Antigenic and genetic characteristics of zoonotic influenza viruses and development of candidate vaccine viruses for pandemic preparedness

September 2018

The development of influenza candidate vaccine viruses (CVVs), coordinated by WHO, remains an essential component of the overall global strategy for pandemic preparedness.

Selection and development of CVVs are the first steps towards timely vaccine production and do not imply a recommendation for initiating manufacture. National authorities may consider the use of one or more of these CVVs for pilot lot vaccine production, clinical trials and other pandemic preparedness purposes based on their assessment of public health risk and need.

Zoonotic influenza viruses continue to be identified and evolve both genetically and antigenically, leading to the need for additional CVVs for pandemic preparedness purposes. Changes in the genetic and antigenic characteristics of these viruses relative to existing CVVs, and their potential risks to public health, justify the need to select and develop new CVVs.

This document summarises the genetic and antigenic characteristics of recent zoonotic influenza viruses and related viruses circulating in animals[1] that are relevant to CVV updates. Institutions interested in receiving these CVVs should contact WHO at gisrs-whohq@who.int or the institutions listed in announcements published on the WHO website[2].

Influenza A(H5)

Since their emergence in 1997, highly pathogenic avian influenza (HPAI) A(H5) viruses of the A/goose/Guangdong/1/96 haemagglutinin (HA) lineage have become enzootic in some countries, have infected wild birds and continue to cause outbreaks in poultry and sporadic human infections. These viruses have diversified genetically and antigenically, including the emergence of viruses with replacement of the N1 gene segment by N2, N3, N5, N6, N8 or N9 gene segments, leading to the need for multiple CVVs. This summary provides updates on the characterisation of A/goose/Guangdong/1/96-lineage A(H5) viruses and the current status of the development of influenza A(H5) CVVs.

Influenza A(H5) activity from 20 February to 24 September 2018

One A(H5N6) human infection in China, where A(H5) infections have also been detected in birds, was reported to WHO. Since 2003 there have been 860 and 20 confirmed human infections with A(H5N1) and A(H5N6) viruses, respectively. A/goose/Guangdong/1/96-lineage A(H5) viruses were detected in poultry and wild birds in many countries (Table 1).

[1] For information relevant to other notifiable influenza virus infections in animals refer to http://www.oie.int/wahis_2/public/wahid.php/Wahidhome/Home

[2] http://www.who.int/influenza/vaccines/virus/candidates_reagents/home/en/

Table 1. Recent A(H5) activity

Country, area or territory	Host	Genetic clade
Bangladesh	Wild birds	2.3.2.1a (H5N1)
	Poultry	2.3.2.1a (H5N1/N2)
Bhutan	Poultry	2.3.2.1a
Bulgaria	Poultry	2.3.4.4 (H5N8)
Cambodia	Poultry	2.3.2.1c (H5N1)
China	Human (1)[#]	unknown (H5N6)
	Poultry	2.3.4.4 (H5N6); unknown (H5N1)
China, Hong Kong SAR	Wild birds	2.3.4.4 (H5N6)
Taiwan, China	Wild birds	2.3.4.4 (H5N2)
Denmark	Wild birds	2.3.4.4 (H5N6)
Egypt	Poultry	2.3.4.4 (H5N6)
Finland	Wild birds	2.3.4.4 (H5N6)
Germany	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
India	Wild birds	2.3.2.1a (H5N1)
	Poultry	2.3.2.1a (H5N1)
Indonesia	Poultry	2.3.2.1c (H5N1)
Iran (Islamic Republic of)	Wild birds	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N6/8)
Iraq	Poultry	2.3.4.4 (H5N8)
Ireland	Wild birds	2.3.4.4 (H5N6)
Italy	Poultry	2.3.4.4 (H5N8)
Japan	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
Malaysia	Poultry	unknown A(H5)
Myanmar	Poultry	2.3.2.1c (H5N1); 2.3.4.4 (H5N6)
Nepal	Poultry	2.3.2.1a (H5N1)
Nigeria	Poultry	2.3.2.1c (H5N1)
Netherlands	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
Republic of Korea	Poultry	2.3.4.4 (H5N6)
Russian Federation	Poultry	2.3.4.4 (H5N2/8)
Saudi Arabia	Poultry	2.3.4.4 (H5N8)
Slovakia	Wild birds	2.3.4.4 (H5N6)
South Africa	Wild birds	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Sweden	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
Togo	Poultry	2.3.2.1c (H5N1)
United Kingdom	Wild birds	2.3.4.4 (H5N6)
Viet Nam	Poultry	2.3.2.1c (H5N1); 2.3.4.4 (H5N6)

# denotes number of human cases reported to WHO within the reporting period (20 February to 24 September 2018)

Antigenic and genetic characteristics of influenza A(H5) viruses

The nomenclature for phylogenetic relationships among the HA genes of A/goose/Guangdong/1/96-lineage A(H5) viruses is defined in consultation with representatives of WHO, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and academic institutions[3].

A(H5) viruses circulating and characterised from 20 February to 24 September 2018 belong to the following clades:

[3] http://onlinelibrary.wiley.com/doi/10.1111/irv.12324/epdf

Clade 2.3.2.1a viruses were detected in birds in Bangladesh, Bhutan, India and Nepal (Figure 1). An increasing proportion of viruses with HA1 amino acid substitutions at positions 154 and 189, which are both within known antigenic sites, reacted poorly with post-infection ferret antiserum raised against the CVVs derived from A/duck/Bangladesh/19097/2013 (Table 2).

Table 2. Haemagglutination inhibition assays of clade 2.3.2.1a A(H5N1) influenza viruses

Reference Antigens	**Clade**	**VN/1203**	**RG30**	**SJ001**
A/Viet Nam/1203/2004	1	**160**	40	<10
A/Hubei/1/2010 PR8 IDCDC-RG30	2.3.2.1a	<10	**160**	80
A/duck/Bangladesh/19097/2013 SJ001	2.3.2.1a	<10	40	**160**
Test antigens				
A/duck/Bangladesh/12-P-10/2018	2.3.2.1a	<10	20	10
A/chicken/Bangladesh/01-P-12/2018	2.3.2.1a	<10	<10	<10
A/chicken/Bangladesh/01-P-21/2018	2.3.2.1a	<10	20	20
A/chicken/Bangladesh/10-P-53/2018	2.3.2.1a	<10	<10	<10
A/chicken/Bangladesh/09-P-59/2018	2.3.2.1a	<10	10	<10
A/duck/Bangladesh/10-P-63/2018	2.3.2.1a	<10	<10	<10
A/duck/Bangladesh/17D1012/2018	2.3.2.1a	<10	10	<10
A/duck/Bangladesh/17D1057/2018	2.3.2.1a	<10	<10	<10
A/duck/Bangladesh/18D1052/2018	2.3.2.1a	<10	<10	<10
A/chicken/Bangladesh/BM-18-B-166/2018	2.3.2.1a	<10	<10	<10

Clade 2.3.2.1c viruses were detected in birds in Cambodia, Indonesia, Myanmar, Nigeria, Togo and Viet Nam. Representative viruses from these countries were genetically similar to viruses detected in previous periods and reacted with post-infection ferret antisera raised against available CVVs, albeit with reduced titres in some instances.

Clade 2.3.4.4 viruses were detected in a human, birds and environmental samples in China and in birds in an additional 22 countries in Africa, Asia and Europe (Table 1). Recently characterised clade 2.3.4.4 viruses showed considerable genetic diversity, similar to what has been seen in previous periods, but the majority of viruses tested remained well inhibited by ferret antisera raised against A/chicken/Viet Nam/NCVD-15A59/2015, A/Hubei/29578/2016, A/duck/Hyogo/1/2016, their corresponding CVVs or closely related viruses. The human A(H5N6) case was a 42-year-old male who reported exposure to poultry and recovered from the infection. Sequence information on the virus from this individual was not available at the time of the consultation and clade designation was inferred based on virus subtype.

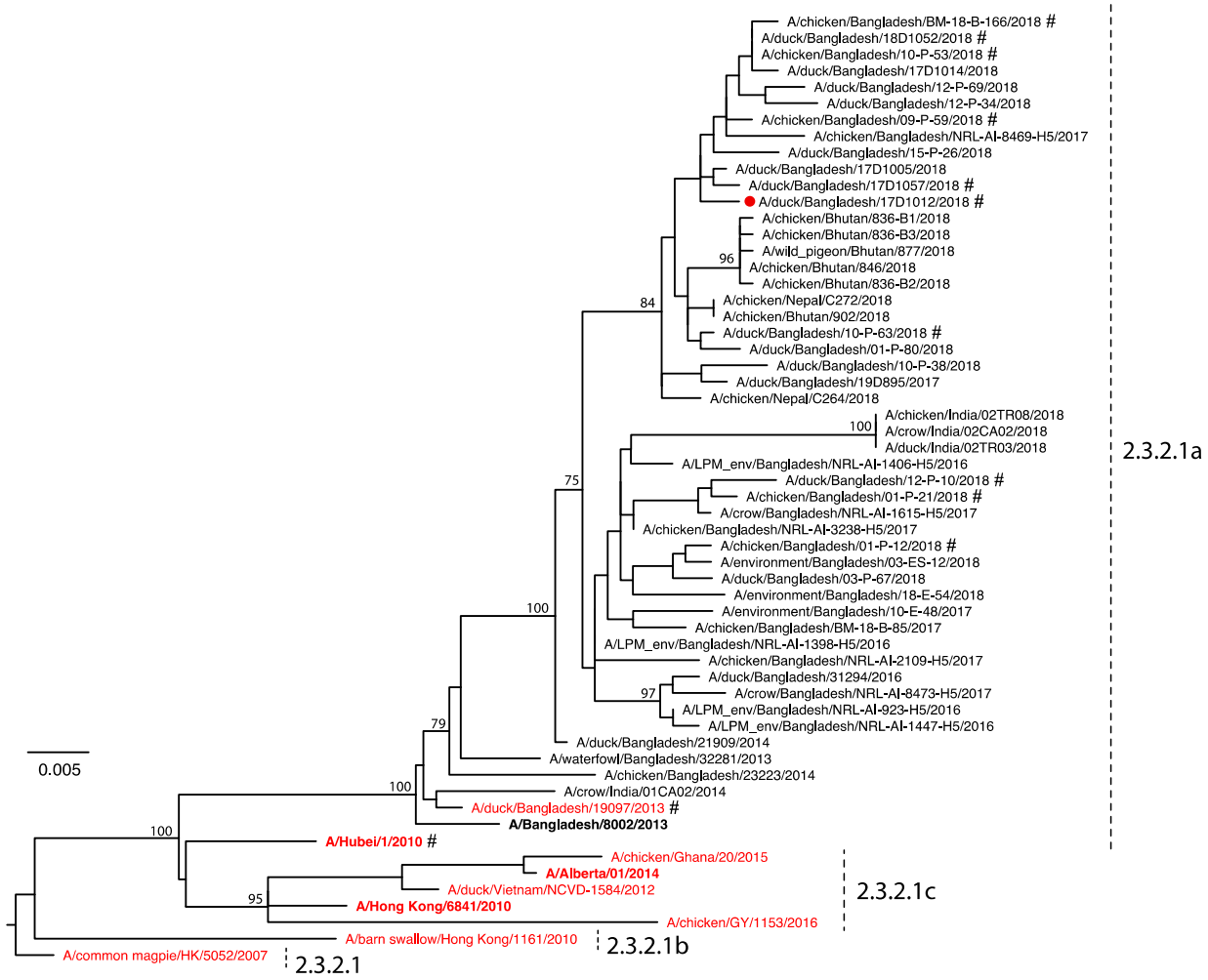

Figure 1. Phylogenetic relationships of A(H5) clade 2.3.2.1 HA genes. CVVs that are available or in preparation are in red. The proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes.

Influenza A(H5) candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, a new A/duck/Bangladesh/17D1012/2018-like A(H5N1) CVV is proposed. The available and pending A(H5) CVVs are listed in Table 3.

Table 3. Status of influenza A(H5) candidate vaccine virus development

Candidate vaccine viruses (like virus)	Clade	Institution*	Available
CDC-RG (A/Viet Nam/1203/2004)	1	CDC	Yes
SJRG-161052 (A/Viet Nam/1203/2004)	1	SJCRH	Yes
NIBRG-14 (A/Viet Nam/1194/2004)	1	NIBSC	Yes
NIBRG-88 (A/Cambodia/R0405050/2007)	1.1	NIBSC	Yes
IDCDC-RG34B (A/Cambodia/X0810301/2013)	1.1.2	CDC	Yes
SJRG-166614 (A/duck/Hunan/795/2002)	2.1.1	SJCRH/HKU	Yes
CDC-RG2 (A/Indonesia/5/2005)	2.1.3.2	CDC	Yes
NIIDRG-9 (A/Indonesia/NIHRD11771/2011)	2.1.3.2a	NIID	Yes
SJRG-163222 (A/bar-headed goose/Qinghai/1A/2005)	2.2	SJCRH/HKU	Yes
IBCDC-RG7 (A/chicken/India/NIV33487/2006)	2.2	CDC/NIV	Yes
SJRG-163243 (A/whooper swan/Mongolia/244/2005)	2.2	SJCRH	Yes
IDCDC-RG11 (A/Egypt/2321-NAMRU3/2007)	2.2.1	CDC	Yes
NIBRG-23 (A/turkey/Turkey/1/2005)	2.2.1	NIBSC	Yes
IDCDC-RG29 (A/Egypt/N03072/2010)	2.2.1	CDC	Yes
IDCDC-RG13 (A/Egypt/3300-NAMRU3/2008)	2.2.1.1	CDC	Yes
NIBRG-306 A/Egypt/N04915/2014)	2.2.1.2	NIBSC	Yes
SJRG-166615 (A/common magpie/Hong Kong/5052/2007)	2.3.2.1	SJCRH/HKU	Yes
IDCDC-RG30 (A/Hubei/1/2010)	2.3.2.1a	CDC	Yes
SJ007 (A/duck/Bangladesh/19097/2013)	2.3.2.1a	SJCRH	Yes
SJ003 (A/barn swallow/Hong Kong/D10-1161/2010)	2.3.2.1b	SJCRH/HKU	Yes
NIBRG-301 (A/duck/Viet Nam/NCVD-1584/2012)	2.3.2.1c	NIBSC	Yes
SJ002 (A/chicken/Hong Kong/AP156/2008)	2.3.4	SJCRH/HKU	Yes
IBCDC-RG6 (A/Anhui/1/2005)	2.3.4	CDC	Yes
CBER-RG1 (A/duck/Laos/3295/2006)	2.3.4	FDA	Yes
SJRG-164281 (A/Japanese white eye/Hong Kong/1038/2006)	2.3.4	SJCRH/HKU	Yes
IDCDC-RG36 (A/chicken/Bangladesh/11rs1984-30/2011)	2.3.4.2	CDC	Yes
IDCDC-RG35 (A/Guizhou/1/2013)	2.3.4.2	CDC/CCDC	Yes
IDCDC-RG42A (A/Sichuan/26221/2014) (H5N6)	2.3.4.4	CDC/CCDC	Yes
CNIC-29578 (A/Hubei/29578/2016) (H5N6)	2.3.4.4	CCDC	Yes
IDCDC-RG43A (A/gyrfalcon/Washington/41088-6/2014) (H5N8)	2.3.4.4	CDC	Yes
NIID-001 (A/duck/Hyogo/1/2016) (H5N6)	2.3.4.4	NIID	Yes
CNIC-21099 (A/Fujian-Sanyuan/21099/2017) (H5N6)	2.3.4.4	CCDC	Yes
SJRG-165396 (A/goose/Guiyang/337/2006)	4	SJCRH/HKU	Yes
IDCDC-RG12 (A/chicken/Viet Nam/NCVD-016/2008)	7.1	CDC	Yes
IDCDC-RG25A (A/chicken/Viet Nam/NCVD-03/2008)	7.1	CDC	Yes
Candidate vaccine viruses in preparation	**Clade**	**Institution**	**Availability**
A/duck/Bangladesh/17D1012/2018-like	2.3.2.1a	CDC	Pending
A/chicken/Guiyang/1153/2016-like	2.3.2.1c	SJCRH/HKU	Pending
A/chicken/Ghana/20/2015-like	2.3.2.1c	CDC	Pending
A/chicken/Viet Nam/NCVD-15A59/2015 (H5N6)-like	2.3.4.4	SJCRH	Pending
A/environment/Hubei/950/2013-like	7.2	CCDC	Pending

* **Institutions developing and/or distributing the candidate vaccine viruses:**
CDC - Centers for Disease Control and Prevention, United States of America
NIV - National Institute of Virology, India
CCDC - Chinese Center for Disease Control and Prevention
FDA - Food and Drug Administration, United States of America
HKU – University of Hong Kong, Hong Kong Special Administrative Region, China.
NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom
NIID - National Institute of Infectious Diseases, Japan
SJCRH - St Jude Children's Research Hospital, United States of America

Influenza A(H7)

Human infections with avian influenza A(H7N9) viruses were first reported to WHO on 31 March 2013. A(H7N9) viruses are enzootic in poultry in China, and reassortment with A(H9N2) and other viruses has generated multiple genotypes. This summary provides updates on the characterisation of A/Anhui/1/2013 HA lineage A(H7) viruses and the current status of the development of corresponding CVVs.

Influenza A(H7) activity from 20 February to 24 September 2018

No human infections with A(H7N9) viruses were reported in this period. The total number of human cases reported since 2013 is 1567, with a case fatality rate of 39%. A(H7) viruses were detected in birds and environmental samples in China, albeit at low levels, and in duck meat smuggled into Japan.

Antigenic and genetic characteristics of influenza A(H7) viruses

Both highly pathogenic (HP) and low pathogenic (LP) avian influenza viruses were detected in birds and environmental samples in China. The HP viruses have accumulated a number of HA amino acid substitutions relative to viruses detected in previous periods and one HP virus has replaced the N9 NA with an N6 NA. The virus detected in Japan was a HP virus that has replaced the N9 NA with an N3 NA. Antigenic characterisation of recent A(H7N9) viruses suggests that they are well covered by existing CVVs; however, the A(H7N3) virus from Japan had reduced reactivity with post-infection ferret antisera raised against available CVVs.

Influenza A(H7N9) candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available A(H7N9) CVVs are listed in Table 4.

Table 4. Status of influenza A(H7N9) candidate vaccine virus development

Candidate vaccine virus (like virus)	Type	Institution*	Available
IDCDC-RG33A (A/Anhui/1/2013)	Reverse genetics	CDC	Yes
NIBRG-268 (A/Anhui/1/2013)	Reverse genetics	NIBSC	Yes
NIIDRG-10.1 (A/Anhui/1/2013)	Reverse genetics	NIID	Yes
SJ005 (A/Anhui/1/2013)	Reverse genetics	SJCRH	Yes
NIBRG-267 (A/Shanghai/2/2013)	Reverse genetics	NIBSC	Yes
CBER-RG4A (A/Shanghai/2/2013)	Reverse genetics	FDA	Yes
IDCDC-RG32A (A/Shanghai/2/2013)	Reverse genetics	CDC	Yes
IDCDC-RG32A.3 (A/Shanghai/2/2013)	Reverse genetics	CDC	Yes
IDCDC-RG56B (A/Hong Kong/125/2017)	Reverse genetics	CDC	Yes
CNIC-GD003 (A/Guangdong/17SF003/2016)	Reverse genetics	CCDC	Yes
IDCDC-RG56N (A/Guangdong/17SF003/2016)	Reverse genetics	CDC	Yes
NIBRG-375 (A/Guangdong/17SF003/2016)	Reverse genetics	NIBSC	Yes
CBER-RG7C (A/Guangdong/17SF003/2016)	Reverse genetics	FDA	Yes
CNIC-HN02650 (A/Hunan/02650/2016)	Reverse genetics	CCDC	Yes

* **Institutions distributing the candidate vaccine viruses:**
CDC - Centers for Disease Control and Prevention, United States of America
CCDC - Chinese Center for Disease Control and Prevention
FDA - Food and Drug Administration, United States of America
NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom
NIID - National Institute of Infectious Diseases, Japan
SJCRH - St Jude Children's Research Hospital, United States of America

Influenza A(H9N2)

Influenza A(H9N2) viruses are enzootic in poultry in parts of Africa, Asia and the Middle East. The majority of viruses sequenced from these regions belong to the A/quail/Hong Kong/G1/97 (G1) and A/chicken/Beijing/1/94 (Y280/G9) lineages. Since 1998, when the first human infection was identified, the detection of A(H9N2) viruses from humans and swine has been reported infrequently. In most human cases the associated illness has been mild and there has been no evidence of human-to-human transmission.

Influenza A(H9N2) activity from 20 February to 24 September 2018

One human case of A(H9N2) virus infection was reported in China in this period. The Y280/G9 lineage A(H9N2) viruses continue to predominate in birds in China and were detected in birds in the Russian Federation, Myanmar and Viet Nam. As in previous reporting periods, G1-lineage viruses were detected in birds in a number of countries in Africa and Asia.

Antigenic and genetic characteristics of influenza A(H9N2) viruses

The reported human A(H9N2) case was a 24-year-old female who fully recovered from the infection. As no virus was recovered from this case antigenic information is not available. All recent A(H9N2) human and poultry infections in China have been caused by viruses of the Y280/G9 lineage (Figure 2) with an increasing proportion showing reduced reactivity to post-infection ferret antiserum raised against A/Hong Kong/308/2014 (Table 5) or its associated CVV.

The majority of poultry viruses from the G1 lineage were antigenically and/or genetically similar to those detected in previous periods and to available CVVs.

Table 5. Haemagglutination inhibition assays of Y280/G9 lineage A(H9N2) influenza viruses

Reference Antigens	Lineage	HK/G9	HK/308	GD/01747	SCBZ/1453	HK/G1
A/chicken/Hong Kong/G9/97	Y280	**640**	40	40	<40	<40
A/Hong Kong/308/2014	Y280	40	**5120**	2560	1280	<40
A/Guangdong/01747/2014	Y280	40	2560	**2560**	1280	<40
A/Sichuan-Bazhou/1453/2014	Y280	40	2560	5120	**2560**	<40
A/quail/Hong Kong/G1/97	G1	<40	40	<40	<40	**1280**
Test Antigens						
A/Anhui-Lujiang/39/2018	Y280	<40	320	640	320	40
A/environment/Hunan/29028/2018	Y280	40	1280	1280	640	<40
A/environment/Hunan/28910/2018	Y280	40	640	1280	640	<40
A/environment/Hunan/28975/2018	Y280	40	640	640	640	<40
A/environment/Chongqing/30179/2018	Y280	<40	640	640	640	<40
A/environment/Jiangxi/27377/2018	Y280	<40	640	1280	640	<40
A/environment/Xinjiang/27373/2018	Y280	<40	320	640	320	40
A/environment/Gansu/25274/2018	Y280	<40	160	320	160	<40
A/environment/Shandong/28173/2018	Y280	<40	2560	2560	1280	<40
A/environment/Guangdong/27994/2018	Y280	<40	320	640	640	<40
A/environment/Guangdong/29635/2018	Y280	<40	320	640	320	<40
A/environment/Guangdong/27987/2018	Y280	<40	640	80	80	<40
A/environment/Heilongjiang/30617/2018	Y280	<40	640	80	80	<40
A/environment/Fujian/30649/2018	Y280	<40	320	640	640	<40
A/environment/Guangxi/13640/2018	Y280	<40	640	640	1280	<40
A/environment/Guangxi/29429/2018	Y280	<40	640	640	640	<40
A/environment/Guangdong/29641/2018	Y280	<40	640	640	640	<40
A/environment/Fujian/04960/2017	Y280	<40	160	320	320	<40
A/environment/Guangxi/40960/2017	Y280	<40	320	320	320	<40
A/environment/Hunan/04908/2017	Y280	<40	160	320	320	<40

Figure 2. Phylogenetic relationships of A(H9) Y280-like HA genes. CVVs that are available or in preparation are in red. The proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes.

Influenza A(H9N2) candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, a new A/Anhui-Lujiang/39/2018-like A(H9N2) CVV is proposed. The available A(H9N2) CVVs are listed in Table 6.

Table 6. Status of influenza A(H9N2) candidate vaccine virus development

Candidate vaccine viruses (like virus)	Type	Clade	Institution*	Available
A/Hong Kong/1073/99	Wild type	G1	NIBSC	Yes
NIBRG-91 (A/chicken/Hong Kong/G9/97)	Reverse genetics	Y280/G9	NIBSC	Yes
IBCDC-2 (A/chicken/Hong Kong/G9/97)	Conventional	Y280/G9	CDC	Yes
IDCDC-RG26 (A/Hong Kong/33982/2009)	Reverse genetics	G1	CDC	Yes
IDCDC-RG31 (A/Bangladesh/994/2011)	Reverse genetics	G1	CDC	Yes
SJ008 (A/Hong Kong/308/2014)	Reverse genetics	Y280/G9	SJCRH	Yes
Candidate vaccine viruses in preparation	**Type**	**Clade**	**Institution**	**Availability**
A/Anhui-Lujiang/39/2018-like	Reverse genetics	Y280/G9	CCDC	Pending
	Conventional	Y280/G9	NIBSC	Pending

* **Institutions distributing the candidate vaccine viruses:**

CDC - Centers for Disease Control and Prevention, United States of America

CCDC - Chinese Center for Disease Control and Prevention

NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom

SJCRH - St Jude Children's Research Hospital, United States of America

Influenza A(H1) variants (v)[4]

Influenza A(H1) viruses circulate in swine populations in many regions of the world. Depending on geographic location, the genetic and antigenic characteristics of these viruses differ. Human infections with swine A(H1) viruses have been documented for many years.

Influenza A(H1)v activity from 20 February to 24 September 2018

Thirteen cases of A(H1N2)v infection were identified in the United States of America (USA). Twelve of the 13 cases reported either exposure to swine or attendance of an agricultural fair during the week preceding illness onset. All but one of these individuals were less than 18 years of age. One individual did not attend a fair and reported no swine exposure, suggesting limited human-to-human transmission. All patients recovered fully.

Antigenic and genetic characteristics of influenza A(H1)v viruses

The A(H1N2)v viruses detected had HA gene segments from the delta 2 sublineage (clade 1B.2) of the swine H1 HA lineage (Figure 3). The HA and NA gene segments of these viruses were closely related to those of the A(H1N2) influenza viruses circulating in the USA swine population. The delta 2 lineage A(H1N2)v viruses possessed 21 HA1 amino acid substitutions relative to the recommended delta 2 lineage CVV derived from A/Ohio/35/2017. All recent A(H1N2)v viruses possessed an NA gene derived from the 1998 lineage of swine influenza viruses, which is distinct from that of A/Ohio/35/2017 (2002 NA lineage). Ferret antiserum raised against A/Ohio/35/2017 reacted well with all of the 2018 A(H1N2)v viruses (Table 7). HI reactivity of pooled post-vaccination sera from children or adults vaccinated with the 2017-2018 vaccine was below the limit of detection for all viruses tested (Table 7).

Table 7. Haemagglutination inhibition assays of A(H1)v influenza viruses

		pdm09	H1N1v (gamma)	H1N1v (gamma)	H1N2v (delta 1)	H1N2v (delta 1)	H1N2v (delta 2)	2017/ 2018	2017/ 2018
Reference Antigens	**Lineage**	**MI/45**	**Ohio/9**	**RG48A**	**MN/19**	**WI/71**	**OH/35**	**Child pool#**	**Adult pool***
A/Michigan/45/2015 H1N1	pdm09	**5120**	80	<10	<10	<10	<10	80	1280
A/Ohio/9/2015 H1N1v	gamma	40	**2560**	640	<10	<10	<10	<10	40
A/Ohio/9/2015 IDCDC-RG48A	gamma	80	5120	**1280**	<10	<10	<10	<10	160
A/Minnesota/19/2011 H1N2v	delta 1	<10	<10	<10	**2560**	1280	10	<10	20
A/Wisconsin/71/2016 H1N2v	delta 1	<10	<10	<10	160	**2560**	10	<10	10
A/Ohio/35/2017 H1N2v	delta 2	<10	<10	<10	<10	80	**320**	<10	<10
Test Antigens									
A/Michigan/382/2018	delta 2	<10	<10	<10	<10	40	160	<10	<10
A/Michigan/383/2018	delta 2	<10	<10	<10	<10	40	320	<10	<10
A/Ohio/24/2018	delta 2	<10	<10	<10	<10	20	160	<10	<10
A/Michigan/384/2018	delta 2	<10	<10	<10	<10	20	160	<10	<10

#2017-2018 post-vaccine immune serum pool from child (0-3 yrs) vaccinees (A/Michigan/45/2015 vaccine)
*2017-2018 post-vaccine immune serum pool from adult (19-49 yrs) vaccinees (A/Michigan/45/2015 vaccine)

[4] http://www.who.int/influenza/gisrs_laboratory/terminology_variant/en/
[5] http://www.eurosurveillance.org/images/dynamic/EE/V19N18/art20793.pdf

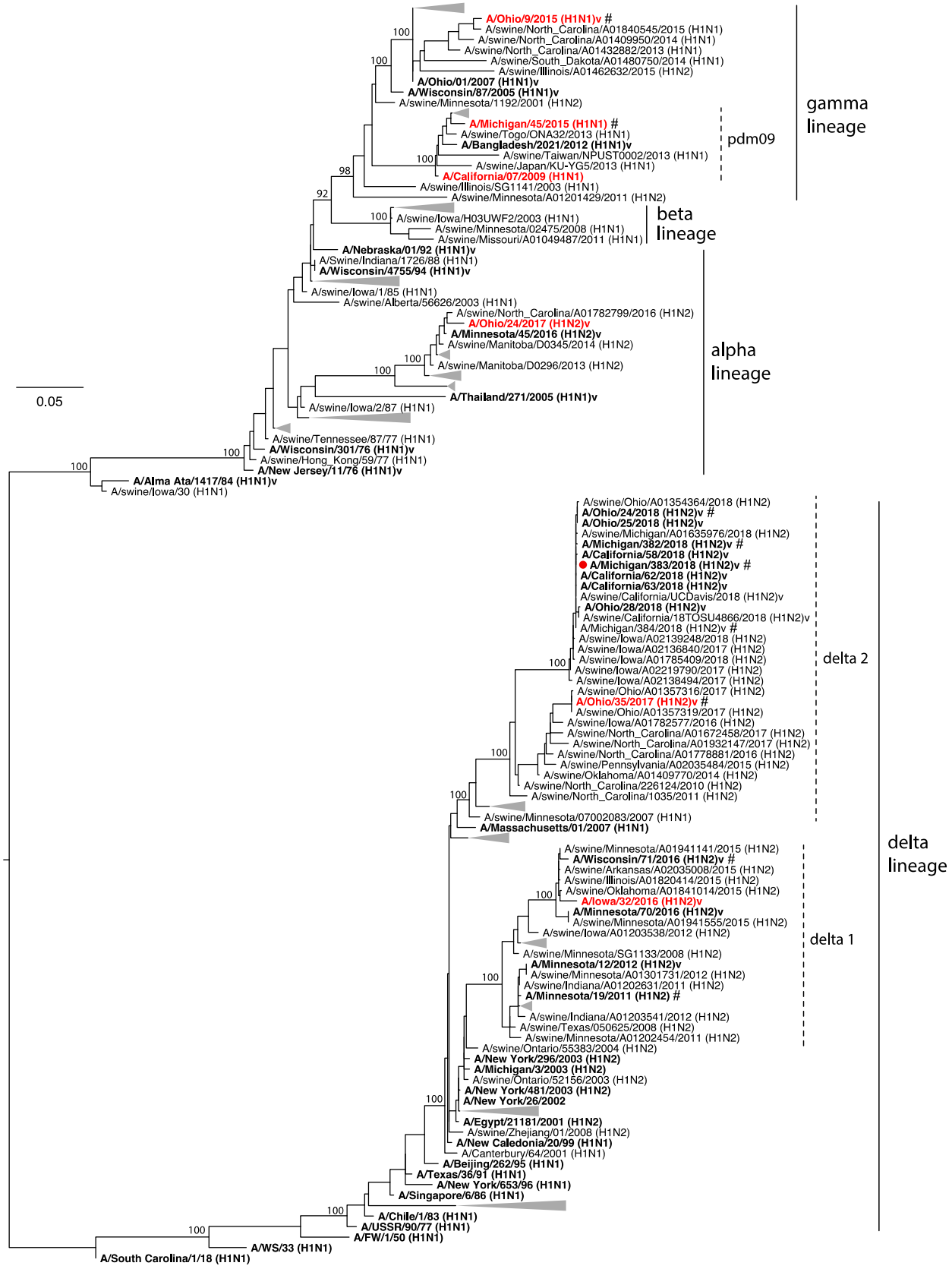

Figure 3. Phylogenetic relationships of A(H1) HA genes. CVVs that are available or in preparation are in red. The proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes. Some branches of virus strains are collapsed into grey triangles for clarity.

Influenza A(H1)v candidate vaccine viruses

Based on the current genetic and epidemiologic data, a new A/Michigan/383/2018-like A(H1N2)v CVV is proposed. The available A(H1)v CVVs are listed in Table 8.

Table 8. Status of A(H1)v candidate vaccine virus development

Candidate vaccine viruses (like viruses)	**Type**	**Institution***	**Available**
IDCDC-RG48A (A/Ohio/9/2015) (H1N1)	Reverse genetics	CDC	Yes
CNIC-1601 (A/Hunan/42443/2015) (H1N1)	Conventional and reverse genetics	CCDC	Yes
Candidate vaccine viruses in preparation	**Type**	**Institution**	**Availability**
A/Iowa/32/2016-like (H1N2)	Reverse genetics	CDC	Pending
A/Netherlands/3315/2016-like (H1N1)	Conventional	NIBSC	Pending
A/Ohio/24/2017-like (H1N2)	Reverse genetics	CDC	Pending
A/Ohio/35/2017-like (H1N2)	Reverse genetics	NIBSC	Pending
A/Michigan/383/2018-like (H1N2)	Reverse genetics	CDC	Pending

***Institution distributing the candidate vaccine virus:**

CDC - Centers for Disease Control and Prevention, United States of America

CCDC - Chinese Center for Disease Control and Prevention, China

NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom

Influenza A(H3N2)v[4]

Influenza A(H3N2) viruses are enzootic in swine populations in most regions of the world. Depending on geographic location, the genetic and antigenic characteristics of these viruses differ. Human infections with swine influenza A(H3N2) viruses have been documented in Asia, Europe and North America[5].

Influenza A(H3N2)v activity from 20 February to 24 September 2018
One A(H3N2)v virus infection was reported in a child from the United States of America. The child, who recovered from mild illness, had exposure to swine at an agricultural fair where swine were found to be infected with closely related viruses.

Antigenic and genetic characteristics of influenza A(H3N2)v viruses
The A(H3N2)v virus isolated from the reported case was closely related genetically to viruses that have circulated in swine in the USA for a number of years and previously been identified in humans in 2016 and 2017. These viruses have HA gene segments derived from a seasonal human A(H3) virus that was likely transmitted to swine from humans in 2010. Reactivity of antisera raised to A/Ohio/13/2017, from which a CVV has been proposed, to the A(H3N2)v virus was reduced 8-fold compared to the homologous virus titre despite the viruses being genetically similar. Pooled adult post-vaccination antisera reacted with the virus at titres that were within 4-fold to those against the homologous reference virus, A/Michigan/15/2014, representing the A(H3N2) component of the 2017-2018 seasonal influenza vaccines. Pooled post-vaccination antisera collected from young children had highly reduced titres to the 2018 virus as compared to the A/Michigan/15/2014 homologous virus titre.

Influenza A(H3N2)v candidate vaccine viruses
Based on the available antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available A(H3N2)v CVVs are listed in Table 9.

Table 9. Status of A(H3N2)v candidate vaccine virus development

Candidate vaccine viruses (like virus)	Type	Institution*	Available
NYMC X-203 (A/Minnesota/11/2010)	Conventional	CDC	Yes
NYMC X-213 (A/Indiana/10/2011)	Conventional	CDC	Yes
IDCDC-RG55C (A/Ohio/28/2016)	Reverse genetics	CDC	Yes
Candidate vaccine viruses in Preparation	**Type**	**Institution**	**Availability**
A/Ohio/13/2017-like	Reverse genetics	CDC	Pending

* **Institution distributing the candidate vaccine viruses:**
CDC - Centers for Disease Control and Prevention, United States of America

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[4] http://www.who.int/influenza/gisrs_laboratory/terminology_variant/en/
[5] http://www.eurosurveillance.org/images/dynamic/EE/V19N18/art20793.pdf