Antigenic and genetic characteristics of zoonotic influenza A 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 influenza 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, leading to the need for multiple CVVs. Notably, H5 viruses have been detected with the N1 gene segment replaced by N2, N3, N5, N6, N8 or N9 gene segments. This summary provides updates on the characterization 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 25 February to 30 September 2020

No human infections with A/goose/Guangdong/1/96-lineage viruses were reported in this period. Since 2003, there have been 24 A(H5N6) and 861 A(H5N1) human infections confirmed. A/goose/Guangdong/1/96-lineage A(H5) viruses were detected in domestic and wild birds in several 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. H5 activity reported to international agencies since February 2020

Country, area or territory	Host	Genetic clade* (subtype)
Bangladesh	Poultry	2.3.2.1a (H5N1), 2.3.4.4h (H5N6)
Bulgaria	Poultry	2.3.4.4b (H5N8)
Cambodia	Poultry	2.3.4.4h (H5N6)
	Poultry	2.3.2.1c (H5N1)
China	Poultry	2.3.4.4h (H5N6)
China, Taiwan province	Poultry	2.3.4.4c (H5N2)
	Poultry	2.3.4.4c (H5N5)
Czech Republic	Poultry	2.3.4.4b (H5N8)
Egypt	Poultry	2.3.4.4b (H5N8)
Germany	Wild bird	2.3.4.4b (H5N8)
	Poultry	2.3.4.4b (H5N8)
Hungary	Poultry	2.3.4.4b (H5N8)
India	Wild bird	2.3.2.1a (H5N1)
	Poultry	2.3.2.1a (H5N1)
Iraq	Poultry	TBD† (H5N8)
Kazakhstan	Poultry	TBD (H5)
	Wild bird	TBD (H5)
Poland	Poultry	TBD (H5N6)
	Poultry	TBD (H5N8)
Republic of the Philippines	Poultry	TBD (H5N6)
Romania	Poultry	2.3.4.4b (H5N8)
Russian Federation	Poultry	2.3.4.4b (H5N8)
	Wild bird	2.3.4.4b (H5N8)
Viet Nam	Poultry	2.3.2.1c (H5N1); 2.3.4.4g (H5N6); 2.3.4.4h (H5N6)

* Utilizing proposed update to the unified nomenclature for HPAI A(H5) viruses

† To be determined

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/or characterized from 25 February to 30 September 2020 belong to the following clades:

Clade 2.3.2.1a viruses were detected in poultry in Bangladesh and India. The majority of viruses tested from Bangladesh reacted well with a post-infection ferret antiserum raised against A/duck/Bangladesh/17D1012/2018, for which a CVV is in development.

Clade 2.3.2.1c viruses were detected in poultry in Viet Nam and Cambodia. Viruses from Viet Nam reacted well with post-infection ferret antisera raised against A/duck/Vietnam/NCVD-1584/2012 and its corresponding CVV.

Clade 2.3.4.4b viruses were detected in poultry and/or wild birds in Bulgaria, Czech Republic, Egypt, Germany, Hungary, Romania and the Russian Federation, with evidence of multiple separate introductions into some countries. Most recent clade 2.3.4.4b viruses reacted well with post-infection ferret antiserum raised against the CVV developed from A/Fujian-Sanyuan/21099/2017.

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

Clade 2.3.4.4c viruses were detected in poultry in Taiwan, province of China. Compared with the most closely related CVV, A/gyrfalcon/Washington/41088-6/2014, there were up to 9 amino acid differences in the HA. No antigenic data are available for these viruses.

Clade 2.3.4.4g viruses were detected in poultry in Viet Nam. These viruses were genetically related to viruses detected in Viet Nam in previous years (Figure 1), which were recognised well by antisera raised against the A/Fujian-Sanyuan/21099/2017 (clade 2.3.4.4b) CVV and A/chicken/Vietnam/NCVD-15A59/2015, the wild type virus recommended for the development of a clade 2.3.4.4f CVV. However, the recently detected viruses reacted poorly with these antisera (Table 2).

Clade 2.3.4.4h viruses were detected in poultry and/or wild birds in Bangladesh, Cambodia, China and Viet Nam. The HAs of most of these viruses had fewer than 10 amino acid differences relative to that of A/Guangdong/18SF020/2018, the closest virus from which a CVV has been proposed. Preparation of post-infection ferret antisera against clade 2.3.4.4h viruses is underway to allow antigenic characterization of these viruses.

Table 2. Haemagglutination inhibition assay of recent clade 2.3.4.4g influenza A(H5N6) viruses

Reference Antigens	Clade	IDCDC-RG42A	CNIC-FJ21099	ck/15A59	dk/17A231
IDCDC-RG42A (A/Sichuan/26221/2014-like)	2.3.4.4a	**320**	160	80	160
CNIC-FJ21099 (A/Fujian-Sanyuan/21099/2017-like)	2.3.4.4b	20	**80**	80	80
A/chicken/Vietnam/NCVD-15A59/2015	2.3.4.4f	40	40	**80**	40
A/duck/Vietnam/NCVD-17A231/2016	2.3.4.4g	20	20	40	**40**
Test Antigens					
A/chicken/Vietnam/RAHO6-19-18283/2019	2.3.4.4g	<10	10	10	20
A/chicken/Vietnam/RAHO6-19-20801-2/2019	2.3.4.4g	20	40	80	80
A/chicken/Vietnam/RAHO6-19-21077/2019	2.3.4.4g	<10	<10	<10	10
A/duck/Vietnam/RAHO6-19-39044/2019	2.3.4.4g	<10	<10	10	10
A/chicken/Vietnam/RAHO4-CD-19-7446/2019	2.3.4.4g	<10	10	10	40
A/chicken/Vietnam/RAHO4-CD-19-11259/2019	2.3.4.4g	<10	<10	<10	<10
A/chicken/Vietnam/RAHO4-CD-20-421/2020	2.3.4.4g	<10	10	10	20

Influenza A(H5) candidate vaccine viruses

Based on current antigenic, genetic and epidemiologic data, a new A(H5N6) clade 2.3.4.4g CVV antigenically like A/chicken/Vietnam/RAHO4-CD-20-421/2020 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/Vietnam/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)	2.3.4.4a	CDC/CCDC	Yes
IDCDC-RG43A (A/gyrfalcon/Washington/41088-6/2014) (H5N8)	2.3.4.4c	CDC	Yes
NIID-001 (A/duck/Hyogo/1/2016) (H5N6)	2.3.4.4e	NIID	Yes
SJRG-165396 (A/goose/Guiyang/337/2006)	4	SJCRH/HKU	Yes
IDCDC-RG12 (A/chicken/Vietnam/NCVD-016/2008)	7.1	CDC	Yes
IDCDC-RG25A (A/chicken/Vietnam/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	2.3.2.1d	SJCRH/HKU	Pending
A/chicken/Ghana/20/2015-like	2.3.2.1f	CDC	Pending
A/chicken/Vietnam/NCVD-15A59/2015 (H5N6)-like	2.3.4.4f	SJCRH	Pending
A/Guangdong/18SF020/2018 (H5N6)-like	2.3.4.4h	CDC/CCDC	Pending
A/Fujian-Sanyuan/21099/2017 (H5N6)-like	2.3.4.4b	CCDC	Pending
A/Hubei/29578/2016 (H5N6)-like	2.3.4.4d	CCDC	Pending
A/chicken/Vietnam/RAHO4-CD-20-421/2020 (H5N6)-like	2.3.4.4g	CDC	Pending

[*] All listed CVVs have been produced using reverse genetics

[†] Where not indicated, the virus subtype is H5N1

[‡] 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 – The 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

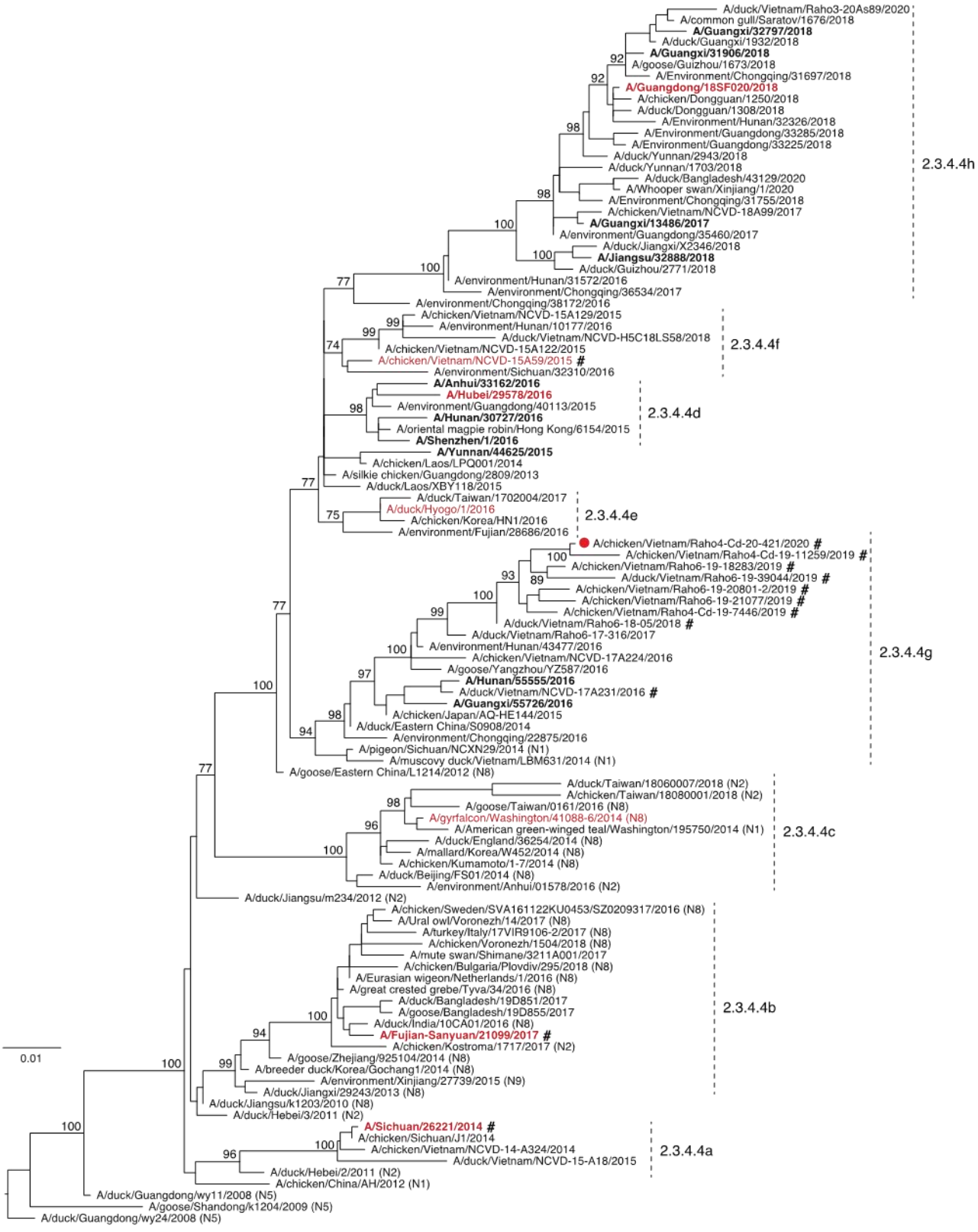

Figure 1. Phylogenetic relationships of A(H5) clade 2.3.4.4 HA genes. Available CVVs are in red. Proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). NA subtypes other than N6 are specified. The tree was built from the nucleotide sequences coding for the mature HA1 protein. The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes.

Influenza A(H7)

Human infections with A/Anhui/1/2013 HA lineage avian influenza A(H7N9) viruses were first reported to WHO on 31 March 2013. Other lineages of A(H7) viruses have also caused zoonotic infections in previous years. This summary provides updates on the characterisation of A(H7) viruses related to these zoonotic viruses and the current status of the development of corresponding CVVs.

Influenza A(H7) activity from 25 February to 30 September 2020

No human infections with A(H7), including A/Anhui/1/2013-lineage A(H7N9) viruses, have been detected in this period. Low pathogenicity and/or highly pathogenic A(H7) viruses belonging to different HA lineages were detected in poultry in Australia and the United States of America but were successfully eradicated through control measures.

Influenza A(H7) candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available and pending CVVs for A(H7) viruses including A(H7N9) are listed in Table 4.

Table 4. Status of influenza A(H7) candidate vaccine virus development

Candidate vaccine virus (like virus)	Lineage (subtype)	Type	Institution*	Available
IDCDC-RG33A (A/Anhui/1/2013)	A/Anhui/1/2013 (H7N9)	Reverse genetics	CDC	Yes
NIBRG-268 (A/Anhui/1/2013)	A/Anhui/1/2013 (H7N9)	Reverse genetics	NIBSC	Yes
NIIDRG-10.1 (A/Anhui/1/2013)	A/Anhui/1/2013 (H7N9)	Reverse genetics	NIID	Yes
SJ005 (A/Anhui/1/2013)	A/Anhui/1/2013 (H7N9)	Reverse genetics	SJCRH	Yes
NIBRG-267 (A/Shanghai/2/2013)	A/Anhui/1/2013 (H7N9)	Reverse genetics	NIBSC	Yes
CBER-RG4A (A/Shanghai/2/2013)	A/Anhui/1/2013 (H7N9)	Reverse genetics	FDA	Yes
IDCDC-RG32A (A/Shanghai/2/2013)	A/Anhui/1/2013 (H7N9)	Reverse genetics	CDC	Yes
IDCDC-RG32A.3 (A/Shanghai/2/2013)	A/Anhui/1/2013 (H7N9)	Reverse genetics	CDC	Yes
IDCDC-RG56B (A/Hong Kong/125/2017)	A/Anhui/1/2013 (H7N9)	Reverse genetics	CDC	Yes
IDCDC-RG56N (A/Guangdong/17SF003/2016)	A/Anhui/1/2013 (H7N9)	Reverse genetics	CDC	Yes
NIBRG-375 (A/Guangdong/17SF003/2016)	A/Anhui/1/2013 (H7N9)	Reverse genetics	NIBSC	Yes
CBER-RG7C (A/Guangdong/17SF003/2016)	A/Anhui/1/2013 (H7N9)	Reverse genetics	FDA	Yes
CBER-RG7D (A/Guangdong/17SF003/2016)	A/Anhui/1/2013 (H7N9)	Reverse genetics	FDA	Yes
IDCDC-RG64A (A/Gansu/23277/2019-like)	A/Anhui/1/2013 (H7N9)	Reverse genetics	CDC	Yes
IBCDC-5 (A/turkey/Virginia/4529/2002)	American (H7N2)	Conventional	CDC	Yes
SJRG-161984-B (A/Canada/rv444/2004)	American (H7N3)	Reverse genetics	SJCRH	Yes
NIBRG-109 (A/New York/107/2003)	American (H7N2)	Conventional	NIBSC	Yes
IBCDC-1 (A/mallard/Netherlands/12/2000)	Eurasian (H7N7)	Conventional	CDC	Yes
NIBRG-60 (A/mallard/Netherlands/12/2000)	Eurasian (H7N3)	Reverse genetics	NIBSC	Yes
NIBRG-63 (A/mallard/Netherlands/12/2000)	Eurasian (H7N1)	Reverse genetics	NIBSC	Yes
Candidate vaccine virus in preparation	**Lineage (subtype)**	**Type**	**Institution***	**Available**
A/chicken/Jiangsu/1/2018-like	Eurasian (H7N4)	Reverse genetics	CCDC	Pending
A/Hunan/02650/2016-like	A/Anhui/1/2013 (H7N9)	Reverse genetics	CCDC	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
FDA – Food and Drug Administration, United States of America
HKU – The 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(H9N2)

Influenza A(H9N2) viruses are enzootic in poultry in parts of Africa, Asia and the Middle East with the majority of viruses belonging to either the A/quail/Hong Kong/G1/97 (G1) or A/chicken/Beijing/1/94 (Y280/G9) lineages. Since the late 1990s, when the first human infection was identified, the detection of A(H9N2) viruses in human and swine specimens has been reported sporadically with associated mild disease in most human cases and no evidence for human-to-human transmission. Since 1998 a total of 57 A(H9N2) human infections had been documented. An additional 16 human cases from January and February of 2019 were published recently.[4] These cases, that included several with severe disease, were detected in Hubei Province, China. The national authorities are currently gathering more information.

Influenza A(H9N2) activity from 25 February to 30 September 2020
Five human cases of A(H9N2) virus infection were detected in China in this period. All cases were mild and in children less than eight years of age.

Y280/G9-lineage viruses continue to predominate in environmental and poultry samples in China and Viet Nam. G1-lineage viruses were detected in poultry in a number of countries in Africa and Asia.

Antigenic and genetic characteristics of influenza A(H9N2) viruses
All recent A(H9N2) human and poultry infections in China, and poultry infections in Viet Nam, were caused by viruses of the Y280/G9-lineage. Four of the viruses detected in humans in 2020 were sequenced; three had HA genes showing greatest similarity to the A/Anhui-Lujiang/39/2018 CVV, while the fourth was most similar to the A/Hong Kong/308/2014 CVV (Figure 2). The viruses from humans infected in 2020 reacted well with post-infection ferret antiserum raised against A/Anhui-Lujiang/39/2018 (Table 5). Currently available CVVs were antigenically representative of most A(H9N2) Y280/G9- and G1-lineage viruses detected in birds, despite some genetic divergence.

Table 5. Haemagglutination inhibition assay of recent human A(H9N2) influenza viruses

Reference antigens	Lineage	HK/G9	HK/308	Gd/01747	AL/39	HK/G1
A/chicken/Hong Kong/G9/97	Y280/G9	**640**	80	20	<20	<20
A/Hong Kong/308/2014	Y280/G9	80	**5120**	5120	640	40
A/Guangdong/01747/2014	Y280/G9	40	2560	**2560**	1280	20
A/Anhui-Luijang/39/2018	Y280/G9	20	640	640	**2560**	<20
A/quail/Hong Kong/G1/97	G1	<20	<20	<20	<20	**320**
Test antigens						
A/Guangdong/11172/2020	Y280/G9	40	640	640	1280	<20
A/Hunan/11173/2020	Y280/G9	80	1280	1280	2560	<20
A/Fujian-Sanyuan/2881/2019	Y280/G9	40	640	640	640	<20
A/Anhui-Yingzhou/12340/2019	Y280/G9	ND*	ND	640	1280	<20
A/Fujian-Siming/1348/2020	Y280/G9	40	1280	640	640	<20
A/environment/Gansu/01447/2019	Y280/G9	40	1280	1280	640	<20
A/environment/Sichuan/01159/2019	Y280/G9	<20	640	640	2560	<20

* Not Determined

[4] Dong X et al. Human H9N2 Avian Influenza Infection: Epidemiological and Clinical Characterization of 16 Cases in China. Virol Sin. 2020 Jul 6:1–4.

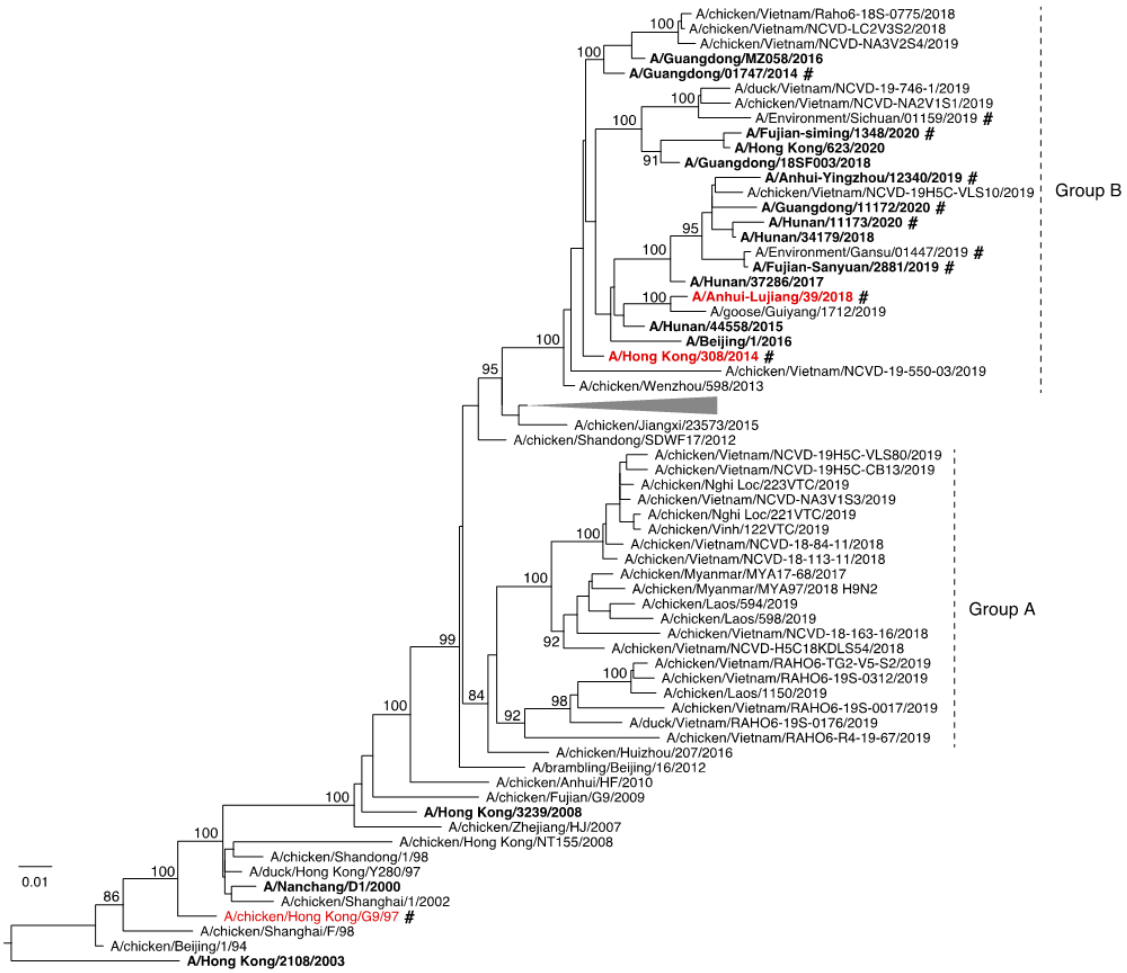

Figure 2. Phylogenetic relationships of A(H9N2) Y280-like HA genes. CVVs that are available or in preparation are in red. Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The tree was built from the nucleotide sequences coding for the mature HA1 protein. 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(H9N2) candidate vaccine viruses

Based on the available antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available and pending A(H9N2) CVVs are listed in Table 6.

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

Candidate vaccine viruses (like virus)	Clade	Type	Institution*	Available
A/Hong Kong/1073/99	G1	Wild type	NIBSC	Yes
NIBRG-91 (A/chicken/Hong Kong/G9/97)	Y280/G9	Reverse genetics	NIBSC	Yes
IBCDC-2 (A/chicken/Hong Kong/G9/97)	Y280/G9	Conventional	CDC	Yes
IDCDC-RG26 (A/Hong Kong/33982/2009)	G1	Reverse genetics	CDC	Yes
IDCDC-RG31 (A/Bangladesh/994/2011)	G1	Reverse genetics	CDC	Yes
SJ008 (A/Hong Kong/308/2014)	Y280/G9	Reverse genetics	SJCRH	Yes
IDCDC-RG61A (A/Anhui-Lujiang/39/2018)	Y280/G9	Reverse genetics	CDC/CCDC	Yes
Candidate vaccine viruses in preparation	**Type**	**Clade**	**Institution**	**Availability**
A/Oman/2747/2019-like	Reverse genetics	G1	CDC	Pending

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

CCDC – Chinese Center for Disease Control and Prevention

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

HKU – The 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

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

Influenza A(H1)v[5]

Influenza A(H1) 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(H1) viruses (designated as A(H1)v viruses) have been documented previously in Asia, Europe and the Americas.

Influenza A(H1)v activity from 25 February to 30 September 2020

One case each of A(H1N1)v and A(H1N2)v human infection was identified in Germany and Brazil, respectively. This was the first case of an A(H1N1)v virus infection reported in Germany and the second case of an A(H1N2)v virus infection reported in Brazil. Additionally, a case of A(H1N1)v virus infection in the Netherlands in September 2019 was identified retrospectively. All individuals had an uncomplicated course of illness.

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

The A(H1N1)v infections were caused by viruses from the 1C.2.2[6] (Eurasian avian-like) swine influenza virus clade, whereas the A(H1N2)v virus was classified as clade 1B.2. Each virus was genetically related to circulating swine influenza viruses from their respective country (Figure 3). The A(H1N1)v 1C.2.2 virus detected in Germany, A/Hessen/47/2020, had an HA1 that differed by 31 amino acids from that of A/Netherlands/3315/2016 from which a clade 1C.2.1 CVV had been recommended. Similarly, the A/Hessen/47/2020 HA1 differed from that of A/Hunan/42443/2020, from which a clade 1C.2.3 CVV has been recommended, by 30 amino acids. A/Hessen/47/2020 was recognised poorly by ferret antisera raised against A/Netherlands/3315/2016, but was well recognised by ferret antisera raised against clade 1C.2.2 swine influenza viruses and clade 1C.2.3 influenza viruses (Table 7). The A(H1N2)v virus detected in Brazil could not be isolated for antigenic characterisation.

Table 7. Haemagglutination inhibition assay of recent A(H1N1)v influenza viruses

Reference Antigens	Clade	A/Neth/ 3315	A/Pavia/ 65	sw/Cd'A 324	sw/IV/ 1455	CNIC- 1601
A/Netherlands/3315/2016	1C.2.1	**320**	40	40	<40	<40
A/Pavia/65/2016	1C.2.1	<40	**320**	<40	80	<40
A/swine/Côtes d'Armor/324/2007	1C.2.2	80	<40	**320**	40	80
A/swine/Ille et Vilaine/1455/99	1C.2.3	<40	40	<40	**160**	80
CNIC-1601 (A/Hunan/42443/2015)	1C.2.3	40	<40	160	160	**320**
Test Antigens						
A/Hessen/47/2020	1C.2.2	40	<40	160	160	320

Influenza A(H1)v candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, a new clade 1C.2.2 CVV antigenically like A/Hessen/47/2020 is proposed. The available and pending A(H1)v CVVs are listed in Table 8.

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

Candidate vaccine viruses (like viruses)	Clade	Type	Institution*	Available
CNIC-1601 (A/Hunan/42443/2015) (H1N1)	1C.2.3	Conventional	CCDC	Yes
IDCDC-RG48A (A/Ohio/9/2015) (H1N1)	1A.3.3.3	Reverse genetics	CDC	Yes
IDCDC-RG58A (A/Michigan/383/2018) (H1N2)	1B.2.1	Reverse genetics	CDC	Yes
IDCDC-RG59 (A/Ohio/24/2017) (H1N2)	1A.1.1	Reverse genetics	CDC	Yes
Candidate vaccine viruses in preparation		**Type**	**Institution**	**Availability**
A/Iowa/32/2016-like (H1N2)	1B.2.2.1	Reverse genetics	CDC	Pending
A/Netherlands/3315/2016-like (H1N1)	1C.2.1	Conventional	NIBSC	Pending
A/Ohio/35/2017-like (H1N2)	1B.2.1	Conventional	NIBSC	Pending
A/Hessen/47/2020-like (H1N1)	1C.2.2	Conventional	NIBSC	Pending

* Institution 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

[5] http://www.who.int/influenza/gisrs_laboratory/terminology_variant/en/
[6] https://msphere.asm.org/content/1/6/e00275-16

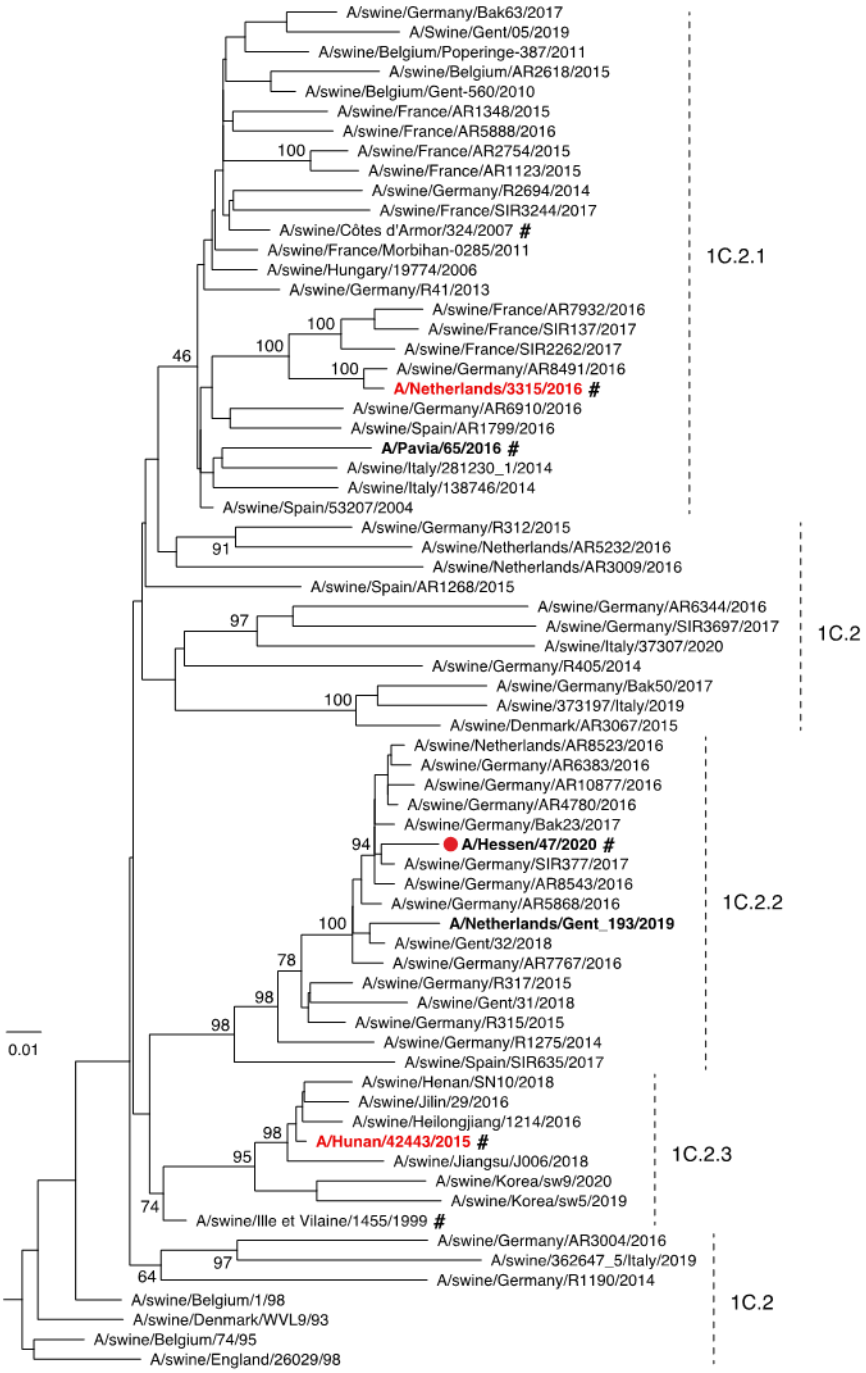

Figure 3. Phylogenetic relationships of Eurasian avian-like influenza A(H1N1)v HA genes. CVVs that are available or in preparation are in red. Proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The tree was built from the nucleotide sequences coding for the mature HA1 protein. The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes.

Influenza A(H3N2)v

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[7].

Influenza A(H3N2)v activity from 25 February to 30 September 2020

A human case of A(H3N2)v virus infection was reported in the United States of America. The case reported no known exposure to swine, had mild illness, and recovered. Since reporting of novel influenza A viruses became nationally notifiable in 2005, 438 human infections with A(H3N2)v viruses have been reported in the United States of America.

Antigenic and genetic characteristics of influenza A(H3N2)v viruses

The human A(H3N2)v virus had an HA gene showing greatest similarity to that of currently circulating swine influenza viruses that are derived from a live attenuated swine influenza vaccine used in the United States of America. This vaccine virus in this vaccine contains the HA and NA genes from a swine A(H3N2) influenza virus from 1998. The A(H3N2)v virus reacted well to pooled post-vaccination adult human sera, but not to pooled post-vaccination sera from children. The virus also reacted well to post-infection ferret antiserum raised against A/Beijing/32/92, a previous seasonal A(H3N2) vaccine component.

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 influenza A(H3N2)v candidate vaccine virus development

Candidate vaccine viruses	Clade	Type	Institution*	Available
A/Minnesota/11/2010 (NYMC X-203)	3.1990.4.A	Conventional	CDC	Yes
A/Indiana/10/2011 (NYMC X-213)	3.1990.4.A	Conventional	CDC	Yes
IDCDC-RG55C (A/Ohio/28/2016-like)	3.2010.1	Reverse Genetics	CDC	Yes
Candidate vaccine viruses in preparation		**Type**	**Institution**	**Availability**
A/Ohio/13/2017-like	3.2010.1	Reverse Genetics	CDC	Pending
A/Ohio/28/2016-like	3.2010.1	Conventional	NIBSC	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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[5] http://www.eurosurveillance.org/images/dynamic/EE/V19N18/art20793.pdf