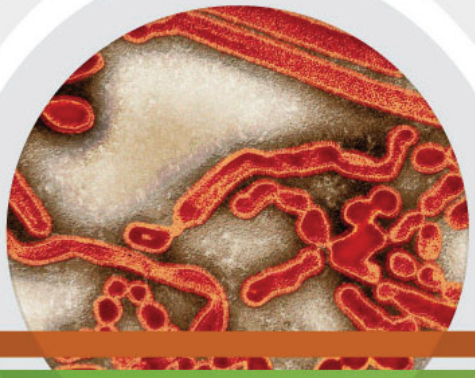

SURVEILLANCE REPORT

Influenza virus characterisation

Summary Europe, October 2012

Summary

Since 1 January 2012 Influenza A(H1N1)pdm09, Influenza A(H3N2) and Influenza B/Victoria and B/Yamagata lineage viruses have been detected in ECDC-affiliated countries.

- Type A viruses have predominated over type B.
- A(H3N2) viruses have predominated over A(H1N1)pdm09 viruses.
- A(H1N1)pdm09 viruses continue to show genetic drift from the vaccine virus, A/California/07/2009, but the vast majority remain antigenically similar to it.
- Recent B/Victoria lineage viruses fell within the B/Brisbane/60/2008 genetic clade and were antigenically similar to reference cell-propagated viruses of the B/Brisbane/60/2008 genetic clade.
- Recent B/Yamagata-lineage viruses fell into two genetic clades, represented by the recommended vaccine component for the 2012/2013 influenza season, B/Wisconsin/1/2010 (clade 3), or B/Estonia/55669/2012 (clade 2); viruses in these clades are antigenically distinguishable.

A summary table of viruses received by the MRC National Institute for Medical Research, the WHO Collaborating Centre for Reference, and Research on Influenza from EU and EAA countries since 1 January 2012 is shown in Table 1.

Viruses and/or clinical samples have been received from 21 EU/EAA countries. The majority (68%) of viruses received have been influenza A(H3N2) viruses; among influenza B receipts, viruses of the B/Yamagata and B/Victoria lineages were received in approximately equal proportions; influenza A(H1N1)pdm09 viruses were received in low numbers and from eight countries only, with Norway providing nearly 50% (18/37). The table is an update of the one shown in the previous report (September 2012). The new viruses in the table have all come from Norway with collection dates in April, June and September.

This report was prepared by Rod Daniels, Vicki Gregory and John McCauley on behalf of the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL), under contract to the European Centre for Disease Prevention and Control (ECDC).

Influenza A(H1N1)pdm09 virus analyses

No new HI assays on Influenza A(H1N1) viruses have been carried out since the previous report.

Influenza A(H3N2) virus analyses

As described before, A(H3N2) viruses have continued to be difficult to characterise antigenically by HI assay due to variable agglutination of red blood cells from guinea pigs, turkeys and humans. Influenza A(H3N2) viruses were analysed by HI assay using guinea pig red blood cells in the presence of 20nM oseltamivir, added to circumvent the NA-mediated binding of H3N2 viruses to the red blood cells (Lin et al. 2010).

The results of an HI assay carried out to examine the two A(H3N2) viruses received from Norway since the September report are shown in Table 2. With post-infection ferret antiserum raised against the recommended, egg-isolated and propagated, vaccine virus for the Northern Hemisphere 2012/2013 influenza season, A/Victoria/361/2011, both test viruses gave an HI titre >8-fold reduced compared with the titre of the homologous virus. In contrast, with antiserum raised against cell-culture isolated and propagated A/Victoria/361/2011, both test viruses showed good reactivity with titres within 2-fold of that of the titre of the homologous virus (Table 2). Both test viruses also showed good reactivity with post-infection ferret antisera raised against other reference viruses propagated exclusively in cell culture, regardless of HA genetic group: A/Alabama/5/2010 (group 5), A/Stockholm/18/2011 (subgroup 3A), A/Athens/GR112/2012 (subgroup 3B), and A/Berlin/93/2011 (subgroup 3C). However, both test viruses reacted poorly with post-infection ferret antisera raised against other egg-propagated reference viruses, A/Victoria/208/2009 and A/Iowa/19/2010, compared to the HI-reactivity of the homologous egg-propagated viruses. As described in the September report the low reactivity of test viruses with antisera raised against each of the egg-adapted viruses, importantly including the new vaccine virus A/Victoria/361/2011, suggests that egg adaptation of the H3N2 reference viruses influences the immune response of the ferret and consequently the results of the HI assay.

Influenza B virus analyses

B/Victoria lineage virus

HI results of a single influenza B virus of the B/Victoria lineage performed since the last report are shown in Table 3. The test virus showed reduced reactivity (an 8-fold reduction in titre compared with the homologous titre) with post-infection ferret antiserum raised against the egg-propagated vaccine virus recommended for the Northern Hemisphere 2011/2012 season, B/Brisbane/60/2008. In contrast, it reacted well with antisera raised against viruses genetically closely related to the vaccine virus but propagated in cells. These antisera were raised against B/Paris/1762/2008, B/Hong Kong/514/2009 and B/Odessa/3886/2010, which are surrogate cell-propagated antigens for the egg-propagated vaccine virus. The reactivity of test viruses with antiserum raised against B/Malta/MV636714/2011, another egg isolate, was also low.

B/Yamagata lineage viruses

Three influenza B viruses of the B/Yamagata lineage have been received since the last report. Table 4 shows the results of HI assays for these viruses, all three showed reduced reactivity with reductions in titre of ≥ 8-fold of that of the homologous virus with the post-infection ferret antiserum raised against the recommended egg-propagated vaccine virus for the Northern Hemisphere 2012/2013 influenza season, B/Wisconsin/1/2010. Two of the three viruses react well with post-infection ferret antiserum raised against B/Estonia/55669/2011, a clade 2 virus antigenically distinguishable from B/Wisconsin/1/2010. All three viruses react well with serum raised against B/Hong Kong/3577/2012, another clade 2 virus, and two of the three viruses react well with antiserum raised against B/Novosibirsk/1/2012, a virus that, like B/Wisconsin/1/2010, falls into clade 3.

Influenza A(H3N2)v virus

As we have described previously, on 3 August, the United States CDC issued a Health Advisory describing an increase in the number of influenza A(H3N2)v infections in three US states and CDC have prepared further background information and have provided updates. Of the 306 confirmed cases, the last reported illness onset was on 7 September 2012. Antigenic and genetic characterisation of H3N2v viruses has been described by Lindstrom et al, 2012. The virus was characterised as being antigenically distinct from currently circulating human seasonal influenza viruses and to be a reassortant virus with seven genes from swine influenza 'triple reassortant' H3N2 viruses and the M-gene from an influenza A(H1N1)pdm09 virus.

Risk assessments for these A(H3N2)v viruses, as a risk to public health, have been posted by the United States CDC and ECDC.

A description of results generated by the WHO Collaborating Centre for Reference and Research on Influenza, based at the MRC National Institute for Medical Research in London, and evaluated at the WHO Vaccine Composition Meetings held at WHO Geneva on 20–22 February 2012 and Beijing, China on 17–19 September 2012 can be found at: http://www.nimr.mrc.ac.uk/documents/about/interim-report-feb-2012.pdf and http://www.nimr.mrc.ac.uk/documents/about/Interim_Report_September_2012_2.pdf

Table 1. Summary of clinical samples and isolates received from ECDC-affiliated countries, collection dates since 2012-01-01.

MONTH	TOTAL RECEIVED	A	H1N1pdm09		H3N2		B	B Victoria lineage		B Yamagata lineage	
		Not subtyped					Lineage unknown				
Country			Number received	Number propagated[1]	Number received	Number propagated[2]		Number received	Number propagated[1]	Number received	Number propagated[1]
UNKNOWN											
Czech Republic[3]	26				10	10		14	10	2	2
JANUARY											
Austria	6				4	4		1	1	1	1
Bulgaria	4				4	3					
Denmark	2				2	1					
Estonia	1				1	0					
Finland	3				3	2					
France	4				4	4					
Germany	15				14	13				1	1
Greece	18				8	7	5	1	1	4	4
Iceland	9				9	7					
Ireland	9				7	2		1	1	1	1
Italy	14				13	12				1	1
Latvia	7				6	5		1	1		
Netherlands	2				2	2					
Norway	16		5	2	11	11					
Portugal	7				7	4					
Romania	3				3	3					
Slovenia	3				3	3					
Spain	21		1	0	18	10		2	2		
Sweden	11		2	2	8	7		1	1		
United Kingdom	4				3	3		1	1		
FEBRUARY											
Bulgaria	8				8	8					
Denmark	11				6	4		2	2	3	3
Estonia	18				18	2					
Finland	5				4	2		1	1		
France	5		2	2	3	3					
Greece	24				14	13	4	2	2	4	4
Iceland	11				11	11					
Ireland	3		1	1	1	1		1	1		
Italy	12				6	5		1	1	5	5
Norway	29		10	6	15	15		1	1	3	3
Portugal	3				1	1				2	1
Slovenia	12		1	1	9	7		1	0	1	0
Sweden	5		3	3				1	1	1	1
United Kingdom	7				5	4		1	1	1	1
MARCH											
Denmark	13		3	0	8	7		1	0	1	0
Estonia	11				11	7					
Finland	1				1	1					
France	19		2	2	11	10		4	4	2	2
Iceland	3				3	2					
Ireland	4				4	4					
Italy	11				4	1		1	0	6	6
Norway	14		3	0	6	6		2	1	3	3
Portugal	10				6	4		1	1	3	2
Slovenia	16		1	0	9	7		4	1	2	0
Sweden	2				1	1				1	1
United Kingdom	10		1	1	7	4		1	1	1	1
APRIL											
Denmark	6				4	3		1	1	1	0
Estonia	8				7	3				1	1
France	6							3	3	3	3
Iceland	1				1	1					
Ireland	10				10	2					
Norway	12				9	9		1	1	2	2
Slovenia	2				1	1	1				
Sweden	5		1	1	3	2				1	1
United Kingdom	10				7	6		2	2	1	1
MAY											
Finland	1							1	1		
Norway	2				2	2					
United Kingdom	3				2	2		1	1		
JUNE											
Norway	3				1	1		1	1	1	1
United Kingdom	1									1	1
AUGUST											
Ireland	1		1	0							
United Kingdom	2				2	2					
SEPTEMBER											
Norway	2									2	2
	527	0	37	21	361	277	10	57	46	62	55
				7.0%		68.5%			10.8%		11.8%

1. Propagated to sufficient titre to perform HI assay
2. Propagated to sufficient titre to perform HI assay in presence of 20nM oseltamivir
3. Package received 2012-05-10

Table 2. Antigenic analysis of A(H3N2) viruses by HI (guinea pig RBCs with 20nM Oseltamivir).

Viruses	Collection Date	Passage History	Haemagglutination inhibition titre[1]								
			A/Perth 16/09	A/Vic 208/09	A/Ala 5/10	A/Stock 18/11	A/Iowa 19/10	A/Vic 361/11	A/Berlin 93/11	A/Vic 361/11	A/Athens 112/12
			F35/11	F7/10	F27/10	F28/11	F15/11	Egg F05/12	T/C F11/12	T/C F14/12	F16/12
Genetic group					group 5	group 3A	group 6	group 3C	group 3C	group 3C	group 3B
REFERENCE VIRUSES											
A/Perth/16/2009	2009-07-04	E3/E1	1280	80	160	160	160	160	320	320	640
A/Victoria/208/2009	2009-06-02	E3/E1	1280	5120	2560	2560	5120	5120	5120	5120	5120
A/Alabama/5/2010	2010-07-13	MK1/C2/SIAT2	<	<	160	160	160	40	160	640	320
A/Stockholm/18/2011	2011-03-28	MDCK2/SIAT5	40	40	80	640	160	160	640	640	640
A/Iowa/19/2010	2010-12-30	E3/E2	320	640	640	640	1280	1280	1280	1280	1280
A/Victoria/361/2011	2011-10-24	E3/E2	320	640	320	160	640	5120	640	640	160
A/Berlin/93/2011	2011-12-07	NVD3/SIAT4	160	160	320	640	640	640	1280	2560	1280
A/Victoria/361/2011	2011-10-24	MDCK2/SIAT3	160	160	320	640	640	640	1280	2560	1280
A/Athens/112/2012	2012-02-01	SIAT5	160	160	320	320	320	320	640	1280	1280
TEST VIRUSES											
A/Norway/1422/2012	2012-04-02	MDCK1/MDCK1	80	80	320	160	320	160	640	1280	640
A/Norway/1443/2012	2012-06-07	MDCK1/MDCK1	80	80	320	320	320	160	640	1280	640

1. < = <40

Table 3. Antigenic analysis of Influenza B/Victoria-lineage viruses by HI (turkey RBCs).

Viruses	Collection date	Passage History	Haemagglutination inhibition titre[1]							
			Post infection ferret sera							
			B/Bris[2] 60/08 Sh 523	B/Mal 2506/04 F28/05	B/England 393/08 F05/11	B/Bris 60/08 F22/12	B/Paris 1762/08 F17/11	B/HK 514/09 F13/10	B/Odessa 3886/10 F19/11	B/Malta 636714/11 F33/11
REFERENCE VIRUSES										
B/Malaysia/2506/2004	2004-12-06	E3/E5	1280	640	80	160	<	<	<	160
B/England/393/2008	2008-08-29	E1/E1	2560	80	640	640	80	40	80	640
B/Brisbane/60/2008	2008-08-04	E4/E3	2560	160	640	640	80	80	160	640
B/Paris/1762/2008	2009-02-09	C2/MDCK1	5120	<	20	80	80	80	80	40
B/Hong Kong/514/2009	2009-10-11	MDCK1/MDCK3	5120	<	20	80	80	80	160	40
B/Odessa/3886/2010	2010-03-19	MDCK2/MDCK1	5120	<	20	40	80	80	160	20
B/Malta/636714/2011	2011-03-07	E4/E1	2560	10	640	640	40	40	80	640
TEST VIRUSES										
B/Norway/1477/2012	2012-06-11	MDCK1/MDCK1	5120	<	20	80	160	80	160	40

1. < = <10; 2. hyperimmune sheep serum

Table 4. Antigenic analysis of Influenza B/Yamagata-lineage viruses by HI (turkey RBCs).

Viruses	Collection date	Passage History	Haemagglutination inhibition titre									
			Post infection ferret sera									
			B/Fl[3] 4/06 SH479	B/Eg[1] 144/05 F3/07	B/Fl[1] 4/06 F01/10	B/Bris[2] 3/07 F21/12	B/Wis[2] 1/10 F23/10	B/Stock[2] 12/2011 F34/11	B/Estonia[2] 55669/2011 F26/11	B/Serbia[2] 1894/2011 F25/11	B/Stock[2] 12/2011 T/C F8/12	B/Novo 1/2012 F31/12	B/HK 3577/2012 F33/12
REFERENCE VIRUSES													
B/Egypt/144/2005	2005-05-01	E3/E5	5120	320	2560	1280	320	640	320	40	640	160	1280
B/Florida/4/2006	2006-12-15	E3/E3	5120	160	2560	1280	320	640	320	20	640	80	1280
B/Brisbane/3/2007	2007-09-03	E2/E1	5120	160	1280	1280	160	320	320	10	640	80	640
B/Wisconsin/1/2010	2007-08-07	E3/E1	5120	160	640	320	320	160	40	80	640	320	160
B/Stockholm/12/2011	2007-08-07	E4/E1	5120	80	640	320	160	1280	20	40	640	160	160
B/Estonia/55669/2011	2011-03-14	MDCK2/MDCK2	5120	40	160	160	20	160	1280	160	80	640	640
B/Serbia/1894/2011	2011-03-08	MDCK1/MDCK4	5120	40	160	160	80	320	160	320	320	640	640
B/Stockholm/12/2011	2011-03-28	Cx/MDCK3	5120	40	320	160	80	320	160	320	320	320	1280
B/Novosibirsk/1/2012	2012-02-14	C2/MDCK2	2560	40	160	160	40	160	160	40	320	640	640
B/Hong Kong/3577/2012	2012-06-13	MDCK2/MDCK1	2560	<	320	160	20	320	1280	160	80	160	1280
TEST VIRUSES													
B/Norway/1494/2012	2012-06-12	MDCK1/MDCK1	5120	<	160	160	20	160	640	40	40	80	1280
B/Norway/1836/2012	2012-09-07	MDCK2/MDCK1	5120	<	160	160	20	160	1280	80	80	320	1280
B/Norway/1864/2012	2012-09-16	MDCK2/MDCK1	5120	40	160	160	40	320	160	160	160	640	640

1. < = <40; 2. < =<10 ; 3. hyperimmune sheep serum