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

September 2022

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 summarizes 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 across a wide geographic area. These viruses have diversified genetically and antigenically, leading to the need for multiple CVVs. Detected viruses with H5 HA gene segments have been paired with a variety of neuraminidase (NA) subtypes (N1, N2, N3, N4, N5, N6, N8 or N9). This summary provides updates on the characterization of A/goose/Guangdong/1/96-lineage A(H5) viruses and the status of the development of influenza A(H5) CVVs.

Influenza A(H5) activity from 24 February through 19 September 2022

Eight human infections with A/goose/Guangdong/1/96-lineage viruses have been reported in this period. Since 2003, there have been 3 A(H5), 7 A(H5N8), 81 A(H5N6) and 865 A(H5N1) human infections reported. Since February 2022, A/goose/Guangdong/1/96-lineage A(H5) viruses have been detected in both domestic and wild birds in many countries, with sporadic detections in wild mammals in Asia, Europe and North America (Table 1).

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 (WOAH) and academic institutions.[3]

[1] For information relevant to other notifiable influenza virus infections in animals refer to https://wahis.woah.org/#/home

[2] https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations/candidate-vaccine-viruses

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

Table 1. H5 activity reported to international agencies since February 2022

Country, area or territory	Host	Genetic clade
Albania	poultry	2.3.4.4b (H5N8)
	wild birds	2.3.4.4b (H5N1)
Austria	wild birds	unknown (H5N1)
Bangladesh	poultry	2.3.4.4b (H5N1); 2.3.2.1a (H5N1)
Belgium	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Bulgaria	poultry	unknown (H5)
	wild birds	
Cambodia	poultry	2.3.2.1c (H5N1); 2.3.4.4b (H5N1/8)
Canada	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
	mammals (skunk, red fox, wild fox, mink, harbor seal)	2.3.4.4b (H5N1)
China	human (7)*	2.3.4.4b (H5N6)
	poultry	2.3.4.4b (H5N1)
	wild birds	unknown (H5N1/8)
China, Hong Kong SAR	wild birds	unknown (H5N1)
Taiwan, China	poultry	unknown (H5N1/2)
	wild birds	unknown (H5N1/2)
Croatia	poultry	unknown (H5N1)
	wild birds	unknown (H5N1)
Czechia	poultry	2.3.4.4b (H5N1)
Denmark	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Egypt	poultry	2.3.4.4b (H5N1/8)
Estonia	wild birds	unknown (H5N1)
Faroe Islands	wild birds	unknown (H5N1)
Finland	wild birds	unknown (H5N1)
	mammal (lynx)	2.3.4.4b (H5N1)
France	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Gabon	poultry	unknown (H5N1)
Germany	poultry	unknown (H5N1)
	wild birds	2.3.4.4b (H5N1/2)
Ghana	poultry	unknown (H5N1)
Greece	wild birds	2.3.4.4b (H5N1)
Guernsey	wild birds	unknown (H5N1)
Guinea	poultry	2.3.4.4b (H5N1)
Hungary	poultry	unknown (H5N1)
	wild birds	unknown (H5N1)
Iceland	poultry	unknown (H5N1)
	wild birds	unknown (H5N1)
India	poultry	2.3.2.1a (H5N1)
Indonesia	poultry	2.3.2.1e (H5N1)
Iraq	poultry	unknown (H5N8)
Ireland	wild birds	2.3.4.4b (H5N1)
	mammal (fox)	2.3.4.4b (H5N1)
Isle of Man	wild bird	unknown (H5N1)
Israel	wild birds	unknown (H5N8)

Italy	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Japan	poultry	unknown (H5N1)
	wild birds	2.3.4.4b (H5N1)
	mammals (fox, raccoon dog)	2.3.4.4b (H5N1)
Jersey	poultry	2.3.4.4b (H5N1)
Kazakhstan	wild birds	unknown (H5)
Kosovo †	poultry	2.3.4.4b (H5N8)
Latvia	wild birds	unknown (H5N1)
Lithuania	wild birds	2.3.4.4b (H5N1)
Luxembourg	wild birds	2.3.4.4b (H5N1)
Mali	poultry	2.3.4.4b (H5N1)
Montenegro	wild birds	unknown (H5N1)
Nepal	poultry	2.3.2.1a (H5N1)
	wild birds	unknown (H5N1)
Netherlands	poultry	unknown (H5N1)
	wild birds	2.3.4.4b (H5N1)
	mammals (fox, polecat)	2.3.4.4b (H5N1)
Niger	poultry	unknown (H5N1)
Nigeria	poultry	2.3.4.4b (H5N1)
North Macedonia	wild birds	unknown (H5N1)
Norway	wild birds	2.3.4.4b (H5N1/5)
Philippines	poultry	2.3.4.4b (H5N1/8)
Poland	poultry	2.3.4.4b (H5N1); 2.3.4.4b (H5N2)
	wild birds	2.3.4.4b (H5N1)
Portugal	poultry	unknown (H5N1)
	wild birds	unknown (H5N1)
Republic of Korea	poultry	unknown (H5N1)
	wild birds	unknown (H5N1)
Republic of Moldova	poultry	unknown (H5N1)
Romania	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Russian Federation	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1); unknown (H5)
Slovakia	poultry	unknown (H5N1)
	wild birds	unknown (H5N1)
South Africa	poultry	unknown (H5N1)
	wild birds	unknown (H5N1)
Spain	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Svalbard and Jan Mayen Islands	wild birds	unknown (H5N1/5)
Sweden	poultry	unknown (H5N1)
	wild birds	2.3.4.4b (H5N1)
	mammal (porpoise)	2.3.4.4b (H5N1)
Switzerland	wild birds	unknown (H5N1)
United Kingdom of Great Britain and Northern Ireland	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)

United States of America	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1); unknown (H5)
	human (1)*	2.3.4.4b (H5N1)
	mammals (red fox, skunk, fox, coyote, wild fox, bobcat, harbor seal, bottlenose dolphin)	2.3.4.4b (H5N1)
Viet Nam	poultry	2.3.4.4b (H5N1/8); 2.3.2.1c (H5N1); 2.3.4.4h (H5N6)

* Number of reported human cases

† All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)

Antigenic and genetic characteristics of influenza A(H5) viruses

Since the February 2022 influenza Vaccine Composition Meeting (VCM), eight new infections with A/goose/Guangdong/1/96-lineage viruses have been reported. All cases were caused by clade 2.3.4.4b viruses. Seven were A(H5N6) infections identified in China and one was an A(H5N1) virus detection in the United States of America. The HAs of the sequenced viruses contained 2 to 5 amino acid substitutions compared to the HA of A/Astrakhan/3212/2020, from which a 2.3.4.4b CVV has been developed. No virus was recovered from the A(H5N1) case and antigenic characterization is pending for three viruses isolated from the A(H5N6) cases.

A(H5) viruses circulating in birds and non-human mammals from February 2022 through September 2022 belong to the following clades:

Clade 2.3.2.1a viruses were detected in poultry in Bangladesh, India and Nepal. There were between 1 and 11 amino acid substitutions between the A/duck/Bangladesh/17D1012/2018 2.3.2.1a CVV HA and recent strains. The viruses from Bangladesh and Nepal and one virus from India formed two genetic groups with the other strain from India being a genetic outlier. Some tested viruses from Bangladesh were well-recognized by post-infection ferret antiserum raised against the A/duck/Bangladesh/17D1012/2018 2.3.2.1a CVV. Conversely, all tested viruses from Nepal and half the tested viruses from Bangladesh were not as well recognized by the antiserum raised against this CVV.

Clade 2.3.2.1c viruses were detected in birds in Cambodia and Viet Nam. The HAs of these viruses had accumulated up to 9 amino acid substitutions relative to the A/duck/Vietnam/NCVD-1584/2012 2.3.2.1c CVV. Despite the emergence of multiple genetic subgroups, approximately half of the tested viruses from Viet Nam were well-recognized by ferret antisera raised against this CVV. These viruses will continue to be monitored for antigenic drift.

A clade 2.3.2.1e virus was detected in Indonesia. The virus had accumulated many amino acid substitutions when compared with the sequences of 2.3.2.1e viruses available in public sequence databases. No antigenic data were available.

Clade 2.3.4.4b viruses were detected in birds in many countries in Africa, Asia, Europe and North America. Additionally, viruses were detected in non-human mammals in some countries in Asia, Europe and North America. Viruses from Canada and the United States of America had HAs that were genetically similar to the A/Astrakhan/3212/2020 CVV (Fig. 1). However, geographical clustering of phylogenetic groups has become increasingly pronounced and viruses from some countries in eastern Europe and West Africa, Cambodia and Viet Nam were less well recognized by an antiserum raised against the A/Astrakhan/3212/2020 2.3.4.4b CVV. The viruses from eastern Europe and West Africa were well recognized by post-infection ferret antisera raised against recent viruses circulating in poultry in West Africa (Table 2).

Clade 2.3.4.4h viruses were detected in Viet Nam. The viruses had accumulated up to 10 HA amino acid substitutions compared to the A/Guangdong/18SF020/2018 CVV, but most of the viruses tested were antigenically similar to this CVV.

Table 2. Haemagglutination inhibition assay* of clade 2.3.4.4b A(H5) viruses

Reference Antigen	Clade	Subtype	CNIC-21099	IDCDC-RG71A	poultry/ Niger	ck/ Ghana	hen/ Bulgaria
CNIC-FJ21099 (A/Fujian-Sanyuan/21099/2017)	2.3.4.4b	H5N6	**40**	160	1280	1280	640
IDCDC-RG71A (A/Astrakhan/3212/2020-like)	2.3.4.4b	H5N8	80	**160**	1280	640	640
A/poultry/Niger/ET3HALAL21VIR2131-33/2021	2.3.4.4b	H5N1	10	40	**640**	320	160
A/chicken/Ghana/AVL-76321VIR7050-39/2021	2.3.4.4b	H5N1	10	20	640	**320**	80
A/hen/Bulgaria/722-1_22VIR778-1/2021	2.3.4.4b	H5N1	10	40	2560	640	**640**
Test Antigen							
A/laying-hen/Moldova/68-1_22VIR638-1/2022	2.3.4.4b	H5N1	10	40	640	320	320
A/ferret/Slovenia/308MZ_22VIR777-9/2022	2.3.4.4b	H5N1	10	10	1280	640	640
A/mute swan/Romania/16790_21VIR11355/2021	2.3.4.4b	H5N1	10	10	1280	320	320
A/avian/Burkina Faso/21VIR11911-3/2021	2.3.4.4b	H5N1	10	20	320	640	80
A/chicken/Mali/T1-17722VIR6104-1/2021	2.3.4.4b	H5N1	10	20	320	640	80
A/avian/Nigeria/711_22VIR3286-17/2021	2.3.4.4b	H5N1	10	40	320	320	40
A/chicken/Nigeria/040_22VIR3286-50/2022	2.3.4.4b	H5N1	10	40	320	320	40
A/chicken/Nigeria/128_22VIR3286-63/2022	2.3.4.4b	H5N1	10	40	320	640	80
A/chicken/Nigeria/717_22VIR3286-19/2021	2.3.4.4b	H5N1	10	40	320	320	40
A/chicken/Nigeria/164A_22VIR3286-69/2022	2.3.4.4b	H5N1	10	40	320	320	40
A/chicken/Nigeria/653_22VIR3286-6/2021	2.3.4.4b	H5N1	20	40	1280	320	320
A/chicken/Nigeria/064_22VIR3286-55/2022	2.3.4.4b	H5N1	10	80	640	320	40
A/chicken/Nigeria/709_22VIR3286-15/2021	2.3.4.4b	H5N1	10	40	320	320	40
A/chicken/Nigeria/601_22VIR3286-2/2021	2.3.4.4b	H5N1	10	80	640	320	80

* Haemagglutination inhibition assay was conducted using turkey red blood cells.

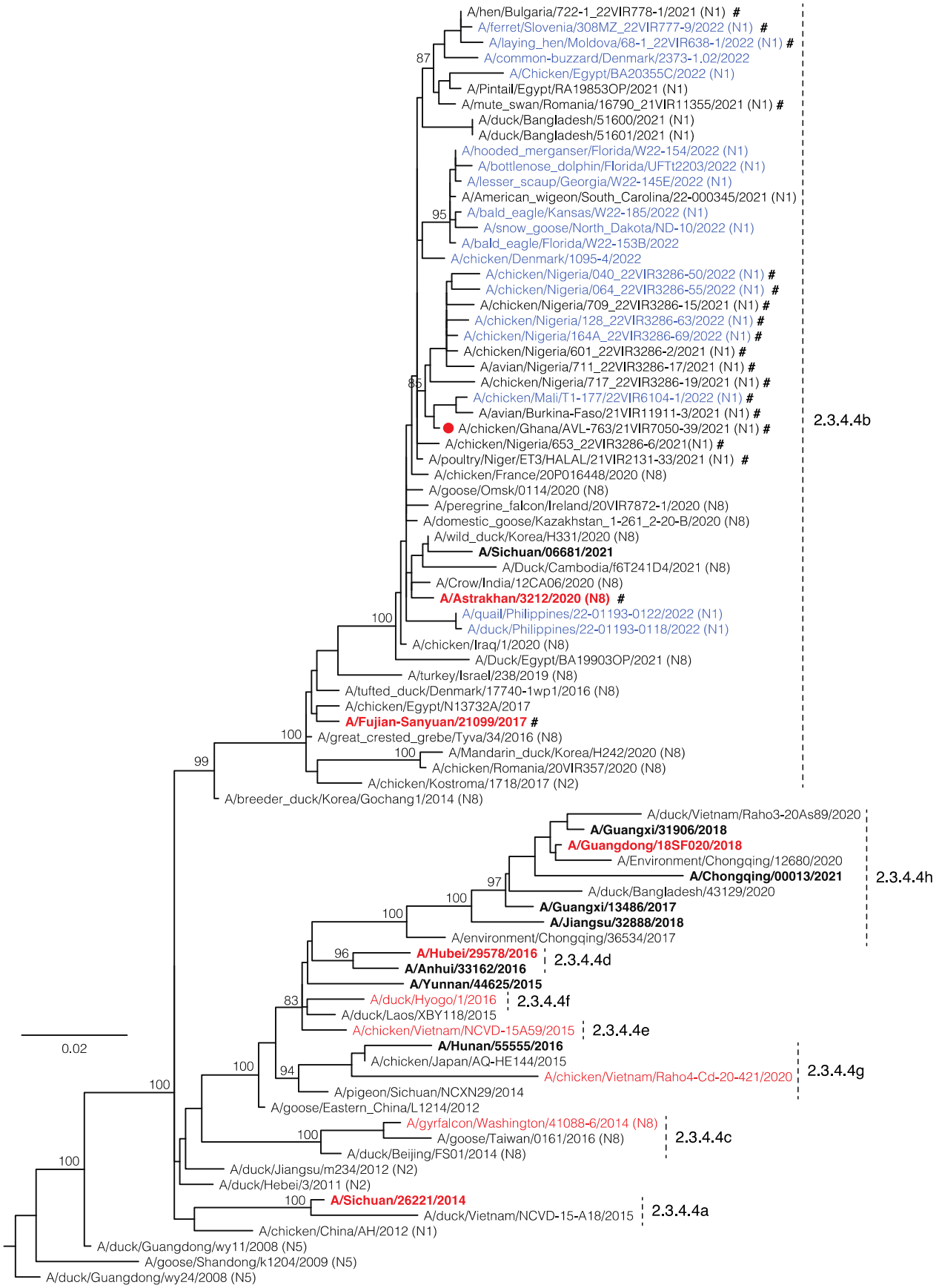

Figure 1. Phylogenetic relationships of A(H5) clade 2.3.4.4 HA genes. The available CVVs are in red. The proposed CVV is indicated by a red dot(●). Human viruses are in bold font. Viruses collected in years 2022 are in blue. The viruses tested in haemagglutination inhibition assays are indicated by hashes (#). 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(H5) candidate vaccine viruses

Based on current antigenic, genetic and epidemiologic data, a new clade 2.3.4.4b CVV that is antigenically like recently circulating viruses from West Africa 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 (MHRA)	Yes
NIBRG-88 (A/Cambodia/R0405050/2007)	1.1	NIBSC (MHRA)	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 (MHRA)	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 (MHRA)	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 (MHRA)	Yes
SJ009 (A/chicken/Guiyang/1153/2016)	2.3.2.1d	SJCRH/HKU	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-RG71A (A/Astrakhan/3212/2020) (H5N8)	2.3.4.4b	CDC	Yes
CBER-RG8A (A/Astrakhan/3212/2020) (H5N8)	2.3.4.4b	FDA	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
IDCDC-RG65A (A/Guangdong/18SF020/2018) (H5N6)	2.3.4.4h	CDC	Yes
Candidate vaccine viruses in preparation	**Clade**	**Institution**	**Availability**
IDCDC-RG63A (A/duck/Bangladesh/17D1012/2018-like)	2.3.2.1a	CDC	Pending
IDCDC-RG75A (A/chicken/Ghana/20/2015-like)	2.3.2.1f	CDC	Pending
A/chicken/Vietnam/NCVD-15A59/2015-like (H5N6)	2.3.4.4f	SJCRH	Pending
A/Guangdong/18SF020/2018-like (H5N6)	2.3.4.4h	CCDC	Pending
CNIC-HB29578 (A/Hubei/29578/2016-like) (H5N6)	2.3.4.4d	CCDC	Pending
CNIC-FJ21099 (A/Fujian-Sanyuan/21099/2017-like) (H5N6)	2.3.4.4b	CCDC	Pending
IDCDC-RG69A (A/ck/Vietnam/RAHO4-CD-20-421/2020-like) (H5N6)	2.3.4.4g	CDC	Pending
A/chicken/Ghana/AVL-76321VIR7050-39/2021-like	2.3.4.4b	To be determined	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 (MHRA)– National Institute for Biological Standards and Control, a centre of the Medicines and Health care 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(H3N8)

A(H3) viruses are present in birds in many regions of the world and detections of A(H3N8) viruses in live poultry markets in Asia have been reported. A(H3N8) virus infections have been detected in dogs, horses, pigs, donkeys and seals.

Influenza A(H3N8) activity from 24 February through 19 September 2022

The first two cases of human infections with A(H3N8) viruses, both associated with poultry exposure, were reported from China. Both infections were in children, one of which resulted in severe disease.

Antigenic and genetic characteristics of influenza A(H3N8) viruses

Genetic analyses of the A(H3N8) viruses from the human cases confirmed they were of avian origin with Eurasian and Pacific Flyway lineage HA and NA genes, respectively. The remaining gene segments were most similar to A(H9N2) viruses. Related viruses were detected in samples from live bird markets in China.

Transmission studies with an A(H3N8) poultry virus in ferrets demonstrated both direct contact and airborne transmission. This, together with detection of molecular changes associated with mammalian adaptation in the HA and PB2 genes of the virus detected in the case with severe disease, warrants close monitoring for avian origin reassortant A(H3N8) viruses.

Influenza A(H3N8) candidate vaccine viruses

Based on current serologic, genetic and epidemiologic data, a new A/Henan/4-10CNIC/2022 CVV is proposed. The pending A(H3N8) CVV is listed in Table 4.

Table 4. Status of influenza A(H3N8) candidate vaccine virus development

Candidate vaccine viruses (like virus)	Clade	Type	Institution *	Available
A/Henan/4-10CNIC/2022	Eurasian	Reverse Genetics	CDC/CCDC	pending

* Institutions distributing the candidate vaccine virus:
CDC – Centers for Disease Control and Prevention, United States of America
CCDC – Chinese Center for Disease Control and Prevention

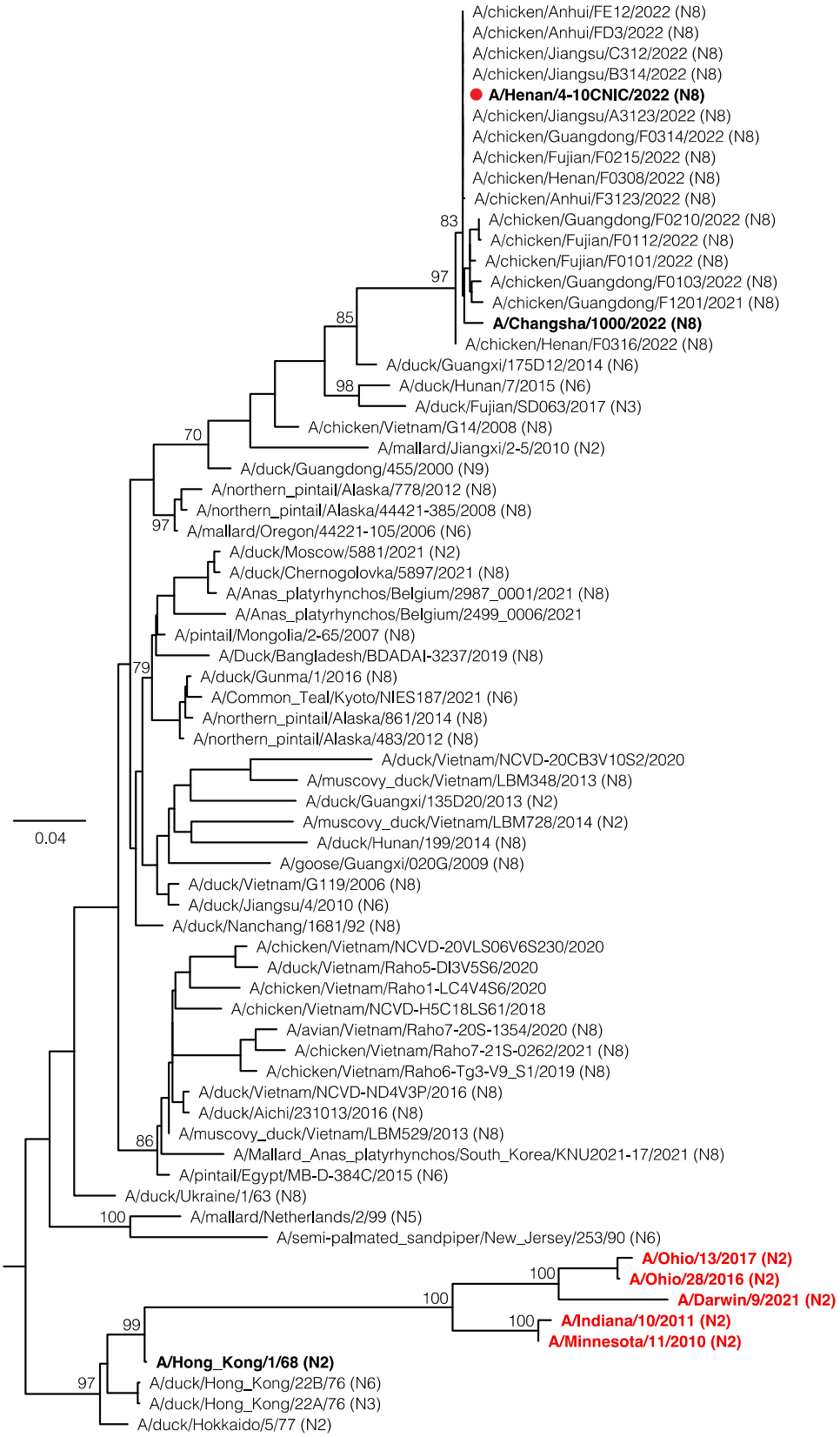

Figure 2. Phylogenetic relationships of influenza A(H3) HA genes. CVVs that are available or in preparation are in red. Proposed CVV is indicated by a red dot(●). Human viruses are in bold font. NA subtypes are specified within parantheses if known. The tree was built from the nucleotide sequences coding 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 HPAI A(H7) viruses of the A/Anhui/1/2013 HA lineage were first reported to WHO on 31 March 2013. Viruses from other A(H7) lineages have also caused zoonotic infections. This summary provides updates on the characterization of A(H7) viruses and the status of the development of corresponding CVVs.

Influenza A(H7) activity from 24 February through 19 September 2022

No human infections with A(H7), including A/Anhui/1/2013-lineage A(H7N9) viruses, have been detected in this reporting period. In addition, no A/Anhui/1/2013-lineage A(H7N9) infections in birds were reported in this period.

Influenza A(H7) candidate vaccine viruses

Based on the current epidemiologic data, no new CVVs are proposed. The available and pending CVVs for A(H7) viruses including A(H7N9) are listed in Table 5.

Table 5. 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 (MHRA)	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 (MHRA)	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 (MHRA)	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 (MHRA)	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 (MHRA)	Yes
NIBRG-63 (A/mallard/Netherlands/12/2000)	Eurasian (H7N1)	Reverse genetics	NIBSC (MHRA)	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 (MHRA)– National Institute for Biological Standards and Control, a centre of the Medicines and Health care 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) lineage. Since the late 1990s, when the first human infection was identified, sporadic detections of A(H9N2) viruses in humans and pigs have been reported, with associated mild disease in most human cases and no evidence for human-to-human transmission.

Influenza A(H9N2) activity from 24 February through 19 September 2022

Since the February 2022 VCM, six A(H9N2) human infections have been identified, five in China and one in Cambodia.

Antigenic and genetic characteristics of influenza A(H9N2) viruses

The three human viruses, two from China and one from Cambodia, from which sequence data were generated belonged to the Y280/G9 lineage. No antigenic data were available for these viruses.

The Y280/G9 lineage A(H9N2) viruses continued to predominate in birds in China and similar viruses were detected in birds in Cambodia and Viet Nam. Viruses from this lineage were genetically diverse but post-infection ferret antisera raised against the A/Anhui-Lujiang/39/2018 CVV reacted well with most of the viruses that were antigenically characterized.

G1 lineage A(H9N2) viruses were detected in birds in Bangladesh and Egypt. Ferret antisera raised against the A/Bangladesh/994/2011 and A/Oman/2747/2019 CVVs reacted well with most of the viruses that were antigenically characterized.

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 (MHRA)	Yes
NIBRG-91 (A/chicken/Hong Kong/G9/97)	Y280/G9	Reverse genetics	NIBSC (MHRA)	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	**Clade**	**Type**	**Institution**	**Availability**
IDCDC-RG66A (A/Oman/2747/2019-like)	G1	Reverse genetics	CDC	Pending
A/Anhui-Lujiang/39/2018-like	Y280/G9	Conventional	NIBSC (MHRA)	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 (MHRA)– National Institute for Biological Standards and Control, a centre of the Medicines and Health care products Regulatory Agency (MHRA), United Kingdom
SJCRH – St Jude Children's Research Hospital, United States of America

Influenza A(H10)

A(H10) viruses are frequently detected in birds in many regions of the world. Prior to this reporting period, A(H10N8), A(H10N7) and A(H10N3) human infections have been reported.

Influenza A(H10) activity from 24 February through 19 September 2022.

A single case of A(H10N3) human infection was identified in China. The illness was severe, but the patient recovered.

Antigenic and genetic characteristics of influenza A(H10) viruses.

The HA and NA of the human virus were genetically similar to viruses recently detected in China including the human A(H10N3) virus from 2021. The remaining gene segments of the virus were most similar to A(H9N2) viruses detected in chickens in the region. No antigenic data were available.

Influenza A(H10) candidate vaccine viruses

Based on the available epidemiologic data, no CVVs are proposed.

Influenza A(H1)v[4]

Influenza A(H1) viruses are enzootic in swine populations in most regions of the world. The genetic and antigenic characteristics of the viruses circulating in different regions are diverse. Human infections with swine influenza A(H1) viruses (designated as A(H1)variant [A(H1)v] viruses) have been, and continue to be, documented in the Americas, Asia and Europe.

Influenza A(H1)v activity from 24 February through 19 September 2022

Single A(H1N1)v virus infections in humans were identified in China (clade 1C.2.3) and Germany (clade 1C.2.2). Five human cases of A(H1N2)v virus infection were reported by the United States of America: the detected viruses belonged to clades 1B.2.1 (3), 1A.1.1 (1) and 1A.3.3.2 (1).

Antigenic and genetic characteristics of influenza A(H1) viruses

The A(H1N1)v virus from China had 14 HA amino acid substitutions relative to the A/Hunan/42443/2015 CVV. Antigenic characterization is underway. The HA of the virus from Germany, A/Nordrhein-Westfalen/8/2022, had 15 amino acid substitutions compared to the clade 1C.2.2 recommended A/Hessen/47/2020 CVV. Haemagglutination inhibition analysis showed post-infection ferret antiserum raised against A/Hessen/47/2020 reacted poorly with A/Nordrhein-Westfalen/8/2022. The 1B.2.1 viruses were genetically related to influenza viruses detected in pigs sampled at agricultural fairs in the United States of America and had nine or 10 HA amino acid substitutions relative to the A/Michigan/383/2018 CVV. These viruses were well inhibited by ferret antisera raised against this CVV. The 1A.1.1 and 1A.3.3.2 viruses were genetically related to viruses detected in pig populations in the United States of America and are awaiting antigenic characterization.

Influenza A(H1)v candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available and pending A(H1)v CVVs are listed in Table 7.

Table 7. Status of influenza A(H1)v candidate vaccine virus development

Candidate vaccine viruses (like viruses)	Lineage	Type	Institution*	Available
CNIC-1601 (A/Hunan/42443/2015) (H1N1)v	1C.2.3	Conventional	CCDC	Yes
IDCDC-RG48A (A/Ohio/9/2015) (H1N1)v	1A.3.3.3	Reverse genetics	CDC	Yes
IDCDC-RG58A (A/Michigan/383/2018) (H1N2)v	1B.2.1	Reverse genetics	CDC	Yes
IDCDC-RG59 (A/Ohio/24/2017) (H1N2)v	1A.1.1	Reverse genetics	CDC	Yes
Candidate vaccine viruses in preparation		**Type**	**Institution**	**Availability**
A/Iowa/32/2016-like (H1N2)v	1B.2.2.1	Reverse genetics	CDC	Pending
A/Netherlands/3315/2016-like (H1N1)v	1C.2.1	Reverse genetics	NIBSC (MHRA)	Pending
A/Ohio/35/2017-like (H1N2)v	1B.2.1	Reverse genetics	NIBSC (MHRA)	Pending
A/Hessen/47/2020-like (H1N1)v	1C.2.2	Conventional	NIBSC (MHRA)	Pending
A/Netherlands/10370-1b/2020 (H1N1)v	1C.2.1	Reverse genetics	NIBSC (MHRA)	Pending
A/Bretagne/24241/2021 (H1N2)v	1C.2.4	Reverse genetics/Conventional	SJCRH/NIBSC (MHRA)	Pending
A/Wisconsin/03/2021 (H1N1)v	1A.3.3.3	Reverse genetics	CDC	Pending
A/California/71/2021 (H1N2)v	1A.1.1	Reverse genetics	CDC	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 (MHRA) – National Institute for Biological Standards and Control, a centre of the Medicines and Health care products Regulatory Agency (MHRA), United Kingdom
SJCRH – St Jude Children's Research Hospital, United States of America

[4] standardization_of_terminology_influenza_virus_variants_update.pdf (who.int)

Influenza A(H3N2)v

Influenza A(H3N2) viruses are enzootic in pig populations in most regions of the world. The genetic and antigenic characteristics of the viruses circulating in different regions are diverse. Human infections with influenza A(H3N2)v viruses, originating from pigs, have been documented in Asia, Australia, Europe and North America.

Influenza A(H3N2)v activity from 24 February through 19 September 2022

Three human cases of A(H3N2)v virus infection were reported by the United States of America. These viruses belonged to clade 3.2010.1. The majority of A(H3N2)v infections have been detected in the United States of America where a total of 444 cases have been reported since 2005, when human infections with a novel influenza A virus became nationally notifiable.

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

The human viruses were genetically similar to clade 3.2010.1 A(H3N2) swine influenza viruses detected in the United States of America in 2022 and were antigenically similar to the recommended A/Ohio/13/2017-like CVV.

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 8.

Table 8. Status of influenza A(H3N2)v candidate vaccine virus development

Candidate vaccine viruses (like viruses)	Lineage	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)	3.2010.1	Reverse Genetics	CDC	Yes
Candidate vaccine viruses in preparation		**Type**	**Institution**	**Availability**
A/Ohio/28/2016-like	3.2010.1	Conventional	NIBSC (MHRA)	Pending
IDCDC-RG60A (A/Ohio/13/2017-like)	3.2010.1	Reverse Genetics	CDC	Pending

* Institution distributing the candidate vaccine viruses:

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

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

Acknowledgements

We acknowledge the WHO Global Influenza Surveillance and Response System (GISRS) which provides the mechanism for detection and monitoring of zoonotic influenza viruses. We thank the National Influenza Centres (NICs) of GISRS who contributed information, clinical specimens and viruses, and associated data; WHO collaborating centres of GISRS for their in-depth characterization and analysis of viruses and preparation of CVVs; and WHO Essential Regulatory Laboratories of GISRS and WHO H5 Reference Laboratories for their complementary analyses and preparation of CVVs. We thank the WOAH/FAO Network of Expertise on Animal Influenza (OFFLU) laboratories for their in-depth characterization and comprehensive analysis of viruses and other national institutions for contributing information and viruses. We also acknowledge the Global Initiative on Sharing All Influenza Data (GISAID) for the EpiFlu™ database, and other sequence databases which were used to share gene sequences and associated information.