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

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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 26 September 2017 to 19 February 2018

Two A(H5N6) human infections in China, where A(H5) infections have also been detected in birds, have been reported to WHO. Since 2003 there have been 860 and 19 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 (subtype)
Afghanistan	Wild birds	Unknown
Bangladesh	Wild birds	2.3.2.1a (H5N1)
	Poultry	2.3.4.4 (H5N6); 2.3.2.1a (H5N1)
Bulgaria	Poultry	2.3.4.4 (H5N8)
Cambodia	Poultry	2.3.2.1c (H5N1)
China	Human (2)[#]	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
China Hong Kong SAR	Wild birds	2.3.4.4 (H5N6)
Taiwan, China	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N2)
Cyprus	Wild birds	2.3.4.4 (H5N8)
Germany	Wild birds	2.3.4.4 (H5N6/N8)
India	Poultry	2.3.4.4 (H5N8)
Indonesia	Poultry	2.3.2.1c (H5N1)
Iraq	Poultry	2.3.2.1c (H5N1); 2.3.4.4 (H5N8)
Iran (Islamic Republic of)	Wild birds	2.3.4.4 (H5N6)
Ireland	Wild birds	2.3.4.4 (H5N6)
Israel	Wild birds	2.3.4.4 (H5N8)
Italy	Wild birds	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Japan	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
Netherlands	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
Nigeria	Poultry	2.3.4.4 (H5N8)
Republic of Korea	Wild birds	2.3.4.4 (H5N6)
	Poultry	2.3.4.4 (H5N6)
Russian Federation	Poultry	2.3.4.4 (H5N8/N2)
Saudi Arabia	Poultry	2.3.4.4 (H5N8)
South Africa	Wild birds	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Sweden	Wild birds	2.3.4.4 (H5N6)
Switzerland	Wild birds	2.3.4.4 (H5N6)
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 (26 September 2017 to 19 February 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 26 September 2017 to 19 February 2018 belong to the following clades:

Clade 2.3.2.1a viruses were detected in birds in Bangladesh. The viruses were similar to viruses detected

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

in the region in previous periods and most reacted well with post-infection ferret antiserum raised against the CVV derived from A/duck/Bangladesh/19097/2013.

Clade 2.3.2.1c viruses were detected in birds in Cambodia, Indonesia, Iraq and Viet Nam. The HA genes of these viruses were similar to those from viruses detected previously in the respective countries. Although there was some diversity in antigenic profiles of the small number of viruses tested, most reacted well with post-infection ferret antiserum raised against available CVVs.

Clade 2.3.4.4 viruses were detected in two humans and birds in China and in birds in an additional 24 countries in Africa, Asia and Europe (Table 1). There is considerable genetic diversity in viruses of this clade, and the nomenclature for clade 2.3.4.4 viruses is under review. The two A(H5N6) viruses from humans had HA gene segments that were phylogenetically distinct from each other. The virus isolated from the case detected in Guangxi province had an HA gene genetically related to previous A(H5N6) viruses detected in China. This virus was well inhibited by ferret antisera raised against a clade 2.3.4.4 CVV, A/Hubei/29578/2016. The virus from Fujian province had an HA gene that was genetically similar to viruses recently detected in poultry and wild birds in Bangladesh, Japan, and many countries in Africa, Europe and Middle East (Figure 1). Representative viruses of this HA lineage reacted less well with post-infection ferret antiserum raised against the available CVVs including that produced from A/Sichuan/26221/2014 (Table 2 and 3). Viruses of this HA lineage in Europe have undergone reassortment with viruses from wild birds.

Table 2. Haemagglutination inhibition assays of clade 2.3.4.4 A(H5) influenza viruses

Reference antigens	**Subtype**	**Anhui/1**	**RG42A**	**d/E/36254**	**V/A324**	**V/15A59**	**Hyogo/1**
A/Anhui/1/2005	H5N1	**640**	<10	20	<10	40	80
A/Sichuan/26221/2014 IDCDC-RG42A	H5N6	<10	**160**	160	640	160	320
A/duck/England/36254/2014	H5N8	<10	20	**80**	80	160	40
A/chicken/Vietnam/NCVD-14-A324/2014	H5N6	<10	40	40	**320**	40	160
A/chicken/Vietnam/NCVD-15A59/2015	H5N6	<10	20	20	320	**80**	320
A/duck/Hyogo/1/2016	H5N6	<10	<10	<10	<10	<10	**160**
Test antigens							
A/duck/Bangladesh/19D770/2017	H5N6	<10	20	40	40	40	40
A/goose/Bangladesh/19D820/2017	H5N6	<10	<10	40	40	40	40
A/duck/Bangladesh/19D849/2017	H5N6	10	10	20	20	20	10
A/duck/Bangladesh/19D851/2017	H5N6	10	10	20	20	10	10
A/goose/Bangladesh/19D855/2017	H5N6	10	10	40	40	20	40
A/duck/Bangladesh/19D857/2017	H5N6	10	10	20	20	20	20

Table 3. Haemagglutination inhibition assays of clade 2.3.4.4 A(H5) influenza viruses

Reference antigens	**Subtype**	**Anhui/1**	**RG42A**	**H/29578**
A/Anhui/1/2005 RG	H5N1	**2560**	<20	<20
A/Sichuan/26221/2014 IDCDC-RG42A	H5N6	<20	**1280**	80
A/Hubei/29578/2016 RG	H5N6	<20	<20	**640**
A/Hubei/29578/2016	H5N6	<20	<20	**320**
Test antigens				
A/Guangxi/13486/2017	H5N6	<20	<20	320
A/environment/Guangdong/35460/2017	H5N6	<20	<20	80
A/environment/Chongqing/36534/2017	H5N6	<20	<20	160
A/environment/Guangdong/40564/2017	H5N6	<20	<20	20
A/Fujian-Sanyuan/21099/2017	H5N6	<20	160	<20

Influenza A(H5) candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, a new A/Fujian-Sanyuan/21099/2017-like A(H5N6) CVV is proposed. The available and pending A(H5) CVVs are listed in Table 4.

Table 4. Status of influenza A(H5) candidate vaccine virus development

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

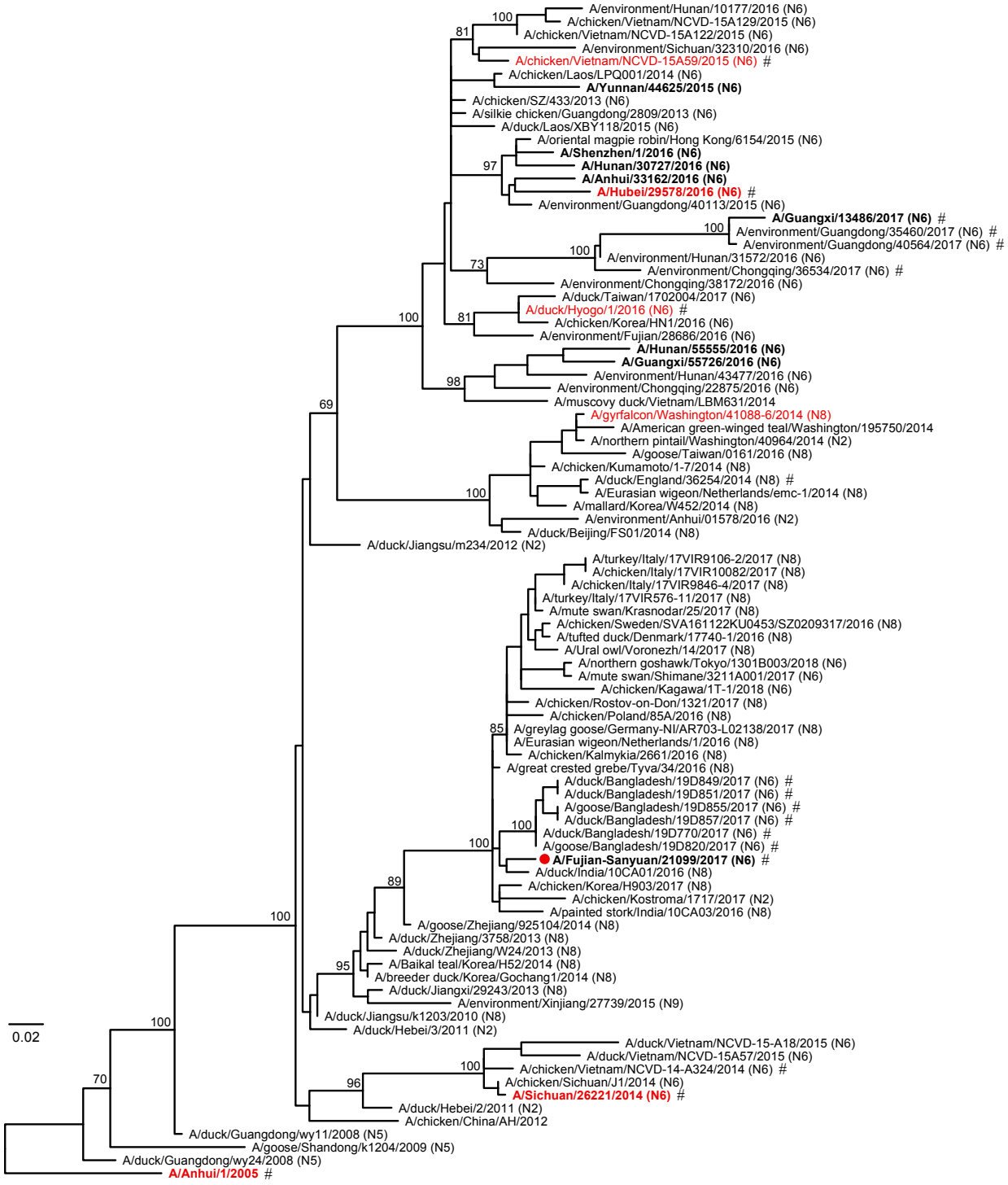

Figure 1. Phylogenetic relationships of A(H5) clade 2.3.4.4 HA genes. The available CVVs are in red. The proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). NA subtypes other than N1 are specified. The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes. A/Anhui/1/2005 (clade 2.3.4) is used to root the tree.

Influenza A(H7N9)

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) viruses has continued to generate multiple genotypes. This summary provides updates on the characterisation of A/Anhui/1/2013 HA lineage A(H7N9) viruses and the current status of the development of corresponding CVVs.

Influenza A(H7N9) activity from 26 September 2017 to 19 February 2018

During the sixth wave of human infections (starting October 2017), three cases of A(H7N9) virus infection with one death were reported from mainland China. The three human cases were reported from Guangdong, Xinjiang and Yunnan provinces. The total number of cases reported since 2013 is 1567 with a case fatality rate of 39%. The Yunnan virus was a HPAI virus and the Xinjiang virus was a low pathogenicity avian influenza (LPAI) virus. Data is not yet available for the virus from Guangdong. During this period in China, reports associated with LPAI in poultry were dramatically reduced and there was only one report of HPAI. Japan reported the detection of an HPAI A(H7N9) virus in a duck carcass originating from China.

Antigenic and genetic characteristics of influenza A(H7N9) viruses

Since 2013, a number of phylogenetically distinct HA groups have been detected within the A(H7N9) viruses. The HA genes of the HPAI and LPAI viruses are genetically distinct and further diversification has been seen within both groups. Viruses characterized in this period were genetically and antigenically related to previously detected viruses and 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 5.

Table 5. Status of influenza A(H7N9) candidate vaccine virus development

Candidate vaccine 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-like)	Reverse genetics	CDC	Yes
CNIC-GD003 (A/Guangdong/17SF003/2016-like)	Reverse genetics	CCDC	Yes
IDCDC-RG56N (A/Guangdong/17SF003/2016-like)	Reverse genetics	CDC	Yes
NIBRG-375 (A/Guangdong/17SF003/2016-like)	Reverse genetics	NIBSC	Yes
CBER-RG7C (A/Guangdong/17SF003/2016-like)	Reverse genetics	FDA	Yes
CNIC-HN02650 (A/Hunan/02650/2016-like)	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(H7N4)

Influenza A(H7N4) activity from 26 September 2017 to 19 February 2018

The first human case of influenza A(H7N4) virus infection was reported by China. The case was from Jiangsu province, and the individual developed severe pneumonia and survived. The throat swab collected from the patient tested positive for A(H7N4) by real-time RT-PCR and sequencing. The individual had slaughtered chickens prior to illness onset and LPAI A(H7N4) viruses were detected in ducks and chickens on the premises. None of the close contacts of the infected individual reported symptoms and all tested negative for influenza.

Genetic characteristics of the influenza A(H7N4) virus

Viral gene sequence analysis generated from clinical material showed that all segments of the human virus shared high identity with wild bird avian influenza viruses. The HA gene was distinct from the A(H7N9) viruses circulating in China and was characterised as low pathogenicity by HA cleavage site sequence. No mutations associated with reduced susceptibility to neuraminidase inhibitors, amantadine or rimantadine, were found. The PB2 carried the 627K marker associated with mammalian adaptation. Virus has not been isolated from the infected individual.

Influenza A(H7) candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available A(H7) CVVs, excluding A(H7N9) CVVs listed above, are listed in Table 6.

Table 6. Status of influenza A(H7) candidate vaccine virus development (excluding A(H7N9))

Candidate vaccine virus	Subtype	Type	Institution*	Available
A/mallard/Netherlands/12/2000 (NIBRG-63)	H7N1	Reverse genetics	NIBSC	Yes
A/turkey/Italy/3889/99	H7N1	Wild type	NIBSC	Yes
A/turkey/Virginia/4529/2002 (IBCDC-5)	H7N2	Reverse genetics	CDC	Yes
A/New York/107/2003 (NIBRG-109)	H7N2	Reverse genetics	NIBSC	Yes
A/Canada/rv444/2004 (SJRG-161984)	H7N3	Reverse genetics	SJCRH	Yes
A/mallard/Netherlands/12/2000 (NIBRG-60)	H7N3	Reverse genetics	NIBSC	Yes
A/mallard/Netherlands/12/2000 (IBCDC-1)	H7N7	Conventional	CDC	Yes

*** Institutions distributing the candidate vaccine viruses:**
CDC - Centers for Disease Control and Prevention, 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
SJCRH - St Jude Children's Research Hospital, United States of America

Influenza A(H9N2)

Influenza A(H9N2) viruses are enzootic in poultry populations in parts of Africa, Asia and the Middle East. The majority of viruses that have been 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 influenza-like symptoms have been mild and there has been no evidence of human-to-human transmission.

Influenza A(H9N2) activity from 26 September 2017 to 19 February 2018
Five human cases of A(H9N2) virus infection have been reported in China in this period; one case had disease onset in mid-September 2017. Four of the infections were in children (from 9 months to 9 years of age) with mild disease. The other infection was in a 51-year-old who was hospitalised. A(H9N2) viruses were detected in birds in many countries.

Antigenic and genetic characteristics of influenza A(H9N2) viruses
Two A(H9N2) viruses were isolated from the human cases in China and both belonged to the Y280/G9-lineage. Antigenic testing of these human viruses indicated that they were antigenically similar to available CVVs and to viruses detected in birds in China. The majority of tested poultry viruses from both G1 and Y280/G9 lineages were antigenically and/or genetically similar to those detected in previous periods and to available CVVs.

Influenza A(H9N2) candidate vaccine viruses
Based on the current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available A(H9N2) CVVs are listed in Table 7.

Table 7. Status of influenza A(H9N2) candidate vaccine virus development

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

*** Institutions distributing the candidate vaccine viruses:**
CDC - Centers for Disease Control and Prevention, 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
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 26 September 2017 to 19 February 2018
One case of A(H1N1)v and one case of A(H1N2)v infection in the United States of America (United States) and one case of suspected A(H1N1)v infection in Switzerland were detected during this reporting period. The virus from Switzerland is undergoing further genetic characterisation. All cases were adults who developed mild disease following exposure to pigs.

Antigenic and genetic characteristics of influenza A(H1)v viruses
Phylogenetic analysis of the A(H1N2)v virus A/Colorado/16/2017 showed that it had an HA gene of the swine H1 delta 1 lineage[5]. The A(H1N1)v virus A/Iowa/33/2017 had HA and NA gene segments derived from a seasonal A(H1N1)pdm09 (clade 6B.1) virus that circulated in humans around 2016. The virus from the case in Switzerland had gene segments closely related to Eurasian avian-like swine influenza viruses. In all three cases, the variant viruses were related to viruses known to circulate in swine. Antigenic testing demonstrated that ferret antisera raised against a delta 1 lineage virus that was genetically and antigenically related to the previously recommended CVV reacted well with the A(H1N2)v virus from Colorado. The reactivity of pooled, adult human sera collected post-vaccination with the 2016-2017 vaccine was reduced against this virus. The A(H1N1)v virus from Iowa was well inhibited by ferret antisera raised against seasonal human A(H1N1)pdm09 viruses, A/California/7/2009 and A/Michigan/45/2015. Virus has not yet been isolated from the case reported in Switzerland.

Influenza A(H1)v candidate vaccine viruses
Based on the current antigenic, genetic and epidemiologic data, no new CVVs are 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	Type	Institution*	Available
A/Ohio/9/2015 (IDCDC-RG48A)	Reverse genetics	CDC	Yes
A/Hunan/42443/2015 (CNIC-1601)	Conventional and reverse genetics	CCDC	Yes
Candidate vaccine viruses in preparation	**Type**	**Institution**	**Availability**
A/Iowa/32/2016-like	Reverse genetics	CDC	Pending
A/Netherlands/3315/2016-like	Conventional	NIBSC	Pending
A/Ohio/24/2017-like	Reverse genetics	CDC	Pending
A/Ohio/35/2017-like	Conventional	NIBSC	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

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

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 26 September 2017 to 19 February 2018
Thirty-one cases of A(H3N2)v infection were detected in the United States during this reporting period in the States of Maryland [26], Michigan [2], Nebraska [1], Delaware [1] and Iowa [1] following exposure to swine at agricultural fairs. Twenty-seven cases (87%) were less than 18 years of age. One instance of possible human-to-human transmission was detected.

Antigenic and genetic characteristics of influenza A(H3N2)v viruses
All of the A(H3N2)v viruses had HA gene segments derived from a seasonal human A(H3) virus that was likely transmitted to swine from humans in 2010. The viruses were closely related to A(H3N2)v viruses previously identified in humans in 2016/2017 and viruses known to circulate in swine in the United States.

The A(H3N2)v viruses were well inhibited by ferret antisera raised against A/Ohio/13/2017, from which a CVV has been recommended. Pooled, adult post-vaccination sera reacted with these viruses at titres that were comparable to those against A/Michigan/15/2014, representing the A(H3N2) component of the seasonal influenza vaccine. However, pooled, post-vaccination sera collected from children (0-3 years of age) had reduced titres compared to the homologous virus and titres detected in pooled adult sera.

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	Type	Institution*	Available
NYMC X-203 (A/Minnesota/11/2010-like)	Conventional	CDC	Yes
NYMC X-213 (A/Indiana/10/2011-like)	Conventional	CDC	Yes
IDCDC-RG55C (A/Ohio/28/2016-like)	Conventional	NIBSC	pending
	and 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
NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom

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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