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 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 September 2021 through 23 February 2022

Twenty-six human infections with A/goose/Guangdong/1/96-lineage viruses were reported in this period. Since 2003, there have been 3 A(H5), 7 A(H5N8), 74 A(H5N6) and 864 A(H5N1) human infections reported. Since September 2021, A/goose/Guangdong/1/96-lineage A(H5) viruses have been detected in both domestic and wild birds in many countries, and also in wild mammals in Europe (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 (OIE) and academic institutions.[3]

[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] 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 from September 2021

Country, area or territory	Host	Genetic clade*
Austria	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
Bangladesh	Poultry	2.3.2.1a (H5N1)
Belgium	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1)
Benin	Poultry	2.3.4.4b (H5N1)
Bosnia and Herzegovina	Wild Birds	unknown (H5N1)
Botswana	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1)
Bulgaria	Poultry	unknown (H5)
Burkina Faso	Poultry	unknown (H5N1)
Cambodia	Poultry	2.3.2.1c (H5N1); 2.3.4.4b (H5N8)
Cameroon	Poultry	unknown (H5N1)
Canada	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1)
China	Human (25)†	2.3.4.4b (H5N6); unknown (H5N6)
	Poultry	2.3.4.4b (H5N8)
	Environmental	2.3.4.4h (H5N6)
	Wild Birds	unknown (H5N1)
China, Hong Kong SAR	Wild Birds	unknown (H5N1)
Taiwan, China	Poultry	unknown (H5N2/N5)
	Wild Birds	unknown (H5N1/N2)
Cote d'Ivoire	Poultry	unknown (H5N1)
Croatia	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1)
Czech Republic	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1)
Denmark	Poultry	unknown (H5N1/N8)
	Wild Birds	unknown ((H5N1/N8)
	Mammal ‡	2.3.4.4b (H5N8)
Egypt	Poultry	2.3.4.4b (H5N1/N8)
Estonia	Poultry	unknown (H5N8)
	Wild Birds	2.3.4.4b (H5N1/N8)
	Mammal‡	2.3.4.4b (H5N1)
Faroe Islands	Wild Birds	unknown (H5N1)
Finland	Wild Birds	2.3.4.4b (H5N1); unknown (H5N8)
	Mammal‡	2.3.4.4b (H5N1)
France	Poultry	2.3.4.4b (H5N1/N8)
	Wild Birds	2.3.4.4b (H5N1)
Germany	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1); unknown (H5N2/N3)
Ghana	Poultry	unknown (H5N1)
Greece	Wild Birds	unknown (H5N1)
Hungary	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
India	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1/N8)
Iran (The Islamic Republic of)	Poultry	unknown (H5N5)
Ireland	Poultry	unknown (H5N1)
	Wild Birds	2.3.4.4b (H5N1)
Isle of Man	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
Israel	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
Italy	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1)

Japan	Poultry	2.3.4.4b (H5N1/N8)
	Wild Birds	2.3.4.4b (H5N8)
Kazakhstan	Poultry	2.3.4.4b (H5N1)
Lao People's Democratic Republic	Poultry	2.3.2.1c (H5N1); 2.3.4.4b (H5N6/N8)
Latvia	Wild Birds	unknown (H5N1)
Luxembourg	Poultry	unknown (H5N1)
	Wild Birds	2.3.4.4b (H5N8)
Mauritania	Wild Birds	unknown (H5)
Namibia	Wild Birds	unknown (H5N1)
Nepal	Poultry	unknown (H5N1)
Netherlands	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1/N3/N8)
Niger	Poultry	unknown (H5N1)
Nigeria	Poultry	unknown (H5N1)
North Macedonia	Wild birds	unknown (H5N1)
Norway	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
Pakistan	Poultry	unknown (H5)
Poland	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1)
Portugal	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
Republic of Korea	Poultry	2.3.4.4b (H5N1/N8)
	Wild birds	2.3.4.4b (H5N1/N8)
Republic of Moldova	Poultry	unknown (H5N1)
Romania	Wild Birds	2.3.4.4b (H5N1)
Russian Federation	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1/N5)
Senegal	Wild Birds	unknown (H5N1)
Serbia	Wild Birds	unknown (H5N1/N2/N8)
Slovakia	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
Slovenia	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
South Africa	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
Spain	Poultry	unknown (H5N1)
	Wild Birds	unknown (H5N1)
Sweden	Poultry	2.3.4.4b (H5N1)
	Wild Birds	2.3.4.4b (H5N1/N8)
	Mammal[‡]	unknown (H5N1)
Switzerland	Poultry	unknown (H5N1)
Togo	Poultry	unknown (H5N1)
Ukraine	Poultry	unknown (H5)
United Kingdom of Great Britain and Northern Ireland	Human (1)	2.3.4.4b (H5N1)
	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)
Viet Nam	Poultry	2.3.2.1c (H5N1); 2.3.4.4b (H5N8); 2.3.4.4h (H5N6)

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

[†] Number of reported human cases

[‡] Mammal includes fox, harbour seal and otter as detailed below

Antigenic and genetic characteristics of influenza A(H5) viruses

Twenty-five of the human infections were identified in China and one in the United Kingdom of Great Britain and Northern Ireland (United Kingdom). The human infections in China were caused by A(H5N6) viruses and sequence data generated from 16 of the cases identified A(H5) clade 2.3.4.4b viruses. The HAs of these viruses

were similar to A/Astrakhan/3212/2020 (1 to 4 amino acid differences), from which a clade 2.3.4.4b CVV has been developed. A post infection ferret antiserum raised against the A/Astrakhan/3212/2020 CVV reacted well to most, but not all, of the viruses isolated in China. The human infection in the United Kingdom was caused by an A(H5N1) clade 2.3.4.4b virus that had an HA with one amino acid substitution relative to A/Astrakhan/3212/2020. No virus was isolated from this case.

A(H5) viruses circulating in birds and non-human mammals from September 2021 through February 2022 belong to the following clades:

Clade 2.3.2.1a viruses were detected in poultry in Bangladesh and were genetically similar to viruses reported in previous years. The tested viruses reacted well to post-infection ferret antisera raised to the A/duck/Bangladesh/19097/2013 or A/duck/Bangladesh/17D1012/2018 2.3.2.1a CVVs.

Clade 2.3.2.1c viruses were detected in birds in Cambodia, Lao People's Democratic Republic and Viet Nam. The HAs of these viruses have accumulated up to 11 amino acid substitutions relative to the 2.3.2.1c CVV A/duck/Vietnam/NCVD-1584/2012.

Clade 2.3.4.4b viruses of the A(H5N1/N3/N5/N6/N8) subtypes were detected in birds in many countries in Africa, Asia, Europe and, for the first time since 2016, in North America. These viruses had HAs that were antigenically and genetically similar to the 2.3.4.4b A/Astrakhan/3212/2020 CVV. A(H5N1) 2.3.4.4.b viruses were also detected in two foxes (*Vulpes vulpes*) and an otter (*Lutra lutra*) in Finland and foxes (*Vulpes vulpes*) in Estonia and Sweden. An A(H5N8) 2.3.4.4b virus was detected in a harbour seal (*Phoca vitulina*) in Denmark. Pigs associated with an A(H5N1) 2.3.4.4b poultry outbreak in Italy were seropositive for H5.

Clade 2.3.4.4h viruses were detected in China and Viet Nam and were genetically similar to viruses previously detected in these countries. However, the HAs of these viruses have accumulated up to 17 amino acid substitutions relative to the A/Guangdong/18SF020/2018 2.3.4.4h CVV and some antigenic heterogeneity was detected.

Influenza A(H5) candidate vaccine viruses

Based on current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available and pending A(H5) CVVs are listed in Table 2.

Table 2. 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-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
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-like (H5N6)	2.3.4.4f	SJCRH	Pending
A/Guangdong/18SF020/2018-like (H5N6)	2.3.4.4h	CDC/CCDC	Pending
A/Hubei/29578/2016-like (H5N6)	2.3.4.4d	CCDC	Pending
A/Fujian-Sanyuan/21099/2017-like (H5N6)	2.3.4.4b	CCDC	Pending
A/chicken/Vietnam/RAHO4-CD-20-421/2020-like (H5N6)	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

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 September 2021 through 23 February 2022

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

HPAI A(H7N9) viruses of the A/Anhui/1/2013-lineage were detected in chickens in Yunnan Province, China. They were genetically similar to viruses detected in this region in early 2021 and had up to 15 amino acid substitutions in HA relative to the A/Gansu/23277/2019 CVV.

In this reporting period, A(H7N7) and A(H7N3) viruses were detected in ducks in Cambodia and had accumulated 10 amino acid substitutions in the HA compared to the Eurasian lineage A(H7N4) A/chicken/Jiangsu/1/2018 CVV.

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 3.

Table 3. 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***	**Availability**
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 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 September 2021 through 23 February 2022

Since 24 September 2021, 15 A(H9N2) human infections have been identified in China. The seven viruses for which sequence data were generated belonged to the Y280/G9 lineage, and the five viruses tested by haemagglutination inhibition (HI) assay reacted well to a post-infection ferret antiserum raised against the A/Anhui-Lujiang/39/2018 CVV.

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. While the majority of viruses tested were antigenically similar to available CVVs, viruses from this lineage are becoming increasingly diverse.

G1 lineage A(H9N2) viruses were detected in birds in Bangladesh, Egypt, Kenya, Niger and Nigeria. Although the HAs of these viruses had up to 29 amino acid substitutions relative to the A/Bangladesh/994/2011 and A/Oman/2747/2019 CVVs, post-infection ferret antisera raised against these CVVs reacted well with those 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 4.

Table 4. 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	**Clade**	**Type**	**Institution**	**Availability**
A/Oman/2747/2019-like	G1	Reverse genetics	CDC	Pending
A/Anhui-Lujiang/39/2018-like	Y280/G9	Conventional	NIBSC	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 Health care products Regulatory Agency (MHRA), United Kingdom
SJCRH – St Jude Children's Research Hospital, United States of America

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 September 2021 through 23 February 2022

Eight cases of A(H1)v infection were identified in Canada (1), Denmark (1), and the United States of America (USA) (6). Three cases resulted from A(H1N2)v infections, four were due to A(H1N1)v infections, and one case could not be sequenced for HA lineage designation or neuraminidase subtype identification. All individuals reported exposure to swine prior to illness onset and all recovered. The A(H1)v viruses were similar to viruses known to be enzootic in swine populations in the respective regions/countries.

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

Three A(H1N1)v viruses from the USA and one from Denmark belonged to the 1A.3.3.2 lineage and were related to circulating A(H1N1)pdm09-like influenza viruses in pigs. A(H1N1)v viruses from the USA reacted

[4] https://cdn.who.int/media/docs/default-source/influenza/global-influenza-surveillance-and-response-system/nomenclature/standardization_of_terminology_influenza_virus_variants_update.pdf?sfvrsn=d201f1d5_6

well to post-infection ferret antisera raised against recent seasonal influenza vaccine viruses and serum pools from vaccinated children and adults. Antigenic testing is pending for swine viruses genetically related to the 1A.3.3.2 A(H1N1)v virus from Denmark (no virus was isolated from the infected individual). One A(H1N2)v virus identified in the USA belonged to the 1B.2.1 lineage and was related to circulating swine influenza viruses. This A(H1N2)v virus reacted well to a post-infection ferret antiserum raised against the A/Michigan/383/2018-like 1B.2.1 lineage CVV. Viruses from the A(H1)v case in Canada and from one of the USA cases could not be isolated for antigenic characterization.

The A(H1N2)v virus detected in California, USA (A/California/71/2021) belonged to the 1A.1.1 lineage and was related to swine influenza viruses circulating in the region (Fig. 1). Ferret antisera raised against the 1A.1.1 lineage A/Ohio/24/2017-like CVV, reacted poorly with A/California/71/2021. Pools of antisera from children and adults who received seasonal influenza vaccine also showed poor cross-reactivity with this virus (Table 5).

Table 5. Haemagglutination inhibition* assay of A(H1)v viruses

Reference antigens	**Lineage**	**Vic/2570**	**OH/24/17**	**RG59**	**Adult** †	**Child** ‡
A/Victoria/2570/2019	pdm09	**5120**	80	80	5120	320
A/Ohio/24/2017	1A.1.1	<10	**2560**	1280	160	<10
IDCDC-RG59 (A/Ohio/24/2017-like)	1A.1.1	<10	1280	**1280**	160	<10
Test antigens						
A/California/71/2021	1A.1.1	<10	20	<10	80	10

*Haemagglutination inhibition assay was conducted using turkey red blood cells.
†19-49 yrs (adult) pool; post-immunization with 2021-2022 seasonal vaccine
‡0-3 yrs (paediatric) pool; post-immunization with 2021-2022 seasonal vaccine

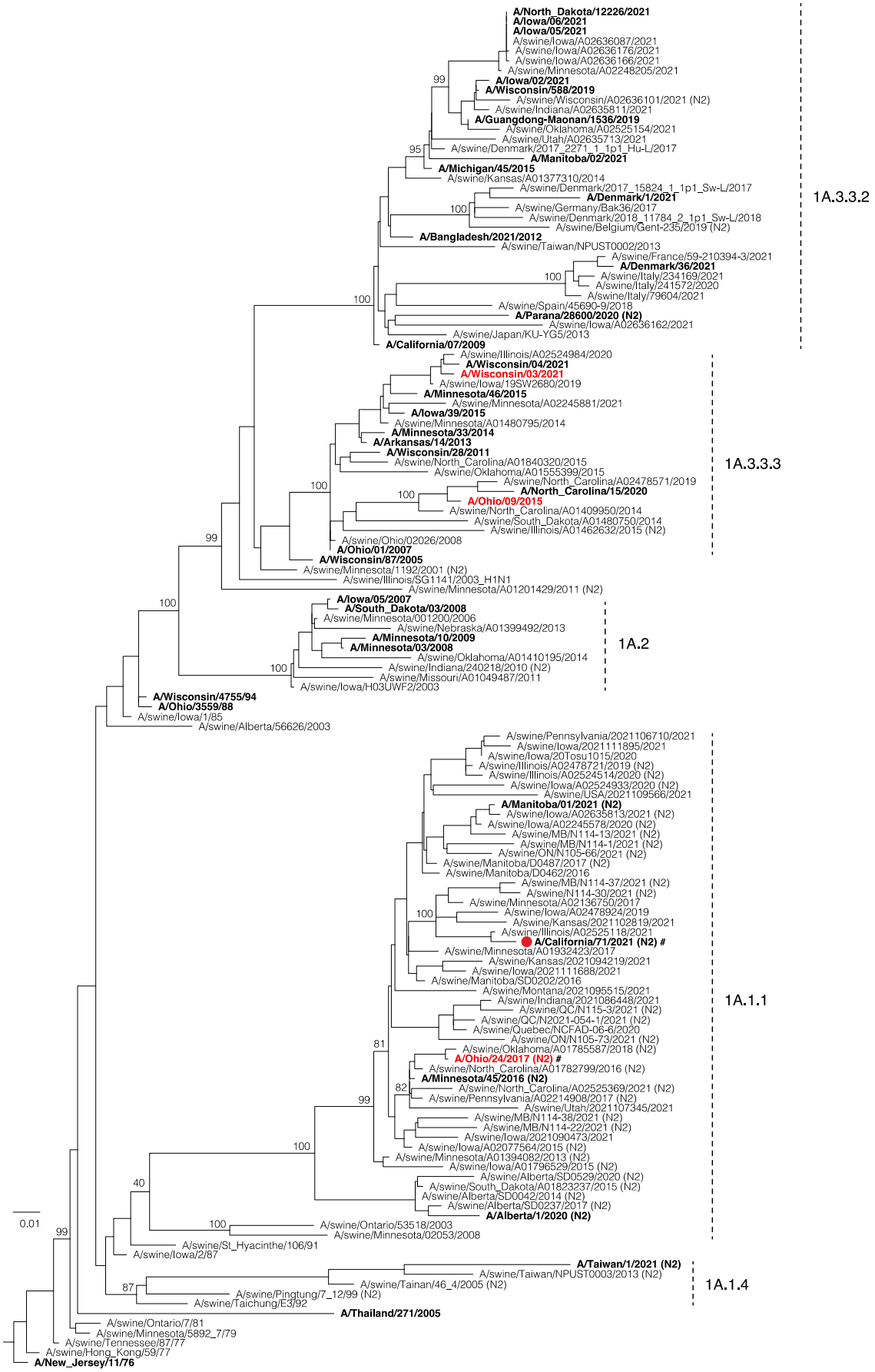

Figure 1. Phylogenetic relationships of influenza A(H1)v HA genes of 1A clades. CVVs that are available or in preparation are in red. Proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). Viruses are N1 or undetermined NA subtype if the NA subtype is not specified inside the parentheses. 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(H1)v candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, a new 1A.1.1 lineage CVV antigenically like A/California/71/2021 is proposed. The available and pending A(H1)v CVVs are listed in Table 6.

Table 6. 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	Conventional	NIBSC	Pending
A/Ohio/35/2017-like (H1N2)v	1B.2.1	Reverse genetics	NIBSC	Pending
A/Hessen/47/2020-like (H1N1)v	1C.2.2	Conventional	NIBSC	Pending
A/Netherlands/10370-1b/2020 (H1N1)v	1C.2.1	Conventional	NIBSC	Pending
A/Bretagne/24241/2021 (H1N2)v	1C.2.4	Reverse genetics/Conventional	SJCRH/NIBSC	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 – 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(H3N2)v

Influenza A(H3N2) 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 influenza A(H3N2)v viruses, originating from swine, have been documented in Asia, Australia, Europe and North America.

Influenza A(H3N2)v activity from 24 September 2021 through 23 February 2022

One case of A(H3N2)v virus infection was reported from the USA. This case did not report exposure to swine and recovered following mild illness. The majority of A(H3N2)v infections have been detected in the USA where a total of 441 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

Virus gene sequences (A/Ohio/06/2021) from the case showed a close genetic relationship to 3.2010.1 lineage A(H3N2) swine influenza viruses detected in the USA during 2021-2022 and the recommended A/Ohio/28/2016-like CVV. The virus was not recovered.

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 7.

Table 7. 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/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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