Recommended composition of influenza virus vaccines for use in the 2013-2014 northern hemisphere influenza season

February 2013

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 the northern and southern hemispheres, respectively. This recommendation relates to the influenza vaccines for the forthcoming influenza season in the northern hemisphere (2013-2014). A recommendation will be made in September 2013 relating to vaccines that will be used for the influenza season in the southern hemisphere (2014). For countries in equatorial regions, epidemiological considerations influence which recommendation (February or September) individual national and regional authorities consider appropriate.

Seasonal influenza activity, September 2012 –January 2013

Between September 2012 and January 2013, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. Influenza A(H1N1)pdm09[3] viruses circulated at low levels in general except in some countries in Africa, Asia, Central and South America and Europe. Influenza A(H3N2) viruses were predominant in most of North America, some countries in northern Africa, some parts of Asia and, early in the season, in some European countries as well as China. Influenza B viruses circulated in many countries and were the predominant viruses in some.

In the northern hemisphere, influenza activity was low in September and October. Increased activity was reported in North America in November, in Europe from December onwards and in a number of countries in Asia in December or January.

Regional A(H1N1)pdm09 activity was reported by a few countries in Asia and central America. An increase in activity was reported in many countries in northern, eastern and central Europe, with regional and widespread outbreaks in January. In northern Africa, widespread outbreaks were reported in Algeria in January. Localized and sporadic activity was also reported in many other countries in northern Africa, Asia and North America.

Influenza A(H3N2) virus activity was low in the Americas in September and October. Activity then increased in November and caused widespread outbreaks in Canada and the United States of America where it was the predominant circulating virus. In Asia, regional outbreaks occurred in Cambodia from September to November. Regional and

[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
[3] Standardization of terminology of the pandemic A(H1N1)2009 virus: http://www.who.int/influenza/gisrs_laboratory/terminology_ah1n1pdm09/en/

widespread outbreaks were reported in the Republic of Korea and Japan respectively in January. Low level activity was reported in Europe from September to November but increased in December and January in a number of countries. In northern Africa, activity increased in January with widespread outbreaks reported in Algeria.

Influenza B virus activity increased in North America from November with regional outbreaks reported by Mexico and the United States of America and influenza B virus became predominant in Mexico. In Europe, widespread outbreaks were reported in many countries in January. In Asia activity was generally low. Localized and sporadic B activity was also reported by a number of countries in northern Africa.

In the southern hemisphere, influenza activity generally declined from September onwards. Some South American countries reported regional outbreaks in September and October due to A(H1N1)pdm09, A(H3N2) and B viruses.

A(H1N1)pdm09 activity was reported at low levels with the exception of regional outbreaks in a few countries in central Africa and South America. Regional A(H3N2) outbreaks were reported in Cameroon in October. Influenza B viruses co-circulated with A(H1N1)pdm09 and A(H3N2) in Argentina causing regional outbreaks in September and October.

Sporadic and localized A(H1N1)pdm09, A(H3N2) and B virus activity was reported in Oceania, central and southern Africa and a number of countries in South America.

In tropical areas, many countries reported outbreaks of varying intensity of A(H1N1)pdm09, A(H3N2) and B viruses. Cambodia reported regional A(H3N2) activity throughout most of this period, declining in January.

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

Zoonotic influenza infections caused by A(H5N1), A(H3N2) variant (v)[4], A(H1N1)v, A(H1N2)v, A(H7N3) and A(H9N2) viruses

From 19 September 2012 to 15 February 2013, 12 confirmed human cases of A(H5N1), 8 of which were fatal, were reported from Cambodia, China, Egypt, and Indonesia, where highly pathogenic avian influenza A(H5N1) is present in poultry. Since December 2003, a total of 620 cases with 367 deaths have been confirmed in 15 countries[5]. To date there has been no evidence of sustained human-to-human transmission.

One case of influenza A(H3N2)v was detected in November 2012 in the United States of America[6]. Since August 2011, a total of 321 cases with one death have been confirmed in the United States of America. To date there has been no evidence of sustained human-to-human transmission.

[4] http://www.who.int/influenza/gisrs_laboratory/terminology_ah3n2v/en/
[5] http://www.who.int/influenza/human_animal_interface/EN_GIP_20130215CumulativeNumberH5N1cases.pdf
[6] http://www.cdc.gov/flu/swineflu/h3n2v-situation.htm

No human cases of influenza A(H1N1)v, A(H1N2)v, A(H7N3) or A(H9N2) were detected during the period 19 September 2012 to 18 February 2013.

Antigenic and genetic characteristics of recent seasonal influenza viruses

Influenza A(H1N1)pdm09 viruses

Between September 2012 and January 2013, 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. The majority of viruses recently circulating belong to clades 6 and 7, which share the S185T and S451N changes 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 carried amino acid substitutions in the region corresponding to positions 153-157 of HA, consistent with results obtained since May 2009.

Influenza A(H3N2) viruses

Antigenic characteristics of A(H3N2) viruses collected from September 2012 to January 2013 were assessed with panels of post-infection ferret antisera in HI and virus neutralization assays. The majority of recent A(H3N2) viruses tested were antigenically similar to the cell- propagated reference viruses A/Victoria/361/2011 and egg and cell-propagated A/Texas/50/2012. However, post-infection ferret antisera raised against egg propagated A/Victoria/361/2011 virus had titres against most recent cell-propagated viruses that were at least 8-fold lower in HI and neutralization tests, compared to the homologous titre (Table 1). The HA genes of most recent A(H3N2) viruses fell into phylogenetic clade 3C while the remainder fell into other phylogenetic clades such as 3A, 3B, 5 and 6. These genetic clades, including those clade 3C viruses with amino acid substitutions T128A, R142G and N145S, were antigenically indistinguishable in HI (Table 1) 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/Victoria/2/87 lineage were prevalent in some countries; B/Yamagata/16/88 lineage viruses have continued to increase in proportion becoming dominant in many countries.

The HA gene sequences of most B/Victoria/2/87 lineage viruses belonged to the B/Brisbane/60/2008 genetic clade 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.

The HA genes of most B/Yamagata/16/88 lineage viruses fell within genetic clades 2 or 3, with the proportion of viruses in clade 2 markedly increasing in many areas

during this period. Many viruses with HA genes in these clades could be distinguished antigenically in HI tests with some post-infection ferret antisera (Tables 2a and 2b).

Resistance to influenza antiviral drugs

Neuraminidase inhibitors

The majority of A(H1N1)pdm09 viruses were sensitive to oseltamivir. Of the small number of oseltamivir-resistant A(H1N1)pdm09 viruses detected, some were linked to the use of this drug for prophylaxis or treatment. In all instances, resistance was due to a histidine to tyrosine substitution at amino acid 275 (H275Y) in the neuraminidase; all viruses remained sensitive to zanamivir. All A(H3N2) and B viruses tested were sensitive to oseltamivir and zanamivir. A smaller number of viruses were also tested for susceptibility to peramivir and laninamivir and all were sensitive.

M2 inhibitors

M gene sequencing of A(H1N1)pdm09 and A(H3N2) viruses revealed that all those analysed, with one A(H3N2) exception, 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 two panels of sera from children, five from adults and four from older adults who had received seasonal trivalent inactivated vaccines. In addition, for A(H3N2) viruses, virus neutralization assays were used for a subset of sera. The trivalent vaccines contained the antigens of the vaccine for the northern hemisphere 2012-2013 season (A/California/7/2009 (H1N1)pdm09, A/Victoria/361/2011 (H3N2) and B/Wisconsin/1/2010-like (Yamagata lineage) viruses).

Vaccines containing A/California/7/2009 antigens induced anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and the majority of representative recent A(H1N1)pdm09 viruses.

Vaccines containing A/Victoria/361/2011 antigens induced antibodies of reduced geometric mean HI titres to the majority of recent cell-propagated A(H3N2) viruses compared to the egg–propagated vaccine virus (average reductions for cell-propagated A(H3N2) viruses: adults, 66%; older adults, 68%; children, 64%).

Vaccines containing influenza B/Wisconsin/1/2010-like antigens generally induced 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. However, significant reductions in GMT were observed more frequently for some serum panels when testing clade 2 viruses as compared to clade 3 viruses. Geometric mean HI titres to recent B/Victoria/2/87 lineage viruses were reduced (average reductions: adults, 56%; older adults, 49%; children, 65%).

Recommended composition of influenza virus vaccines for use in the 2013-2014 northern hemisphere influenza season

A(H1N1)pdm09 viruses co-circulated in varying proportions with A(H3N2) and B viruses during the period of September 2012 to January 2013, with low activity in many countries. The majority of A(H1N1)pdm09 viruses were antigenically similar to A/California/7/2009. Vaccines containing A/California/7/2009 antigens induced 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 isolated in cells were antigenically and genetically similar to cell-propagated A/Victoria/361/2011 (HA clade 3C) and A/Victoria/361/2011-like reference viruses such as A/Texas/50/2012. However, ferret antisera raised against egg-propagated A/Victoria/361/2011 had high homologous titres but showed reduced titres against recently circulating cell-propagated viruses. Antisera raised against egg propagated A/Texas/50/2012 showed higher reactivity against recent cell-propagated viruses compared to those raised against egg-propagated A/Victoria/361/2011. Current vaccines containing A/Victoria/361/2011 antigens induced antibodies in humans that reacted less well to most recent influenza A(H3N2) cell-propagated viruses.

Influenza B activity was reported in many countries. The proportion of B/Yamagata/16/88 lineage viruses increased in many parts of the world but B/Victoria/2/87 lineage viruses predominated in some countries, including Australia and China. The majority of recent B/Victoria/2/87 lineage viruses were antigenically and genetically closely related to B/Brisbane/60/2008. The majority of recently reported B/Yamagata/16/88 viruses belonged to the HA phylogenetic clade 2, except in China where they belonged to clade 3. Most recently isolated B/Yamagata/16/88 lineage viruses were antigenically distinguishable from the previous vaccine virus B/Wisconsin/1/2010 (clade 3) and were more closely related to B/Massachusetts/2/2012-like (clade 2) viruses. Current vaccines containing B/Wisconsin/1/2010 antigens induced anti-HA antibodies in humans that had similar titres against the vaccine viruses and recent viruses of the B/Yamagata/16/88 lineage; however, significant reductions in GMT were observed more frequently for some serum panels when testing clade 2 viruses as compared to clade 3 viruses. Titres were lower to recent viruses of the B/Victoria/2/87 lineage.

It is recommended that vaccines for use in the 2013-2014 influenza season (northern hemisphere winter) contain the following:

– an A/California/7/2009 (H1N1)pdm09-like virus[a];
– an A(H3N2) virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011[b] [*];
– 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[c].

[a] A/Christchurch/16/2010 is an A/California/7/2009-like virus;
[b] A/Texas/50/2012 is an A(H3N2) virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011;
[c] B/Brisbane/33/2008 is a B/Brisbane/60/2008-like virus.

*** It is recommended that A/Texas/50/2012 is used as the A(H3N2) vaccine component because of antigenic changes in earlier A/Victoria/361/2011-like vaccine viruses (such as IVR-165) resulting from adaptation to propagation in eggs.**

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[7]. Candidate vaccine viruses for A(H5N1), A(H9N2), A(H7) and A(H3N2)v 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[8].

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: +61 2 6232 8564, email: influenza.standards@tga.gov.au; web site: http://www.tga.gov.au); Division of Virology, National Institute for Biological Standards and Control, Health Protection Agency, Blanche Lane, South Mimms, Potters Bar, Hertfordshire, EN6 3QG UK (fax: +44 1707 641050, e-mail: enquiries@nibsc.hpa.org.uk, 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: +81 42 561 6156, 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: +61 3 9342 3939, 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: +81 42 561 6149 or +81 42 565 2498, web site: http://www.nih.go.jp/niid/index.html); 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: +1 404 639 0080, web site: http://www.cdc.gov/flu/, email:

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

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: +44 208 906 4477, 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 web site[9].

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

Table 1. Haemagglutination inhibition reactions of influenza H3N2 viruses (guinea pig red blood cells)

		REFERENCE FERRET ANTISERA						
		EGG	MDCK	EGG	MDCK	EGG	HA	SEQ
REFERENCE ANTIGENS		VIC/361	VIC/361	TX/50	TX/50	X-223	GROUP	CHANGES
1	A/VICTORIA/361/2011[1] Egg	1280	320	320	320	320	3C	H156Q, G186V, S219Y
2	A/VICTORIA/361/2011 Cell	40	160	160	160	160	3C	
3	A/TEXAS/50/2012 Egg	640	1280	320	640	640	3C	T128N, G186V, S198P, S219F[2]
4	A/TEXAS/50/2012 Cell	40	160	160	160	160	3C	T128N, S198P[2]
5	A/TEXAS/50/2012 X-223	640	640	320	320	640	3C	I226N[3]
6	A/TEXAS/50/2012 X-223A	640	640	320	320	640	3C	I226N[3]
TEST ANTIGENS[4]								
7	A/ARKANSAS/05/2012	80	640	320	320	320	3A	
8	A/VIRGINIA/03/2013	80	320	320	320	160	3C	T128A, R142G, N145S[2]
9	A/NEW HAMPSHIRE/21/2012	40	160	160	160	160	3C	T128A, R142G, N145S[2]
10	A/SOUTH CAROLINA/16/2012	80	160	160	160	160	5	
11	A/COTE D'IVOIRE/1331/2012	80	160	160	320	80	nt	
12	A/SAPPORO/125/2012	40	160	160	160	160	3C	N145S[2]
13	A/HUBEI-HONGSHAN/1368/2012	80	160	160	160	nt[5]	3C	N145S[2]
14	A/JIANGSU-XIUCHENG/1358/2012	80	160	320	160	nt	3C	T128A, R142G, N145S[2]
15	A/LAOS/717/2012	80	320	160	320	nt	nt	

1. Egg-propagated A/Victoria/361/2011 differs from the cell-propagated A/Victoria/361/2011 at the 3 positions indicated.
2. Substitution in the HAs of the clade 3C viruses compared to cell-propagated A/Victoria/361/2011.
3. Substitution in the HAs of the A/Texas/50/2012 reassortants compared to egg-propagated A/Texas/50/2012.
4. All test viruses were cell-propagated.
5. Not tested

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

Viruses	Genetic Clade	Haemagglutination Titre: Post-infection ferret sera: B/Wis Egg	B/Estonia Cell	B/HK Cell	B/Mass Egg	B/Mass Cell
REFERENCE VIRUSES						
B/Wisconsin/1/2010	3	640	40	160	640	40
B/Estonia/55669/2011	2	80	640	1280	320	640
B/Hong Kong/3577/2012	2	40	640	640	160	640
B/Massachusetts/02/2012	2	160	80	320	640	40
B/Massachusetts/02/2012	2	40	160	640	640	160
TEST VIRUSES*						
B/Paris/1443/2012	3	160	40	320	320	80
B/Ghana/DILI-0859/2012	3	80	40	320	320	80
B/Hyogo/4002/2012	3	80	40	160	320	80
B/Paris/1448/2012	2	40	640	640	320	160
B/New Mexico/04/2012	2	40	640	640	320	160
B/Yokohama/82/2012	2	40	320	320	160	160
Homologous Titre		2012-13 Vaccine				

* Cell isolated and propagated

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

Viruses	Genetic Clade	HI- titre[1]: Post-infection ferret antiserum: WISC Egg	MAL Cell	WELL Cell	WELL Egg	BRIS Egg
REFERENCE VIRUSES						
B/WISCONSIN/1/2010	3	640	<	160	40	640
B/MALAYSIA/412/2012	2	80	320	640	640	640
B/WELLINGTON/3/20121	2	20	160	640	1280	640
B/WELLINGTON/3/20121	2	20	160	640	640	640
B/BRISBANE/36/2012	2	80	80	160	160	640
TEST VIRUSES*						
B/MALAYSIA/878/2012	3	320	<	80	20	320
B/HYOGO/4002/2012	3	160	<	320	80	160
B/VICTORIA/1028/2012	3	160	<	320	80	160
B/DENMARK/31/2012	2	320	640	640	640	1280
B/VICTORIA/834/2012	2	160	320	640	640	1280
B/MASSACHUSETTS/02/2012	2	40	320	320	320	640
B/YOKOHAMA/82/2012	2	40	320	320	320	640
B/NEWCASTLE/1/2013	2	40	320	320	320	640
Homologous Titre		2012-13 vaccine				

1. < = <20; * Cell isolated and propagated

Annex 1

Declarations of interest

The WHO recommendation on the composition of influenza virus vaccines for the northern hemisphere 2013-2014 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, all Directors of the WHO CCs and WHO 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 3 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
WHO CC Memphis	Dr Richard Webby	None
WHO CC and ERL Tokyo	Dr Masato Tashiro	None
WHO ERL Washington	Dr Zhiping Ye	None
WHO ERL London	Dr Othmar Engelhardt	Travel cost (flights and hotel) to a conference related to influenza vaccine development under GAP[10] program as invited speaker by the vaccine manufacturer BIRMEX
WHO ERL 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.

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

Annex 2. Extent and type of influenza activity worldwide, August 2012 – January 2013

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Africa						
Algeria	0	0	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, **B	****H1(pdm09), ***H3, ****B
Burkina Faso	0	*H1(pdm09), *H3	*H3	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B
Cameroon	*H3	**H3, *B	***H3, *B	**H3, *B	*H3, **B	*H3, *B
Central African Republic	**H3	*H3	*H3	0	*H3, *B	*H1(pdm09), *B
Côte d'Ivoire	*H1(pdm09), *H3, *B	*A, *H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0
Democratic Republic of the Congo	0	0	*H1(pdm09), *H3	**H1(pdm09)	***H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Egypt	*H3	*H3		*H3	*H1(pdm09), **H3, *B	*H3, *B
Ethiopia	*H1(pdm09)	*H1(pdm09)	**H1(pdm09)	**H1(pdm09)	*H1(pdm09), *H3	*H1(pdm09)
Ghana	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	**H1(pdm09)	**H1(pdm09), *H3, *B	*H1(pdm09), *H3
Kenya	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	*H3, *B	0
Madagascar	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B	**B	*B	*H3*B

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Mali	*H3	**H3	*H3	*B	0	*B
Mauritius	0	*H1(pdm09), *B	0	0	0	0
Morocco		*B	*B	*B	*B	
Niger	*H3	*H3	*H3	*H3		
Nigeria	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B			
Rwanda	0	0	*H3	*B	0	*H1(pdm09), *H3, *B
Senegal	*H3	*H1(pdm09), **H3	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*B
Sierra Leone	*H1(pdm09), *B	0				
South Africa	*H1(pdm09), **H3, **B	*H3, **B	*H3, *B	*H3, *B	0	*H1(pdm09), *H3, *B
Togo	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	0	
Tunisia		0	0	0	*B	*H1(pdm09), *H3, *B
Uganda	*H3, *B	**H3, *B	**H3	*H3, *B		
United Republic of Tanzania	*A, *B	*B	*A			*H1(pdm09), *B

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Zambia	*H3, *B	*A, *B	*A, *B	*A, *B	*A, *B	
America						
Argentina	***H1(pdm09), ***H3, ***B	**H1(pdm09), ***H3, ***B	**H1(pdm09), *H3, ***B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B
Bolivia (Plurinational State of)	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	**H3, *B	*H3, *B
Brazil	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B	**H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	*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	*H3;*B	*H1(pdm09), *H3, **B	*H3;**B	*H3;**B	*H1(pdm09), *H3, *B	*B
Colombia	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3
Costa Rica	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Cuba	*H1(pdm09), **B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B
Dominica						*H1(pdm09)
Dominican Republic	0	*B	*B	*B	*B	*H1(pdm09)
Ecuador	*B	*B	*B	*H3, *B	*H3, *B	0

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
El Salvador	*H1(pdm09), **B	*H3, *B	*H3, *B	*H3, *B	*H3	0
France, French Guiana	*B	*B	*B	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
France, Guadeloupe						*H1(pdm09)
France, Martinique	0	0	0	0	0	0
Guatemala	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3	*H3
Honduras	*H1(pdm09)	0	*H3, *B	*H1(pdm09), **H3, *B	*H3, *B	
Jamaica	*B	*H3, *B	*H3, *B	*H3, *B	*H3, *B	*B
Mexico	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, **B	*H3, **B	*H3, ***B	*H1(pdm09), **H3, **B
Nicaragua	*H1(pdm09), *H3, **B	*H3, **B	*H3, **B	*H3, **B	*H3, *B	*H3, *B
Panama	*H3, *B	*H3, *B	*B	*H3, *B	*H3, *B	*H3
Paraguay	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	*H3, *B	**H3, *B
Peru	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H1(pdm09), *H3	*H1(pdm09), *H3
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

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Uruguay	*H3, *B	0				
Asia						
Armenia	0	0	0	0	0	*B
Azerbaijan						0
Bahrain	*H1(pdm09)	*H1(pdm09)	*H1(pdm09)	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B
Georgia						*H1(pdm09), *B
Bangladesh	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B		
Bhutan	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3
Cambodia	*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	*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
Taiwan, China		*H3				
India	*H1(pdm09), *H3, *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	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Indonesia	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	
Iran (Islamic Republic of)	0	*B	0	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B
Iraq	0	0	0	0	0	*H1(pdm09)
Israel			*H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, *B
Japan	**H3, *B	*H1(pdm09), **H3	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), ***H3, *B	*H1(pdm09), ****H3, *B
Jordan	0	0	*H1(pdm09)	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B
Kazakhstan	0	0	0	0	*H3	*H3, *B
Kyrgyzstan	0	0	0	0	*B	*H1(pdm09), *B
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	
Malaysia	0					
Mongolia	0	0	*H3	*H3		*H1(pdm09), **H3
Nepal	*H1(pdm09), **B	**H1(pdm09), **B	*H1(pdm09), *B	0	0	*H1(pdm09)
Oman	*H1(pdm09)	*H1(pdm09)	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *B	

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Pakistan	*H3	*H3	*H3	*H3;*B	*H1(pdm09), *H3, *B	*H3, *B
Philippines	*H3;*B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3;*B	*B	
Qatar	0	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B
Republic of Korea	*H3	*H3	0	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	**H1(pdm09), ***H3, *B
Singapore	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B			
Sri Lanka	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
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
Turkey	0	0	0	*H3, *B	*H1(pdm09), *H3, *B	****H1(pdm09), *H3, *B
Uzbekistan						*H1(pdm09), *H3, *B
Viet Nam	*H3, *B	*H3, *B	*H3, *B	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B
Europe						
Albania		0	0	0	0	*H1(pdm09), *B
Austria	0	0	0	*H3	*H1(pdm09), *H3, *B	***H1(pdm09), *H3, ***B

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Belarus	0	0	0	0	*H1(pdm09)	**H1(pdm09), *H3
Belgium	*H3	0	0	*H1(pdm09), *B	**H1(pdm09), *H3, ***B	****H1(pdm09), *H3, ****B
Bosnia and Herzegovina	0	0	0	0	0	*H1(pdm09), **H3, *B
Bulgaria	0	0	0	0	0	*H1(pdm09), *B
Croatia		0	0	0	*H1(pdm09), *B	****H1(pdm09), *H3, ****B
Czech Republic		0	*H3, *B	*H1(pdm09)	**H1(pdm09), *H3, *B	****H1(pdm09), *H3, ***B
Denmark	*H3	*H3, *B	*B	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	**H1(pdm09), ****H3, ****B
Estonia	0	0	0	*B	*H1(pdm09)*B	*H1(pdm09), *H3, ****B
Finland	0	0	0	*H3, *B	*H1(pdm09)	****H1(pdm09), ****H3, ****B
France	0	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	***H1(pdm09), **H3, ***B	****H1(pdm09), ***H3, ***B
Germany	*H3	*H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, *B	****H1(pdm09), ***H3, ***B
Greece	0	0	0	0	*H3	*H1(pdm09), *H3, *B
Hungary			0	0	*H1(pdm09)	*H1(pdm09), *H3, *B

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Iceland	0	0	*B	*H3	*H1(pdm09), *H3, *B	****H1(pdm09), ***H3, *B
Ireland	*B	0	*B	*H3, *B	*H1(pdm09), *H3, **B	**H1(pdm09), **H3, ****B
Italy				*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, ***B
Latvia		0	0	0	*H1(pdm09), *H3, *B	***H1(pdm09), **H3, **B
Lithuania	0	0	0	0	*B	***H1(pdm09), *H3, **B
Luxembourg		0	0	*B	*H3, *B	****H1(pdm09), **H3, ****B
Malta		0	*B	*B	**H1(pdm09)*B	
Netherlands	*H1(pdm09)	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, *B	****H1(pdm09), ****H3, ***B
Norway	*H3	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, **B	***H1(pdm09), *H3, ***B	****H1(pdm09), **H3, ****B
Poland	0	0	0	0	*H1(pdm09)	****H1(pdm09), *H3, *B
Portugal	0	*B	*H3	*H3, *B	*H1(pdm09), *H3, *B	****H1(pdm09), *H3, **B
Republic of Moldova	0	0	0	0	0	***H1(pdm09), ***B
Romania	0	0	*H3	0	0	*H1(pdm09), *H3, *B

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Russian Federation	*H1(pdm09), *H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, *B
Serbia		0	0	0	*H3	***H1(pdm09), ***H3, ***B
Slovakia	*H3	0	*H1(pdm09)	0	0	**H1(pdm09), **H3, **B
Slovenia	0	0	0	0	*H1(pdm09), *H3, *B	****H1(pdm09), *H3, **B
Spain	0	0	*H3, *B	*H3, *B	*H1(pdm09), *H3, **B	***H1(pdm09), *H3, ****B
Sweden	*H1(pdm09)	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	****H1(pdm09), *H3, ****B
Switzerland		0	*B	*H1(pdm09), *B	*H1(pdm09), *H3, *B	**H1(pdm09), **H3, ****B
Ukraine	0	0	0	*H3	*B	***H1(pdm09), **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, ****B
Oceania						
Australia	*H1(pdm09), ****H3, ****B	*H1(pdm09), **H3, **B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H1(pdm09), *H3, *B
France, New Caledonia	*H3, *B	*H3, *B	0	0	0	

Geographical region / Country, area or territory	August 2012	September 2012	October 2012	November 2012	December 2012	January 2013
Micronesia (Federated States of)	*H3					
New Zealand	*H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B				
United States of America, American Samoa	*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