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

September 2017

The development of candidate influenza vaccine viruses (CVVs), coordinated by the World Health Organization (WHO), remains an essential component of the overall global strategy for pandemic preparedness.

Selection and development of CVVs are the first steps towards timely vaccine production and do not imply a recommendation for initiating manufacture. National authorities may consider the use of one or more of these CVVs for pilot lot vaccine production, clinical trials and other pandemic preparedness purposes based on their assessment of public health risk and need.

Zoonotic influenza viruses continue to be identified and evolve both genetically and antigenically, leading to the need for additional CVVs for pandemic preparedness purposes. Changes in the genetic and antigenic characteristics of these viruses relative to existing CVVs, and their potential risks to public health, justify the need to select and develop new CVVs.

This document summarises the genetic and antigenic characteristics of recent zoonotic influenza viruses and related viruses circulating in animals[1] that are relevant to CVV updates. Institutions interested in receiving these CVVs should contact WHO at GISRS-whohq@who.int or the institutions listed in announcements published on the WHO website[2].

[1] For information relevant to other notifiable influenza virus infections in animals refer to http://www.oie.int/wahis_2/public/wahid.php/Wahidhome/Home

[2] http://www.who.int/influenza/vaccines/virus/en/

Influenza A(H5)

Since their emergence in 1997, highly pathogenic avian influenza (HPAI) A(H5) viruses of the A/goose/Guangdong/1/96 haemagglutinin (HA) lineage have become enzootic in some countries, have infected wild birds, and continue to cause outbreaks in poultry and sporadic human infections. These viruses have diversified genetically and antigenically, including the emergence of viruses with replacement of the N1 gene segment by N2, N3, N5, N6, N8 or N9 gene segments, leading to the need for multiple CVVs. This summary provides updates on the characterisation of A/goose/Guangdong/1/96-lineage A(H5) viruses and the current status of the development of influenza A(H5) CVVs.

Influenza A(H5) activity from 28 February to 25 September 2017

An A(H5N1) human infection in Egypt, where A(H5) infections have also been detected in birds, has been reported to WHO. In addition, one fatal human case of A(H5N1) was reported from Bali Province, Indonesia. This is the first human case of A(H5N1) reported from Indonesia since March 2015. Globally, since 2003 there have been 860 and 16 confirmed human infections with A(H5N1) and A(H5N6) viruses, respectively. A/goose/Guangdong/1/96-lineage A(H5) viruses were detected in poultry and wild birds in many countries (Annex 1).

Antigenic and genetic characteristics of influenza A(H5) viruses

The nomenclature for phylogenetic relationships among the HA genes of A/goose/Guangdong/1/96-lineage A(H5) viruses is defined in consultation with representatives of WHO, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and academic institutions[3].

A(H5) viruses circulating and characterised from 28 February to 25 September 2017 belong to the following clades:

Clade 2.2.1.2 viruses were detected in poultry in Egypt. The HAs of the 2017 viruses had a limited number of amino acid substitutions relative to A/Egypt/N04915/2014, from which a CVV has been developed. No antigenic or genetic data are available for the reported A(H5N1) human virus from Egypt.

Clade 2.3.2.1a viruses were detected in birds in Bangladesh, India and Nepal. The HA genes of these viruses were similar to viruses detected in the region in previous periods. Viruses from Nepal and most viruses from Bangladesh reacted well with post-infection ferret antiserum raised against the A/duck/Bangladesh/19097/2013 CVV.

Clade 2.3.2.1c viruses were detected in birds in Cameroon, China, Indonesia, Lao People's Democratic Republic, Malaysia, Myanmar, Nigeria, Togo and Viet Nam. The viruses from Africa were genetically and antigenically similar to those detected previously, including A/chicken/Ghana/20/2015 from which a CVV is under development. The viruses from Asia were also similar to viruses previously detected in the region and the corresponding CVVs. No antigenic or genetic data are currently available for the reported A(H5N1) human virus from Indonesia.

Clade 2.3.4.4 viruses were detected in birds in 40 countries in Africa, Asia and Europe (Annex 1). The clade 2.3.4.4 viruses from Africa and Europe were primarily of the A(H5N8) subtype, those in Asia were primarily A(H5N6). The majority of characterised viruses were antigenically and/or genetically similar to available CVVs.

Influenza A(H5) candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available and pending A(H5) CVVs are listed in Table 1.

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

Table 1. Status of influenza A(H5) candidate vaccine virus development

Candidate vaccine viruses	Clade	Institution*	Available
A/Viet Nam/1203/2004 (CDC-RG; SJRG-161052)	1	CDC and SJCRH	Yes
A/Viet Nam/1194/2004 (NIBRG-14)	1	NIBSC	Yes
A/Cambodia/R0405050/2007 (NIBRG-88)	1.1	NIBSC	Yes
A/Cambodia/X0810301/2013 (IDCDC-RG34B)	1.1.2	CDC	Yes
A/duck/Hunan/795/2002 (SJRG-166614)	2.1.1	SJCRH/HKU	Yes
A/Indonesia/5/2005 (CDC-RG2)	2.1.3.2	CDC	Yes
A/Indonesia/NIHRD11771/2011 (NIIDRG-9)	2.1.3.2a	NIID	Yes
A/bar-headed goose/Qinghai/1A/2005 (SJRG-163222)	2.2	SJCRH/HKU	Yes
A/chicken/India/NIV33487/2006 (IBCDC-RG7)	2.2	CDC/NIV	Yes
A/whooper swan/Mongolia/244/2005 (SJRG-163243)	2.2	SJCRH	Yes
A/Egypt/2321-NAMRU3/2007 (IDCDC-RG11)	2.2.1	CDC	Yes
A/turkey/Turkey/1/2005 (NIBRG-23)	2.2.1	NIBSC	Yes
A/Egypt/N03072/2010 (IDCDC-RG29)	2.2.1	CDC	Yes
A/Egypt/3300-NAMRU3/2008 (IDCDC-RG13)	2.2.1.1	CDC	Yes
A/Egypt/N04915/2014 (NIBRG-306)	2.2.1.2	NIBSC	Yes
A/common magpie/Hong Kong/5052/2007 (SJRG-166615)	2.3.2.1	SJCRH/HKU	Yes
A/Hubei/1/2010 (IDCDC-RG30)	2.3.2.1a	CDC	Yes
A/duck/Bangladesh/19097/2013 (SJ007)	2.3.2.1a	SJCRH	Yes
A/barn swallow/Hong Kong/D10-1161/2010 (SJ003)	2.3.2.1b	SJCRH/HKU	Yes
A/duck/Viet Nam/NCVD-1584/2012 (NIBRG-301)	2.3.2.1c	NIBSC	Yes
A/chicken/Hong Kong/AP156/2008 (SJ002)	2.3.4	SJCRH/HKU	Yes
A/Anhui/1/2005 (IBCDC-RG6)	2.3.4	CDC	Yes
A/duck/Laos/3295/2006 (CBER-RG1)	2.3.4	FDA	Yes
A/Japanese white eye/Hong Kong/1038/2006 (SJRG-164281)	2.3.4	SJCRH/HKU	Yes
A/chicken/Bangladesh/11rs1984-30/2011 (IDCDC-RG36)	2.3.4.2	CDC	Yes
A/Guizhou/1/2013 (IDCDC-RG35)	2.3.4.2	CDC/CCDC	Yes
A/Sichuan/26221/2014 (IDCDC-RG42A) (H5N6)	2.3.4.4	CDC/CCDC	Yes
A/gyrfalcon/Washington/41088-6/2014 (IDCDC-RG43A) (H5N8)	2.3.4.4	CDC	Yes
A/duck/Hyogo/1/2016 (NIID-001) (H5N6)	2.3.4.4	NIID	Yes
A/goose/Guiyang/337/2006 (SJRG-165396)	4	SJCRH/HKU	Yes
A/chicken/Viet Nam/NCVD-016/2008 (IDCDC-RG12)	7.1	CDC	Yes
A/chicken/Viet Nam/NCDV-03/2008 (IDCDC-RG25A)	7.1	CDC	Yes
Candidate vaccine viruses in preparation	**Clade**	**Institution**	**Availability**
A/chicken/Guiyang/1153/2016-like	2.3.2.1c	SJCRH/HKU	Pending
A/chicken/Ghana/20/2015-like	2.3.2.1c	CDC	Pending
A/chicken/Viet Nam/NCVD-15A59/2015-like (H5N6)	2.3.4.4	SJCRH	Pending
A/Hubei/29578/2016-like (H5N6)	2.3.4.4	CCDC	Pending
A/environment/Hubei/950/2013	7.2	CDC/CCDC	Pending

* **Institutions developing and/or distributing the candidate vaccine viruses:**
CDC - Centers for Disease Control and Prevention, United States of America
NIV - National Institute of Virology, India
CCDC - Chinese Center for Disease Control and Prevention
FDA - Food and Drug Administration, United States of America
HKU – University of Hong Kong, Hong Kong Special Administrative Region, China.
NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom
NIID - National Institute of Infectious Diseases, Japan
SJCRH - St Jude Children's Research Hospital, United States of America

Influenza A(H7N9)

Human infections with avian influenza A(H7N9) viruses were first reported to WHO on 31 March 2013. A(H7N9) viruses are enzootic in poultry in China and reassortment with A(H9N2) viruses has continued to generate multiple genotypes. This summary provides updates on the characterisation of A/Anhui/1/2013 HA lineage A(H7N9) viruses and the current status of the development of corresponding CVVs.

Influenza A(H7N9) activity from 28 February to 25 September 2017

During the fifth wave of human infection (starting October 2016), 758 cases of A(H7N9) virus infection with 288 deaths were reported in mainland China. Five human cases were reported from China Hong Kong Special Administrative Region, two cases from China Macao Special Administrative Region and one case from Taiwan, China. Since 28 February 2017, 306 cases of human infection have been reported. The total number of cases reported since 2013 is 1564 with 610 deaths and a case fatality rate of 39%. HPAI A(H7N9) viruses have been detected in samples from 28 human cases across six provinces in China. HPAI and low pathogenic avian influenza (LPAI) A(H7N9) viruses have also been detected in birds in China.

Antigenic and genetic characteristics of influenza A(H7N9) viruses

A number of phylogenetically distinct HA groups have been detected within the A(H7N9) viruses. The HA genes of the HPAI and LPAI viruses are genetically distinct and further diversification has been seen within both virus groups (Figure 1). Post-infection ferret antisera raised against A/Hong Kong/125/2017 and A/Hunan/2650/2016 CVVs reacted well against LPAI viruses but not HPAI viruses. Post-infection ferret antisera raised against HPAI viruses or the associated CVV reacted well with the majority of early wave 5 HPAI and LPAI viruses. Antigenic characterisation of more recent wave 5 viruses with post-infection ferret antisera raised to available CVVs is ongoing.

Influenza A(H7N9) candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available and pending A(H7N9) CVVs are listed in Table 2.

Table 2. Status of influenza A(H7N9) candidate vaccine virus development

Candidate vaccine virus	Type	Institution*	Available
A/Anhui/1/2013 (IDCDC-RG33A)	Reverse genetics	CDC	Yes
A/Anhui/1/2013 (NIBRG-268)	Reverse genetics	NIBSC	Yes
A/Anhui/1/2013 (NIIDRG-10.1)	Reverse genetics	NIID	Yes
A/Anhui/1/2013 (SJ005)	Reverse genetics	SJCRH	Yes
A/Shanghai/2/2013 (NIBRG-267)	Reverse genetics	NIBSC	Yes
A/Shanghai/2/2013 (CBER-RG4A)	Reverse genetics	FDA	Yes
A/Shanghai/2/2013 (IDCDC-RG32A)	Reverse genetics	CDC	Yes
A/Shanghai/2/2013 (IDCDC-RG32A.3)	Reverse genetics	CDC	Yes
IDCDC-RG56B (A/Hong Kong/125/2017-like)	Reverse genetics	CDC	Yes
Candidate vaccine viruses in preparation	**Type**	**Institution**	**Availability**
A/Guangdong/17SF003/2016-like	Reverse genetics	CCDC, CDC, FDA, NIBSC	Pending
A/Hunan/2650/2016-like	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
NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom
NIID - National Institute of Infectious Diseases, Japan
SJCRH - St Jude Children's Research Hospital, United States of America

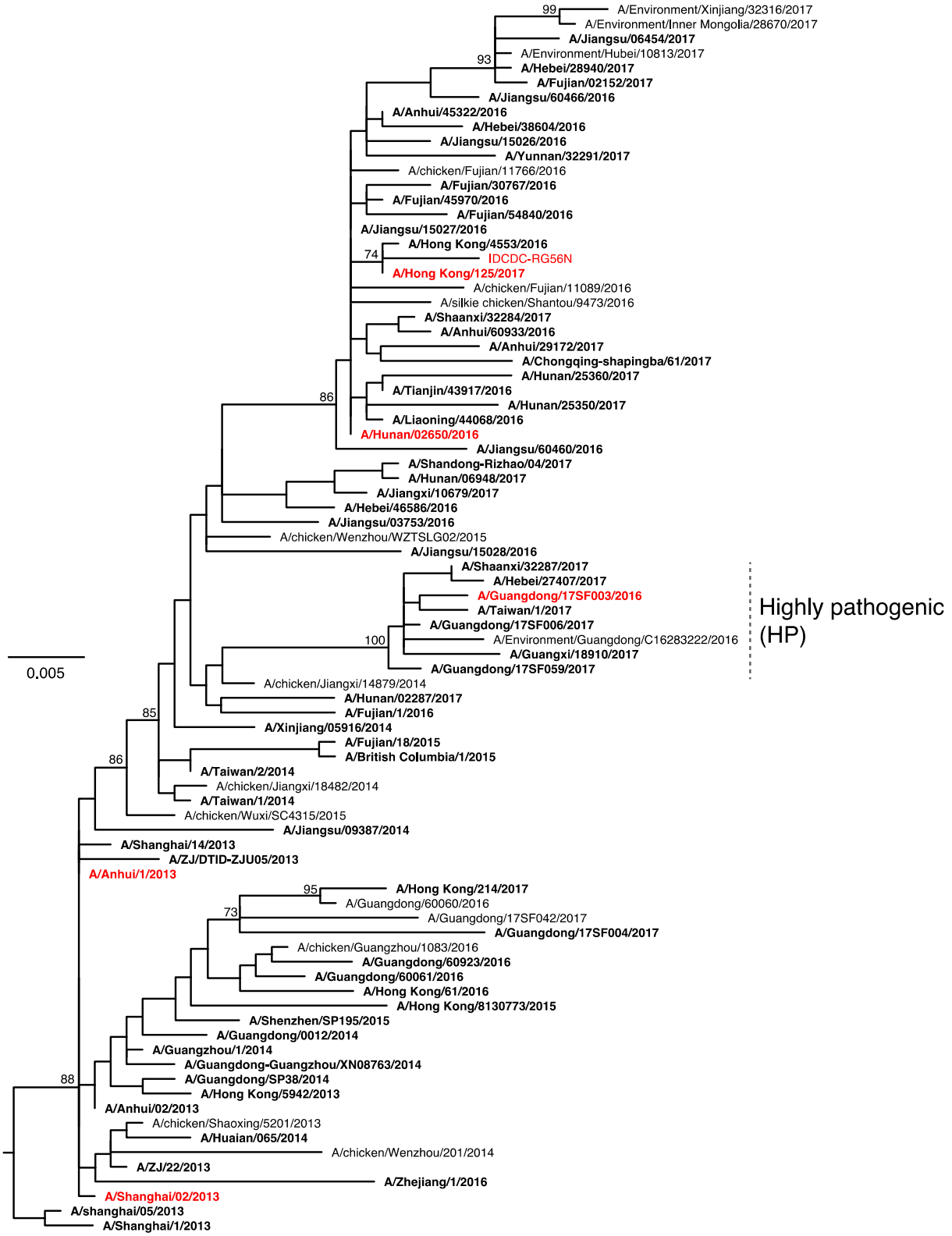

Figure 1. Phylogenetic relationships of A(H7N9) HA genes. CVVs that are available or in preparation are in red. The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes.

Influenza A(H9N2)

Influenza A(H9N2) viruses are enzootic in poultry populations in parts of Africa, Asia and the Middle East. The majority of viruses that have been sequenced belong to the A/quail/Hong Kong/G1/97 (G1) and A/chicken/Beijing/1/94 (Y280/G9) lineages. Since 1998, when the first human infection was identified, the detection of A(H9N2) viruses from humans and swine has been reported infrequently. In most human cases the associated influenza-like symptoms have been mild and there has been no evidence of human-to-human transmission.

Influenza A(H9N2) activity from 28 February to 25 September 2017
Four human cases of A(H9N2) infections have been reported in China in this period; one case had disease onset in early February. Three of the four infections were in young children and all infections were mild. A(H9N2) viruses were detected in birds in many countries.

Antigenic and genetic characteristics of influenza A(H9N2) viruses
No antigenic or genetic information could be generated from the human case samples in China. Y280/G9-lineage A(H9N2) viruses dominated in birds in China. A(H9N2) viruses from birds were characterised from a number of other countries including Bangladesh, Burkina Faso, Côte d'Ivoire, India, Indonesia, Senegal, Uganda and Viet Nam, with most being antigenically and/or genetically similar to those detected in previous periods and available CVVs.

Influenza A(H9N2) candidate vaccine viruses
Based on the current antigenic, genetic and epidemiologic data, no new CVVs are proposed. The available A(H9N2) CVVs are listed in Table 3.

Table 3. Status of influenza A(H9N2) candidate vaccine virus development

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

* **Institutions distributing the candidate vaccine viruses:**
CDC - Centers for Disease Control and Prevention, United States of America
NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom
SJCRH - St Jude Children's Research Hospital, United States of America

Influenza A(H1N2) variants (v)[4]

Influenza A(H1) viruses circulate in swine populations in many regions of the world. Depending on geographic location, the genetic characteristics of these viruses differ. Human infections with swine A(H1) viruses have been documented for many years.

Influenza A(H1N2)v activity from 28 February to 25 September 2017

Two cases of A(H1N2)v were detected in the United States of America during this reporting period. Both were in children who developed mild disease following direct contact with pigs. Phylogenetic analysis of the HA gene of A/Ohio/24/2017 showed it was of the swine H1 alpha lineage similar to viruses isolated from swine in North America in recent years. A/Ohio/35/2017 had a seasonal, human-like H1 HA gene segment that belonged to the delta 2 lineage of swine influenza viruses. This HA gene is closely related to the HA genes of influenza viruses currently circulating in swine in the United States of America (Figure 2).

Antigenic and genetic characteristics of influenza A(H1N2)v viruses

Antigenic testing demonstrated that ferret antisera raised against current CVVs reacted poorly with these two A(H1N2)v viruses. The reactivity of pooled, adult human sera collected post-vaccination with the 2016-2017 vaccine was also reduced against these viruses in haemagglutination inhibition assays (Tables 4 and 5).

Table 4. Haemagglutination inhibition assays of classical swine influenza A(H1) variant viruses.

REFERENCE ANTIGENS	Lineage	CA/7	RG48A	Bris/59	MD/12	NE/01	MN/45	Pooled human sera*
A/California/7/2009	pdm09 H1N1	**5120**	160	<10	1280	320	40	80
A/Ohio/9/2015 IDCDC-RG48A	classical γ H1N1v	20	**1280**	<10	160	80	40	80
A/Brisbane/59/2007	pre-2009 H1N1	<10	<10	**640**	80	80	<10	10
A/Maryland/12/91	classical α H1N2v	640	40	<10	**1280**	640	10	80
A/Nebraska/01/92	classical α H1N2v	640	80	<10	1280	**640**	10	80
A/Minnesota/45/2016	classical α H1N2v	<10	<10	<10	160	40	**640**	<10
TEST ANTIGEN								
A/Ohio/24/2017	classical α H1N2v	640	<10	<10	160	40	640	<10

*2016-2017 post-vaccine immune serum pool from adult (19-49 yrs) vaccinees

Table 5. Haemagglutination inhibition assays of influenza A(H1) variant viruses.

REFERENCE ANTIGENS	Lineage	CA/7 X-179	RG 48A	Bris/59	SI/03	New/ 20	MN/ 19	WI/ 71	Pooled human sera*
A/California/7/09 X-179	pdm09 H1N1	**160**	20	<10	<10	<10	<10	20	640
A/Ohio/9/2015 IDCDC-RG48A	classical γ H1N1v	<10	**1280**	<10	<10	<10	<10	<10	80
A/Brisbane/59/2007	pre-2009 H1N1	<10	<10	**1280**	1280	320	320	20	160
A/Solomon Islands/03/2006	pre-2009 H1N1	<10	<10	80	**320**	80	<10	40	20
A/New Caledonia/20/99	pre-2009 H1N1	<10	<10	40	160	**640**	20	<10	20
A/Minnesota/19/2011	δ-1 H1N2v	<10	<10	40	40	<10	**640**	1280	<10
A/Wisconsin/71/2016	δ-1 H1N2v	<10	<10	10	10	<10	160	**5120**	20
TEST ANTIGENS									
A/Iowa/32/2016	δ-1 H1N2v	<10	<10	10	10	<10	20	640	20
A/Ohio/35/2017	δ-2 H1N2v	<10	<10	<10	<10	<10	<10	40	10

*2016-2017 post-vaccine immune serum pool from adult (19-49 yrs) vaccinees

[4] http://www.who.int/influenza/gisrs_laboratory/terminology_variant/en/

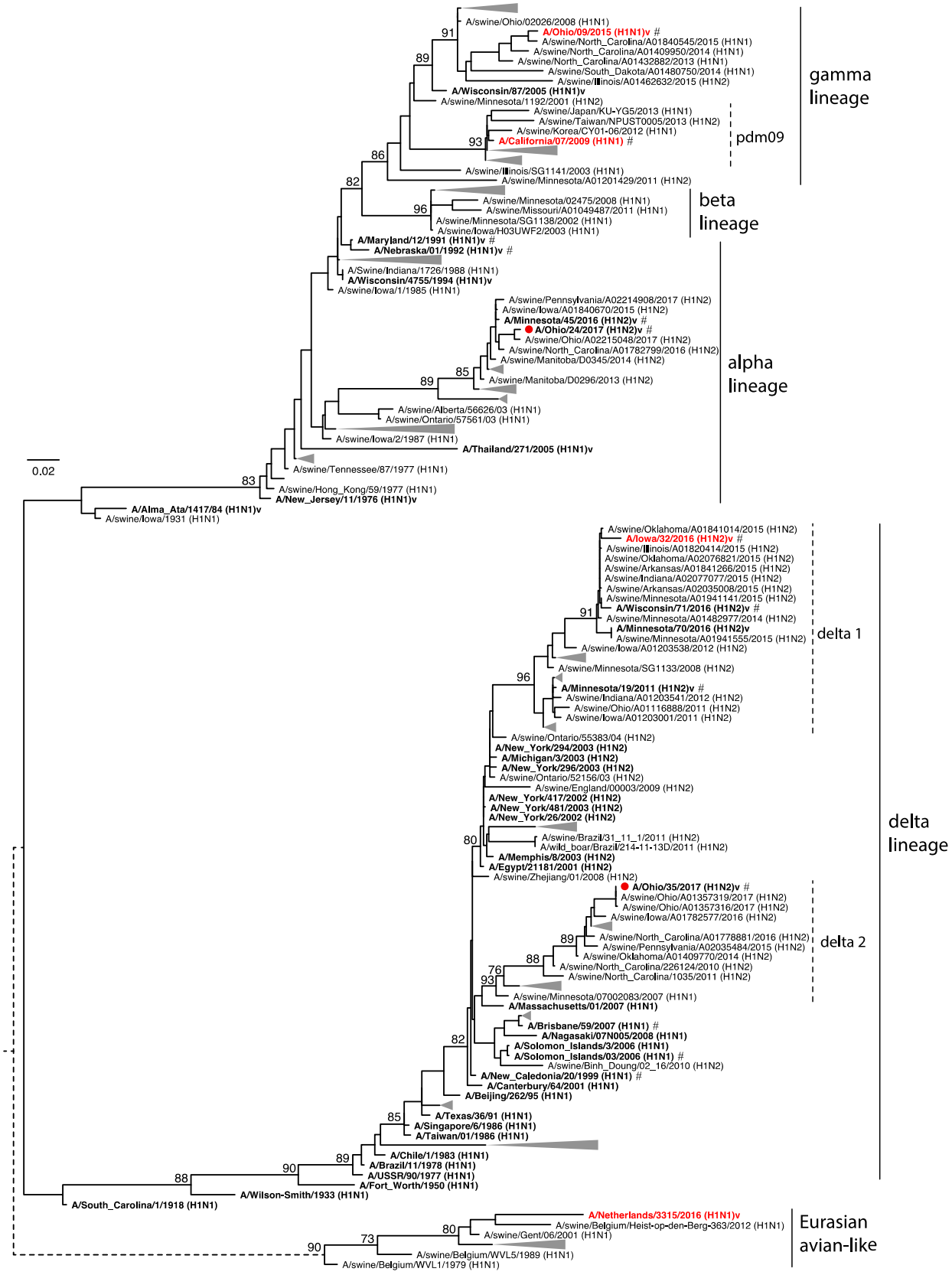

Figure 2. Phylogenetic relationships of A(H1) HA genes. The available CVVs are in red. The proposed CVV is indicated by a red dot(●). Human viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes. Some branches of virus strains are collapsed into grey triangles for clarity.

Influenza A(H1)v candidate vaccine viruses

Based on the current antigenic, genetic and epidemiologic data, new CVVs generated from A/Ohio/24/2017-like and A/Ohio/35/2017-like viruses are proposed. The available A(H1)v CVVs are listed in Table 6.

Table 6. Status of A(H1)v candidate vaccine virus development

Candidate vaccine viruses	**Type**	**Institution***	**Available**
A/Ohio/9/2015 (IDCDC-RG48A)	Reverse genetics	CDC	Yes
A/Hunan/42443/2015 (CNIC-1601)	Conventional and reverse genetics	CCDC	Yes
Candidate vaccine viruses in preparation	**Type**	**Institution**	**Availability**
A/Iowa/32/2016-like	Reverse genetics	CDC	Pending
A/Netherlands/3315/2016-like	Conventional	NIBSC	Pending
A/Ohio/24/2017-like	Reverse genetics	CDC	Pending
A/Ohio/35/2017-like	Conventional	NIBSC	Pending

***Institution distributing the candidate vaccine virus:**

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

CCDC - Chinese Center for Disease Control and Prevention, China

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

Influenza A(H3N2)v

Influenza A(H3N2) viruses are enzootic in swine populations in most regions of the world. Depending on geographic location, the genetic and antigenic characteristics of these viruses differ. Human infections with swine influenza A(H3N2) viruses have been documented in Asia, Europe and North America[5].

Influenza A(H3N2)v activity from 28 February to 25 September 2017

Thirty one cases of A(H3N2)v were detected in the United States of America during this reporting period. The virus from one case in Texas had an HA gene belonging to the IV-A cluster, closely related to A(H3N2) viruses currently circulating in North American swine. The remaining cases of A(H3N2)v virus infection were identified in North Dakota [1], Pennsylvania [1], Maryland [13] and Ohio [15] from July to September following exposure to swine at agricultural fairs. With the exception of three adult cases, all others were among children twelve years of age or younger. No human-to-human transmission was identified. These A(H3N2)v viruses had HA genes derived from a seasonal human H3 virus that was probably introduced to swine by humans in 2010 (Figure 3). The viruses were closely related to A(H3N2)v viruses infecting humans in Ohio and Michigan in 2016 and viruses known to circulate in swine in the United States of America.

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

Characterisation of the cluster IV-A virus revealed that ferret antisera raised against wild type viruses and CVVs reacted well with this virus. Antigenic testing of the viruses with the 2010 human-like H3 gene showed reduced inhibition by post-infection ferret antisera raised against the nearest CVV, IDCDC-RG55C, and seasonal A(H3N2) viruses. Pooled, adult post-vaccination antisera reacted with these viruses at titres that were reduced compared to those against homologous vaccine viruses. A pool of sera collected from vaccinated children showed greater reductions in titre compared with pooled adult sera (Table 7).

Table 7. Haemagglutination inhibition assays of influenza A(H3N2) variant viruses.

REFERENCE STRAINS	Lineage	HK/ 4801	IN/10	MN/11	MN X-203	OH/ 27	RG 55C	OH/ 13	Pooled child sera*	Pooled adult sera†
A/Hong Kong/4801/2014	Seasonal	**320**	<10	<10	<10	10	<10	10	2560	5120
A/Indiana/10/2011	IV-A	<10	**320**	320	320	<10	<10	10	20	80
A/Minnesota/11/2010	IV-A	<10	40	**320**	1280	<10	<10	10	20	20
A/Minnesota/11/2010 X-203	IV-A	20	40	640	**2560**	<10	<10	20	40	20
A/Ohio/27/2016	human-like	10	<10	<10	<10	**5120**	1280	1280	40	320
A/Ohio/28/2016 IDCDC-RG55C	human-like	20	20	20	20	5120	**5120**	640	40	320
A/Ohio/13/2017	human-like	20	10	10	10	160	80	**640**	80	160
TEST ANTIGENS										
A/Ohio/15/2017	human-like	40	<10	20	10	320	160	2560	80	320
A/Ohio/17/2017	human-like	10	<10	10	<10	80	80	640	40	80
A/Ohio/18/2017	human-like	40	10	20	<10	160	160	1280	160	320
A/Ohio/21/2017	human-like	40	20	20	<10	320	80	1280	160	160
A/Ohio/28/2017	human-like	40	40	10	<10	320	80	1280	80	320
A/Ohio/27/2017	human-like	40	10	20	<10	320	80	2560	80	320
A/Ohio/29/2017	human-like	40	20	40	<10	640	160	1280	160	640
A/North Dakota/19/2017	human-like	40	20	40	<10	640	80	1280	160	320

* 2016-2017 post-vaccine immune serum pool from child (0-3 yrs) vaccinees

†2016-2017 post-vaccine immune serum pool from adult (19-49 yrs) vaccinees

[5] http://www.eurosurveillance.org/images/dynamic/EE/V19N18/art20793.pdf

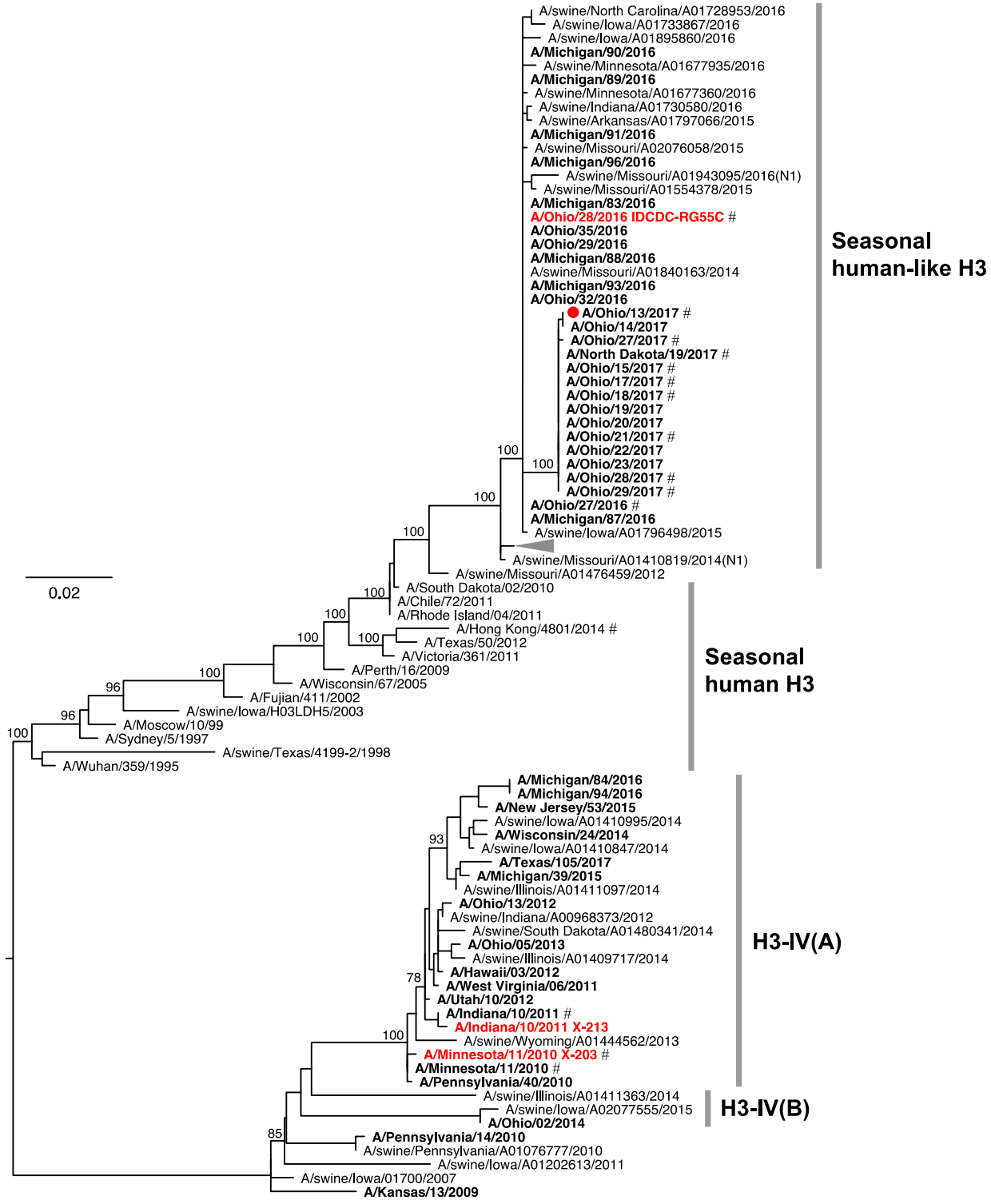

Figure 3. Phylogenetic relationships of A(H3) HA genes. The available CVVs are in red. The proposed CVV is indicated by a red dot(●). The A(H3N2)v viruses are in bold font. The viruses tested in haemagglutination inhibition assay are indicated by hashes (#). The scale bar represents the number of substitutions per site. Bootstrap supports of topology are shown above selected nodes.

Influenza A(H3N2)v candidate vaccine viruses

Based on the available antigenic, genetic and epidemiologic data, a new CVV based on an A/Ohio/13/2017-like virus is proposed. The available A(H3N2)v CVVs are listed in Table 8.

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

Candidate vaccine viruses	**Type**	**Institution***	**Available**
A/Minnesota/11/2010 (NYMC X-203)	Conventional	CDC	Yes
A/Indiana/10/2011 (NYMC X-213)	Conventional	CDC	Yes
IDCDC-RG55C (A/Ohio/28/2016-like)	Conventional	NIBSC	pending
	and reverse genetics	CDC	Yes
Candidate vaccine viruses in Preparation	**Type**	**Institution**	**Availability**
A/Ohio/13/2017-like	Reverse genetics	CDC	pending

* **Institution distributing the candidate vaccine viruses:**
CDC - Centers for Disease Control and Prevention, United States of America
NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom

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Annex 1. Recent A(H5) activity reported to international agencies

Country, area or territory	Host	Genetic clade (subtype)
Austria	Wild bird	2.3.4.4 (H5N8)
Bangladesh	Poultry	2.3.2.1a (H5N1)
Belgium	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Bosnia and Herzegovina	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Bulgaria	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Cameroon	Poultry	2.3.2.1c (H5N1)
China	Poultry	2.3.2.1c (H5N1) 2.3.4.4 (H5N2/N6/N8)
China, Hong Kong SAR	Wild bird	2.3.4.4 (H5N6)
Taiwan, China	Poultry	2.3.4.4 (H5N2/N8)
Croatia	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8/N5)
Czechia	Wild bird	2.3.4.4 (H5N8/N5)
	Poultry	2.3.4.4 (H5N8)
Democratic Republic of the Congo	Poultry	2.3.4.4 (H5N8)
Denmark	Wild bird	2.3.4.4 (H5N8)
Egypt	Human (1)#	unknown (H5N1)
	Poultry	2.2.1.2 (H5N1), 2.3.4.4 (H5N8)
Finland	Wild bird	2.3.4.4 (H5N8)
France	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Georgia	Wild bird	2.3.4.4 (H5N8/N5)
Germany	Wild bird	2.3.4.4 (H5N8/N5)
	Poultry	2.3.4.4 (H5N8/N5)
Greece	Poultry	2.3.4.4 (H5N8)
Hungary	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
India	Poultry	2.3.2.1a (H5N1)
Indonesia	Human (1)#	unknown (H5N1)
	Poultry	2.3.2.1c (H5N1)
Israel	Poultry	2.3.4.4 (H5N8)
Italy	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Japan	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N6)
Lao People's Democratic Republic	Poultry	2.3.2.1c (H5N1)
Lithuania	Wild bird	2.3.4.4 (H5N8)
Luxembourg	Poultry	2.3.4.4 (H5N8)
Malaysia	Poultry	2.3.2.1c (H5N1)
Myanmar	Poultry	2.3.2.1c (H5N1)
Nepal	Wild bird	2.3.2.1a (H5N1)
	Poultry	2.3.4.4 (H5N8)
Netherlands	Wild bird	2.3.4.4 (H5N8/N5)
Nigeria	Poultry	2.3.2.1c (H5N1)
Philippines	Poultry	2.3.4.4 (H5N6)
Poland	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Republic of Korea	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N6/N8)

Country, area or territory	Host	Genetic clade (subtype)
Romania	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Russian Federation	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Serbia	Wild bird	2.3.4.4 (H5N8)
Slovakia	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Slovenia	Wild bird	2.3.4.4 (H5N8)
South Africa	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Spain	Wild bird	2.3.4.4 (H5N8)
Sweden	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Switzerland	Wild bird	2.3.4.4 (H5N8)
Togo	Poultry	2.3.2.1c (H5N1)
United Kingdom	Wild bird	2.3.4.4 (H5N8)
	Poultry	2.3.4.4 (H5N8)
Viet Nam	Poultry	2.3.2.1c (H5N1) 2.3.4.4 (H5N6)
Zimbabwe	Poultry	2.3.4.4 (H5N8)

# denotes number of human cases reported to WHO within the reporting period (28 February to 25 September 2017)