Genetic and antigenic characteristics of zoonotic influenza A viruses and development of candidate vaccine viruses for pandemic preparedness

September 2024

The development of influenza candidate vaccine viruses (CVVs), coordinated by the World Health Organization (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 antigenically and genetically, leading to the need for additional CVVs for pandemic preparedness purposes. Changes in the antigenic and genetic characteristics of these viruses relative to existing CVVs and their potential risks to public health justify the need to develop new CVVs.

This document summarizes the antigenic and genetic 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, high pathogenicity avian influenza (HPAI) A(H5) viruses of the A/goose/Guangdong/1/96 haemagglutinin (HA) lineage have become enzootic in many countries, have infected wild birds and continue to cause outbreaks in poultry and sporadic human and other mammalian infections across a wide geographic area. In the United States of America (USA), an outbreak of HPAI A(H5N1) in dairy cattle has been reported since March 2024. A(H5) HA gene segments have paired with a variety of neuraminidase (NA) subtypes (N1, N2, N3, N4, N5, N6, N8 or N9). These viruses have diversified genetically and antigenically, leading to the need for multiple CVVs. 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 20 February to 23 September 2024

Since 2003, eight A(H5), seven A(H5N8), 93 A(H5N6) and 904 A(H5N1) human infections have been reported. Twenty-six human infections with A/goose/Guangdong/1/96-lineage viruses have been reported to WHO in this period. Since February 2024, A/goose/Guangdong/1/96-lineage A(H5) viruses have been detected in both domestic and wild birds with spillover to mammals in many countries, and sustained circulation in dairy cattle in the USA (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 Organization 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/zoonotic-influenza-viruses-and-candidate-vaccine-viruses
[3] https://onlinelibrary.wiley.com/doi/10.1111/irv.12324

Table 1. Influenza A(H5) activity reported to international agencies from 20 February to 23 September 2024

Country, area or territory	Host	Genetic clade
Algeria	poultry	Unknown† (HPAI)
Antarctica	mammal (southern elephant seal)	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Australia	human (1)*	2.3.2.1a (H5N1)
Austria	wild birds	2.3.4.4b (H5N1)
Bangladesh	poultry	2.3.2.1a, 2.3.4.4b (H5N1)
Belgium	wild birds	2.3.4.4b (H5N1)
Bhutan	poultry	unknown (H5N1)
Brazil	wild birds	2.3.4.4b (H5N1)
Bulgaria	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Burkina Faso	poultry	2.3.4.4b (H5N1)
Cambodia	human (6) *	2.3.2.1c (H5N1)
	poultry	2.3.2.1c, 2.3.4.4b (H5N1)
Canada	mammal (skunk, racoon)	2.3.4.4b (H5N5)
	poultry	unknown (H5N1)
	wild birds	2.3.4.4b (H5N1/5)
China	human (4)*	2.3.4.4b (H5N6), 2.3.4.4h (H5N6), unknown (H5N1)
	poultry	2.3.4.4b (H5N1/6), 2.3.4.4h (H5N6)
	wild birds	2.3.4.4b (H5N1/6)
Taiwan, China	Poultry	unknown (H5N1)
	wild birds	(H5N1)
Croatia	wild birds	2.3.4.4b (H5N1)
Czechia	captive birds	2.3.4.4b (H5N1)
	wild birds	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)
Ecuador	poultry	unknown (H5N1)
Falkland Islands (Malvinas)	wild birds	unknown (HPAI)
France	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Gabon	poultry	unknown (H5N1)
Germany	mammal (red fox)	2.3.4.4b (H5N1)
	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Hungary	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
India	poultry	2.3.2.1a, 2.3.4.4b (H5N1)
Indonesia	poultry	unknown (H5N1)
Iraq	wild birds	unknown (H5N1)
Israel	poultry	unknown (H5N1)
Italy	poultry	2.3.4.4b (H5N1)
Japan	poultry	2.3.4.4b (H5N1/6)
	wild birds	2.3.4.4b (H5N1/5/6)
Latvia	wild birds	2.3.4.4b (H5N1)
	poultry	2.3.4.4b (H5N1)
Mexico	poultry	2.3.4.4b (H5N1/2)
Moldova, Republic of	wild birds	unknown (H5N1)
Netherlands (Kingdom of the)	wild birds	2.3.4.4b (H5N1)
Nigeria	poultry	2.3.4.4b (H5N1)
Norway	mammal (red fox)	2.3.4.4b (H5N5)
	wild birds	2.3.4.4b (H5N1)
Pakistan	poultry	unknown (H5N1)
Peru	poultry	unknown (H5)
	wild birds	unknown (H5)
Philippines	poultry	unknown (H5N1)
Poland	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Portugal	captive birds	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)

Republic of Korea	poultry	unknown (H5N1)
Romania	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Slovakia	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Slovenia	wild birds	unknown (H5N1)
South Africa	wild birds	2.3.4.4b (H5N1)
South Georgia and the South Sandwich Islands	mammal (South American fur seal, southern elephant seal)	unknown (HPAI)
	wild birds	unknown (HPAI)
Spain	captive birds	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Sweden	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
United Kingdom of Great Britain and Northern Ireland	wild birds	2.3.4.4b (H5N1/5)
Ukraine	wild birds	unknown (H5N1)
United States of America	human (14)*	2.3.4.4b (H5N1), unknown (H5)
	mammal (alpaca, bobcat, cats, dairy cattle, desert cottontail, goats, house mouse, mink, red fox)	2.3.4.4b (H5N1)
	poultry	2.3.4.4b (H5N1)
	wild birds	2.3.4.4b (H5N1)
Viet Nam	human (1)*	2.3.2.1c (H5N1)
	poultry	2.3.2.1c, 2.3.4.4b (H5N1)

†unknown: denotes instances where specific lineage designations were not available
*Number of cases and/or detections

Genetic and antigenic characteristics of influenza A(H5) viruses

Twenty-six new human infections or detections with A/goose/Guangdong/1/96-lineage viruses were reported. Most infected individuals had recent exposure to birds or dairy cattle. A single clade 2.3.2.1a A(H5N1) human infection was reported in Australia in a child who had recently travelled from India. The HA of the virus isolated from this case had nine amino acid substitutions relative to A/duck/Bangladesh/17D1012/2018, from which a CVV has been developed. The virus reacted, albeit with reduced titres, to post-infection ferret antisera raised against available CVVs. Seven human infections of clade 2.3.2.1c A(H5N1) were identified, one in Viet Nam and six in Cambodia (one with an illness onset date in the prior reporting period) (Figure 1). The individual from Viet Nam and one individual from Cambodia died; the remaining cases from Cambodia were hospitalized but recovered. Antigenic analysis of A/Cambodia/SVH240441/2024 and a reassortant virus with the HA and NA of A/Viet Nam/Khanh Hoa/RV1-005/2024 showed reduced reactivity to a post-infection ferret antiserum raised against the A/duck/Viet Nam/NCVD-1584/2012 CVV. This trend in reduced cross-reactivity was observed for other 2.3.2.1c human viruses detected in recent reporting periods (Table 2).

Table 2. Haemagglutination inhibition assay of A(H5) clade 2.3.2.1c viruses

			Post-infection ferret antisera		
Reference antigens	**Subtype**	**Clade**	**SJ001**	**duck/VN/ 1584**	**NIBRG-301**
SJ001 (A/duck/Bangladesh/19097/2013-like)	H5N1	2.3.2.1a	**80**	80	160
A/duck/Viet Nam/NCVD-1584/2012	H5N1	2.3.2.1c	20	**80**	160
NIBRG-301 (A/duck/Viet Nam/NCVD-1584/2012)	H5N1	2.3.2.1c	80	160	**640**
Test antigens					
A/Cambodia/24020155/2024 (January 2024)	H5N1	2.3.2.1c	<10	40	80
A/Cambodia/24020179/2024 (February 2024)	H5N1	2.3.2.1c	<10	20	80
A/Cambodia/SVH240441/2024 (July 2024)	H5N1	2.3.2.1c	<10	20	40
A/Viet Nam/Khanh Hoa/RV1-005/2024 x PR8	H5N1	2.3.2.1c	<10	20	80

One clade 2.3.4.4b A(H5N6) and two clade 2.3.4.4h A(H5N6) avian influenza virus infections in human were identified in China; all individuals died. The HA of the clade 2.3.4.4b virus had four amino acid substitutions relative to the A/Astrakhan/3212/2020 CVV, and those of the 2.3.4.4h viruses had 14 amino acid changes relative to the A/Guangdong/18SF020/2018 CVV. Antigenic analysis is ongoing for these viruses. An additional A(H5N1) human infection was detected in China from an individual who had recently travelled from Viet Nam. No sequence data was available for the virus. Fourteen A(H5) human infections were identified in

the USA of which nine were confirmed as clade 2.3.4.4b A(H5N1). All but one case reported exposure to dairy cattle or poultry, and mild illness was reported in all cases except one where underlying comorbidities were present. The HAs were genetically similar to viruses detected in dairy cattle (Figure 2) and had between two and six amino acid substitutions relative to A/American Wigeon/South Carolina/22-000345-001/2021, from which a CVV has been developed. The viruses that were tested antigenically reacted well to post-infection ferret antisera raised against the A/Astrakhan/3212/2020, A/American Wigeon/South Carolina/22-000345-001/2021 and A/chicken/Ghana/AVL-763_21VIR7050-39/2021 CVVs (Table 3).

Table 3. Haemagglutination inhibition assay of human derived A(H5) clade 2.3.4.4b viruses

			Post-infection ferret antisera					
Reference antigens	**Subtype**	**Clade**	**VN/ 1203**	**CNIC-21099**	**IDCDC-RG71A**	**IDCDC-RG78A**	**IDCDC-RG80A**	**TX/37**
A/Viet Nam/1203/2004	H5N1	1	**2560**	<10	<10	<10	<10	<10
CNIC-21099 (A/Fujian-Sanyuan/21099/2017)	H5N6	2.3.4.4b	20	**80**	160	80	1280	40
IDCDC-RG71A (A/Astrakhan/3212/2020-like)	H5N8	2.3.4.4b	10	80	**320**	160	1280	80
IDCDC-RG78A (A/American Wigeon/South Carolina/22-000345-001/2021)	H5N1	2.3.4.4b	10	80	640	**320**	1280	80
IDCDC-RG80A (A/chicken/Ghana/AVL-763_21VIR7050-39/2021)*	H5N1	2.3.4.4b	<10	10	80	40	**1280**	80
A/Texas/37/2024	H5N1	2.3.4.4b	10	40	320	160	1280	**80**
Test antigens								
A/Colorado/109/2024	H5N1	2.3.4.4	10	10	320	320	1280	80
A/Colorado/134/2024	H5N1	2.3.4.4	10	10	160	160	1280	80
A/Colorado/137/2024	H5N1	2.3.4.4	10	10	160	320	1280	80
A/Colorado/138/2024	H5N1	2.3.4.4	10	40	160	160	1280	80
A/Michigan/90/2024	H5N1	2.3.4.4	10	40	160	320	1280	80

*Availability pending

A(H5) viruses from birds and non-human mammals belonged to the following clades:

Clade 2.3.2.1a viruses were detected in poultry in Bangladesh and India. There were up to 11 amino acid substitutions in the HA of recent viruses compared to the A/duck/Bangladesh/17D1012/2018 CVV. The majority of recent viruses from Bangladesh reacted well with post-infection ferret antisera raised against either the A/duck/Bangladesh/19097/2013 or A/duck/Bangladesh/17D1012/2018 CVV. However, a small number of viruses reacted poorly.

Clade 2.3.2.1c viruses were detected in poultry in Cambodia and Viet Nam (Figure 1). The HAs of these viruses had accumulated up to 11 amino acid substitutions compared to the 2.3.2.1c A/duck/Viet Nam/NCVD-1584/2012 CVV. An increasing proportion of clade 2.3.2.1c viruses from Viet Nam had reduced reactivity with post-infection ferret antiserum raised against the 2.3.2.1c A/duck/Viet Nam/NCVD-1584/2012 CVV. Limited antigenic data were available for recent viruses from poultry in Cambodia.

Clade 2.3.4.4b viruses were detected in birds in many countries, areas and territories in Africa, Antarctica, Asia, Europe, North America and South America. A(H5N1) viruses have continued to circulate in birds in most regions; A(H5N6) viruses have been detected in China and Japan; A(H5N5) viruses have been detected in Asia, Europe and North America. Infections in wild and captive mammals have continued to be reported, as well as the ongoing outbreak in dairy cattle with subsequent spread to poultry and peri-domestic birds and mammals in the USA. Sequence analyses for viruses from dairy cattle indicate that the ongoing outbreak was caused by a single introduction that has subsequently spread to over 200 herds in 14 states. The majority of HAs from the characterized 2.3.4.4b viruses had less than 10 amino acid substitutions compared to the 2.3.4.4b CVVs and most viruses tested reacted well to at least one of the post-infection ferret antisera raised against the 2.3.4.4b CVVs. Dairy cattle viruses with HA substitutions in antigenic sites and reduced reactivity to post-infection ferret antisera to available CVVs (Table 4) have been identified, but these viruses are sporadically detected and, and based on available data, do not represent viruses with currently sustained circulation (Figure 2).

Table 4. Haemagglutination inhibition assay of A(H5) clade 2.3.4.4b viruses

			Post-infection ferret antisera			
Reference antigens	**Subtype**	**Clade**	**IDCDC-RG71A**	**IDCDC-RG78A**	**IDCDC-RG80A**	**bald eagle/FL**
IDCDC-RG71A (A/Astrakhan/3212/2020-like)	H5N8	2.3.4.4b	**160**	10	2560	40
IDCDC-RG78A (A/American Wigeon/South Carolina/22-000345-001/2021)	H5N1	2.3.4.4b	320	**80**	2560	320
IDCDC-RG80A (A/chicken/Ghana/AVL-763_21VIR7050-39/2021)*	H5N1	2.3.4.4b	40	20	**2560**	40
rg-A/bald eagle/Florida/W22-134-OP/2022	H5N1	2.3.4.4b	160	40	2560	**160**
Test antigens						
A/bovine/USA/C-5/2024	H5N1	2.3.4.4b	160	40	2560	160
A/bovine/USA/12/2024	H5N1	2.3.4.4b	160	20	2560	160
A/bovine/USA/A-1/2024	H5N1	2.3.4.4b	80	40	2560	160
A/bovine/USA/K-6/2024	H5N1	2.3.4.4b	20	10	2560	80
A/bovine/Ohio/B24OSU-368/2024	H5N1	2.3.4.4b	<10	10	640	20

**Availability pending*

Clade 2.3.4.4h viruses were detected in poultry in China. Detections of 2.3.4.4h viruses have been low to absent over recent periods. Some of the recent A(H5N6) viruses have accumulated over 15 HA amino acid substitutions relative to available CVVs with antigenic characterization pending.

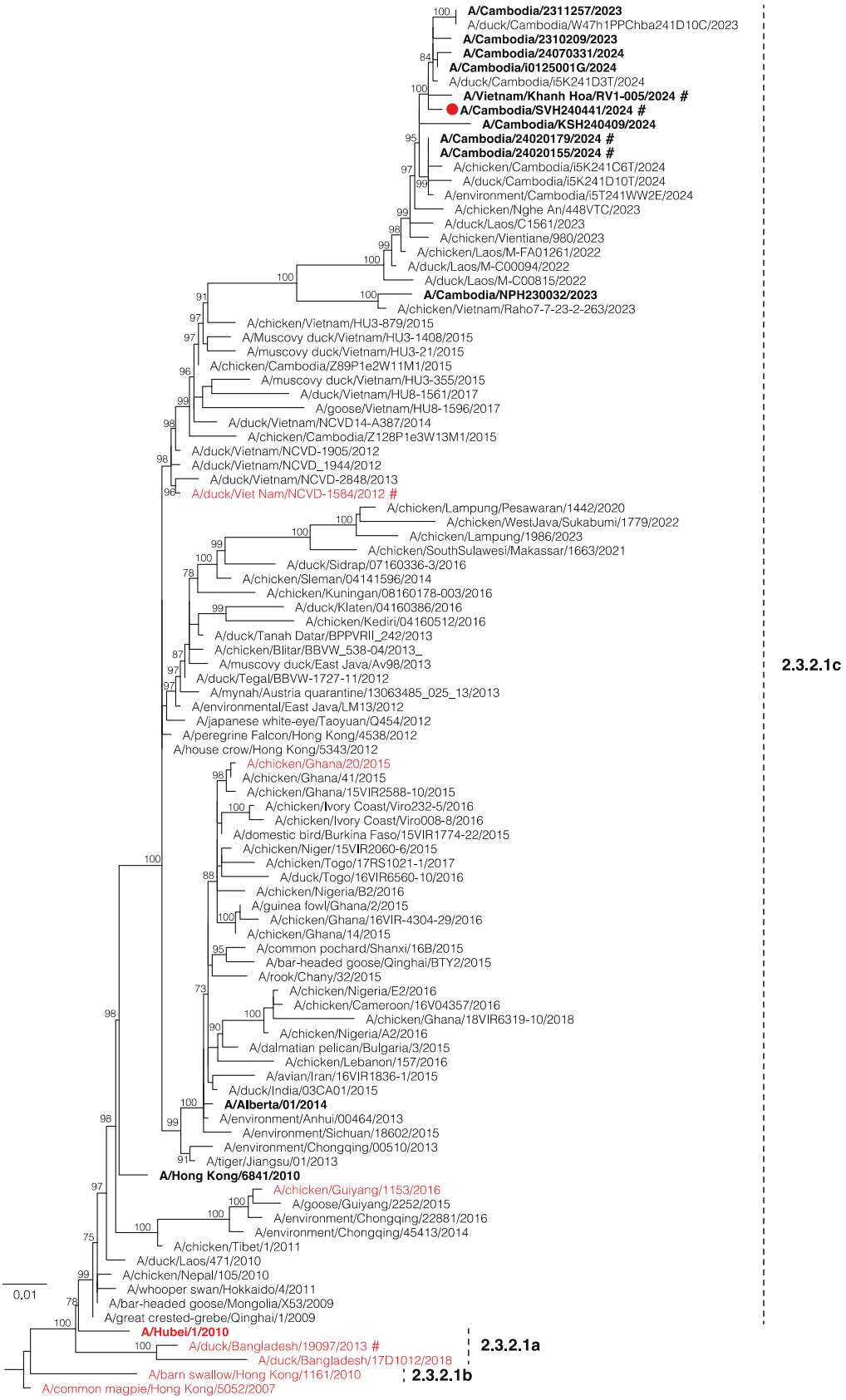

Figure 1. Phylogenetic relationships of A(H5) clade 2.3.2.1 HA genes. CVVs that are available or in preparation are in red. The proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The scale bar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

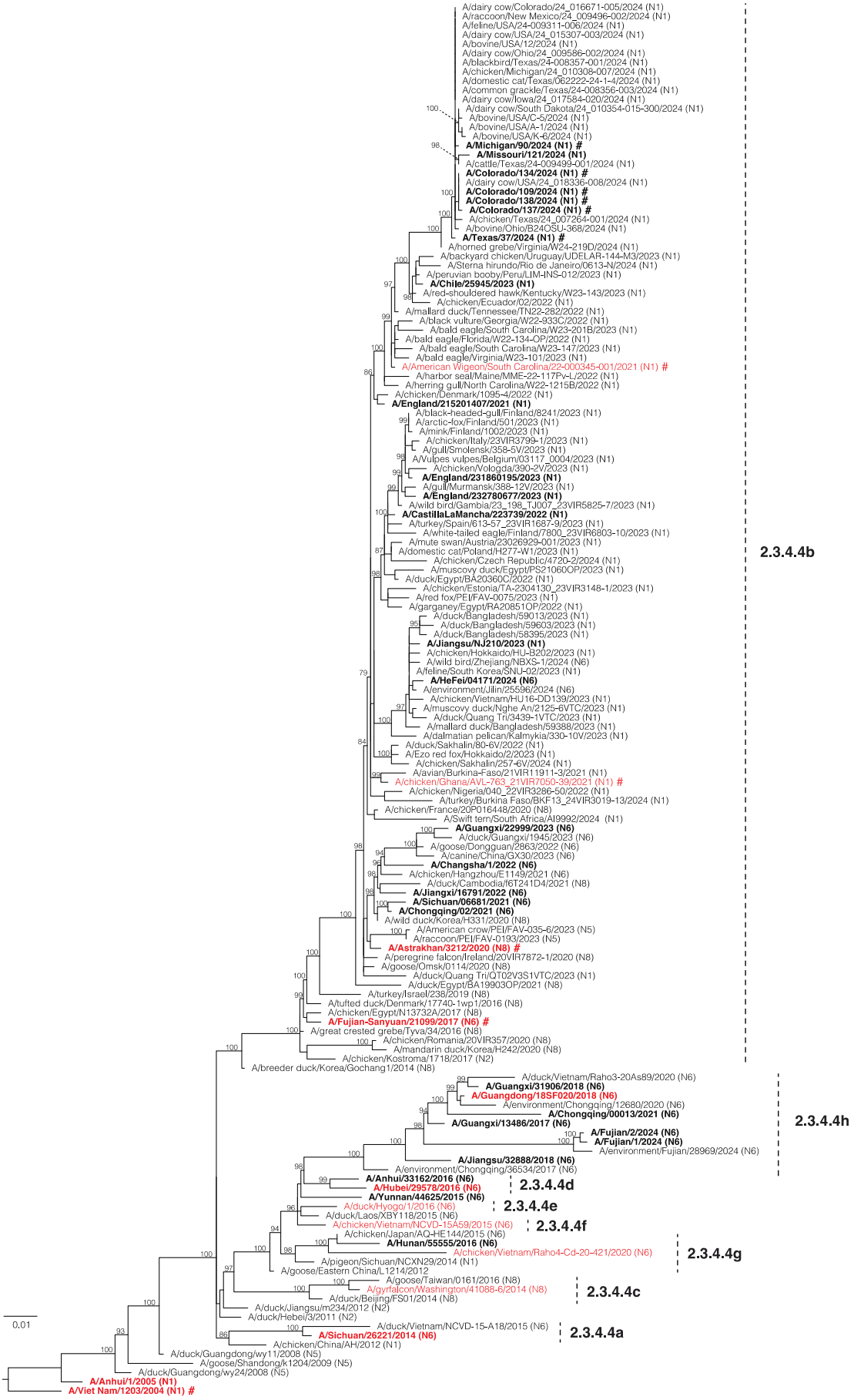

Figure 2. Phylogenetic relationships of A(H5) clade 2.3.4.4 HA genes. CVVs that are available or in preparation are in red. Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The tree was built from the nucleotide sequences coding for the mature HA1 protein. The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes.

Influenza A(H5) candidate vaccine viruses

Based on current genetic, antigenic and epidemiologic data, a new clade 2.3.2.1c CVV that is antigenically like A/Cambodia/SVH240441/2024 is proposed. The available and pending A(H5) CVVs are listed in Table 5.

Table 5. 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	MHRA	Yes
NIBRG-88 (A/Cambodia/R0405050/2007)	1.1	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	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	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
IDCDC-RG63A (A/duck/Bangladesh/17D1012/2018)	2.3.2.1a	CDC	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	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-RG78A (A/Am. Wigeon/South Carolina/22-000345-001/2021)	2.3.4.4b	CDC	Yes
NIID-002 (A/Ezo red fox/Hokkaido/1/2022)	2.3.4.4b	NIID	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
IDCDC-RG65A (A/Guangdong/18SF020/2018) (H5N6)	2.3.4.4h	CDC	Yes
IDCDC-RG69A (A/ck/Vietnam/RAHO4-CD-20-421/2020-like)(H5N6)	2.3.4.4g	CDC	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/Cambodia/SVH240441/2024-like	2.3.2.1c	CDC	Pending
IDCDC-RG75A (A/chicken/Ghana/20/2015-like)	2.3.2.1f	CDC	Pending
CNIC-FJ21099 (A/Fujian-Sanyuan/21099/2017-like) (H5N6)	2.3.4.4b	CCDC	Pending
A/chicken/Ghana/AVL-76321VIR7050-39/2021-like	2.3.4.4b	CDC	Pending
CNIC-HB29578 (A/Hubei/29578/2016-like) (H5N6)	2.3.4.4d	CCDC	Pending
SJ010 (A/chicken/Vietnam/NCVD-15A59/2015) (H5N6)	2.3.4.4f	SJCRH	Pending
A/Guangdong/18SF020/2018-like (H5N6)	2.3.4.4h	CCDC	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, USA
NIV – National Institute of Virology, India
CCDC – Chinese Center for Disease Control and Prevention, China
FDA – Food and Drug Administration, USA

HKU – The University of Hong Kong, Hong Kong Special Administrative Region (SAR), China
MHRA – Medicines and Healthcare products Regulatory Agency (previously known as NIBSC), United Kingdom of Great Britain and Northern Ireland
NIID – National Institute of Infectious Diseases, Japan
SJCRH – St. Jude Children's Research Hospital, USA

Low pathogenicity avian influenza (LPAI) A(H5N2) – non-A/goose/Guangdong/1/96-lineage

Low pathogenicity avian influenza (LPAI) non-A/goose/Guangdong/1/96-lineage A(H5) viruses circulate in birds globally. The genetic and antigenic characteristics of the viruses circulating in different regions of the world are diverse. LPAI A(H5N2) viruses are enzootic in poultry populations in some countries, including Mexico where they have been detected since 1993 and have occasionally mutated to high pathogenicity strains.

LPAI A(H5N2) Activity from 20 February to 23 September 2024
The first ever human case of infection with an LPAI A(H5N2) virus was reported in Mexico. The person had severe underlying comorbidities and died.

Genetic and antigenic characteristics of LPAI A(H5N2) viruses
The virus from the human case was closely related genetically to LPAI A(H5N2) viruses known to circulate in poultry in Mexico. Post-infection ferret antiserum raised against the virus isolated from the human case, A/Mexico/Mex_InDRE_F3546/2024, reacted poorly with other A(H5N2) viruses detected in North America.

LPAI A(H5N2) candidate vaccine viruses
Based on the available antigenic, genetic and epidemiologic data, no new CVVs are proposed.

Influenza A(H9N2)

Influenza A(H9N2) viruses are enzootic in poultry in many parts of Africa, Asia and the Middle East with the majority of viruses belonging to either the A/quail/Hong Kong/G1/97 G (G1) or A/chicken/Beijing/1/94 B (Y280/G9) lineage[4]. 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 sustained human-to-human transmission.

Influenza A(H9N2) activity from 20 February to 23 September 2024
Seven A(H9N2) human infections have been identified in China and one each in Ghana, India and Viet Nam. Four cases from China had illness onset dates outside of this reporting period. The majority of cases reported exposure to poultry and recovered from mild disease. The case from Viet Nam had severe underlying comorbidities and died.

Genetic and antigenic characteristics of influenza A(H9N2) viruses
Sequence information was available for six of the 10 viruses detected in humans. Viruses from the cases from China and Viet Nam belonged to the B4.7 (Y280/G9) lineage and had accumulated many HA substitutions relative to the closest CVV. The virus from the human case detected in Hong Kong SAR, China reacted with a post-infection ferret antiserum raised against the A/Anhui-Lujiang/39/2018 CVV, albeit with reduced titres. Antigenic data for the other A(H9N2) viruses detected in humans in China and Viet Nam were not available. The viruses from Ghana and India belonged to the G5.5 and G5.7 (G1) lineages, respectively, and reacted well with post-infection ferret antiserum raised against the A/Oman/-2747/2019 CVV.

A(H9N2) viruses from birds belonged to the following lineages:

B4.7 (Y280/G9) lineage A(H9N2) viruses from poultry in Cambodia, China and Viet Nam were characterised and continued to diversify genetically. Although post-infection ferret antisera raised against the A/Anhui-Lujiang/39/2018 and the A/Anhui-Tianjiaan/11086/2022 CVVs reacted well with many of the tested viruses,

[4] https://wwwnc.cdc.gov/eid/article/30/8/23-1176_article

reduced reactivity was observed with some viruses detected in live bird markets in China. Further reagent generation is planned to determine if additional CVVs are warranted.

G5.5 and G5.7 lineage A(H9N2) viruses were characterized from birds in Africa and Asia, respectively, and remained genetically and antigenically similar to viruses detected in previous periods. The majority of the tested viruses reacted well to post-infection ferret antisera raised against available CVVs, while one virus from Bangladesh showed reduced reactivity.

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	G-like (G1)	Wild type	MHRA	Yes
NIBRG-91 (A/chicken/Hong Kong/G9/97)	B-like (Y280/G9)	Reverse genetics	MHRA	Yes
IBCDC-2 (A/chicken/Hong Kong/G9/97)	B-like (Y280/G9)	Conventional	CDC	Yes
IDCDC-RG26 (A/Hong Kong/33982/2009)	G4 (G1)	Reverse genetics	CDC	Yes
IDCDC-RG31 (A/Bangladesh/994/2011)	G5.7 (G1)	Reverse genetics	CDC	Yes
SJ008 (A/Hong Kong/308/2014)	B4.7 (Y280/G9)	Reverse genetics	SJCRH	Yes
IDCDC-RG61A (A/Anhui-Lujiang/39/2018)	B4.7.4 (Y280/G9)	Reverse genetics	CDC/CCDC	Yes
IDCDC-RG66A (A/Oman/2747/2019)	G5.5 (G1)	Reverse genetics	CDC	Yes
Candidate vaccine viruses in preparation	**Clade**	**Type**	**Institution**	**Availability**
A/Anhui-Lujiang/39/2018-like	B4.7.4 (Y280/G9)	Conventional	MHRA	Pending
A/Anhui-Tianjiaan/11086/2022-like	B4.7.2 (Y280/G9)	Reverse genetics	CDC	Pending

*Institutions distributing the candidate vaccine viruses:
CCDC – Chinese Center for Disease Control and Prevention, China
CDC – Centers for Disease Control and Prevention, USA
HKU – The University of Hong Kong, Hong Kong SAR, China
MHRA – Medicines and Healthcare products Regulatory Agency (previously known as NIBSC), United Kingdom of Great Britain and Northern Ireland
SJCRH – St. Jude Children's Research Hospital, USA
† Note on nomenclature

Influenza A(H10)

A(H10) viruses are frequently detected in birds in many regions of the world and are considered endemic in poultry in China, with rare human infections reported. Prior to this reporting period, two A(H10N3), one A(H10N5), four A(H10N7) and three A(H10N8) human infections have been detected.

Influenza A(H10) activity from 20 February to 23 September 2024

A single A(H10N3) human infection was identified in China. The illness was severe but the patient recovered. The patient had a history of raising and slaughtering birds including chickens and geese, although viruses could not be detected from the environment or poultry carcasses associated with the case. No transmission to contacts of the case was detected.

Antigenic and genetic characteristics of influenza A(H10N3) viruses

The HA and NA genes of the A/Yunnan/YJ24001/2024 virus from the human case were genetically similar to those from A(H10N3) viruses associated with human infections detected in China in 2021. The HA sequence was phylogenetically distinct from that of the A(H10N5) human virus from 2023 (Figure 3). The six internal gene segments of the A(H10N3) virus were derived from A(H9N2) viruses. The human A(H10N3) virus had mixed amino acids at HA position 226 that included 226L in 76% of the virus population and PB2 701N. Both are mutations associated with mammalian adaptation. Virus isolation from the clinical sample from the 2024 human case was unsuccessful but a genetically related virus, A/Jiangsu/428/2021, is available for further characterization.

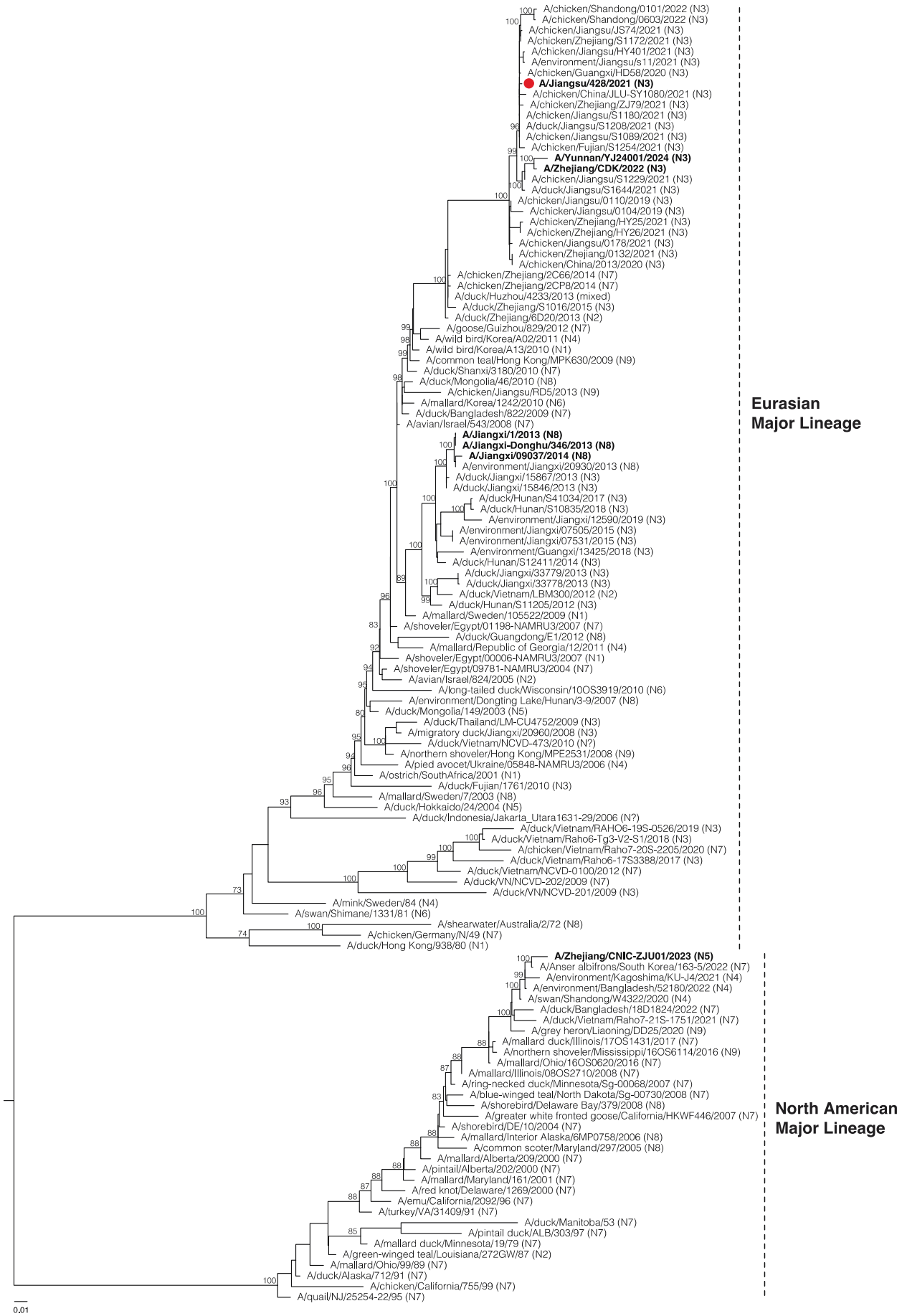

Figure 3. Phylogenetic relationships of A(H10) HA genes. Human viruses are in bold font. The proposed CVV is indicated by a red dot(●). The tree was built from the nucleotide sequences coding for the mature HA1 protein. The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes.

Influenza A(H10N3) candidate vaccine viruses
Based on the available genetic and epidemiologic data, a new A/Jiangsu/428/2021-like CVV is proposed. The pending A(H10N3) CVV is listed in Table 7.

Table 7. Status of influenza A(H10N3) candidate vaccine virus development

Candidate vaccine viruses (like virus)	Lineage	Type	Institution*	Available
A/Jiangsu/428/2021	Eurasian	Reverse Genetics	CDC	Pending

Influenza A(H1)v[5]

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. Viruses isolated from human infections with swine influenza A(H1) viruses are designated as A(H1) variant ((H1)v) viruses and have been previously detected in the Americas, Asia and Europe.

Influenza A(H1)v activity from 20 February to 23 September 2024
Multiple clades of A(H1) viruses were detected in swine populations globally with one A(H1N1)v and four A(H1N2)v infections detected in the USA and one A(H1N1)v identified in Viet Nam (Table 8).

Table 8. Recent swine and A(H1)v activity shared with international agencies and/or collected from sequence repositories.

Country, area or territory	Host	Genetic clade
Austria	Swine	1C.2.4.1
Belgium	Swine	1A.3.3.2; 1B.1.2.1; 1C.2.2
Canada	Swine	1A.1.1.3; 1A.2; 1A.3.3.2
Czechia	Swine	1A.3.3.2; 1C.2.4.3
Denmark	Swine	1A.3.3.2; 1C.2; 1C.2.2; 1C.2.4.1; 1C.2.4.2; 1C.2.4.3; 1C.2.5
France	Swine	1A.3.3.2; 1C.2.1; 1C.2.2; 1C.2.4.2
Germany	Swine	1A.3.3.2; 1B.1.2.1; 1C.2.2; 1C.2.4.3
Italy	Swine	1A.3.3.2; 1C.2.1; 1C.2.2; 1C.2.4.3
Russian Federation	Swine	1A.3.3.2; 1C.2.1
Switzerland	Swine	1C.2.2
United Kingdom of Great Britain and Northern Ireland	Swine	1A.3.3.2; 1B.1.1.2; 1B.2.7;^ 1C.2.2
United States of America	Human (5)* Swine	1A.1.1.3 1A.1.1.3; 1A.3.3.2; 1A.3.3.3-c1; 1A.3.3.3-c3; 1A.4; 1B.2.1; 1B.2.2.1; 1B.2.2.2
Viet Nam	Human (1)*	1C.2.3

^Detected prior to reporting period; included as a newly designated clade.
*Number of cases and/or detections

Genetic and antigenic characteristics of influenza A(H1)v viruses
The viruses from the USA A(H1)v cases were genetically similar to clade 1A.1.1.3 viruses circulating in swine in similar geographic regions. The virus from the human case in Viet Nam was a clade 1C.2.3 virus closely related to swine viruses circulating in the region. The USA human viruses were poorly reactive with post-infection ferret antisera raised against the A/Ohio/24/2017 CVV and the wildtype A/California/71/2021 virus, which was previously proposed as a CVV. However, post-infection ferret antiserum raised against the A(H1N2)v virus, A/Pennsylvania/27/2024, reacted well with all related 1A.1.1.3 viruses (Table 9). Post-

[5] Standardization of terminology for the influenza virus variants infecting humans: Update 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

infection ferret antiserum raised against the 1C.2.3 CVV, A/Hunan/42443/2015, reacted well with the virus isolated from the human case in Viet Nam.

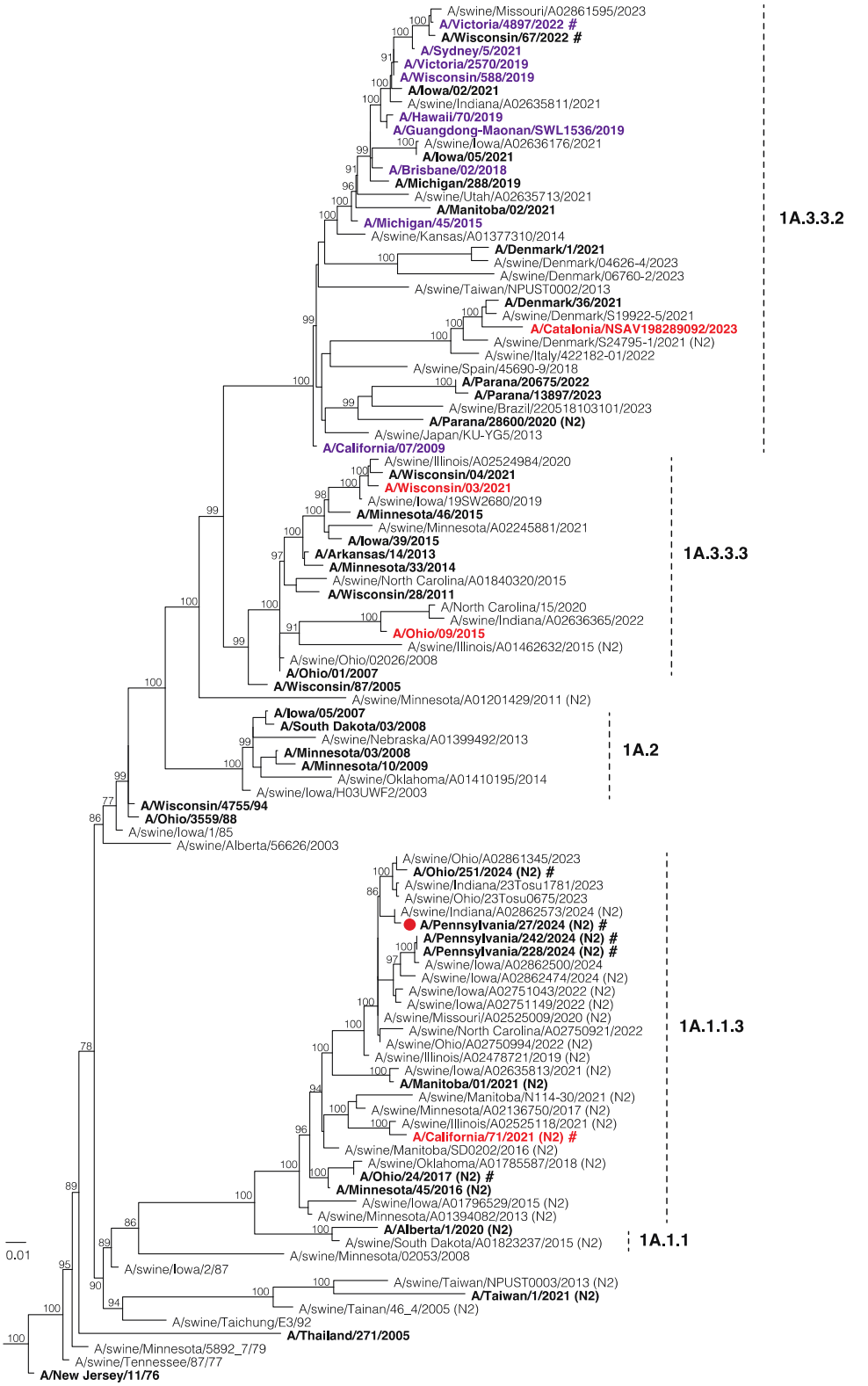

Figure 4 . Phylogenetic relationships of influenza A(H1)v HA genes of 1A lineages. CVVs that are available or in preparation are in red. Seasonal vaccine viruses are in purple. Proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition 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.

Table 9. Haemagglutination inhibition assays of A(H1N1)pdm09 viruses and a clade 1A.1.1.3 A(H1N2)v virus

		Post-infection ferret antisera						
Reference antigens	**Subtype (clade)**	**Vic/4897**	**IDCDC-RG59A**	**CA/71**	**IDCDC-RG81A**	**PA/27**	**Adult***	**Child^**
A/Victoria/4897/2019	H1N1pdm09	**2560**	<10	10	10	10	640	160
IDCDC-RG59 (A/Ohio/24/2017)	H1N2v (1A.1.1.3)	<10	**2560**	20	<10	320	160	<10
A/California/71/2021	H1N2v (1A.1.1.3)	<10	<10	**>5120**	640	160	80	<10
IDCDC-RG81A (A/CA/71/2021-like)	H1N2v (1A.1.1.3)	<10	<10	1280	**1280**	160	10	<10
A/Pennsylvania/27/2024	H1N2v (1A.1.1.3)	<10	10	80	<10	**5120**	20	<10
Test antigens								
A/Pennsylvania/228/2024	H1N2v (1A.1.1.3)	<10	20	80	<10	2560	20	<10
A/Ohio/251/2024	H1N2v (1A.1.1.3)	<10	20	20	<10	2560	20	<10
A/Pennsylvania/242/2024	H1N2v (1A.1.1.3)	<10	20	80	<10	2560	20	<10

*19-49 yrs (adult) pool; post-immunization with 2023-2024 seasonal vaccine

^6 months-3 yrs (pediatric) pool; post-immunization with 2023-2024 seasonal vaccine

Influenza A(H1)v candidate vaccine viruses

Based on the current genetic, antigenic and epidemiologic data, a new clade 1A.1.1.3 CVV that is antigenically like A/Pennsylvania/27/2024 is proposed. The available and pending A(H1)v CVVs are listed in Table 10.

Table 10. 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)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.1.1.3	Reverse genetics	CDC	Yes
Candidate vaccine viruses in preparation	**Clade**	**Type**	**Institution**	**Availability**
A/Catalonia/NSAV198289092/2023-like (H1N1)v	1A.3.3.2	Pending	MHRA	Pending
A/England/234600203/2023-like (H1N2)v	1B.1.1.1	Reverse genetics	MHRA	Pending
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	MHRA	Pending
A/Ohio/35/2017-like (H1N2)v	1B.2.1	Reverse genetics	MHRA	Pending
A/Netherlands/10370-1b/2020 (H1N1)v	1C.2.1	Reverse genetics	MHRA	Pending
NIB-124 (A/Hessen/47/2020) (H1N1)v	1C.2.2	Conventional	MHRA	Pending
A/Bretagne/24241/2021 (H1N2)v	1C.2.4	Reverse genetics	SJCRH	Pending
NIB-131 (A/Bretagne/24241/2021 (H1N2)v		Conventional	MHRA	Pending
A/Wisconsin/03/2021 (H1N1)v	1A.3.3.3	Reverse genetics	CDC	Pending
A/California/71/2021 (H1N2)v	1A.1.1.3	Reverse genetics	CDC	Pending
A/Catalonia/NSAV198289092/2023 (H1N1)v	1A.3.3.2	Conventional	MHRA	Pending
A/England/234600203/2023 (H1N2)v	1B.1.1.1	Conventional	MHRA	Pending
A/Pennsylvania/27/2024 (H1N2)v	1A.1.1.3	Reverse genetics	CDC	Pending
		Conventional	MHRA	Pending

*Institution distributing the candidate vaccine viruses:
CDC – Centers for Disease Control and Prevention, USA
CCDC – Chinese Center for Disease Control and Prevention, China
MHRA – Medicines and Healthcare products Regulatory Agency (previously known as NIBSC), United Kingdom of Great Britain and Northern Ireland
SJCRH – St. Jude Children's Research Hospital, USA

Influenza A(H3N2)v

Influenza A(H3N2) viruses with diverse genetic and antigenic characteristics are enzootic in swine populations in most regions of the world. Human infections with influenza A(H3N2)v viruses originating from swine have been previously documented in Asia, Australia, Europe and the Americas.

Influenza A(H3N2)v activity from 20 February to 23 September 2024
A(H3N2) viruses were detected in swine in Canada, Kazakhstan and the USA and five A(H3N2)v virus infections were detected in the USA and one in Canada (Table 1). The viruses from the USA were genetically similar to viruses circulating in swine in similar geographic regions as the human cases and belonged to clade 1990.4a and 2010.1.

Table 11. Recent swine and A(H3)v activity shared with international agencies and/or collected from sequence repositories.

Country, area or territory	Host	Genetic clade
Canada	Human (1)*	1990.4
	Swine	1990.4; 1990.4.b2; 1990.4.c; 1990.4.i; 2010.1
Kazakhstan	Swine	other/human
United States of America (the)	Human (4)*	1990.4.a; 2010.1
	Swine	1990.4; 1990.4.a; 1990.4.b1; 1990.4.i; 2010.1; 2010.2; 2020.1

*Number of cases and/or detections

Antigenic and genetic characteristics of influenza A(H3N2)v viruses
The viruses isolated from the human cases in the USA reacted well with post-infection ferret antisera raised against the 2010.1 CVV, IDCDC-RG60A (A/Ohio/13/2017-like), and A/swine/Iowa/23TOSU0850/2023, from which a CVV has been previously proposed. The virus from the case detected in Canada was genetically similar to viruses circulating in swine in the region and belonged to clade 1990.4. Antigenic analysis of the virus from the case detected in Canada was not performed because virus could not be recovered from the sample.

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 12.

Table 12. Status of influenza A(H3N2)v candidate vaccine virus development

Candidate vaccine viruses (like viruses)	Lineage	Type	Institution*	Available
NYMC X-203 (A/Minnesota/11/2010)	3.1990.4.A	Conventional	CDC	Yes
NYMC X-213 (A/Indiana/10/2011)	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	MHRA	Pending
A/swine/Iowa/23TOSU0850/2023	3.1990.4A	Reverse Genetics	CDC	Pending

*Institution distributing the candidate vaccine viruses:
CDC – Centers for Disease Control and Prevention, USA

MHRA – Medicines and Healthcare products Regulatory Agency (previously known as NIBSC), United Kingdom of Great Britain and Northern Ireland

[1] Standardization of terminology for the influenza virus variants infecting humans: Update 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

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