Recommended composition of influenza virus vaccines for use in the 2015 southern hemisphere influenza season

September 2014

The World Health Organization (WHO) convenes technical consultations[1] in February and September each year to recommend viruses for inclusion in influenza vaccines[2] for use in the northern and southern hemisphere influenza seasons. This recommendation relates to the influenza vaccines for the forthcoming influenza season in the southern hemisphere (2015). A recommendation will be made in February 2015 relating to vaccines that will be used for the influenza season in the northern hemisphere (2015-2016). For countries in equatorial regions, epidemiological considerations influence which recommendation (February or September) individual national and regional authorities consider appropriate.

Influenza activity, February – September 2014

Between February and September 2014, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. Activity varied from low or moderate to high due to the circulation of influenza A(H1N1)pdm09, A(H3N2) and influenza B viruses.

In the northern hemisphere, influenza activity was high from February to April and started to decline from April onwards with the exception of a few countries. In the southern hemisphere, activity remained low from February until May when moderate to high activity was reported from a number of countries.

Influenza A(H1N1)pdm09 viruses

Influenza A(H1N1)pdm09 activity was variable in Africa, the Americas, Asia, Europe and Oceania. Regional and widespread outbreaks occurred in Asia, Europe and North America between February and April. Activity was low from May until September in the northern hemisphere. Regional outbreaks occurred in Brazil from May to August and in Paraguay during May and June. There were widespread outbreaks in the Plurinational State of Bolivia in June. Activity in Australia increased from May and caused widespread outbreaks in August and September. New Zealand had regional outbreaks in September. In general, low A(H1N1)pdm09 activity was recorded in Africa with the exception of Egypt where regional and widespread outbreaks were reported in February and March.

Influenza A(H3N2) viruses

Influenza A(H3N2) activity was generally moderate to high in parts of Africa, the Americas, Asia, Europe and Oceania. In Africa, local and regional outbreaks were reported in February and March in Egypt, Madagascar and Tunisia and during July and August in South Africa. In the Americas, local and regional outbreaks were reported by Canada, Mexico and the United States of America between February and March, while regional outbreaks occurred in a

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

[2] Description of the process of influenza vaccine virus selection and development available at: http://www.who.int/gb/pip/pdf_files/Fluvaccvirusselection.pdf

number of South American countries (Bolivia (Plurinational State of), Brazil, Colombia, Paraguay and Peru) from May onwards. Widespread outbreaks occurred in Chile from June to August. In Asia regional outbreaks were reported by China, Japan and the Republic of Korea in February and March, in Singapore during June, and in Nepal in August. There were widespread outbreaks in Japan in February, Georgia and Israel in February and March, and Cambodia from May to July. In Europe, many countries reported regional or widespread outbreaks of A(H3N2) between February and April with co-circulation of A(H1N1)pdm09 virus. In Oceania, sporadic activity occurred from February until April. Regional outbreaks were reported in Australia from May until August with co-circulation of both A(H1N1)pdm09 and influenza B viruses. In September widespread A(H3N2) outbreaks occurred in Australia and regional outbreaks occurred in New Caledonia and New Zealand.

Influenza B viruses

In general influenza B activity was low in most of Africa and Europe with the exception of the Democratic Republic of the Congo and Egypt where regional outbreaks occurred in February and May respectively. In Asia, widespread and regional outbreaks occurred in Japan from February until May. Regional outbreaks were reported by China in February and March and by the Republic of Korea from February to April. Regional and widespread activity occurred in Canada from February to May. In Central and South America regional activity was reported in Paraguay from May to July, El Salvador in June, Brazil in July and August, and Nicaragua in September. In Oceania, regional outbreaks occurred in Australia from July onwards.

The extent and type of seasonal influenza activity worldwide are summarized in Annex 2.

Zoonotic influenza infections caused by A(H5), A(H7N9) and A(H3N2)v viruses

From 18 February 2014 to 23 September 2014, 15 confirmed human cases of A(H5N1), 7 of which were fatal, were reported from Cambodia, China, Egypt and Indonesia. Highly pathogenic avian influenza A(H5N1) is present in poultry in these countries. Since December 2003, a total of 667 human cases with 393 deaths have been confirmed in 16 countries[3]. To date there has been no evidence of sustained human-to-human transmission. In addition a single fatal case of A(H5N6) was reported in China. This was the first reported human infection with this virus.

During this period 99 additional cases of avian influenza A(H7N9) virus infection were reported in China. Since February 2013, a total of 454 cases with at least 171 deaths have been confirmed[4].

Two cases of non-fatal A(H3N2)v were reported in the United States of America. No cases of A(H9N2) or A(H10N8) were reported in this period.

Antigenic and genetic characteristics of recent seasonal influenza viruses

Influenza A(H1N1)pdm09 viruses

Antigenic characteristics of A(H1N1)pdm09 viruses collected from February to September 2014 were assessed with panels of post-infection ferret antisera in haemagglutination inhibition (HI) tests. HI tests indicated that the vast majority of A(H1N1)pdm09 viruses remained antigenically homogeneous and closely related to the vaccine virus

[3] http://www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_27June14.pdf
[4] Communication from Chinese Center for Disease Control and Prevention (CCDC)

A/California/7/2009. Sequence analysis of the HA genes of A(H1N1)pdm09 viruses indicated that recently circulating viruses fell into two genetic clades, 6 and 7, which were antigenically indistinguishable. Most of the circulating viruses belonged to clade 6B while a small number of viruses from Africa and China belonged to clade 6C. A single virus from China belonged to clade 7. A small proportion of viruses showed reductions in reactivity in HI assays with ferret antisera raised against A/California/7/2009-like reference viruses; most of these viruses carried amino acid substitutions in the region corresponding to positions 153-157 of HA, often associated with propagation in cells.

Influenza A(H3N2) viruses

Antigenic characteristics of A(H3N2) viruses collected from February to September 2014 were assessed with panels of post-infection ferret antisera in HI and virus neutralization assays. While many recent A(H3N2) viruses were well inhibited by ferret antisera raised against cell-propagated reference viruses such as A/Victoria/361/2011 and A/Texas/50/2012, an increasing proportion was poorly inhibited by post-infection ferret antisera raised against these cell-propagated viruses as well as egg-propagated A/Texas/50/2012 (Table 1). The HA genes of viruses that were poorly inhibited by these ferret antisera fell into phylogenetic clades 3C.2a and 3C.3a. Compared to cell propagated A/Texas/50/2012 the HAs of clade 3C.2a viruses had amino acid changes at L3I, N144S, N145S, F159Y, K160T, N225D and Q311H while HAs of viruses in clade 3C.3a had amino acid changes in residues T128A, A138T, R142G, N145S, F159S and N225D. Viruses in these 2 new genetic clades were antigenically indistinguishable from each other in HI and neutralization assays.

Influenza B viruses

Influenza B viruses of the B/Victoria/2/87 and the B/Yamagata/16/88 lineages co-circulated. Viruses of the B/Yamagata/16/88 lineage predominated in all countries reporting influenza B infections.

The HA genes of B/Yamagata/16/88 lineage viruses fell within genetic clades 2 or 3, with the majority being in clade 3 over recent months. Most of the clade 3 viruses from China were reassortants that carried the NA gene from the B/Victoria lineage. Viruses with HA genes in these clades could be distinguished antigenically in HI tests by some post-infection ferret antisera. Post-infection ferret antisera raised against the egg-propagated vaccine virus B/Massachusetts/2/2012 (a clade 2 virus) recognised the majority of recent viruses but with a significantly increased proportion of recently circulating viruses showing 4-fold reductions in HI titre compared to homologous titres (Table 2). Recent circulating viruses were generally better inhibited by ferret antisera raised against egg-propagated clade 3 viruses (e.g. B/Phuket/3073/2013).

The HA gene sequences of the vast majority of B/Victoria/2/87 lineage viruses belonged to the B/Brisbane/60/2008 genetic clade 1A. In HI tests with post-infection ferret antisera most viruses were antigenically closely related to the vaccine virus, B/Brisbane/60/2008, and viruses closely related to B/Brisbane/60/2008 that were propagated in cells. Some viruses recovered in China showed reduced HI titres compared to homologous titres.

Resistance to influenza antiviral drugs

Neuraminidase inhibitors

The majority of A(H1N1)pdm09 viruses tested were sensitive to oseltamivir and zanamivir. A small proportion of A(H1N1)pdm09 viruses with highly reduced inhibition (HRI) by oseltamivir were detected globally. In Japan, a small proportion (2.7%) showed HRI with

oseltamivir and peramivir, and one virus showed reduced inhibition to zanamivir and laninamivir. In all cases resistance was due to a histidine to tyrosine substitution at amino acid 275 (H275Y) in the neuraminidase and the majority were from cases that were not treated with antiviral drugs. In one case there was an additional change (I223R) resulting in HRI by oseltamivir and peramivir and reduced inhibition by zanamivir and laninamivir. The vast majority of A(H3N2) and B viruses tested were sensitive to oseltamivir, peramivir, laninamivir and zanamivir.

M2 inhibitors

M gene sequencing of A(H1N1)pdm09 and A(H3N2) viruses revealed that all those analysed had the serine to asparagine substitution at amino acid 31 (S31N) of the M2 protein which is known to confer resistance to the M2 inhibitors, amantadine and rimantadine.

Human serology studies with inactivated influenza virus vaccines

HI assays were used to measure the presence of antibodies to recent virus isolates in panels of sera from children, adults and older adults who had received seasonal trivalent inactivated vaccines. For A(H3N2) viruses, virus neutralization assays were used for a subset of sera. Five panels of sera from adults and older adults as well as two panels from children were from trials of egg-grown trivalent vaccine of the composition recommended for the northern hemisphere 2013-14 and southern hemisphere 2014 seasons (A/California/7/2009 (H1N1)pdm09-like, A/Texas/50/2012 (H3N2)-like and B/Massachusetts/2/2012-like viruses); one panel of sera from adults and older adults was from a trial of cell-grown trivalent vaccine of the same composition.

For the majority of panels tested, geometric mean HI titres of antibodies against representative recent A(H1N1)pdm09 viruses were not reduced significantly as compared to HI titres to the vaccine virus.

Geometric mean HI titres against clade 3C.3a A(H3N2) viruses were significantly reduced compared to HI titres against both cell-propagated and egg-propagated A/Texas/50/2012 viruses (average reductions for 3C.3a viruses compared to egg propagated A/Texas/50/2012: adults, 79%; older adults, 77%; children, 70%; average reductions compared to cell propagated A/Texas/50/2012: adults, 67%; older adults, 72%; children, 52%).

Serum panels were tested against representative recent B/Yamagata/16/88 lineage viruses of genetic groups 2 and 3 as well as against B/Victoria/2/87 lineage viruses. Geometric mean HI titres of antibodies against representative recent group 2 B/Yamagata/16/88 lineage viruses were not reduced significantly compared to HI titres to the vaccine virus. However, for a majority of panels tested, geometric mean HI titres against group 3 viruses were significantly reduced compared to HI titres against the group 2 vaccine virus. As expected, geometric mean HI titres to B/Victoria/2/87 lineage viruses also were reduced.

Recommended composition of influenza virus vaccines for use in the 2015 southern hemisphere influenza season

A(H1N1)pdm09 viruses co-circulated in varying proportions with A(H3N2) and B viruses during the period February - September 2014, with outbreaks in several countries. The majority of A(H1N1)pdm09 viruses were antigenically similar to A/California/7/2009. Vaccines containing A/California/7/2009 - like antigens elicited anti-HA antibodies in humans of similar titres against the vaccine virus and recent A(H1N1)pdm09 viruses.

Influenza A(H3N2) viruses were associated with outbreaks in several countries. The majority of recent viruses were antigenically distinguishable from the previous vaccine virus A/Texas/50/2012 and more closely related to A/Switzerland/9715293/2013. Current vaccines containing A/Texas/50/2012 antigens induced antibodies in humans that reacted less well to A(H3N2) clade 3C.3a viruses.

Influenza B activity was reported in many countries. B/Yamagata/16/88 remained dominant over B/Victoria/2/87 lineage viruses. The majority of recent B/Victoria/2/87 lineage viruses were antigenically and genetically closely related to B/Brisbane/60/2008. Most recently isolated B/Yamagata/16/88 lineage viruses were antigenically distinguishable from the current vaccine virus B/Massachusetts/2/2012 (clade 2) and were more closely related to B/Phuket/3073/2013-like (clade 3) viruses. Current vaccines containing B/Massachusetts/2/2012 antigens induced anti-HA antibodies that reacted well to B/Yamagata/16/88 lineage clade 2 viruses; however, significant reductions in GMT were observed more frequently when testing clade 3 viruses.

It is recommended that vaccines for use in the 2015 influenza season (southern hemisphere winter) contain the following:

– an A/California/7/2009 (H1N1)pdm09-like virus;
– an A/Switzerland/9715293/2013 (H3N2)-like virus[a];
– a B/Phuket/3073/2013-like virus.

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus.

[a] A/South Australia/55/2014, A/Norway/466/2014 and A/Stockholm/6/2014 are A/Switzerland/9715293/2013-like viruses

Lists of candidate influenza vaccine viruses that are available or under development and reagents for vaccine standardization, including those for this recommendation, can be found on the WHO website[5]. Candidate vaccine viruses for zoonotic influenza viruses are updated on the same website.

As in previous years, national or regional authorities approve the composition and formulation of vaccines used in each country. National public health authorities are responsible for making recommendations regarding the use of the vaccine. WHO has published recommendations on the prevention of influenza[6].

Candidate vaccine viruses (including reassortants) and reagents for use in the laboratory standardization of inactivated vaccine may be obtained from: Immunobiology, Office of Laboratory and Scientific Services, Monitoring and Compliance Group, Therapeutic Goods Administration, P.O. Box 100, Woden, ACT, 2606, Australia (fax: +61262328564, email: influenza.standards@tga.gov.au; web site: http://www.tga.gov.au); Division of Virology, National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG UK (fax: +441707641050, e-mail: enquiries@nibsc.org, web site: http://www.nibsc.ac.uk/spotlight/influenza_resource_centre/reagents.aspx); Division of Biological Standards and Quality Control, Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20892, United States

[5] http://www.who.int/influenza/vaccines/virus/candidates_reagents/home
[6] http://www.who.int/wer/2012/wer8747.pdf

(fax: +1 301 480 9748); Center for Influenza Virus Research, National Institute of Infectious Diseases, Gakuen 4-7-1, Musashi-Murayama, Tokyo 208-0011, Japan (fax: +81425616156, email: flu-vaccine@nih.go.jp).

Requests for reference viruses should be addressed to the WHO Collaborating Centre for Reference and Research on Influenza, VIDRL, 792 Elizabeth Street, Melbourne, Victoria 3000, Australia (fax: +61393429329, web site: http://www.influenzacentre.org, email: whoflu@influenzacentre.org); the WHO Collaborating Centre for Reference and Research on Influenza, National Institute of Infectious Diseases, Gakuen 4-7-1, Musashi-Murayama, Tokyo 208-0011, Japan (fax: +81425616149 or +81425652498, email: whocc-flu@nih.go.jp the WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza, Centers for Disease Control and Prevention, 1600 Clifton Road, Mail Stop G16, Atlanta, GA 30333, United States (fax: +14046390080, web site: http://www.cdc.gov/flu/, email: influenzavirussurveillance@cdc.gov); the WHO Collaborating Centre for Reference and Research on Influenza, MRC National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, UK (fax: +442089064477, web site: http://www.nimr.mrc.ac.uk/wic/, email: whocc@nimr.mrc.ac.uk) or the WHO Collaborating Centre for Reference and Research on Influenza, National Institute for Viral Disease Control and Prevention, China CDC, 155 Changbai Road, Changping District, 102206, Beijing, P.R. China. (tel: +86 10 5890 0851, fax: +86 10 5890 0851, email: whocc-china@cnic.org.cn, website: http://www.cnic.org.cn/eng/).

Influenza surveillance information is updated on the WHO Global Influenza Programme web site[7].

[7] http://www.who.int/influenza

Table 1. Haemagglutination inhibition reactions of influenza A(H3N2) viruses

				REFERENCE FERRET ANTISERA							
				3C.1	3C.1	3C.3	3C.2a	3C.3a	3C.3a	3C.3a	
		Collection	Passage	EGG	SIAT	EGG	MDCK	MDCK	SIAT	EGG	HA
	REFERENCE ANTIGENS	Date	History[1]	TX/50	TX/50	WA/18	NE/4	CA/2	PU/6759	SZ/9715293	CLADE
1	A/TEXAS/50/2012	2012-04-15	E5	640	320	320	320	80	80	320	3C.1
2	A/TEXAS/50/2012	2012-04-15	MK/MDCK1/SIAT2	320	640	320	640	320	320	320	3C.1
3	A/WASHINGTON/18/2013	2013-11-29	E5	320	320	640	320	20	80	320	3C.3
4	A/NEBRASKA/4/2014	2014-03-11	MDCK3	160	160	80	160	160	160	160	3C.2a
5	A/CALIFORNIA/2/14	2014-01-16	MDCK1SIAT2	40	40	40	160	160	80	80	3C.3a
6	A/PALAU/6759/2014	2014-03-26	SIAT2	40	40	20	80	80	160	80	3C.3a
7	A/SWITZERLAND/9715293/2013	2013-12-06	E4/E2	160	40	80	320	80	160	320	3C.3a
	TEST ANTIGENS										
8	A/HAWAII/34/2014	2014-06-11	SIAT1	320	320	640	320	160	320	160	3C.3
9	A/BOLIVIA/841/2014	2014-06-30	SIAT2	320	320	160	320	160	320	160	3C.3
10	A/BRAZIL/45230/2014	2014-05-08	MDCK1/SIAT2	160	160	80	160	160	320	160	3C.3
11	A/MONTANA/6/2014	2014-06-04	SIAT1	80	80	80	1280	160	320	160	3C.2a
12	A/ALASKA/33/2014	2014-06-17	SIAT1	80	40	40	160	160	320	160	3C.3a
13	A/HAWAII/26/2014	2014-06-27	SIAT1	80	40	20	160	160	320	80	3C.3a
14	A/CAMBODIA/585/2014	2014-05-17	SIAT2	80	40	40	320	320	320	320	3C.3a

[1] E, egg; MK, Monkey kidney cells; MDCK cells; MDCK-SIAT1 cells

Table 2. Haemagglutination inhibition reactions of influenza B (Yamagata lineage) viruses

Viruses	Genetic Clade	Collection date	Passage History[2]	Haemagglution Inhibition Titre[1]					
				Post infection ferret antisera					
				2	2	2	3	3	3
				MDCK B/Estonia	Egg B/Mass	MDCK B/Mass	Egg B/Wis	Egg B/Stock	Egg B/Phuket
				55669/11	2/12	2/12	1/10	12/11	3073/13
REFERENCE VIRUSES									
B/Estonia/55669/2011	2	2011-03-14	MDCK1/MDCK1	640	320	640	80	80	160
B/Massachusetts/2/2012	2	2012-03-13	E3/E4	160	1280	320	320	1280	1280
B/Massachusetts/2/2012	2	2012-03-13	MDCK1/C2/MDCK3	640	1280	640	320	640	1280
B/Wisconsin/1/2010	3	2010-02-20	E3/E2	<	320	40	320	640	640
B/Stockholm/12/2011	3	2011-03-28	E4/E1	<	320	40	80	320	320
B/Phuket/3073/2013	3	2013-11-21	E4/E1	<	320	40	160	320	640
TEST VIRUSES									
B/Phuket/3073/2013	3	2013-11-21	MDCK2/MDCK1	80	320	160	20	320	640
B/Norway/1877/2014	3	2014-05-21	MDCK1	80	320	160	20	320	320
B/Norway/2011/2014	3	2014-06-19	MDCK1	40	320	80	20	320	320
B/Brisbane/9/2014	3	2014-03-24	E4/E1	<	160	40	160	320	320
B/Norway/2045/2014		2014-05-28	MDCK2	80	160	160	160	320	ND
B/Cameroon/1640/2014	2	2014-03-10	MDCK1/MDCK1	640	320	640	10	160	320
B/Cameroon/2082/2014	2	2014-03-20	MDCK1/MDCK1	640	160	640	10	160	160

[1] < = <10; ND = Not done
[2] E, egg; MDCK cells

Annex 1

Declarations of interest

The WHO recommendation on composition of influenza vaccines for the southern hemisphere 2014 was made through a technical consultation with relevant WHO Collaborating Centres on Influenza (CCs) and WHO Essential Regulatory Laboratories (ERLs).

In accordance with WHO policy, Directors and experts of the relevant WHO CCs and ERLs, in their capacity as representatives of their respective institutions ("Advisers") completed the WHO form for Declaration of Interests for WHO experts before being invited to the consultation. At the start of the consultation, the interests declared by the Advisers were disclosed to all consultation participants.

The Advisers declared the following personal current or recent (within the past 4 years) financial or other interests relevant to the subject of work:

Institution	Representative	Personal interest
WHO CC Atlanta	Dr Nancy Cox	None
WHO CC Beijing	Dr Yuelong Shu	None
WHO CC London	Dr John McCauley	None
WHO CC Melbourne	Dr Anne Kelso	Shareholdings (significant) in the company CSL Limited.
WHO CC Memphis	Dr Richard Webby	None
WHO CC Tokyo WHO ERL NIID Tokyo	Dr Takato Odagiri	None
WHO ERL CBER Bethesda	Dr Zhiping Ye	None
WHO ERL NIBSC Potters Bar	Dr Othmar Engelhardt	Travel cost (flights and hotel) to a conference related to influenza vaccine development under GAP[8] program as invited speaker by the vaccine manufacturer BIRMEX
WHO ERL TGA Canberra	Dr Gary Grohmann	None

Based on the WHO assessment of the interest declared by Dr Kelso, it was concluded that Dr Kelso should continue to serve as an Adviser, considering that the interest was disclosed at the beginning of the consultation, and that, in accordance with the conditions required of all WHO CC Melbourne staff, Dr Kelso has agreed to refrain from acquiring additional shares in companies involved in influenza vaccine manufacture.

The interest declared by Dr Engelhardt was reviewed by WHO and determined not to present a conflict of interest with the objectives of the technical consultation.

In view of the foregoing, Dr Kelso and Dr Engelhardt participated in the consultation as Advisers.

[8] http://www.who.int/influenza_vaccines_plan/objectives/en/

Annex 2. Extent and type of influenza activity worldwide, from end of January to early September 2014

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Africa								
Algeria	*H1(pdm09), ***H3, *B	*H1(pdm09), **H3	*H1(pdm09), *H3, *B	0	*H1(pdm09), *B	*H1(pdm09), *B	0	0
Burkina Faso	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09)		*H3, *B			
Cameroon	*H1(pdm09), *H3, *B	*B	*H1(pdm09), *B	*H1(pdm09), **H3, **B	**H3, *B	*H1(pdm09), **H3, *B	0	*B
Central African Republic	*H3, *B	*B						
Côte d'Ivoire	*H1(pdm09), **H3, *B	0	*B	*H3, *B	*H3, *B	*H3, *B	*H3, *B	*H3, *B
Democratic Republic of the Congo	*H3, ***B	*H3, *B	*H3, *B	*H3, *B	*H3, *B	0		
Egypt	***H1(pdm09), ***H3, **B	****H1(pdm09), ***H3, **B	**H1(pdm09), *H3, *B	**H1(pdm09), *H3, ***B	*H1(pdm09)*H3, *B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), *B
Ethiopia	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B						
Ghana	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3	*H1(pdm09), *B
Kenya	*H1(pdm09), **H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0	0	*H3, *B
Madagascar	***H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*B	*H3, **B	*H1(pdm09), **H3, *B	**H3, **B
Mauritius	*H1(pdm09), *H3	**H1(pdm09), **H3, *B						
Morocco	**H3	0	0	0	0	0	0	0
Mozambique	*H3, *B	*H3, *B	*H3, *B	0	0	0	0	0
Niger	*H1(pdm09), *B	*H1(pdm09)	*B					

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Nigeria	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H3	*H1(pdm09), *H3	0	0	0
Rwanda	*H3	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H3	
Senegal	*H1(pdm09), *H3	*H1(pdm09), *B	*H1(pdm09)	*H1(pdm09), *H3	*H1(pdm09)	*H3	**H3	
Sierra Leone	*A	0						
South Africa		*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *H3	*H1(pdm09), **H3, *B	*H1(pdm09), ***H3	*H1(pdm09), ***H3, *B	*H1(pdm09), **H3, *B
Togo	*H3, **B	*H3, *B						
Tunisia	***H3	**H3	**H3, *B	*H3;*B	*H1(pdm09), *H3, *B			
Uganda	*B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B				
United Republic of Tanzania	*H1(pdm09), **H3	**H1(pdm09), *H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	0	0
Zambia	0	*B	*B	*B	*B	*H3;*B	*H3;*B	*H3;*B
America								
Argentina	*H1(pdm09), *H3	*B	*H3, *B	*H1(pdm09), *H3	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, **B	*H1(pdm09), **H3, **B	*H3, *B
Bahamas		*H1(pdm09)						
Bolivia (Plurinational State of)	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H3	*H1(pdm09), ***H3, *B	****H1(pdm09), ***H3, *B	**H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B
Brazil	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	***H1(pdm09), ***H3, *B	**H1(pdm09), ***H3, *B	***H1(pdm09), ***H3, ***B	***H1(pdm09), ***H3, ***B	*H1(pdm09), ***H3, *B
Canada	****H1(pdm09), **H3, ***B	****H1(pdm09), **H3, ****B	***H1(pdm09), **H3, ****B	*H1(pdm09), **H3, ***B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Chile	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	***H3, *B	****H3, **B	****H3, **B	*H1(pdm09), ****H3, **B	*H1(pdm09), **H3, *B

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Colombia	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), ***H3, *B	*H1(pdm09), ***H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Costa Rica	*H1(pdm09), *H3	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H3, **B	*H1(pdm09), *H3, **B	*H3, **B
Cuba	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09)	*H1(pdm09)	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*B
Dominican Republic	*B	0	*H3, *B	*H3, *B	*H3	*H3	0	*H3, *B
Ecuador	*H1(pdm09)	*H1(pdm09)	*H1(pdm09)	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B
El Salvador	*H1(pdm09), *H3	0	0	*H1(pdm09)	***B	*B	*B	0
France, French Guiana		*H1(pdm09), *H3	*H1(pdm09), *H3				*H3, *B	
France, Guadeloupe	*H3, *B	*H3, *B						
Guatemala	*H1	*H1(pdm09), *H3	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*B	*H1(pdm09), *H3, *B	0
Haiti	0	0	0	0	*B		0	
Honduras	0	*B	*B	**B	**B	*H3, **B	*H3, **B	**B
Jamaica	0	*B	*H3, *B	*B	*B	*B	*B	0
Mexico	***H1(pdm09), **H3;*B	***H1(pdm09), **H3;*B	*H1(pdm09), *H3;*B	*H1(pdm09), *H3;*B	*H1(pdm09), *H3;*B	*B	*H1(pdm09), *H3;*B	0
Nicaragua	*H1(pdm09), *B	*B	0	*H1(pdm09)	0	*H3, *B	**B	***B
Panama	0	*H1(pdm09)	*H1(pdm09), *H3	**H1(pdm09), **B	*H1(pdm09), **B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09)
Paraguay	*H3, *B	*B	*H1(pdm09), *B	*H1(pdm09), ***H3, ***B	*H1(pdm09), ***H3, *B	*H1(pdm09), ***H3, ***B	*H1(pdm09), ***H3, *B	*H1(pdm09), **H3, *B
Peru	0	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	***H1(pdm09), ***H3, *B	***H1(pdm09), ***H3, **B

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Saint Kitts and Nevis		*H1(pdm09)						
Saint Vincent and the Grenadines		*B						
Trinidad and Tobago	*B	*H3, *B						
United Kingdom of Great Britain and Northern Ireland - Bermuda	*H1(pdm09)							
United States of America	****H1(pdm09), ***H3, **B	***H1(pdm09), ***H3, ***B	**H1(pdm09), **H3, **B	**H1(pdm09), **H3, **B	*H1(pdm09), **H3, **B	*H1(pdm09), **H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Uruguay	0	0	0	0	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B
Venezuela (Bolivarian Republic of)	*H1(pdm09), *H3, *B	*H3	*H3, *B	*B	*B	*H3, *B	*H3, *B	0
Asia								
Afghanistan	0	0						
Armenia	*H1(pdm09), *H3	*H1(pdm09), *H3	*H3	0			0	
Azerbaijan	0	*B	*B	*B			0	
Bahrain	**H1(pdm09), *B	**H1(pdm09), **H3, **B	*H3, **B	**H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	**H1(pdm09), *B	*H1(pdm09)	*H1(pdm09), *H3
Bangladesh	*B	*H1(pdm09), *B	*H1(pdm09), *B	*H3, *B	*H3, *B	*H3, *B		
Bhutan	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Cambodia	0	*H1(pdm09), **H3, *B	*H1(pdm09), **H3	**H1(pdm09), ****H3, *B	**H1(pdm09), ****H3, *B	**H1(pdm09), ****H3, *B	*H1(pdm09), ***H3	***H3, *B
China	***H1(pdm09), ***H3, ***B	***H1(pdm09), ***H3, ***B	**H1(pdm09), **H3, **B	**H1(pdm09), **H3, **B	**H1(pdm09), **H3, **B	*H1(pdm09), **H3, **B	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B
China, Hong Kong SAR	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Taiwan, China	*H1(pdm09), **H3, *B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Cyprus	*H1(pdm09), *H3							
Georgia	**H1(pdm09), ****H3, *B	*H1(pdm09), ****H3, *B	*H1(pdm09), ***H3, *B	**B	0		0	0
India	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), ***H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Indonesia	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B
Iran (Islamic Republic of)	*H1(pdm09), **H3, **B	*H1(pdm09), **H3, **B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0
Iraq	0	*H1(pdm09)	0	*B	0	*H1(pdm09)	*H3	0
Israel	***H1(pdm09), ****H3, **B	**H1(pdm09), ****H3, **B	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B				
Japan	****H1(pdm09), ****H3, ****B	****H1(pdm09), ***H3, ****B	**H1(pdm09), **H3, ***B	**H1(pdm09), **H3, ***B	*H1(pdm09), *H3, **B	*H3, *B	*H1(pdm09), *H3, *B	*H3
Jordan	*H3, *B	*H1(pdm09), *B	*H1(pdm09)	*H1(pdm09), *B		*H1(pdm09)		0
Kazakhstan	*H1(pdm09), **H3, *B	*H1(pdm09), ***H3, *B	*H1(pdm09), *H3, *B	0	0	0	0	
Kyrgyzstan	*H1(pdm09), **H3, *B	0	0	0	0	0	0	
Lao People's Democratic Republic	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Malaysia	*H1(pdm09), *H3, *B	0	*H3, *B	*H1(pdm09), *B				
Mongolia	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0	0	0
Nepal	*H1(pdm09), **H3, **B	**H1(pdm09), ***H3, **B	***H1(pdm09), **H3, **B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), ***H3, *B	*H1(pdm09), **H3, *B
Oman	*H1(pdm09), *H3, *B	****H1(pdm09), **H3	****H1(pdm09), **H3, *B	****H1(pdm09), **H3, **B	****H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, *B	*H3, *B
Pakistan	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	*H1(pdm09)	*H1(pdm09)	*H1(pdm09)	0		
Philippines	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *B	*H3, *B	*H3, *B	*H3, *B
Qatar	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	0
Republic of Korea	**H1(pdm09), ***H3, ***B	**H1(pdm09), ***H3, ***B	*H1(pdm09), **H3, ***B	*H1(pdm09), *H3, *B	*B	*H3	*H3	0
Singapore	**H1(pdm09), **H3, **B	**H1(pdm09), **H3, **B	**H1(pdm09), **H3, **B	**H1(pdm09), **H3, **B	**H1(pdm09), ***H3, **B	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B
Sri Lanka	*H3	*H3	*H1(pdm09), *H3	*H1(pdm09), *H3	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H3
Thailand	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	
Turkey	*H1(pdm09), **H3, *B	**B	*H3, **B	*B	0	0	0	0
Uzbekistan	*H1(pdm09), *H3	*H1(pdm09), *H3	0	0	0	0	0	0
Viet Nam	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B
Europe								
Albania	**H1(pdm09), **H3	***H1(pdm09), ***H3	*H1(pdm09)				0	

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Austria	****H1(pdm09), ****H3, **B	****H1(pdm09), ****H3, **B	***H1(pdm09), ***H3, **B	*H1(pdm09), *B	*H1(pdm09)		0	
Belarus	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B			0	
Belgium	****H1(pdm09), ****H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3	0		0	
Bosnia and Herzegovina	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	0			0	
Bulgaria	****H1(pdm09), ***H3	***H1(pdm09), **H3	*H1(pdm09), *B	0	0		0	
Croatia	****H3, *B	****H3, *B	****H3, *B	*H3, *B			0	
Czech Republic	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H1(pdm09), *H3	*H3, *B	*H3		0	
Denmark	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B		0	
Estonia	****H1(pdm09), *H3	****H1(pdm09), *H3	***H1(pdm09), *H3	*A	0		0	
Finland	****H1(pdm09), ****H3, *B	****H1(pdm09), ***H3	*H1(pdm09), *H3	*H1(pdm09), *H3, *B			0	
France	****H1(pdm09), ***H3, **B	****H1(pdm09), ***H3, **B	**H1(pdm09), **H3, **B	**H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09)	0
Germany	***H1(pdm09), ***H3, *B	***H1(pdm09), ***H3, *B	***H1(pdm09), ***H3, *B	**H1(pdm09), **H3, *B	*H1(pdm09)		0	0
Greece	****H1(pdm09), **H3, *B	****H1(pdm09), **H3, *B	****H1(pdm09), **H3, *B	****H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B		0	
Hungary	****H1(pdm09), **H3, *B	****H1(pdm09), ***H3, *B	*H1(pdm09), *H3, *B	0			0	
Iceland	****H1(pdm09), **H3	****H1(pdm09), **H3, **B	**H1(pdm09), *H3, *B	*H1(pdm09), *B	*H3, *B		0	
Ireland	***H1(pdm09), ****H3, **B	**H1(pdm09), ****H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	*H3, *B		0	0

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Italy	****H1(pdm09), ****H3, *B	**H1(pdm09), **H3, *B	*H1(pdm09), *H3				0	
Latvia	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3	*B		0	
Lithuania	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3	*H3	*H1(pdm09)		*H3	0
Luxembourg	****H1(pdm09), **H3, *B	****H1(pdm09), **H3	*H1(pdm09), *H3	*H3		0		
Malta						*H1(pdm09), *B		0
Netherlands	****H1(pdm09), ****H3, *B	****H1(pdm09), ****H3, *B	***H1(pdm09), ***H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B			
Norway	****H1(pdm09), **H3, *B	****H1(pdm09), **H3, *B	***H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	*H3, *B		
Poland	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H1(pdm09)	*H1(pdm09)	*A	0	0
Portugal	****H1(pdm09), ***H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*B	*B	0	*H1(pdm09)	0
Republic of Moldova	*H1(pdm09), ***H3	*H1(pdm09), ***H3	*H1(pdm09), ***H3	0	0	0	0	0
Romania	*H1(pdm09), *H3, *B	**H1(pdm09), ***H3.*B	*H1(pdm09), ***H3.*B	*H3	0	0	0	0
Russian Federation	**H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	**H1(pdm09), **H3, **B	**H1(pdm09), *H3, **B	*H1(pdm09)	0	*H1(pdm09), *H3, *B	0
Serbia	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3	0	0		
Slovakia	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09)			
Slovenia	*H1(pdm09), ****H3, *B	*H1(pdm09), ****H3, *B	*H1(pdm09), **H3, *B	*H3	0			
Spain	****H1(pdm09), ***H3, *B	***H1(pdm09), ***H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	*H3, *B	*A	0

Country, area or territory by geographical region	Week 5-8	Week 9-12	Week 13-16	Week 17-20	Week 21-24	Week 25-28	Week 29-32	Week 33-36
Sweden	****H1(pdm09), ***H3, *B	****H1(pdm09), *H3, *B	***H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0	0	0	0
Switzerland	****H1(pdm09), ***H3, *B	****H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B					
The former Yugoslav Republic of Macedonia	**H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B					
Ukraine	**H1(pdm09), ***H3, *B	**H1(pdm09), ***H3, *B	**H1(pdm09), ***H3, *B	*H1(pdm09), *H3, *B	0	0	0	0
United Kingdom of Great Britain and Northern Ireland	****H1(pdm09), ***H3, *B	****H1(pdm09), ***H3, *B	***H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0	0
Oceania								
Australia	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	***H1(pdm09), ***H3, **B	***H1(pdm09), ***H3, **B	****H1(pdm09), ***H3, ***B	****H1(pdm09), ***H3, ***B	****H1(pdm09), ****H3, ***B
Australia, Tasmania		*H3						
France, New Caledonia	*H1(pdm09)	*H1(pdm09), **H3	*H1(pdm09), **H3	*H1(pdm09), **H3, *B	*H3	*H1(pdm09), *H3	*H1(pdm09), *H3	**H1(pdm09), ***H3
New Zealand	*H1(pdm09)	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	**H1(pdm09), **H3, **B	***H1(pdm09), ***H3, **B
Palau			*H3					

Data in Annex 2 were provided by the Global Influenza Surveillance and Response System and other partners.

* = Sporadic activity	A = Influenza A (not subtyped)
** = Local activity	B = Influenza B
*** = Regional outbreaks	H1(pdm09) = Influenza A(H1N1)pdm09
****= Widespread outbreaks	H3 = Influenza A(H3N2)
	0 = All negative