/2016	Recovered	Fair exhibitor	CDC	No	3000480509	No	Yes	A/Michigan/82/2016
	H3N2v (human-like)	10	M	MI	8/1/2016	Recovered	Fair exhibitor	CDC	Yes	3000480511	9/8/2016	Yes	A/Michigan/83/2016
	H3N2v (Cluster IV)	64	F	MI	8/4/2016	Recovered	Vet working multiple fairs	CDC	Yes	3000478560	9/8/2016	Yes	A/Michigan/84/2016
	H3N2v (human-like)	2	M	MI	8/6/2016	Recovered	Fair attendee	CDC	Yes	3000414190	9/8/2016	Yes	A/Michigan/87/2016
	H3N2v (human-like)	8	M	MI	8/6/2016	Recovered	Fair exhibitor	CDC	No	3000414191	No	Yes	A/Michigan/88/2016
	H3N2v (human-like)	5	M	OH	8/13/2016	Recovered	Fair attendee	CDC	Yes	3000480656	9/8/2016	Yes	A/Ohio/29/2016
	H3N2v (human-like)	2	F	MI	8/6/2016	Recovered	Fair attendee	CDC	No	3000414194	No	Yes	A/Michigan/91/2016
	H3N2v (human-like)	13	F	MI	8/7/2016	Recovered	Fair attendee	CDC	Yes	3000414193	9/8/2016	Yes	A/Michigan/90/2016
	H3N2v (human-like)	3	M	MI	8/8/2016	Recovered	Fair attendee	CDC	No	3000414192	No	Yes	A/Michigan/89/2016
	H3N2v (human-like)	15	M	OH	8/11/2016	Recovered	Fair exhibitor	CDC	No	3000480635	No	Yes	A/Ohio/33/2016
	H3N2v (human-like)	10	F	MI	8/9/2016	Recovered	Fair attendee	CDC	Yes	3000480638	9/8/2016	Yes	A/Michigan/93/2016
	H3N2v (Cluster IV)	4	M	MI	8/8/2016	Recovered	Fair attendee	CDC	Yes	3000480639	9/8/2016	Yes	A/Michigan/94/2016
	H3N2v (human-like)	6	M	MI	8/11/2016	Recovered	Fair exhibitor	CDC	No	3000480640	No	Yes	A/Michigan/95/2016
	H3N2v (human-like)	5 mo	F	MI	8/6/2016	Recovered	Fair attendee	CDC	No	3000480641	No	Yes	A/Michigan/96/2016
	H3N2v (human-like)	19	F	OH	8/13/2016	Recovered	Fair exhibitor	CDC	Yes	3000480643	9/8/2016	Yes	A/Ohio/32/2016
	H3N2v (human-like)	1	F	OH	8/3/2016	Recovered	Fair attendee	CDC	No	3000478835	No	Yes	A/Ohio/35/2016
Canada	H3N2v (Cluster IV)	?	?	ON	10/24/2016	Recovered	exposure to swine	CDC	Yes	3000687667	No	Yes	A/Ontario/RV3236/2016

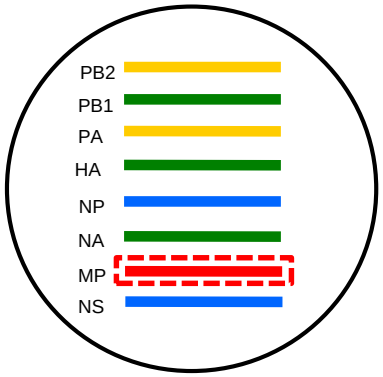
Genome Comparisons of H3N2v 2005-2017



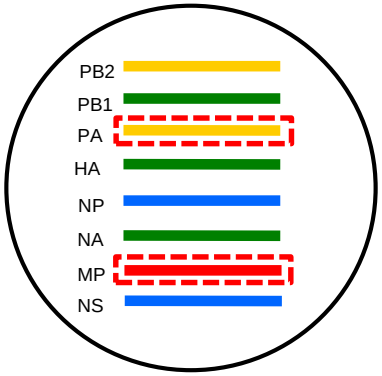
2005-2010



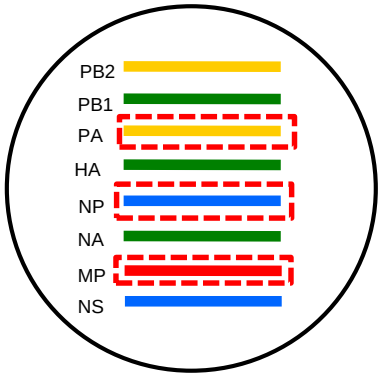
Majority of 2011-2012 (n>300) and 2013 from Indiana (n=13)
A/Minnesota/38/2015
A/Michigan/39/2015
A/New Jersey/53/2015



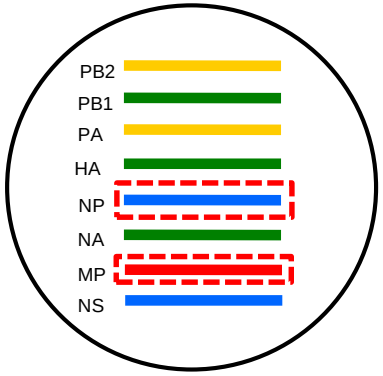
2013 (n=5)
Ohio, Illinois, Indiana, Michigan



2013 (n=1)
Iowa

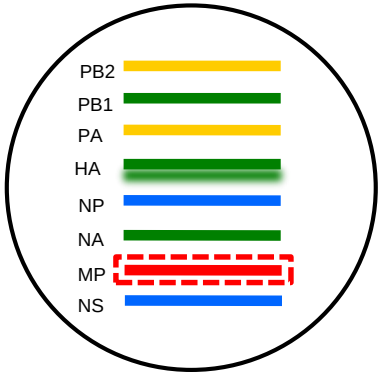


2014 (n=3)
Ohio, Wisconsin

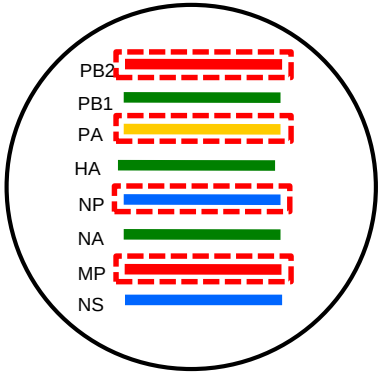


2016 (n=2)
Michigan
IV-A

2016 (n=16)
Ohio, Michigan



2016 (n=1)
Ontario, Canada

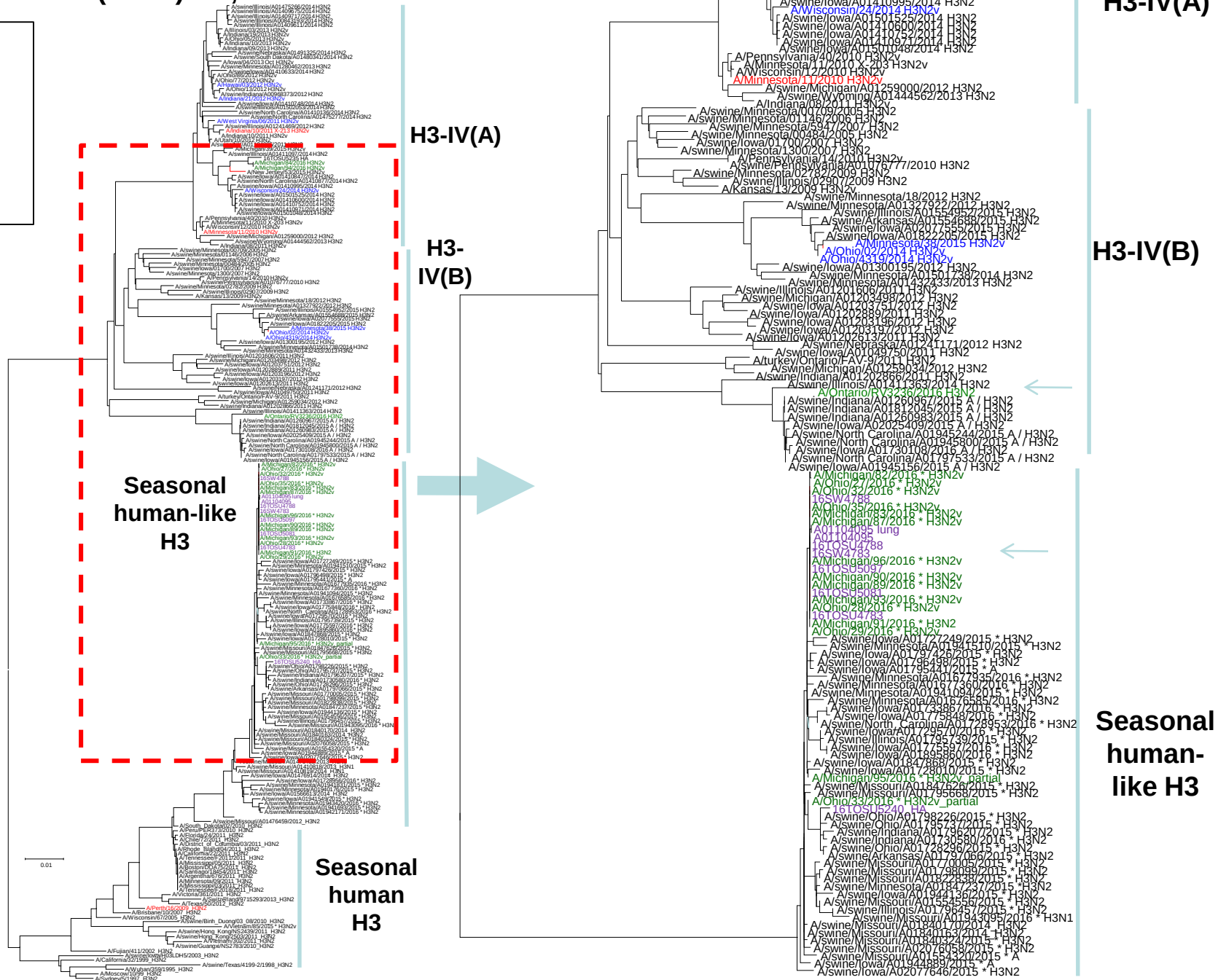


Evolutionary Relationships Among Influenza A Variant (H3N2) HA, 2016

H1v candidate vaccine virus

CDC reference viruses in blue

2016 H3N2v viruses



Antigenic properties of A(H3N2)v viruses

REFERENCE ANTIGENS	H3N2 clade	MOS/99	Perth/09	SWITZ	IN/10	MN/11	MN/11 X-203	child pool*	Adult pool*
A/Moscow/10/99	Seasonal	**1280**	10	<#	20	10	<	<	160
A/Perth/16/2009	Seasonal	10	**640**	10	10	10	<	640	640
A/Switzerland/9715293/2013	Seasonal	10	10	**640**	20	10	<	640	1280
A/Indiana/10/2011	IV-A	10	<	10	**2560**	2560	1280	80	320
A/Minnesota/11/2010	IV-A	10	<	20	1280	**2560**	1280	80	640
A/Minnesota/11/2010 X-203	IV-A	10	80	<	320	640	**2560**	40	40
TEST ANTIGENS									
A/Ohio/27/2016	human-like	20	80	40	160	40	<	160	1280
A/Ohio/28/2016	human-like	20	80	40	160	10	<	320	1280
A/Ohio/29/2016	human-like	20	40	40	160	10	<	320	1280
A/Ohio/32/2016	human-like	20	40	40	80	10	<	160	640
A/Michigan/83/2016	human-like	20	40	40	80	80	40	160	1280
A/Michigan/87/2016	human-like	20	80	40	320	160	160	160	2560
A/Michigan/90/2016	human-like	20	80	40	160	80	80	160	1280
A/Michigan/93/2016	human-like	10	20	10	80	10	<	160	640
A/Michigan/84/2016	IV-A	20	<	10	1280	1280	640	80	320
A/Michigan/94/2016	IV-A	20	10	10	1280	1280	640	80	320

Antigenic characterization

- Antigenic testing of the 'human-like' A(H3N2)v isolates from the USA revealed that ferret antisera generated against existing cluster IV-A wt and CVVs (A/Minnesota/11/2010 and A/Indiana/10/2011) poorly inhibited these viruses.

- Heterologous HI titers of ferret antiserum generated against A/Perth/16/2009, the closest seasonal A(H3N2) vaccine virus based on amino acid relationship, were reduced by 8-fold or greater compared to the homologous virus titer.
    - 23 amino acid differences b/t Perth/16
    - Many found in antigenic sites

- Post-vaccine immune serum from children (0-3 yrs) reacted with the human-like A(H3N2)v viruses with titers ranging from 160-320, whereas HI titers of adult (19-49 yrs) post-vaccine immune serum with these viruses were higher (640-2560)

Status of A(H3N2)v candidate vaccine virus development

Candidate vaccine viruses	Type	Institution
A/Minnesota/11/2010 (NYMC X-203)	Conventional reassortant	CDC
A/Indiana/10/2011 (NYMC X-213)	Conventional reassortant	CDC

Candidate vaccine viruses in preparation	Type	Institution
A/Ohio/28/2016-like	Conventional reassortant	NIBSC
	and reverse genetics	CDC

Influenza A(H1N1)v and A(H1N2)v activity in 2016/2017

Country	subtype	Age	Sex	Location	Onset date	Outcome	Exposure	Confirmed/ Reported	Isolate available	CDC ID/ Source	CDC HI test	HA seq.	Virus name
USA	H1N2v (alpha)	55	M	MN	27-Mar-2016	recovered	potential exposure to swine	Influenza Division, CDC	yes	3000478102	6/23/2016	CDC	A/Minnesota/45/2016
	H1N2v (delta 1)	64	M	WI	1-Jun-2016	recovered	exposure to swine		yes	3000414182	6/23/2016	CDC	A/Wisconsin/71/2016
	H1N2v (delta 1)	7	M	MN	5-Apr 2016	recovered	exposure to swine		yes	3000478188	9/20/2016	CDC	A/Minnesota/70/2016
	H1N2v (delta 1)	52	M	IA	4-Nov-2016	recovered	exposure to swine		yes	3000414195	1/19/17	CDC	A/Iowa/32/2016
Netherlands	H1N1 (Eurasian avian-like)	9	?	?	October 2016	Recovered	exposure to swine	Erasmus Medical Center	Yes	3000687663	1/19/17	GISAID	A/Netherlands/3315/2016
Switzerland	H1N1 (Eurasian avian-like)	23	M	Zurich	20-Dec-2016	recovered	exposure to swine	National Centre of Influenza in Switzerland	No	N/A		GISAID	A/Zurich/19495823/16
Italy	H1N1 (Eurasian avian-like)	40s	M	Pavia	Oct-2016	recovered	exposure to swine	IZSLe, Brescia, Italy	?	N/A		GISAID	A/Pavia/65/2016

Genome Comparisons of H1N1v and H1N2v Viruses 2009-2017

Classical Swine H1N1 – North American Lineage

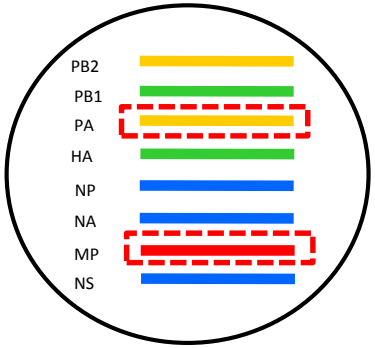
Avian – North American Lineage

Human Seasonal Lineage

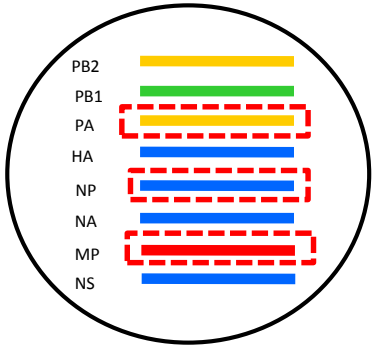
Eurasian Swine Lineage

Genes derived from H1N1 pdm09 virus

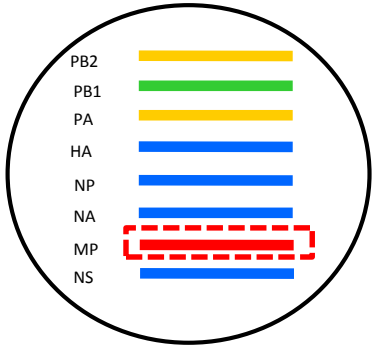
A/Missouri/12/2012
H1N1v - delta



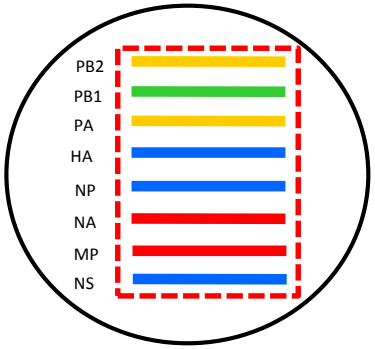
A/Arkansas/14/2013
A/Iowa/39/2015
A/Minnesota/46/2015
H1N1v - gamma



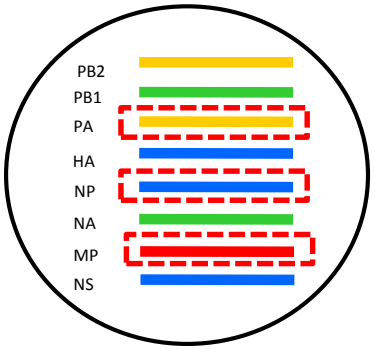
A/Minnesota/33/2014
A/Ohio/09/2015
H1N1v - gamma



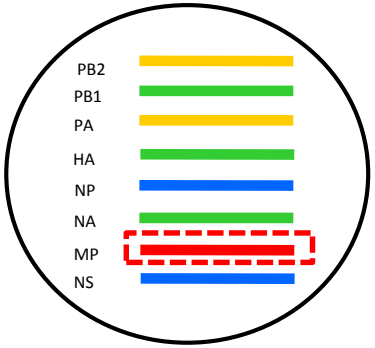
2009 Pandemic H1N1



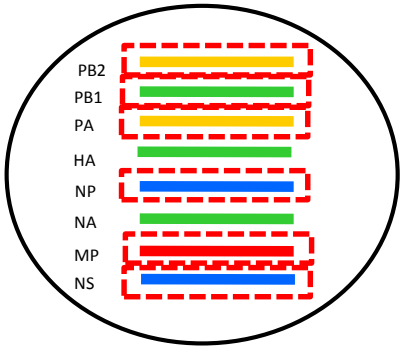
A/Minnesota/45/2016
H1N2v - alpha



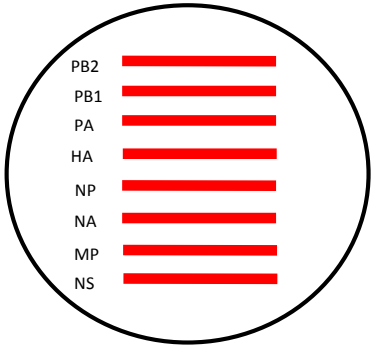
A/Wisconsin/71/2016
A/Minnesota/70/2016
A/Iowa/32/2016
H1N2v – delta 1



A/Parana/720/2015
H1N2v - delta



A/Netherlands/3315/2016
A/Pavia/65/2016
Eurasian avian-like H1N1v



Influenza A Variant (H1)v HA, 2016

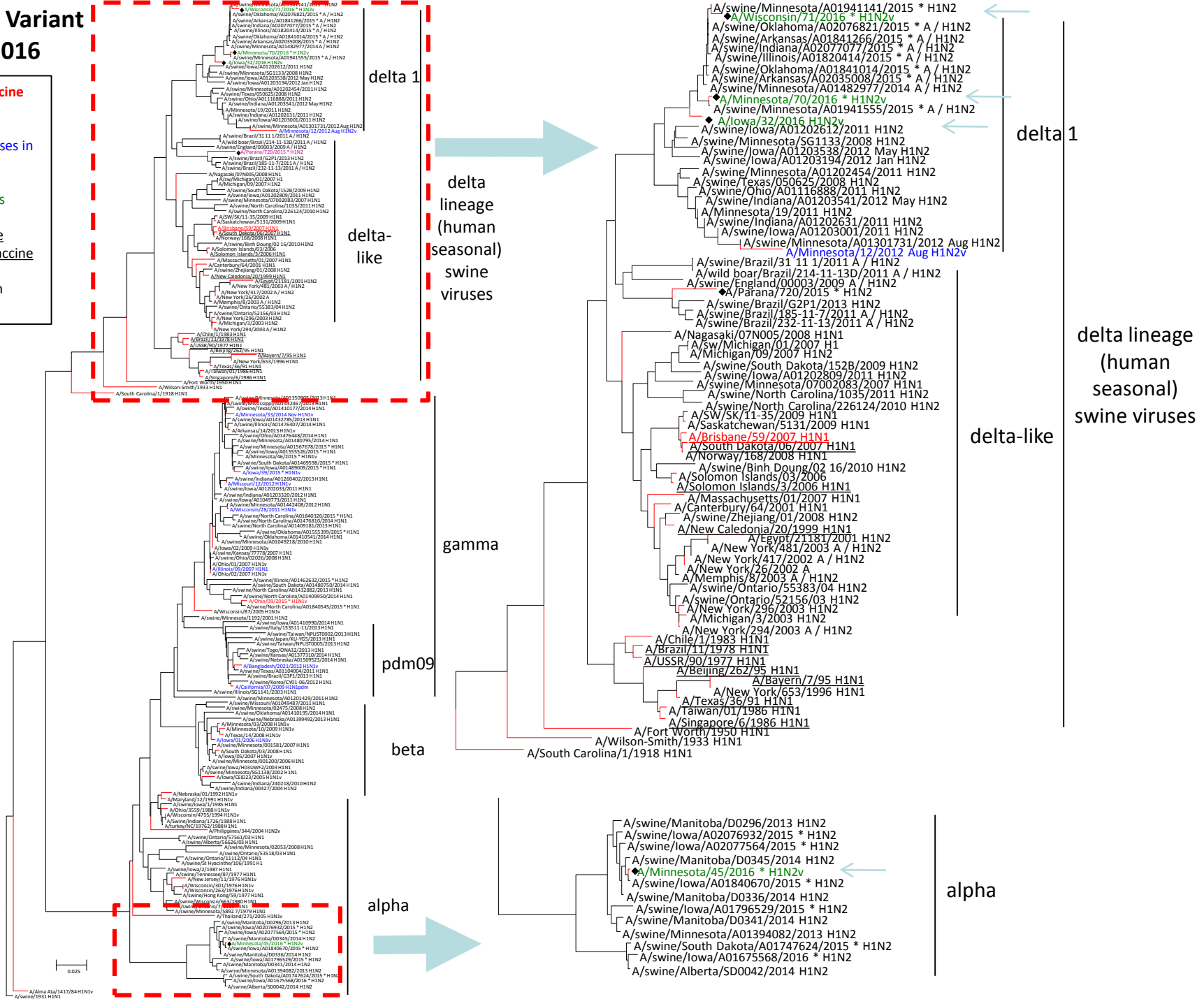
H1v candidate vaccine virus

CDC reference viruses in blue

2016 H1N2v viruses

Underlines indicate human seasonal vaccine

Viruses collected in 2015/2016 (*)



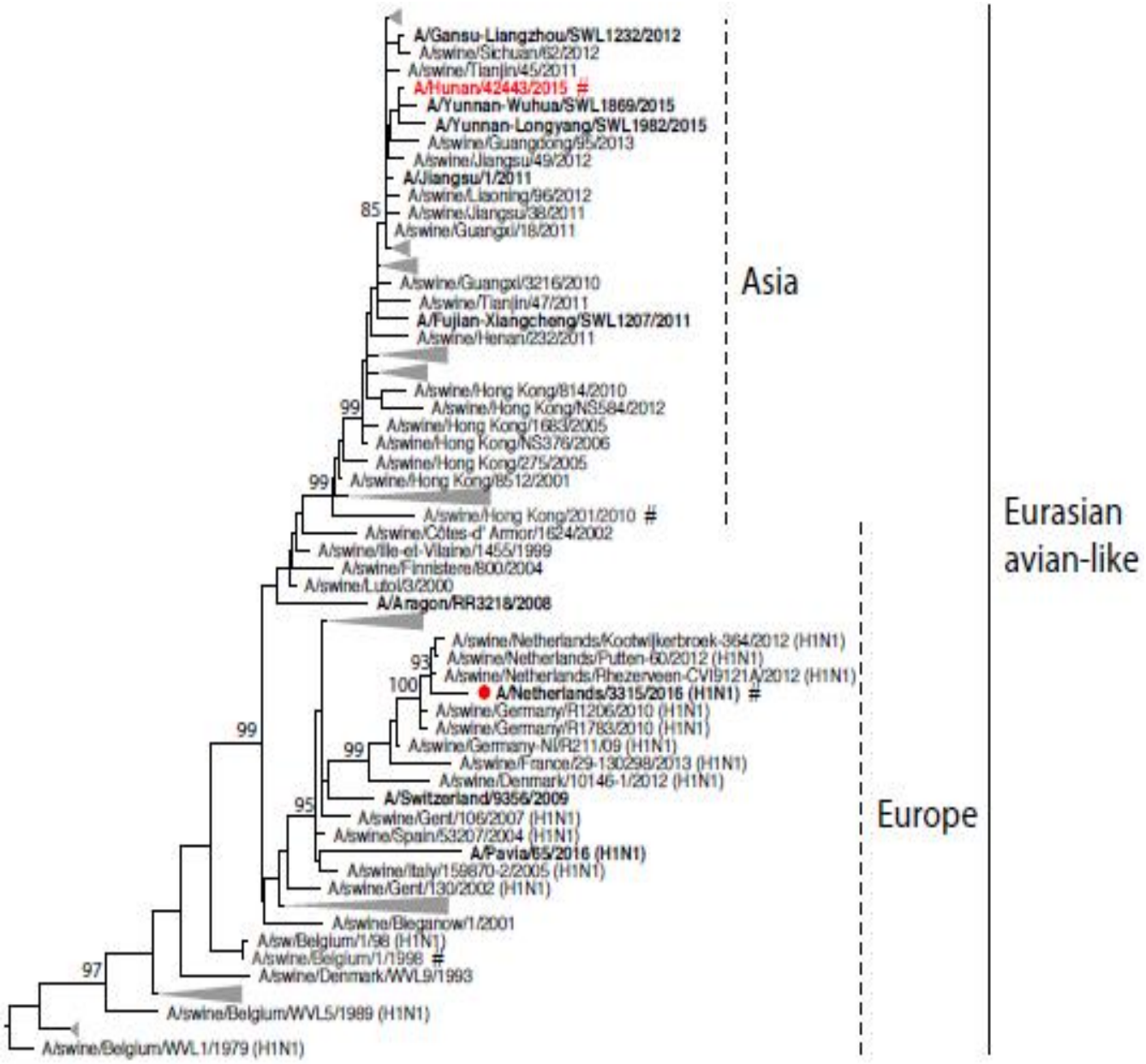
Antigenic properties of A(H1N2)v viruses

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA A(H1)v

													NEW	
			seasonal H1N1	pdm09				beta	gamma					
			2009-165	2014-073	2009-172	2014-074	2015-119	2007-072	2012-033	2013-001	2016-021	2016-009	2015-160	2016-063	2015/2016
	STRAIN DESIGNATION	Lineage	Bris/59	CA/7	X-179	BA/2021	St.P/15	IA/1	WI/28	MO/12	OH/09	RG48A	MN/33	IA/39	HUMAN*
1	A/Brisbane/59/2007	seasonal H1N1	**2560**	10	<10	<10	10	<10	<10	<10	<10	<10	20	10	320
2	A/California/7/2009	pdmH1	<10	**5120**	1280	320	320	2560	80	40	80	<10	1280	160	640
3	A/California/7/09 X-179	pdmH1	<10	640	**640**	640	320	640	<10	20	1280	80	640	640	2560
4	A/Bangladesh/2021/2012	pdmH1 (6A)	<10	640	320	**1280**	160	320	<10	20	160	10	160	320	640
5	A/St Petersburg/61/15	pdmH1 (6B)	<10	640	320	640	**1280**	160	<10	<10	40	<10	320	80	160
6	A/Iowa/1/2006	H1N1v (beta)	10	1280	160	320	10	**320**	<10	<10	5120	640	640	640	640
7	A/Wisconsin/28/2011	H1N1v (gamma)	10	5120	5120	640	640	5120	**640**	640	1280	160	5120	5120	1280
8	A/Missouri/12/2012	H1N1v (gamma)	10	5120	5120	5120	1280	5120	5120	**5120**	5120	1280	5120	5120	5120
9	A/Ohio/9/2015 (155E)	H1N1v (gamma)	<10	<10	<10	<10	<10	<10	<10	<10	**2560**	1280	160	320	80
10	A/Ohio/9/2015 CVV RG48A	H1N1v (gamma)	10	20	10	80	40	80	<10	10	5120	**5120**	2560	2560	320
11	A/Minnesota/33/2014	H1N1v (gamma)	<10	5120	2560	640	640	2560	640	320	640	320	**5120**	1280	640
12	A/Iowa/39/2015	H1N1v (gamma)	<10	320	160	320	160	640	10	10	2560	320	5120	**5120**	1280
	TEST ANTIGENS														
13	A/Minnesota/45/2016	H1N2v (alpha)	10	10	10	20	<10	<10	<10	<10	<10	<10	<10	<10	40
14	A/Minnesota/19/2011	H1N2v (delta)	160	<10	<10	<10	<10	<10	<10	<10	10	<10	<10	<10	20
15	A/Wisconsin/71/2016	H1N2v (delta)	10	<10	<10	<10	<10	<10	<10	<10	<10	<10	<10	<10	40

*** 2015-2016 post-vaccine immune serum pool from adult (19-49 yrs) vaccinees**

Eurasian avian-like H1N1



Haemagglutination inhibition assays of influenza A(H1) variant viruses

REFERENCE ANTIGENS	Lineage	CA/ 7	X-179	RG 48A	Br/59	WI/ 71	sw/ HK	sw/Bg	Hu / 42443	CNIC 1601	pooled human sera
A/California/7/2009	pdm09	**2560**	1280	10	< #	<	1280	640	1280	1280	160
A/California/7/2009 X-179	pdm09	320	**160**	20	<	<	<	20	<	<	80
A/Ohio/9/2015 RG48A	classical γ	<	<	**1280**	<	<	40	160	20	<	20
A/Brisbane/59/2007	pre-2009 H1N1	<	<	10	**640**	10	<	<	<	<	80
A/Wisconsin/71/2016	H1N2v δ	<	<	<	<	**5120**	<	<	<	<	10
A/swine/HK/201/2010	EA† avian	1280	640	10	<	<	**2560**	640	1280	2560	20
A/swine/Belgium/1/98	EA avian	1280	640	20	<	<	640	**2560**	320	640	40
A/Hunan/42443/2015	EA avian	1280	320	<	<	<	1280	640	**1280**	1280	40
A/Hunan/42443/2015 CNIC 1601	EA avian	640	320	<	<	<	1280	640	640	**1280**	<
TEST ANTIGENS											
A/Iowa/32/2016	H1N2v δ	<	<	<	<	1280	<	<	<	<	10
A/Netherlands/3315/2016	EA avian	10	<	10	<	<	160	160	160	10	40

represents a haemagglutination inhibition titre of <10; † Eurasian avian

Status of A(H1N1)v candidate vaccine virus development

Candidate vaccine viruses	Type	Institution
A/Ohio/9/2015 (IDCDC-RG48A)	Reverse genetics	CDC
A/Hunan/42443/2015 (CNIC-1601)	Conventional reassortant	CCDC & NIBSC

Candidate vaccine viruses in preparation	Type	Institution
A/Iowa/32/2016 – A(H1N2)v δ lineage	RG	CDC
A/Netherlands/3315/2016 – EA avian-like	RG & Conventional	NIBSC

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- Gounalan Pavade

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- GIP, WHO
- National Influenza Centers

Association of Public Health Laboratories
- State public health laboratories