Recommended composition of influenza virus vaccines for use in the 2012-2013 northern hemisphere influenza season

February 2012

Influenza activity, September 2011 – January 2012

Between September 2011 and January 2012, influenza activity was reported in Africa, the Americas, Asia, Europe and Oceania. Influenza A(H1N1)pdm09[1] viruses circulated at very low levels in general with the exception of some countries in Asia and the Americas. Influenza A(H3N2) viruses were predominant in Europe, many countries in the Americas and northern Africa and some countries in Asia. Influenza B viruses circulated in many parts of the world and predominated in some countries.

In the northern hemisphere, influenza activity in general was low from September to December 2011, increasing in January 2012 in most countries.

Regional A(H1N1)pdm09 activity was reported by a few countries in Asia and Central America. Widespread activity was reported in Mexico in December 2011 and January 2012. Localized and sporadic activity was reported in northern Africa, Europe and North America.

Influenza A(H3N2) viruses caused regional outbreaks in Asia throughout the period with widespread activity reported in Japan in January 2012. Activity was low in Europe but increased in January 2012 with regional and widespread outbreaks reported in Spain and a number of other countries. Influenza A(H3N2) activity continues to increase in Europe. In northern Africa, activity increased from December 2011 with regional and widespread outbreaks reported. In North America, the United States of America reported regional outbreaks from November 2011 onwards while sporadic and localized activity was reported in Canada and Mexico.

Influenza B virus activity increased in North America from December 2011 with regional outbreaks reported by the United States of America in January 2012. In China, influenza B viruses predominated throughout the period. Sporadic and localized influenza B activity was reported by a number of countries in northern Africa, Asia and Europe.

In the southern hemisphere, influenza activity in general was low with the exception of Australia and New Zealand where regional outbreaks due to co-circulation of influenza A(H1N1)pdm09, A(H3N2) and B viruses were reported in September and October 2011. Some South American countries also reported regional and widespread activity early in the period.

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

A(H1N1)pdm09 was reported at low levels with the exception of regional activity in a few countries in South America and Oceania. Influenza A(H3N2) was the predominant virus in many countries in South America with widespread outbreaks occurring in Paraguay and regional outbreaks in Argentina and Peru in September and October 2011. Sporadic and localized activity of A(H3N2) and B viruses was reported in southern Africa.

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

The extent and type of seasonal influenza activity worldwide are summarized in Annex 1.

Zoonotic influenza infections caused by A(H5N1), A(H3N2) variant (v)[2], A(H1N1)v and A(H1N2)v viruses

From 20 September 2011 to 21 February 2012, 21 confirmed human cases of A(H5N1), 15 of which were fatal, were reported from Cambodia, China, Egypt, Indonesia, and Viet Nam where highly pathogenic avian influenza A(H5N1) is present in poultry and wild birds. Since December 2003, a total of 585 cases with 346 deaths have been confirmed in 15 countries[3]. To date there has been no evidence of sustained human-to-human transmission.

Sporadic human cases of influenza A variant (v) viruses have been detected since September 2011 in the United States of America[4] where a total of 8 infections caused by A(H3N2)v viruses have been reported along with single cases of A(H1N1)v and A(H1N2)v.

No human cases of influenza A(H9N2) were detected during the period 20 September 2011 to 21February 2012.

Antigenic and genetic characteristics of recent seasonal influenza viruses

Influenza A(H1N1)pdm09 viruses

Between September 2011 and February 2012, all influenza A(H1N1) viruses detected worldwide were A(H1N1)pdm09. Haemagglutination inhibition (HI) tests using post-infection ferret antisera indicated that 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 at least eight genetic groups which were antigenically indistinguishable. A small proportion of viruses showed reductions in reactivity in HI assays with ferret antisera against A/California/7/2009-like reference viruses. Most of these viruses with reduced

[2] http://www.who.int/influenza/gisrs_laboratory/terminology_ah3n2v/en/
[3] http://www.who.int/entity/influenza/human_animal_interface/EN_GIP_20120221CumulativeNumberH5N1cases.pdf
[4] http://www.cdc.gov/flu/swineflu/variant.htm

HI titres had amino acid changes in HA positions 153-157, which is consistent with results obtained since May 2009.

Influenza A(H3N2) viruses

Antigenic characteristics of A(H3N2) viruses collected from September 2011 to January 2012 were assessed with panels of post-infection ferret antisera in HI and virus neutralization assays. The recently circulating viruses were antigenically heterogeneous. While many viruses were closely related to A/Perth/16/2009, the vaccine virus for the 2011-2012 northern hemisphere and 2012 southern hemisphere seasons, an increasing proportion of viruses circulating in 2012 showed reduced reactivity with ferret antisera raised against A/Perth/16/2009 virus. These recent A(H3N2) viruses showed higher titres with ferret antisera raised against A/Victoria/361/2011-like reference viruses. The HA genes of recent viruses fell into two phylogenetic groups represented by A/Victoria/361/2011 (genetic group 3) and A/Brisbane/299/2011 (genetic group 6), with the majority falling within genetic group 3. Recently circulating viruses showed higher titres in HI and virus neutralization assays with ferret antisera raised against viruses in genetic groups 3 and 6 compared to ferret antisera raised against A/Perth/16/2009 virus (Tables 1 and 2 respectively).

Influenza B viruses

Influenza B viruses of both the B/Victoria/2/87 and the B/Yamagata/16/88 lineages circulated. The two lineages were observed in similar proportions in some countries, suggesting an increase in the prevalence of viruses of the B/Yamagata/16/88 lineage, although the number of viruses collected was relatively small. In China, however, viruses of the B/Victoria/2/87 lineage predominated, except in China Hong Kong Special Administrative Region (China Hong Kong SAR) where the two lineages were present in approximately equal proportions. In HI tests with post-infection ferret antisera, the majority of viruses of the B/Yamagata/16/88 lineage were antigenically distinguishable from the previous vaccine virus of the B/Yamagata/16/88 lineage, B/Florida/4/2006, and antigenically similar to recent reference viruses, e.g. B/Wisconsin/1/2010, B/Hubei-Wujiagang/158/2009, B/Texas/6/2011 and B/Stockholm/12/2011 (Table 3). The HA genes of most viruses, including the four examples given, were in genetic clade 3.

The majority of viruses of the B/Victoria/2/87 lineage were antigenically closely related to the current vaccine virus B/Brisbane/60/2008 and the HA gene sequences of the viruses predominantly belonged to the B/Brisbane/60/2008 genetic clade.

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 tested, 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 and, in addition for A(H3N2) viruses, virus neutralization assays were used to measure the presence of antibodies to recent virus isolates in two panels of sera from children, five from adults and five from older adults who had received seasonal trivalent inactivated vaccines. The trivalent vaccines contained the antigens of A/California/7/2009 (H1N1)pdm09, A/Perth/16/2009 (H3N2)-like and B/Brisbane/60/2008 viruses.

Vaccines containing A/California/7/2009 antigens stimulated 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 influenza A/Perth/16/2009-like antigens stimulated antibodies with geometric mean HI titres that were lower to the majority of recent isolates than to the vaccine virus (average reductions: adults, 38%; older adults, 40%; children, 38%). For a subset of sera, these HI results were supported by results from microneutralization tests.

Vaccines containing influenza B/Brisbane/60/2008 antigens stimulated anti-HA antibodies of similar geometric mean HI titres to the vaccine virus and the majority of representative recent B/Victoria/2/87 lineage viruses. Geometric mean HI titres were lower to recent B/Yamagata/16/88 lineage viruses than to the most recent B/Victoria/2/87 lineage viruses (average reductions: adults, 41%; older adults, 58%; children, 64%).

Recommended composition of influenza virus vaccines for use in the 2012-2013 influenza season

A(H1N1)pdm09 viruses co-circulated in varying proportions with A(H3N2) and B viruses during the period of September 2011 to February 2012, 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 stimulated anti-HA antibodies 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 distinguishable from the

vaccine virus A/Perth/16/2009 and were more closely related to A/Victoria/361/2011-like reference viruses. Current vaccines containing A/Perth/16/2009 antigens stimulated antibodies of titres that were lower to most recent influenza A(H3N2) 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, notably in China. 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 previous vaccine virus B/Florida/4/2006 and were closely related to B/Wisconsin/1/2010-like viruses. Current vaccines containing B/Brisbane/60/2008 antigens stimulated anti-HA antibodies that had similar titres against the vaccine viruses and recent viruses of the B/Victoria/2/87 lineage; however, titres were lower to recent viruses of the B/Yamagata/16/88 lineage.

It is recommended that vaccines for use in the 2012-2013 influenza season (northern hemisphere winter) contain the following:

– an A/California/7/2009 (H1N1)pdm09-like virus;
– an A/Victoria/361/2011 (H3N2)-like virus;
– a B/Wisconsin/1/2010-like virus.

For those considering the use of a B/Victoria/2/87 lineage vaccine virus, either in trivalent vaccines or in quadrivalent vaccines containing two influenza B viruses, B/Brisbane/60/2008-like viruses continue to be the appropriate vaccine virus.

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[5].

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[6]. Candidate vaccine viruses for A(H5N1), A(H9N2) and A(H3N2)v viruses are also listed on the same website.

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,

[5] http://www.who.int/docstore/wer/pdf/2002/wer7728.pdf
[6] http://www.who.int/influenza/vaccines/virus/en/

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); or Division of Product 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).

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); 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 Center 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/); 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/) or the WHO Collaborating Center 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[7].

[7] http://www.who.int/influenza
Virological web update: http://www.who.int/influenza/gisrs_laboratory/updates/summaryreport/en/
Epidemiological web update:
http://www.who.int/influenza/surveillance_monitoring/updates/latest_update_GIP_surveillance/en/

Table 1. Results of haemagglutination inhibition reactions of influenza A(H3N2) viruses (guinea pig blood cells)

		REFERENCE FERRET ANTISERA						
REFERENCE VIRUSES		**BRIS/10**	**PERTH/16**	**S.AUST/3**	**CHIANG RAI/277**	**BRIS/299**	**KY/5**	**GENETIC GROUP**
1	A/BRISBANE/10/2007	640	20	80	80	40	80	
2	A/PERTH/16/2009	20	320	320	320	320	640	1
3	A/SOUTH AUSTRALIA/03/2011	20	80	160	160	160	160	3
4	A/CHIANG RAI/277/2011	10	40	80	160	80	80	3
5	A/BRISBANE/299/2011	40	80	160	160	160	80	6
6	A/KENTUCKY/05/2011	20	80	160	320	160	160	6
TEST VIRUSES								
8	A/FINLAND/190/2011	160	160	640	640	320	320	3
9	A/SHANGHAI-FENGXIAN/1388/2011	5	160	160	80	160	160	1
10	A/ARKANSAS/01/2012	80	80	320	320	320	160	6
11	A/EGYPT/736/2011	20	80	320	320	80	40	3
12	A/HONG KONG/5063/2011	20	80	160	160	160	160	3
13	A/WISCONSIN/01/2012	20	80	160	160	ND	160	6
14	A/BRITISH COLUMBIA/4791/2011	40	40	160	160	320	160	3
15	A/ENGLAND/258/2011	20	40	80	160	160	40	3
16	A/HONG KONG/4913/2011	20	40	40	160	80	80	3
17	A/KOBE/241/2011	20	40	80	80	80	40	3
18	A/NEBRASKA/01/2012	20	40	80	80	160	160	3
19	A/SHANGHAI-LUWAN/1440/2011	20	40	40	160	80	80	3

ND = Not determined

Table 2. Results of virus neutralization: plaque-reduction assay for influenza A(H3N2) viruses

	VIRUSES	PERTH/16/09	S. AUS/03/11	CHIANG RAI/277/11	KY/05/11	HA GENETIC GROUP
1	A/PERTH/16/2009	2560	1280	640	1280	1
2	A/S. AUSTRALIA/03/2011	640	2560	1280	2560	3
3	A/CHIANG RAI/277/2011	640	2560	640	1280	3
4	A/VICTORIA/361/2011	160	320	320	320	3
5	A/KENTUCKY/05/2011	320	1280	640	1280	6
6	A/BRISBANE/299/2011	640	2560	1280	1280	6
7	A/BANGLADESH/5071/2011	320	1280	640	1280	3
8	A/UTAH/12/2011	320	1280	640	1280	3

Table 3. Results of haemagglutination inhibition reactions of recent influenza B (Yamagata lineage) viruses

	Florida 4/2006	Wisconsin 1/2010	Texas 6/2011 (egg)	Texas 6/2011 (cell)
REFERENCE VIRUSES				
B/FLORIDA/4/2006	**1280**	160	160	160
B/WISCONSIN/1/2010	160	**160**	80	160
B/TEXAS/6/2011 (EGG)	160	160	**160**	160
B/TEXAS/6/2011 (CELL)	160	320	160	**320**
TEST VIRUSES				
B/ARIZONA/1/2012	160	320	160	320
B/IOWA/1/2012	320	320	320	640
B/UTAH/1/2012	320	320	320	320
B/UTAH/2/2012	320	320	320	320
B/WASHINGTON/1/2012	320	160	80	160

Annex 1. Extent and type of influenza activity worldwide, September 2011 – January 2012

Geographical region / Country, area or territory	September 2011	October 2011	November 2011	December 2011	January 2012
Africa					
Algeria	0	*H3	*H3	**H3	***H3
Angola	0	0	0	0	0
Burkina Faso	*H3, *B	*H3, *B	*B	*B	*B
Cameroon	**H1(pdm09), **H3, **B	**H1(pdm09), **H3, **B	**H1(pdm09), **H3, **B	*H1(pdm09), *H3, *B	*H3
Central African Republic	0	0	0	0	0
Côte d'Ivoire	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, **B	*H1(pdm09), *H3, *B	*H3, *B	
Democratic Republic of the Congo	*B	*B	*B	*H3, *B	
Egypt	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H3, *B	*H3	
Ethiopia	*B		*H3, *B	*H3, *B	*B
France, Réunion	*H3	*B	*B		
Ghana	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3, *B	*H3, *B
Kenya	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Madagascar	*H1(pdm09), *H3	0		*H1(pdm09)	*H1(pdm09), *H3, *B
Mali	0	0	0	0	0
Mauritius	*H3, *B	*H3, *B	*B	0	0
Morocco		*H3	*H3	***H3, *B	***H3, *B
Nigeria	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*B	
Rwanda					*B
Senegal	*H1(pdm09), **H3, **B	*H1(pdm09), **H3, **B	*H1(pdm09), **H3, **B	*H1(pdm09), *H3, *B	0
Sierra Leone	*H3	*H1(pdm09), *H3	*H1(pdm09), *H3		
South Africa	*H1(pdm09), **H3, *B	**H3, **B	*H3, *B	*B	*H3, *B
Togo	*H3	**H3, **B	**H3, **B	*H3, *B	**H3, **B
Tunisia		*H3	*H3	***H3	****H3

Geographical region / Country, area or territory	September 2011	October 2011	November 2011	December 2011	January 2012
Uganda	*H1(pdm09), *H3, *B	*H3	*H1(pdm09), *H3, *B	*H1(pdm09), *B	*H3, *B
United Republic of Tanzania	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H1(pdm09), *H3, *B	0
Zambia	*H1(pdm09), *B	0	*H3	0	0
America					
Argentina	**H1(pdm09), ***H3, **B	**H1(pdm09), ***H3, **B	*H1(pdm09), **H3, *B	*B	0
Bolivia (Plurinational State of)	***H1(pdm09), **H3, **B	***H1(pdm09), **H3, **B	**H1(pdm09), *H3, **B	**H1(pdm09), *H3, *B	0
Brazil	*H1(pdm09), *H3, *B	*H1(pdm09), *H3	**H1(pdm09), *H3, *B	**H1(pdm09), *H3, **B	**H1(pdm09), *H3, *B
Canada	*H1(pdm09), *H3, *B	*H3	*H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, **B
Chile	**H1(pdm09), *H3, *B	**H1(pdm09), *H3, *B	*H1(pdm09), *H3	*H1(pdm09), *H3	*H3
Colombia	*H1(pdm09), *H3	*H1(pdm09), *H3	**H1(pdm09), *H3	**H1(pdm09)	*H1(pdm09), *H3
Costa Rica	**H1(pdm09), **H3	**H1(pdm09), **H3	*H1(pdm09), **H3	*H1(pdm09), *H3	*H1(pdm09), *H3, *B
Cuba	*H1(pdm09), ***H3	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H3
Dominican Republic	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *B	0
Ecuador	*H1(pdm09)	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3
El Salvador	***H3, ***B	*H1(pdm09), ***H3, ***B	**H3, **B	**H3, **B	
France, French Guiana					*H1(pdm09)
France, Guadeloupe		*H3		*H1(pdm09), *H3	*H1(pdm09), *H3
France, Martinique					*H1(pdm09), *B
Guatemala	*H3, *B	*H3, *B	*H3, *B	0	*H1(pdm09)
Honduras	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*B	*B
Jamaica		*H1(pdm09), *H3	*H1(pdm09)	*H1(pdm09)	*H1(pdm09)
Mexico	*H3	*H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), *H3, **B	***H1(pdm09), *H3, *B
Nicaragua	**H1(pdm09), **H3	***H1(pdm09), ***H3	***H1(pdm09), **H3	*H1(pdm09), *H3	*B
Panama	*H1(pdm09)	*H1(pdm09)	*H1(pdm09)	*H1(pdm09)	0
Paraguay	*H3	*H1(pdm09), ****H3	**H1(pdm09), *H3, *B	**H1(pdm09), **H3, **B	

Geographical region / Country, area or territory	September 2011	October 2011	November 2011	December 2011	January 2012
Peru	*H1(pdm09), ***H3, *B	*H1(pdm09), ***H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), *B
United States of America	*H1(pdm09), **H3, *B	*H1(pdm09), **H3, *B	*H1(pdm09), ***H3, **B	*H1(pdm09), ***H3, *B	*H1(pdm09), **H3, ***B
Uruguay	*H3				
Venezuela (Bolivarian Republic of)	*A	**A	**A, *H3	**A	0
Asia					
Armenia	0	0	0	0	0
Bangladesh	*H3, *B	*H1(pdm09), *B	*B		
Bhutan	*H3			*B	*B
Cambodia	***H1(pdm09), **H3, ***B	***H1(pdm09), **H3, ***B	***H1(pdm09), **H3, ***B	***H1(pdm09), *H3, *B	*B
China	**H3, *B	*H3, *B	*H3, *B	*H3, **B	*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	*H3, *B,	*H3, *B,	*H3, *B,		
Georgia	0	0	0	0	*H1(pdm09), *H3
India	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H1(pdm09), *H3, *B
Indonesia	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	
Iran (Islamic Republic of)	*B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	**H3, *B
Israel			*H3, *B	*H3, *B	**H3, **B
Japan	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B	*H1(pdm09), ***H3, **B	*H1(pdm09), ****H3, ***B
Jordan	*H3		*H3	*H3	*H3
Kazakhstan					*H1(pdm09), *H3
Kyrgyzstan				*H3	*H3, *B
Lao People's Democratic Republic	*H3	*H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B
Mongolia	0	0	0	0	*B
Myanmar	*H3, *B	*H3	*H3, *B	*H3	

Geographical region / Country, area or territory	September 2011	October 2011	November 2011	December 2011	January 2012
Nepal		H3**, B**	*H3, *B	*H3, *B	*B
Oman	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	**H1(pdm09), **B
Pakistan	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Philippines	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B	
Qatar	*H1(pdm09), *B	*H1(pdm09), *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	
Republic of Korea	*H3	*H3	*H3, *B	***H3, **B	***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	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B
Thailand	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Viet Nam	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H3, *B
Europe					
Albania	0	*H1(pdm09), *B	*H3, *B	0	*H3, *B
Austria				*H3, *B	*H3, *B
Belarus	0	0	0	0	*H1(pdm09), *H3
Belgium		*B	*H1(pdm09), *H3	*H3	*H3, *B
Bosnia and Herzegovina	0	0	0	0	0
Bulgaria	0	0	0	0	***H3
Croatia	0	0	0	0	*H3, *B
Czech Republic		*H1(pdm09)		*H1(pdm09), *B	*H1(pdm09)
Denmark	*H3		*H3	*H3	0
Estonia	0	0	0	0	**H3
Finland		*H3	*H3	*H3	*H1(pdm09), ***H3, *B
France	*H3, *B	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	**H3, *B	*H1(pdm09), **H3, *B
Germany		*B	*H3	*H3, *B	*H3
Greece	0	0	0	0	*H1(pdm09), *H3, *B

Geographical region / Country, area or territory	September 2011	October 2011	November 2011	December 2011	January 2012
Hungary				*H3	*H3, *B
Iceland			*H3	*H3	***H3
Ireland			*H3, *B	*H3, *B	*H3, *B
Italy			*H3	*H1(pdm09), *H3	*H1(pdm09), **H3, *B
Latvia				*H3, *B	*H3, *B
Lithuania	0	0	0	0	0
Luxembourg				*H3	*H3
Malta					*A
Netherlands	*H3	*B	**H3, **B	**H3, **B	**H3
Norway		*H3, *B	*H3, *B	*H1(pdm09), **H3, *B	**H1(pdm09), ***H3, **B
Poland	*B	*B			*B
Portugal			*H3	*H3	*H1(pdm09), *H3
Republic of Moldova	0	0	0	0	0
Romania				*H3	**H3
Russian Federation	*H1(pdm09), *H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B
Serbia				*H3	*H3
Slovakia	0	0	*A	0	0
Slovenia				*H3	*H3
Spain	*H3, *B	*H1(pdm09), *H3, *B	*H3, *B	**H3, *B	**H1(pdm09), ****H3, **B
Sweden	*H3	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B	**H1(pdm09), ***H3, **B
Switzerland		*B	*B	*H3, *B	**H3, **B
Turkey			*H3	**H3, *B	***H3, *B
Ukraine			*H3, *B		*H3
United Kingdom of Great Britain and Northern Ireland	*H3	*H1(pdm09), *H3, *B	*H3, *B	*H1(pdm09), *H3, *B	*H1(pdm09), *H3, *B

Geographical region / Country, area or territory	September 2011	October 2011	November 2011	December 2011	January 2012
Oceania					
Australia	***H1(pdm09), ***H3, ***B	***H1(pdm09), ***H3, ***B	*H1(pdm09), *H3, *B	*H1(pdm09), **H3, *B	*H3, *B
Fiji	0	0	0	0	
France, New Caledonia	**H1(pdm09)	*H1(pdm09)			
New Zealand	**H1(pdm09), ***H3, ***B	*H1(pdm09), **H3, **B			
Palau	*B, H1(pdm09)				
United States of America, American Samoa	*H3				

Data in table 1 were provided by the Global Influenza Surveillance and Response System and other partners.

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

Annex 2

Declarations of interest

The WHO recommendation on the composition of influenza virus vaccines for the northern hemisphere 2012-2013 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[8] 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 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/