

Recommended composition of influenza virus vaccines for use in the 2014-2015 northern hemisphere influenza season

February 2014

The World Health Organization (WHO) convenes technical consultations¹ in February and September each year to recommend viruses for inclusion in influenza vaccines² for the northern and southern hemispheres, respectively. This recommendation relates to the influenza vaccines for the forthcoming influenza season in the northern hemisphere (2014-2015). A recommendation will be made in September 2014 relating to vaccines that will be used for the influenza season in the southern hemisphere (2015). For countries in equatorial regions, epidemiological considerations influence which recommendation (February or September) individual national and regional authorities consider appropriate.

Seasonal influenza activity, September 2013 – January 2014

Between September 2013 and January 2014, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. Activity varied from low to high and was associated with the co-circulation of influenza A(H1N1)pdm09, A(H3N2) and B viruses.

In the northern hemisphere, influenza activity was moderate from November with high activity reported in December and January in North America. Activity was generally low in Europe but increased in January. In the southern hemisphere, activity remained low from September to January except in Oceania where high influenza activity was reported in September and October.

Influenza A(H1N1)pdm09 activity was generally low to sporadic in Africa and in Central and South America, and variable in Asia, Europe, North America and Oceania. In Africa, local activity was reported in Senegal from September to October and in Egypt in November and January. Regional to widespread activity was reported in some European countries in January including Bulgaria, France, Greece, Portugal, Spain, and Switzerland. Regional or widespread outbreaks occurred in Australia in September and October, and in China and North America in December and January, and in Japan in January and February.

Influenza A(H3N2) activity was generally low in Africa, the Americas, and Europe, and variable in Asia and Oceania. In Africa, local activity was reported in the Central African Republic during September, in Côte d'Ivoire during November, and in Madagascar during January. In Asia, local activity was reported from Singapore from September to January, and from the Islamic Republic of Iran and from Japan in November and January. In Turkey local activity was reported in December and regional outbreaks were reported in January. Regional or widespread outbreaks were also reported in France, Ireland, and Spain in January. Regional or widespread outbreaks were reported in Oceania in September and October before activity declined in November. Regional outbreaks were reported in China during December and January.

Influenza B activity was generally low in Africa, the Americas, Europe and Oceania, and variable in Asia. In Africa, local activity was reported in the Central African Republic during

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

September, in Senegal in September and October, becoming regional in November, and in Ghana during January. In Asia, local activity was reported in Japan and the Republic of Korea in December and January. Local activity was reported in Australia in September and October. Regional outbreaks were reported in Cambodia from September to December. In China, local activity was reported from November to January.

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

Zoonotic influenza infections caused by A(H5N1), A(H7N9), A(H9N2) and A(H10N8) viruses

From 24 September 2013 to 17 February 2014, 15 confirmed human cases of A(H5N1), 9 of which were fatal, were reported from Cambodia, Canada, China, Indonesia and Viet Nam. Highly pathogenic avian influenza A(H5N1) is present in poultry in each of these countries except Canada. Since December 2003, a total of 652 cases with 387 deaths have been confirmed in 16 countries. To date there has been no evidence of sustained human-to-human transmission.

During this period 220 additional human cases of avian influenza A(H7N9) virus infection have been reported. All cases were in China with the exception of a single case detected in Malaysia in an individual travelling from Guangdong Province, China. Since February 2013, a total of 355 cases with 112 deaths have been reported³

Two cases of A(H9N2) were reported in this period, one each in China, and China Hong Kong Special Administrative Region. The associated disease in both cases was mild with both viruses belonging to the A/chicken/Hong Kong/Y280/97 genetic lineage.

Three cases of A(H10N8) with two deaths were reported from Jiangxi Province, China during this period.

Antigenic and genetic characteristics of recent seasonal influenza viruses

Influenza A(H1N1)pdm09 viruses

Between September 2013 and February 2014, all seasonal influenza A(H1N1) viruses detected worldwide were A(H1N1)pdm09. Haemagglutination inhibition (HI) tests using post-infection ferret antisera indicated that the majority of A(H1N1)pdm09 viruses remained antigenically homogeneous and closely related to the vaccine virus A/California/7/2009. Sequence analysis of the HA genes of A(H1N1)pdm09 viruses indicated that the viruses fell into several genetic clades which were antigenically indistinguishable. Recently the great majority of circulating viruses belonged to clade 6, defined by the substitution D97N in the HA. 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, consistent with results obtained since May 2009.

³ Communication from Chinese Centers for Disease Control and Prevention (CDC)

Influenza A(H3N2) viruses

Antigenic characteristics of A(H3N2) viruses collected from September 2013 to January 2014 were assessed with panels of post-infection ferret antisera in HI and virus neutralization assays. The majority of recent A(H3N2) viruses were well inhibited by ferret antisera raised against cell-propagated reference viruses such as A/Texas/50/2012 and A/Victoria/361/2011, indicating that significant antigenic drift has not occurred. Inhibition at similar HI titres was observed with post-infection ferret antisera raised against the egg- and cell-propagated A/Texas/50/2012 viruses. However, the majority of recent cell-propagated A(H3N2) viruses had 8-fold or greater HI titre reductions compared to the homologous titre for the egg-propagated A/Texas/50/2012 virus. The HA genes of recent A(H3N2) viruses belong to phylogenetic clades 3C.3 (approximately 80%) and 3C.2 (approximately 20%). Viruses in these two genetic clades have HA N145S amino acid substitution and the 3C.3 clade HAs have T128A and R142G amino acid substitutions. Viruses in both genetic clades were antigenically indistinguishable from each other as well as from viruses in clade 3C.1 (includes A/Texas/50/2012 virus) 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 countries reporting influenza B activity.

The HA genes of B/Yamagata/16/88 lineage viruses fell within genetic clades 2 or 3, in approximately equal numbers. 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 cell-propagated prototype virus B/Massachusetts/2/2012 (a clade 2 virus) recognised the majority of recent viruses.

The HA gene sequences of most B/Victoria/2/87 lineage viruses belonged to the B/Brisbane/60/2008 genetic clade subgroup 1A and, in HI tests with post-infection ferret antisera, the majority of 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.

Resistance to influenza antiviral drugs

Neuraminidase inhibitors

The majority of A(H1N1)pdm09 viruses tested were sensitive to oseltamivir and all were sensitive to zanamivir. A small number of A(H1N1)pdm09 viruses were detected in China, Japan and the United States with highly reduced inhibition (HRI)⁴ by oseltamivir. In Japan a community cluster of viruses with HRI by oseltamivir and peramivir, but sensitive to zanamivir and laninamivir, were reported in the Sapporo city area in Hokkaido; resistant viruses in the United States had a similar antiviral susceptibility profile. In all instances, HRI was due to a histidine to tyrosine substitution at amino acid 275 (H275Y) in the neuraminidase and the majority were from cases not treated with antiviral drugs. The great majority of A(H3N2) and B viruses tested were sensitive to oseltamivir, peramivir and zanamivir. The exceptions were one A(H3N2) virus which showed HRI by oseltamivir and carried the E119V substitution in the neuraminidase and one B/Yamagata-lineage virus which showed reduced inhibition to peramivir. A smaller number of viruses were also tested for susceptibility to laninamivir and all were sensitive.

⁴ <http://www.who.int/wer/2012/wer8739/en/index.html>

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 or quadrivalent inactivated vaccines. For A(H3N2) viruses, virus neutralization assays were used for a subset of sera. One panel of sera from adults and older adults was taken from recipients of vaccine containing the antigens of the vaccine for the southern hemisphere 2013 season (A/California/7/2009 (H1N1)pdm09-like, A/Victoria/361/2011 (H3N2)-like and B/Wisconsin/1/2010-like viruses); five panels of sera from adults and five from older adults as well as two panels from children were from trials of trivalent vaccine of the composition recommended for the northern hemisphere 2013-14 season (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, one from older adults and one from children were from recipients of quadrivalent vaccine containing, in addition to the antigens recommended for trivalent vaccines for the northern hemisphere 2013-14 season, a B/Brisbane/60/2008-like antigen.

In recipients of vaccine containing A/California/7/2009-like antigens, 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.

Vaccines containing A/Texas/50/2012 antigens stimulated antibodies of similar geometric mean HI titres to the vaccine virus and the majority of representative recent A(H3N2) viruses, when measured against cell-propagated A/Texas/50/2012. When compared with egg-grown A/Texas/50/2012, titres against cell-grown representative recent viruses were reduced (average reductions for cell-grown A(H3N2) viruses compared to egg-grown A/Texas/50/2012: adults, 71%; older adults, 69%; children, 75%; average reductions for egg-grown A(H3N2) viruses compared to egg-grown A/Texas/50/2012: adults, 16%; older adults, 18%; children, 19%).

Vaccines containing influenza B/Massachusetts/2/2012-like antigens stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and the majority of representative recent B/Yamagata/16/88 lineage viruses. In panels from recipients of trivalent vaccine containing influenza B/Massachusetts/2/2012-like antigens, geometric mean HI titres to recent B/Victoria/2/87 lineage viruses were reduced (average reductions for B/Victoria/2/87 lineage viruses as compared to titres against egg-grown B/Massachusetts/2/2012-like reference viruses: adults, 76%; older adults, 74%; children, 69%). Quadrivalent vaccine containing influenza B/Massachusetts/2/2012-like and B/Brisbane/60/2008-like antigens stimulated antibodies of similar geometric mean HI titres to the B/Victoria/2/87 lineage vaccine virus and representative recent B/Victoria/2/87 lineage viruses.

Recommended composition of influenza virus vaccines for use in the 2014-2015 northern hemisphere influenza season

A(H1N1)pdm09 viruses co-circulated in varying proportions with A(H3N2) and B viruses during the period of September 2013 - January 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 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 and genetically similar to the cell-propagated A/Texas/50/2012 viruses. Most A(H3N2) viruses isolated since September 2013 were inhibited by ferret antisera raised against A/Texas/50/2012. Vaccines containing A/Texas/50/2012 antigens elicited antibodies in humans of similar geometric mean HI titres to the cell-propagated vaccine virus and the majority of representative recent A(H3N2) viruses.

Influenza B activity was reported in many countries with B/Yamagata/16/88 lineage viruses predominating. Of the small number of recent B/Victoria/2/87 lineage viruses detected the majority was antigenically and genetically closely related to B/Brisbane/60/2008. Recently reported B/Yamagata/16/88 viruses belonged to the HA phylogenetic clades 2 or 3 and were antigenically similar to B/Massachusetts/2/2012-like (clade 2) viruses.

Current vaccines containing B/Massachusetts/2/2012 antigens elicited anti-HA antibodies in humans that had similar titres against the vaccine virus and recent viruses of the B/Yamagata/16/88 lineage.

It is recommended that vaccines for use in the 2014-2015 influenza season (northern hemisphere winter) contain the following:

- an A/California/7/2009 (H1N1)pdm09-like virus;**
- an A/Texas/50/2012 (H3N2)-like virus;**
- a B/Massachusetts/2/2012-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.

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 web site⁵. Candidate vaccine viruses for zoonotic influenza including A(H5N1), A(H9N2), A(H7) and A(H3N2)v viruses are updated on the same web site.

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 influenza⁶.

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

⁵ http://www.who.int/influenza/vaccines/virus/candidates_reagents/home

⁶ <http://www.who.int/wer/2012/wer8747.pdf>.

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 (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, 10 Wreckyn Street, North Melbourne, Victoria 3051, Australia (fax: +61393423939, 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: todayiri@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, web site: <http://www.cnic.org.cn/eng/>).

Influenza surveillance information is updated on the WHO Global Influenza Programme web site⁷.

⁷ <http://www.who.int/influenza>

Annex 1

Declarations of interest

The WHO recommendation on the composition of influenza virus vaccines for the northern hemisphere 2014-2015 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, all Directors of the 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 (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 and ERL Tokyo	Dr Masato Tashiro	None
WHO ERL Canberra	Dr Gary Grohmann	None
WHO ERL London	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 Rockville	Dr Zhiping Ye	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 influenza vaccine manufactures.

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 2013

Geographical region / Country, area or territory	Week 37- 40	Week 41-44	Week 45-48	Week 49 - 52	Week 1-4	Week 5
Africa						
Algeria	0	0	0	0	*H3,*B	***H3
Burkina Faso	*B	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	
Cameroon	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B		*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B
Central African Republic	*H1(pdm09), **H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3			0
Côte d'Ivoire	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09),**H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3
Democratic Republic of the Congo	*H3	*H3, *B				
Egypt	*H1N1(pdm09),*H3 , *B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	****H1(pdm09), *H3, *B
Ethiopia	*H3, *B	**H3, **B	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B	
Ghana	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B
Kenya	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B		*H1(pdm09), *H3	0
Madagascar	*B	A,*B	0	*H3,*B	*H1(pdm09), **H3, *B	**H3, *B
Mali	*H1(pdm09), *H3	*H1(pdm09), *H3	*B	0	0	
Mauritius	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3	*H3	*H1(pdm09)
Niger	*H1(pdm09), *H3, *B	*H3	*H3,*B	*H3,*B		

Geographical region / Country, area or territory	Week 37- 40	Week 41-44	Week 45-48	Week 49 - 52	Week 1-4	Week 5
Nigeria	*H1(pdm09), *H3, *B	*H3, *B	*H3, **B	*B		
Rwanda	0	0				
Senegal	**H1(pdm09), **H3, **B	***H1(pdm09), **B	***H1(pdm09), ***B	*H1(pdm09)		
South Africa	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	*B	*H3, *B	0
Togo	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *H3, *B		*B
Tunisia		0	*H1(pdm09), *H3	*H3	**H3	***H3
Uganda	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*B			
United Republic of Tanzania	*H3, *B	*B	*H3	*H3	*A, *B	
Zambia	*B	0	*B	0		0
America						
Argentina	*H3, *B	*H3, *B	*H3, *B	*B	*H1(pdm09)	
Barbados	*H1(pdm09)					
Belize	*H1(pdm09), *B					
Bolivia (Plurinational State of)	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *H3	*H1(pdm09)	0	0
Brazil	*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
Chile	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, **B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3
Colombia	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *H3

Geographical region / Country, area or territory	Week 37- 40	Week 41-44	Week 45-48	Week 49 - 52	Week 1-4	Week 5
Costa Rica	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09)	*H1(pdm09)
Cuba	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*B	*H1(pdm09), *B
Dominica		*H3				
Dominican Republic	*H3, *B	*H3, *B	*H3, *B	*H3, *B	*B	0
El Salvador	**H1(pdm09)	**H1(pdm09), *H3, **B	***H1(pdm09)	*H1(pdm09)	*H1(pdm09), *H3	
France, French Guiana	*H3	0	0	0	0	
France, Guadeloupe	0	0	0	*A	*A	
France, Martinique	*H1(pdm09), *H3	*H1(pdm09), *H3	*H3	0	*A	
Guatemala	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0	*B	
Honduras	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H1(pdm09), *B		
Jamaica	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3	*H3	0
Mexico	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Nicaragua	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09)	*H1(pdm09), *H3	
Panama	0	0	0	*H3	0	0
Paraguay	*H1(pdm09), *H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*B	*H3, *B	*B
Peru	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *B	*B	0	0
Saint Vincent and the Grenadines		*H1(pdm09)				
Trinidad and Tobago	*H1(pdm09)	*H1(pdm09), *H3				

Geographical region / Country, area or territory	Week 37- 40	Week 41-44	Week 45-48	Week 49 - 52	Week 1-4	Week 5
United Kingdom of Great Britain and Northern Ireland - British Virgin Islands	*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
Uruguay	*H3	0	0	*H3,*B	*H3	
Asia						
Armenia	0	0	0	0	0	*H3
Afghanistan					0	0
Azerbaijan	0	*B	*B	0	0	0
Bahrain	*H3	*H3	**H3,*B	*H1(pdm09), *H3, *B	*H1(pdm09)	
Bangladesh	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	*H3, *B		
Bhutan	*H3	*H3	*B	0	*B	
Cambodia	**H1(pdm09), ***H3, ***B	***H1(pdm09), **H3, ***B	**H1(pdm09), **H3, ***B	**H1(pdm09), **H3, ***B	*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
China, Hong Kong SAR	**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	*H1(pdm09), *H3	*H3, *B	*H3, *B		
India	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B
Indonesia	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B			
Iran (Islamic Republic of)	*H3	*H1(pdm09), *H3, *B	*H1(pdm09), **H3	**H3	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B

Geographical region / Country, area or territory	Week 37- 40	Week 41-44	Week 45-48	Week 49 - 52	Week 1-4	Week 5
Iraq		0	0	*H1(pdm09), *H3, *B	0	
Israel		*H1(pdm09), *H3, *B	*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	***H1(pdm09), *H3, *B
Jordan	0	*H3	*H1(pdm09), **H3	*H3	*H3	
Kazakhstan	0	0	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09)	
Kyrgyzstan	0	0	0	0	0	0
Lao People's Democratic Republic	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	
Malaysia		0	*H1(pdm09), *H3, *B	*H1(pdm09), *H3		
Mongolia	0	0	0	*H3,*B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B
Nepal	*H3	0	*B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	0
Oman	*H1(pdm09)	*H1(pdm09), *B	0			
Pakistan	*H3, *B	*H3, *B	*B	*B	*H1(pdm09)	
Philippines	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	
Qatar	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), **B			
Republic of Korea	0	*B	*H1(pdm09), *B	*H1(pdm09), *H3, **B	**H1(pdm09), *H3, **B	**H1(pdm09), *H3, **B
Singapore	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, **B	
Sri Lanka	*H3, *B	*H1(pdm09)	*B	*H3	*B	0
Thailand	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B

Geographical region / Country, area or territory	Week 37- 40	Week 41-44	Week 45-48	Week 49 - 52	Week 1-4	Week 5
Turkey	0	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	***H3, *B	*H1(pdm09), ***H3, *B
Uzbekistan	0	0	0	*H1(pdm09), *H3		*H1(pdm09), *H3
Viet Nam	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0
Europe						
Albania	0	0	0	0	0	*H1(pdm09), *H3
Austria	0	0	0	*H1(pdm09)	*H1(pdm09), *H3, *B	*H1(pdm09), *H3
Belarus	0	0	0	0	0	*H1(pdm09)
Belgium	*B	0	*H1(pdm09)	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3
Bosnia and Herzegovina	0	0	0	*B	*H1(pdm09),*B	0
Bulgaria	0	0	0	*H1(pdm09),*B	***H1(pdm09), *H3	****H1(pdm09), *H3
Croatia	0	0	0	*H3, *B		
Czech Republic		*B	0	0	*H1(pdm09), *H3	*H1(pdm09), *B
Denmark	*B	*H1(pdm09), *H3	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B
Estonia	0	0	0	0	*H1(pdm09)	*H1(pdm09)
Finland	0	*H1(pdm09)	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3, *B
France	*H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, *B	****H1(pdm09), *H3, *B
Georgia	0	0	0	0	*H3	*H3
Germany	*H1(pdm09)	*H1(pdm09)	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3
Greece	0	0	0	*H1(pdm09)	****H1(pdm09), *H3	****H1(pdm09), *H3

Geographical region / Country, area or territory	Week 37- 40	Week 41-44	Week 45-48	Week 49 - 52	Week 1-4	Week 5
Hungary	0	0	0	0	*H1(pdm09)	*H1(pdm09)
Iceland	0	0	0	*H1(pdm09),*H3,* B	*H1(pdm09)	*H1(pdm09)
Ireland	*B	0	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, *B	**H1(pdm09), **H3
Italy			*H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3
Latvia	0	0	0	*H1(pdm09), *H3	*H1(pdm09)	*H1(pdm09), *H3, *B
Lithuania	0	0	0	0	0	0
Luxembourg	0	0	0	0	*H1(pdm09)	*H1(pdm09), *H3
Malta					*H1(pdm09)	*H1(pdm09), *H3
Netherlands	0	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3
Norway	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B
Poland	0	*A	*H3	*H1(pdm09), *H3	0	*H1(pdm09), *H3
Portugal	0	*H1(pdm09), *B	*H3	*H1(pdm09), *H3	****H1(pdm09), *H3	****H1(pdm09), *H3, *B
Republic of Moldova	0	0	0	*H3	*H3	*H3
Romania	0	0	*H3	*H1(pdm09)	*H1(pdm09), *H3	*H1(pdm09), *H3
Russian Federation	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, *B
Serbia		0	0	0	*H1(pdm09), *H3	*H3
Slovakia	0	0	0	0	*B	0
Slovenia	0	0	0	*H3	*H3, *B	**H3
Spain	*H1(pdm09)	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	****H1(pdm09), **H3, *B	****H1(pdm09), *H3
Sweden	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	***H1(pdm09), *H3, *B

Geographical region / Country, area or territory	Week 37- 40	Week 41-44	Week 45-48	Week 49 - 52	Week 1-4	Week 5
Switzerland	0	0	*B	*H1(pdm09), *H3	**H1(pdm09), *H3,*B	*H1(pdm09), *H3, *B
The former Yugoslav Republic of Macedonia					***H3	*H1(pdm09), ***H3
Ukraine	*H1(pdm09)	*H3	*H3	*H3	*H1(pdm09), *H3, *B	**H3, *B
United Kingdom of Great Britain and Northern Ireland	*H3,*B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	****H1(pdm09), *H3, *B	***H1(pdm09), *H3
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
France, New Caledonia	*H1(pdm09)	*H1(pdm09)	*H1(pdm09)			
New Zealand	*H1(pdm09), ***H3, **B	*H1(pdm09), *H3, *B				

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