INFORMATION FOR THE VACCINE AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE
CBER, FDA

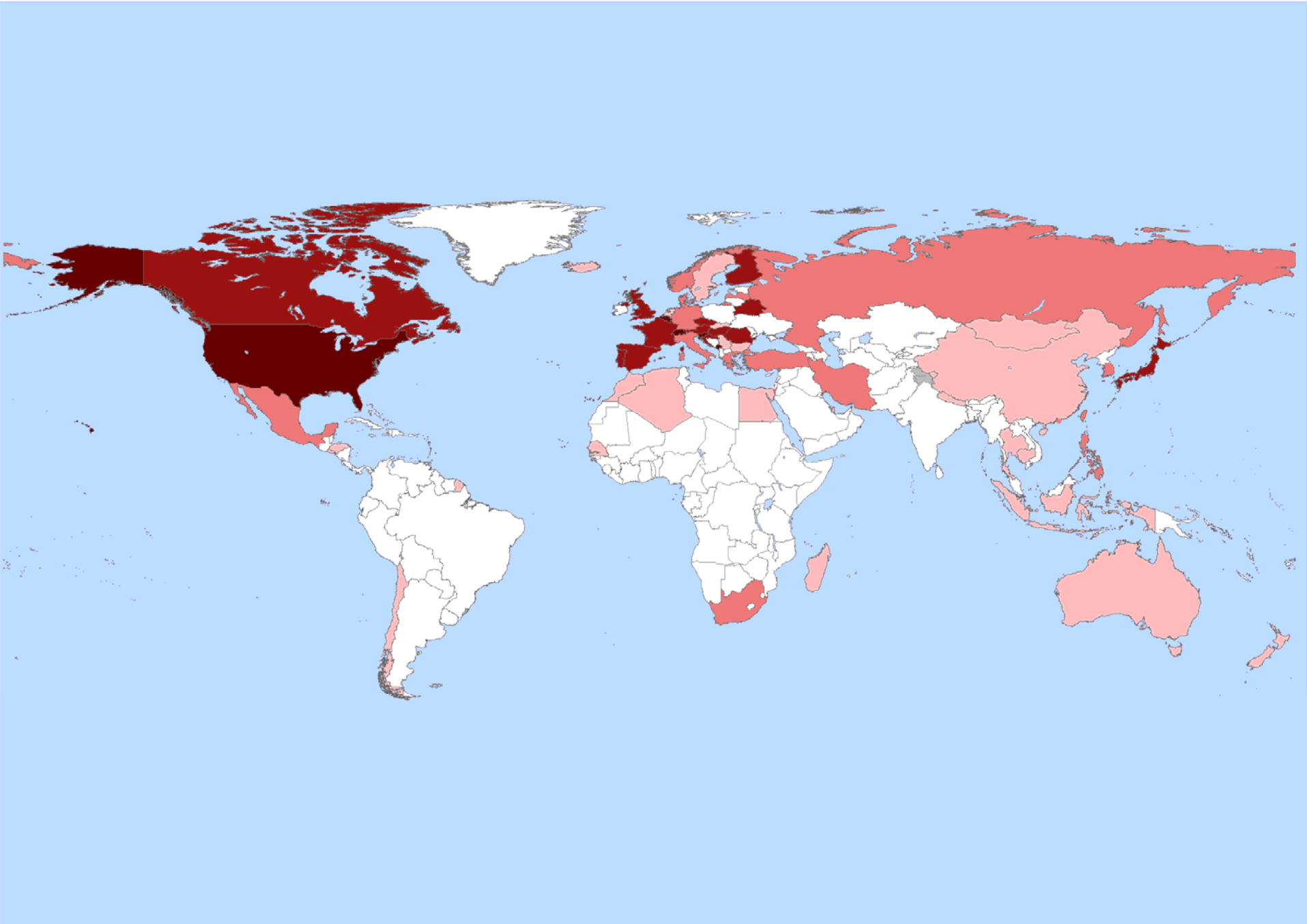
FEBRUARY 21, 2008

WHO COLLABORATING CENTER FOR SURVEILLANCE, EPIDEMIOLOGY AND CONTROL OF INFLUENZA

Influenza Division
National Center for Immunization and Respiratory Diseases
Coordinating Center for Infectious Diseases
Centers for Disease Control and Prevention
Atlanta, GA 30333

Influenza A (H1N1) Viruses

H1N1 activity from September 2007 – January 2008



HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA H1 VIRUSES (02/08/08)

		FERERENCE FERRET ANTISERA							Date	
	REFERENCE ANTIGENS	NC/20	SI/3	AS/59	SD/6	FU/141	HK/2652	CB/0371	collected	Passage
1	A/NEW CALEDONIA/20/99	640	160	160	160	320	160	80	06/09/99	E4/E2
2	A/SOLOMON ISLANDS/3/06 IVR-145*	160	640	320	160	640	320	160	REASS	E9/E1
3	A/BRISBANE/59/07*	80	160	640	640	640	320	320	07/01/07	E2/E1
4	A/SOUTH DAKOTA/6/07*	80	160	640	640	640	320	320	07/17/07	E3
5	A/FUKUSHIMA/141/06	80	160	640	1280	1280	640	640	UNKN	E4/E1
6	A/HONG KONG/2652/06	80	160	640	640	640	1280	2560	07/17/06	E3
7	A/CAMBODIA/0371/07*	40	160	320	320	640	1280	1280	08/09/07	E4
	TEST ANTIGENS									
8	A/FLORIDA/13/2007	80	640	320	320	320	320	160	12/16/07	E2
9	A/FLORIDA/18/2007	80	320	640	320	320	320	160	12/17/07	C2
10	A/FLORIDA/19/2007-EGG	80	320	160	160	320	160	160	12/28/07	E2
11	A/NEW MWXICO/8/2007	80	320	640	320	640	640	640	12/17/07	E2
12	A/PENNSYLVANIA/14/2007-EGG	160	320	1280	1280	1280	640	1280	12/12/07	E3
13	A/PENSYLVANIA/14/2007-MDCK	80	320	320	320	320	320	160	12/12/07	C2
14	A/PENSYLVANIA/03/2008	40	160	640	640	640	320	320	01/02/08	X/C2
15	A/FLORIDA/19/2007-MDCK	80	160	320	320	320	320	160	12/28/07	C2
16	A/NEW MWXICO/01/2008	80	80	640	640	640	320	640	01/03/08	MX/C1
17	A/NEW MWXICO/07/2007	80	80	640	640	640	320	320	12/18/07	E2
18	A/COLORADO/35/2007	80	160	320	320	160	160	80	12/17/07	M2/C1
19	A/THAILAND/749/2007	80	640	320	320	320	320	160	10/08/07	C2/C1
20	A/THAILAND/589/2007	80	320	320	320	320	320	80	08/03/07	C2/C1
21	A/THAILAND/781/2007	80	320	160	160	160	160	80	10/18/07	C2/C1
22	A/THAILAND/C71644/2007	80	160	640	640	320	320	160	09/11/07	C1/C2
23	A/THAILAND/713/2007	80	160	640	1280	640	320	320	09/21/07	C3/C1
24	A/THAILAND/590/2007	40	160	640	640	1280	640	320	08/09/07	C2/C1
25	A/LYON/1323/2007	80	160	320	320	320	320	160	12/11/07	C2/C1
26	A/LYON/1412/2007	80	160	320	320	640	320	160	12/19/07	C2/C2
27	A/LYON/1375/2007	40	80	320	320	640	320	320	12/18/07	C2/C1
28	A/LYON/1321/2007	40	80	320	320	640	320	160	12/10/07	C2/C1
29	A/LYON/1362/2007	40	80	320	320	160	160	80	12/14/07	C2/C1
30	A/HIROSHIMA/93/2007	40	40	320	320	320	320	320	10/30/07	E3/E1

*Serology antigens

CDC

Influenza A(H1N1) Isolates Characterized by CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 2007 – September 2007							
A/N.Caledonia/20/99-like	5	7	11	5	13	1	42 (25.1%)
A/Sol. Islands/03/2006-like	25	1	5	79	4	5	119 (71.3%)
A/Sol. Islands/03/2006 (low)*				4			4 (2.4%)
A/Sol. Islands/03/2006 (low)**				2			2 (1.2%)
						Total	167
October 2007- January 2007							
A/N.Caledonia/20/99-like					2		2 (1%)
A/Sol. Islands/03/2006-like	107	1	5	25			138 (75%)
A/Sol. Islands/03/2006 (low)*	12		3	6			21 (11%)
A/Sol. Islands/03/2006 (low)**	12		6	5			23 (13%)
						Total	184
Total	161	9	30	126	19	6	351

Preliminary Data 02/12/2008

* 4-fold low to A/Solomon Islands/03/2006
** 8-fold or greater low to A/Solomon Islands/03/2006

Antigenic analyses of influenza A H1N1 viruses (London)

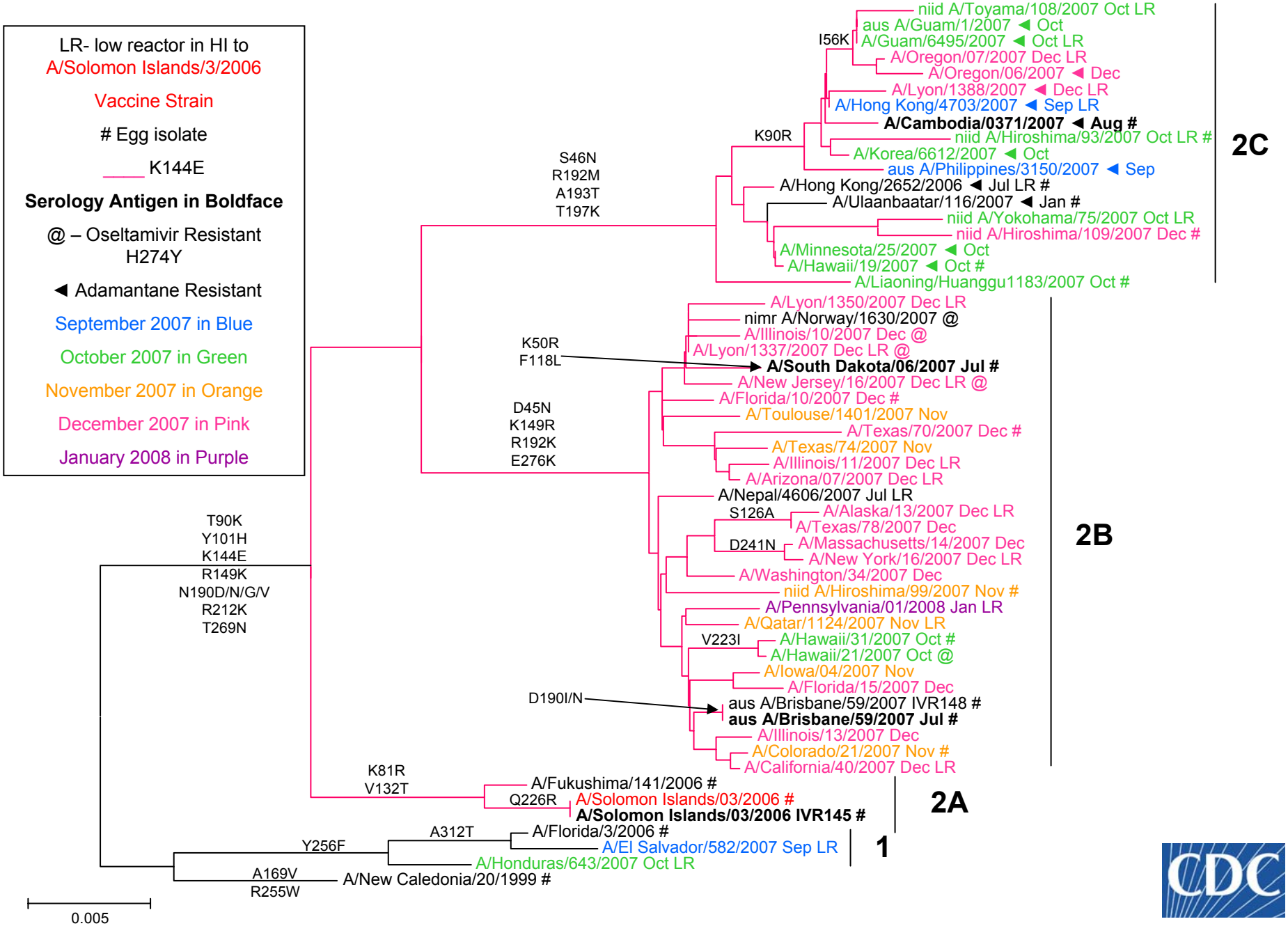
Viruses	Collection Date	Passage	Post infection ferret sera					
			A/NC 20/99	A/HK 2652/06	A/Fuk 141/06	A/SI 3/06	A/Bris 59/07 Aus	A/Bris 59/07
REFERENCE VIRUSES								
A/New Caledonia/20/99	9.6.99	Ex	**320**	40	80	40	80	160
A/Hong Kong/2652/2006	17.7.06	E2 \2	40	**320**	320	320	160	640
A/Fukushima/141/2006	7.2.06	E4 \2	80	160	**640**	640	160	1280
A/Solomon Islands/3/2006	21.8.06	E3 \2	80	320	320	**640**	320	640
A/Brisbane/59/2007	1/7/07	E2 \1	40	160	320	320	**320**	**1280**
A/Brisbane/59/2007	1/7/07	MDCKx+2	<	40	<	<	320	320
TEST VIRUSES								
A/Trieste/4/2008	8/1/08	MDCKsiat1	40	160	160	320	640	640
A/Lisbon/3/2008 #	2/01/2008	MDCK3	40	160	160	320	640	1280
A/Hungary/3/2007	25/12/07	E3 \1	<	160	160	320	80	40
A/Firenze/25/2007	20/12/07	MDCK1	40	80	160	160	160	160
A/Parma/68/07	20/12/07	II MDCK	40	80	160	160	160	160
A/Finland/4/2007	23/12/07	MDCK2	40	80	80	160	320	640
A/Algeria/G195/07	3/11/07	PO1\1	40	80	320	160	160	160
A/Barcelona/00122/2008	5/1/08	MDCK0	40	80	160	160	160	160
A/Paris/0577/07 #	Dec-08	MDCKx	40	80	80	80	320	320
A/Denmark/4/2008	4/1/08	MDCK2	40	80	80	80	320	640
A/Norway/12/2008 #	13/12/07	MDCK1	40	80	40	80	320	640
A/Algeria/G258/07	12/11/07	PO1\1	40	80	40	80	320	640
A/Barcelona/145/2008	5/1/08	MDCK1	<	80	80	80	160	640
A/Bordeaux/1314/07	04/12/07	MDCK3	40	80	40	40	160	320
A/Stockholm/16/2007	11/12/07	MDCK2	<	80	40	40	320	640
A/Stockholm/17/2007	13/12/07	MDCK2	<	80	40	40	320	1280
A/Stockholm/1/2008	Jan-08	MDCK1	<	40	40	40	80	80
A/Dakar/09/07	05/10/07	MDCK2	<	<	40	<	640	320
A/Barcelona/00083/2008	3/1/08	MDCK0	<	40	<	<	160	640
A/Baden-Wurttemberg/2/08	7/01/08	MDCKx	80	40	40	<	40	160

1. < : <40; #, oseltamivir resistant

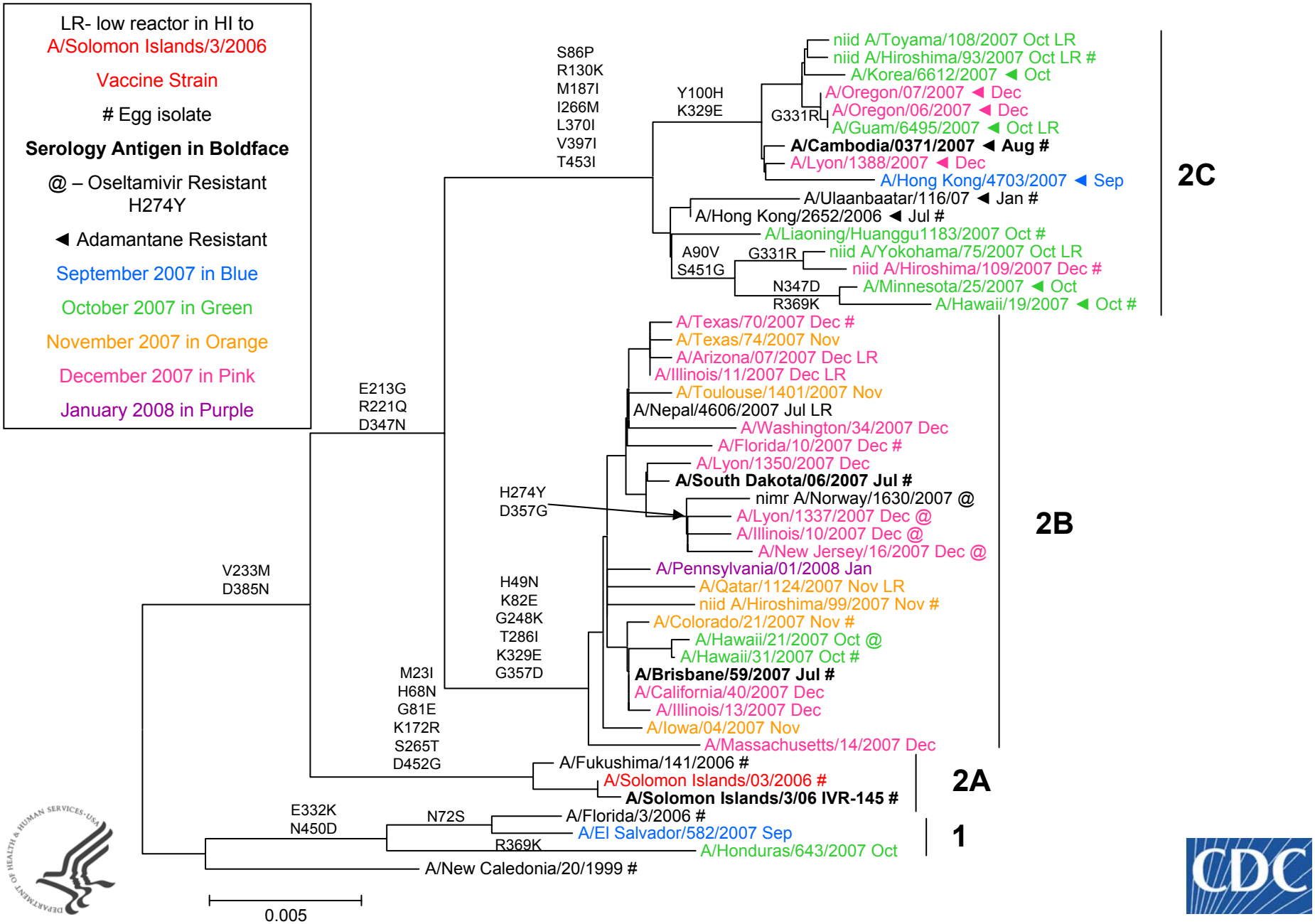
H1 low reactors in HI assays in WHOCCs

	A/SI/3/06-like	low-reactors (≥ 8-f)
• Australia (Oct-)	117 [55%]	97 [45%]
• CDC (Oct -)	137 [96%]	6 [4%]
• NIID (Sept -)	90 [88%]	12 [12%]
• NIMR (Sept -)	72 [54%]	62 [46%]
Total	416 [70%]	177 [30%]

Evolutionary Relationships Among Influenza H1N1 HA (HA1) Genes, 2007-08



Evolutionary Relationships Among Influenza H1N1 NA Genes, 2007-08



HI Antibody Responses to the H1 Component of the 2007 - 2008 Influenza Vaccine

PEDIATRIC POPULATIONS

								% with HI titer ≥ 40			% with HI titer ≥ 80			% with HI titer ≥ 160		
Population	N	Antigen	% Rise 1st	% Rise 2nd	Pre GMT	Post GMT 1st	Post GMT 2nd	Pre	Post 1st	Post 2nd	Pre	Post 1st	Post 2nd	Pre	Post 1st	Post 2nd
USA[1]	15	A/Solomon Islands/03/2006 IVR-145*	93	100	5	36	202	0	80	100	0	13	80	0	7	67
	15	A/Brisbane/59/2007	20	53	5	8	26	0	20	47	0	7	27	0	7	7
	15	A/South Dakota/6/2007	20	67	5	8	23	0	20	47	0	7	13	0	0	7
	15	A/Cambodia/0371/2007	20	47	5	8	15	0	20	40	0	7	7	0	0	7
USA[2]	29	A/Solomon Islands/03/2006 IVR-145*	N/A	96	6	N/A	129	7	N/A	93	3	N/A	90	0	N/A	48
	29	A/Brisbane/59/2007	N/A	69	6	N/A	33	0	N/A	45	0	N/A	31	0	N/A	21
	29	A/South Dakota/6/2007	N/A	52	6	N/A	29	0	N/A	45	0	N/A	31	0	N/A	21
	29	A/Cambodia/0371/2007	N/A	52	6	N/A	25	0	N/A	45	0	N/A	31	0	N/A	21

Preliminary Data 02/01/06

1. Sera were kindly provided by Virginia Commonwealth University, Medical Center, Department of Pediatrics. The populations were vaccinated with 2 doses of the 2007-2008 trivalent influenza vaccine containing 7.5ug each of A/Wisconsin/67/2005 X161B (H3N2)-like, A/Solomon Islands/03/2007(H1N1)-like, and B/Malaysia/2506/2004-like hemagglutinin.
2. Sera were kindly provided by Dr. Zhiping Ye, FDA, Bethesda, MD. The populations were vaccinated with the 2007-2008 trivalent influenza vaccine containing 15ug each of A/Wisconsin/67/2005 X161B (H3N2)-like, A/Solomon Islands/03/2006 (H1N1)-like, and B/Malaysia/2506/2004-like hemagglutinin.

* H1 component of the vaccine.

H1N1 viruses - Summary

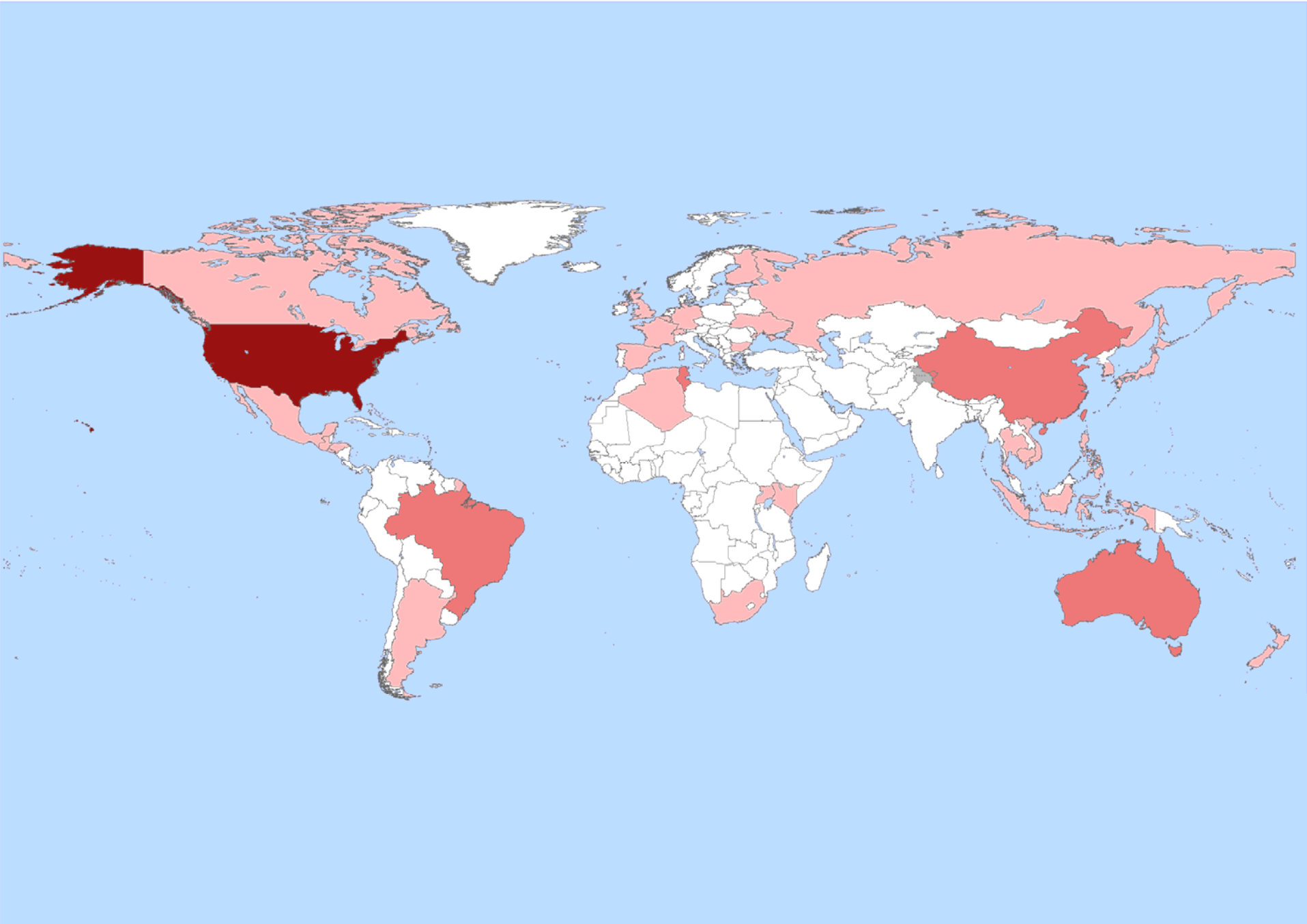
- H1N1 viruses predominated in most countries; caused outbreaks in some countries
- Many viruses were closely related to A/Solomon Islands/3/2006; few were A/New Caledonia/20/99-like
- Increasing proportion antigenically distinct from A/Solomon Islands/3/06 and closely related to A/Brisbane/59/2007
- Majority of HA sequences in clade 2B (represented by A/Brisbane/59/2007)
- Increasing proportion of clade 2B NAs with H274Y mutation, causing oseltamivir resistance
- Oseltamivir-sensitive and -resistant viruses antigenically similar

WHO Recommendations

- It is recommended that vaccines for use in the 2008-2009 influenza season contain:
  - an A/Brisbane/59/2007 (H1N1)-like virus.

Influenza A (H3N2) Viruses

H3N2 activity from September 2007 – January 2008



HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA H3 VIRUSES (02/06/08) GUINEA PIG RED BLOOD CELLS

			BRISBANE				NEPAL	144D		Date	
		X-161B	BRIS/10	X-171A	UG/716	TX/37	NP/921	HE/147	BC/1287	Collected	Passage
1	A/WISCONSIN/67/2005 X PR8 X-161B*	2560	320	320	320	160	320	640	80	REASSORT	EX/E1
2	A/BRISBANE/10/2007*	320	640	1280	1280	1280	1280	5120	320	02/06/07	E2/E1
3	A/BRISBANE/10/2007 X-171A	640	2560	1280	2560	2560	2560	5120	640	REASSORT	EX/E1
4	A/URUGUAY/716/2007*	320	640	1280	640	640	640	2560	160	06/21/07	SpfCK1E4
5	A/TEXAS/37/2007*	320	640	640	640	640	640	1280	640	10/13/07	M1/C2
6	A/NEPAL/921/2006	640	320	1280	1280	640	2560	2560	320	07/11/06	SpfCK2E3
7	A/HENAN/JINSHUI147/2007	160	320	320	640	640	1280	5120	160	01/29/07	E1/E3
8	A/BRITISH/COLUMBIA/RV1287/2007	160	640	320	160	160	160	160	640	09/27/07	C1/C3
TEST ANTIGENS											
9	A/ARKANSAS/01/2008	5120	5120	5120	5120	640	640	2560	320	01/03/08	X/C2
10	A/TENNESSEE/11/2007	1280	640	1280	1280	320	320	1280	320	12/21/07	MX/C1
11	A/WISCONSIN/34/2007	1280	1280	1280	1280	5120	1280	5120	1280	11/28/07	C1
12	A/ALBERTA/RV0141/2007	640	640	640	2560	640	2560	1280	320	12/26/07	X1/C1
13	A/ARIZONA/09/2007	640	640	640	2560	640	10	1280	160	12/23/07	CX/C1
14	A/ARKANSAS/03/2008	640	640	640	1280	640	320	1280	320	01/10/08	X/C2
15	A/NORTH CAROLINA/05/2007	640	1280	2560	1280	320	320	640	160	11/26/07	MX/C1
16	A/WISCONSIN/33/2007	640	1280	640	1280	1280	640	2560	640	11/21/07	C1
17	A/ARIZONA/10/2007	320	1280	640	1280	320	640	640	80	12/14/07	CX/C1
18	A/ARKANSAS/02/2007	320	640	640	1280	640	320	640	320	01/04/08	X/C2
19	A/ARKANSAS/04/2008	320	640	1280	640	320	320	1280	160	01/14/08	X/C1
20	A/ONTARIO/RV0152/2007	160	320	320	320	80	160	320	80	12/30/07	X2/C1
21	A/MEXICO/3701/2007	320	640	1280	640	640	320	1280	160	10/18/07	C4/C1
22	A/GUATEMALA/8247/2007	320	640	640	1280	160	160	320	40	08/28/07	CX/C2
23	A/SINGAPORE/66/2007	320	640	640	1280	640	640	640	160	11/16/07	C3/C2
24	A/THAILAND/738/2007	320	640	320	1280	160	640	640	160	09/25/07	C2/C1
25	A/TOYAMA/119/2007	320	640	640	1280	160	160	640	320	UNKNOWN	C1+2/C2
26	A/GYEONGNAM/4506/07	160	320	320	640	320	320	640	160	11/19/07	C2/C2
27	A/SINGAPORE/65/2007	160	640	320	640	320	320	640	160	10/31/07	C2/C2
28	A/THAILAND/284/2007	160	640	320	640	320	640	640	80	09/18/07	X/C2

*Serology Antigen

Influenza A(H3N2) Isolates Characterized by CDC

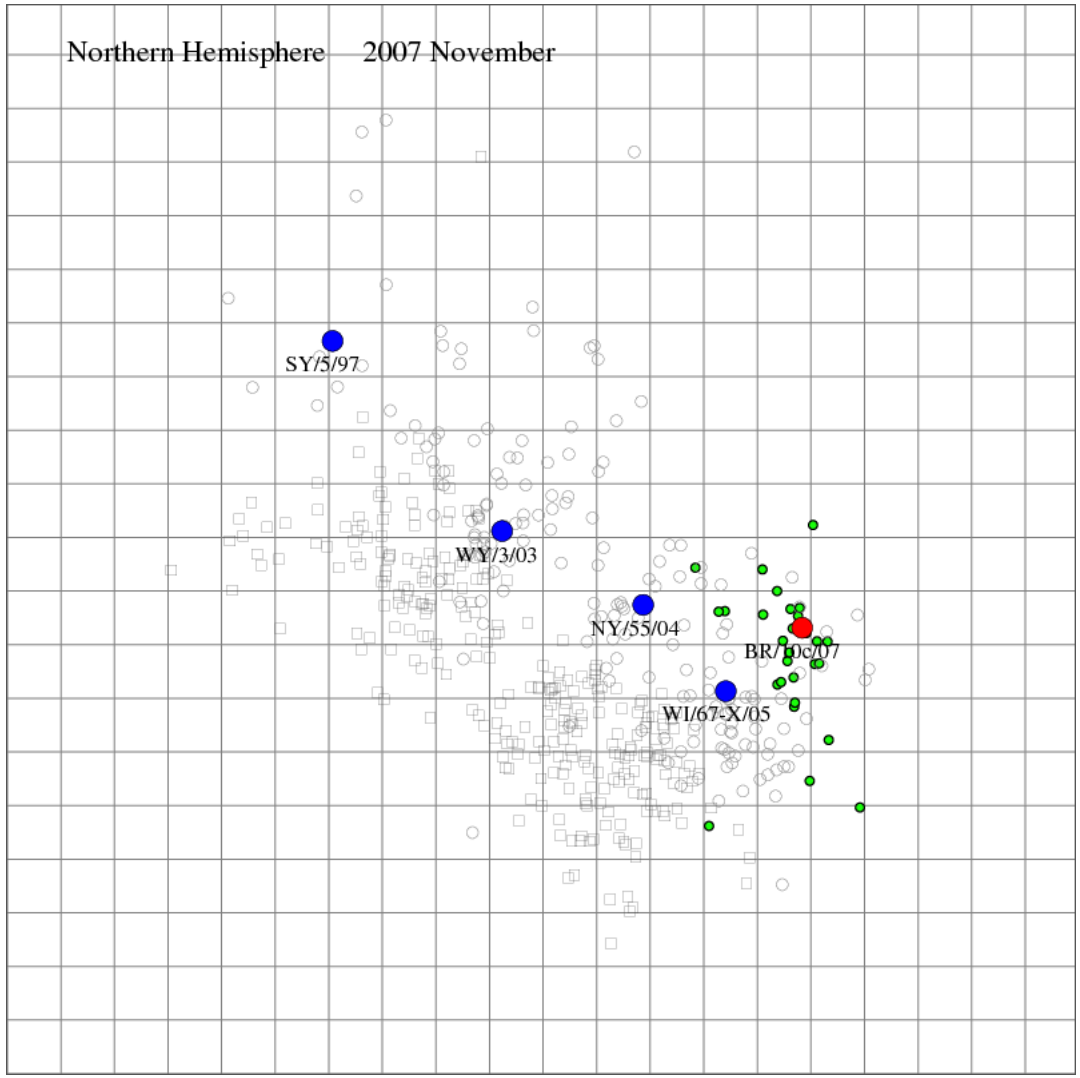
	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 2007 – September 2007							
A/Wisconsin/67/2005-like	22		6	4	16	1	49 (8%)
A/Wisconsin/67/2005-like (low)*	6		5	2	5		18 (3%)
A/Wisconsin/67/2005-like (low)**	27	4	7	28	111	2	179 (30%)
A/Brisbane/10/2007-like	16	19	5	84	211	15	350 (59%)
						Total	596
October 2007 – January 2008							
A/Wisconsin/67/2005-like	8						8 (9%)
A/Brisbane/10/2007-like	54	6		10	4		74 (82%)
A/Brisbane/10/2007-like (low)	5	2			1		8 (9%)
						Total	90
Total	138	31	23	128	348	18	686

Preliminary data 02/07/2008

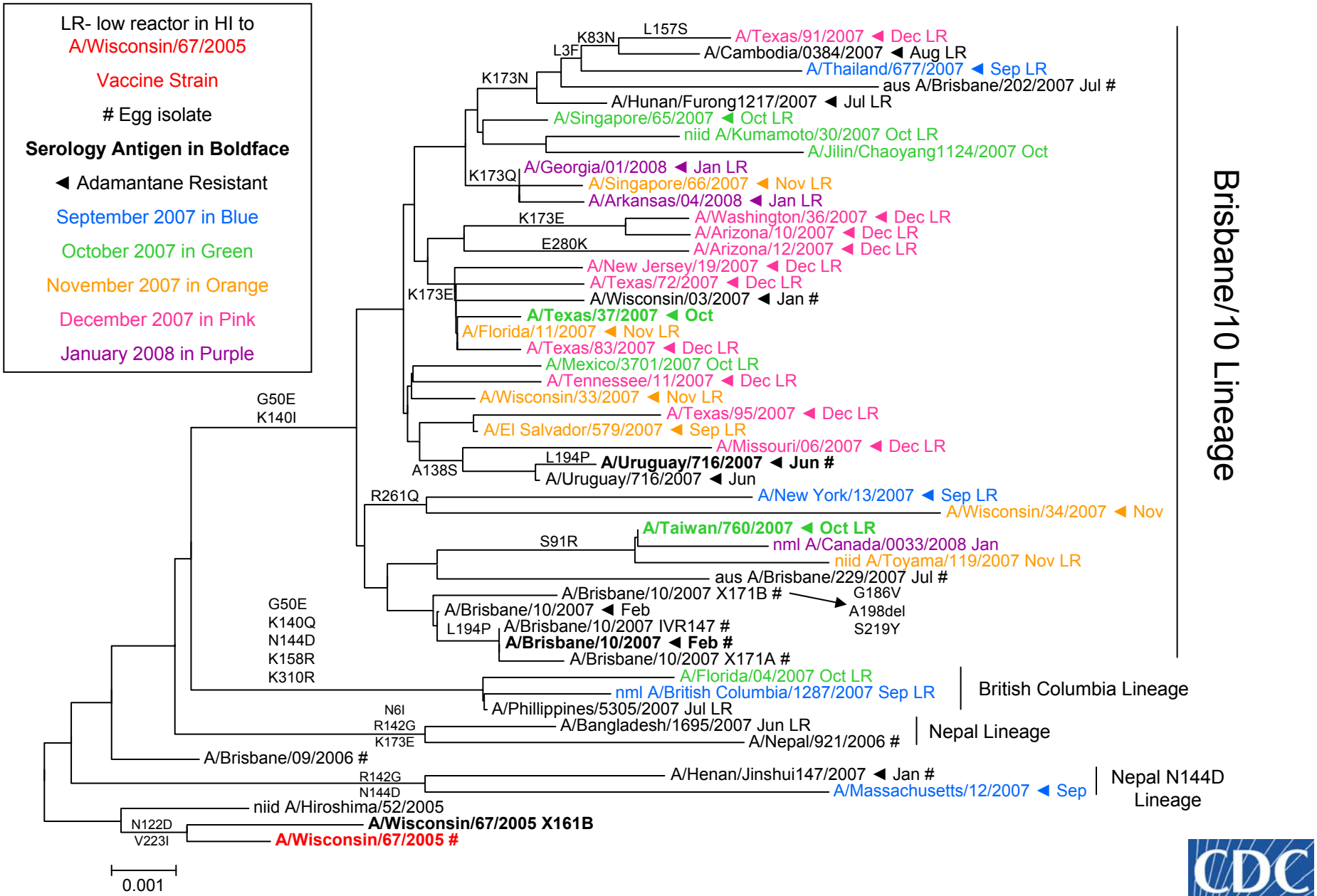
* 4-fold low to A/Wisconsin/67/2005
** 8-fold or greater low to A/Wisconsin/67/2005

		A	B	C	D	E	F	G
		F859	F864	F897	F948	F966	F968	F998
	Reference Strains	CAL/7	WISC/67	BRIS/9	NEP/921	BRIS/4	BRIS/10	BRIS/10
A	A/CALIFORNIA/7/2004	**1280**	320	320	40	640	160	160
B	A/WISCONSIN/67/2005	1280	**640**	1280	160	1280	640	320
C	A/BRISBANE/9/2006	640	640	**1280**	160	1280	320	320
D	A/NEPAL/921/2006	320	320	640	**160**	320	320	320
E	A/BRISBANE/4/2007	640	320	1280	160	**1280**	640	640
F	A/BRISBANE/10/2007	1280	640	640	160	1280	**640**	640
G	A/BRISBANE/10/2007	80	<40	80	40	40	160	**80**
H	A/PERTH/27/2007	160	80	320	80	160	320	320
I	A/PHILIPPINES/1616/2007	80	<40	80	<40	40	80	160
J	A/WISCONSIN/3/2007	1280	640	2560	320	1280	1280	640
K	A/BRISBANE/202/2007	2560	1280	1280	640	2560	2560	2560
L	A/BRISBANE/229/2007	160	320	640	80	640	160	80
	Antigens							
1	A/SINGAPORE/206/2007	640	640	1280	320	1280	1280	1280
2	A/SINGAPORE/211/2007	320	80	640	80	320	640	320
3	A/SINGAPORE/214/2007	320	40	640	80	320	640	320
4	A/THAILAND/994/2007	160	80	640	80	320	640	320
5	A/CHRISTCHURCH/36/2007	320	160	640	80	320	640	320
6	A/SINGAPORE/67/2007	160	40	160	40	40	320	160
7	A/SINGAPORE/208/2007	320	40	640	80	160	320	320
8	A/SINGAPORE/212/2007	160	40	320	40	80	320	320
9	A/THAILAND/966/2007	160	40	320	40	160	320	320
10	A/THAILAND/981/2007	320	80	640	80	320	320	320
11	A/THAILAND/1036/2007	80	40	320	40	160	320	160
12	A/THAILAND/807/2007	160	80	320	80	160	320	160
13	A/CHRISTCHURCH/56/2007	160	40	640	80	160	320	160
14	A/SINGAPORE/56/2007	40	<40	80	<40	40	160	40
15	A/SINGAPORE/50/2007	80	<40	80	40	40	160	80
16	A/PHILIPPINES/3671/2007	80	40	160	40	80	160	160
17	A/THAILAND/829/2007	80	40	160	40	40	160	80
18	A/THAILAND/897/2007	80	<40	80	40	40	160	80
19	A/SINGAPORE/53/2007	40	<40	40	<40	<40	80	40
20	A/SINGAPORE/59/2007	40	<40	40	<40	40	80	40

November 2007



Evolutionary Relationships Among Influenza H3N2 HA (HA1) Genes, 2007-08



Evolutionary Relationships Among Influenza H3N2 NA Genes, 2007-08

LR- low reactor in HI to A/Wisconsin/67/2005

Vaccine Strain

Egg isolate

Serology Antigen in Boldface

◄ Adamantane Resistant

September 2007 in Blue

October 2007 in Green

November 2007 in Orange

December 2007 in Pink

January 2008 in Purple

A/Arkansas/04/2008 ◄ Jan LR
A/Singapore/66/2007 ◄ Nov LR
I215V
A/Jilin/Chaoyang1124/2007 Oct
A/Georgia/01/2008 ◄ Jan LR
niid A/Kumamoto/30/2007 Oct
P45S
A/Thailand/677/2007 ◄ Sep LR
A/Cambodia/0384/2007 ◄ Aug LR
A/Texas/91/2007 ◄ Dec LR
A/Hunan/Furong1217/2007 ◄ Jul LR
P45L
niid A/Toyama/119/2007 Nov
A/Taiwan/760/2007 ◄ Oct LR
I312T
A/Brisbane/10/2007 IVR-147
A/Brisbane/10/2007 X-171B
A/Brisbane/10/2007 ◄ Feb #
A/Brisbane/10/2007 X-171A
A/Brisbane/10/2007 ◄ Feb LR
A/Singapore/65/2007 ◄ Oct LR
A/Texas/95/2007 ◄ Dec LR
A/Tennessee/11/2007 ◄ Dec LR
N147D
R210K
A/Wisconsin/33/2007 ◄ Nov LR
A/Arizona/12/2007 ◄ Dec LR
N402D
A/Florida/11/2007 ◄ Nov LR
A/New Jersey/19/2007 ◄ Dec LR
N387K
I26T
A/Texas/37/2007 ◄ Oct
A/Texas/72/2007 ◄ Dec LR
H150R
D151N/G/S
V194I
Y310H
S372L
A/Wisconsin/03/2007 ◄ Jan #
A/El Salvador/579/2007 ◄ Sep LR
A/Uruguay/716/2007 ◄ Jun
R150H
T267I
A/Uruguay/716/2007 ◄ Jun #
A/New York/13/2007 ◄ Sep LR
A/Wisconsin/34/2007 ◄ Nov
A/Arizona/10/2007 ◄ Dec LR
A/Washington/36/2007 ◄ Dec LR
N93D
L370S
aus A/Brisbane/9/2006 #
I443V
A/British Columbia/1287/2007 Sep LR
A/Florida/04/2007 Oct LR
A/Philippines/5305/2007 Jul LR
N86E/K
H150R
K296R
I307M
S335G
N43S
S315R
A/Bangladesh/1695/2007 Jun LR
A/Nepal/921/2006 Jul #
A/Henan/Jinshui147/2007 ◄ Jan #
A/Massachusetts/12/2007 ◄ Sep
P285L
A/Wisconsin/67/2005 x161B

0.002

Brisbane/10 Lineage

British Columbia Lineage

Nepal Lineage

Nepal N144D Lineage

HI Antibody Responses to the H3 Component of the 2007 - 2008 Influenza Vaccine

PEDIATRIC POPULATIONS

								% with HI titer ≥ 40			% with HI titer ≥ 80			% with HI titer ≥ 160		
Population	N	Antigen	% Rise 1st	% Rise 2nd	Pre GMT	Post GMT 1st	Post GMT 2nd	Pre	Post 1st	Post 2nd	Pre	Post 1st	Post 2nd	Pre	Post 1st	Post 2nd
USA[1]	15	A/Wisconsin/67/2005 X-161B*	47	93	5	17	76	0	20	80	0	20	73	0	13	33
	15	A/Brisbane/10/2007	20	73	5	12	35	0	21	67	0	20	33	0	13	13
	15	A/Uruguay/716/2007	20	60	5	7	15	0	13	27	0	0	7	0	0	0
USA[2]	29	A/Wisconsin/67/2005 X-161B	N/A	86	8	N/A	48	17	N/A	69	10	N/A	42	3	N/A	17
	29	A/Brisbane/10/2007	N/A	48	7	N/A	20	10	N/A	28	10	N/A	10	3	N/A	10
	29	A/Uruguay/716/2007	N/A	28	7	N/A	14	10	N/A	10	7	N/A	10	3	N/A	10

Preliminary Data 02/01/06

1. Sera were kindly provided by Virginia Commonwealth University, Medical Center, Department of Pediatrics. The populations were vaccinated with 2 doses of the 2007-2008 trivalent influenza vaccine containing 7.5ug each of A/Wisconsin/67/2005 X161B (H3N2)-like, A/Solomon Islands/03/2007(H1N1)-like, and B/Malaysia/2506/2004-like hemagglutinin.
2. Sera were kindly provided by Dr. Zhiping Ye, FDA, Bethesda, MD. The populations were vaccinated with the 2007-2008 trivalent influenza vaccine containing 15ug each of A/Wisconsin/67/2005 X161B (H3N2)-like, A/Solomon Islands/03/2006 (H1N1)-like, and B/Malaysia/2506/2004-like hemagglutinin.

* H3 component of the vaccine.

MN Antibody Responses to the H3N2 Component of the 2007-2008 Influenza Vaccine

Adult Populations

						% with MN ≥ 80		% with MN ≥ 160	
Population	N	Antigen	% Rise	Pre GMT	Post GMT	Pre	Post	Pre	Post
Japan[1]	30	A/Wisconsin/67/2005 (X-161B)	20	63	133	63	80	30	60
	30	A/Brisbane/10/2007	20	54	98	47	70	27	47
	30	A/Brisbane/10/2007X-171A	23	29	55	30	47	10	30
	30	A/Brisbane/10/2007X-171	17	47	84	47	70	20	40
	30	A/Uruguay/761/2007	17	32	55	37	47	13	33
USA[2]	24	A/Wisconsin/67/2005 (X-161B)*	54	123	854	58	96	54	92
	24	A/Brisbane/10/2007	46	37	226	33	83	33	75
	24	A/Brisbane/10/2007X-171A	54	46	392	38	83	33	71
	24	A/Brisbane/10/2007X-171	50	90	640	46	83	46	79
	24	A/Uruguay/761/2007	58	41	302	38	79	33	71

02/05/08

1. Sera were kindly provided by Dr. Takato Odagiri, WHO Collaborating Center, Tokyo, Japan. The populations were vaccinated with the 2007-2008 trivalent influenza vaccine containing 15ug each of A/Hiroshima/52/2005(H3N2), A/Solomon Islands/3/2006 (H1N1), and B/Malaysia/2506/2004 hemagglutinin.
2. Sera were kindly provided by Dr. Zhiping Ye, FDA, Bethesda, MD. The populations were vaccinated with the 2007-2008 trivalent influenza vaccine containing 15ug each of A/Wisconsin/67/2005 X161B (H3N2)-like, A/Solomon Isalnds/3/2006 (H1N1)-like, and B/Malaysia/2506/2004-like hemagglutinin.

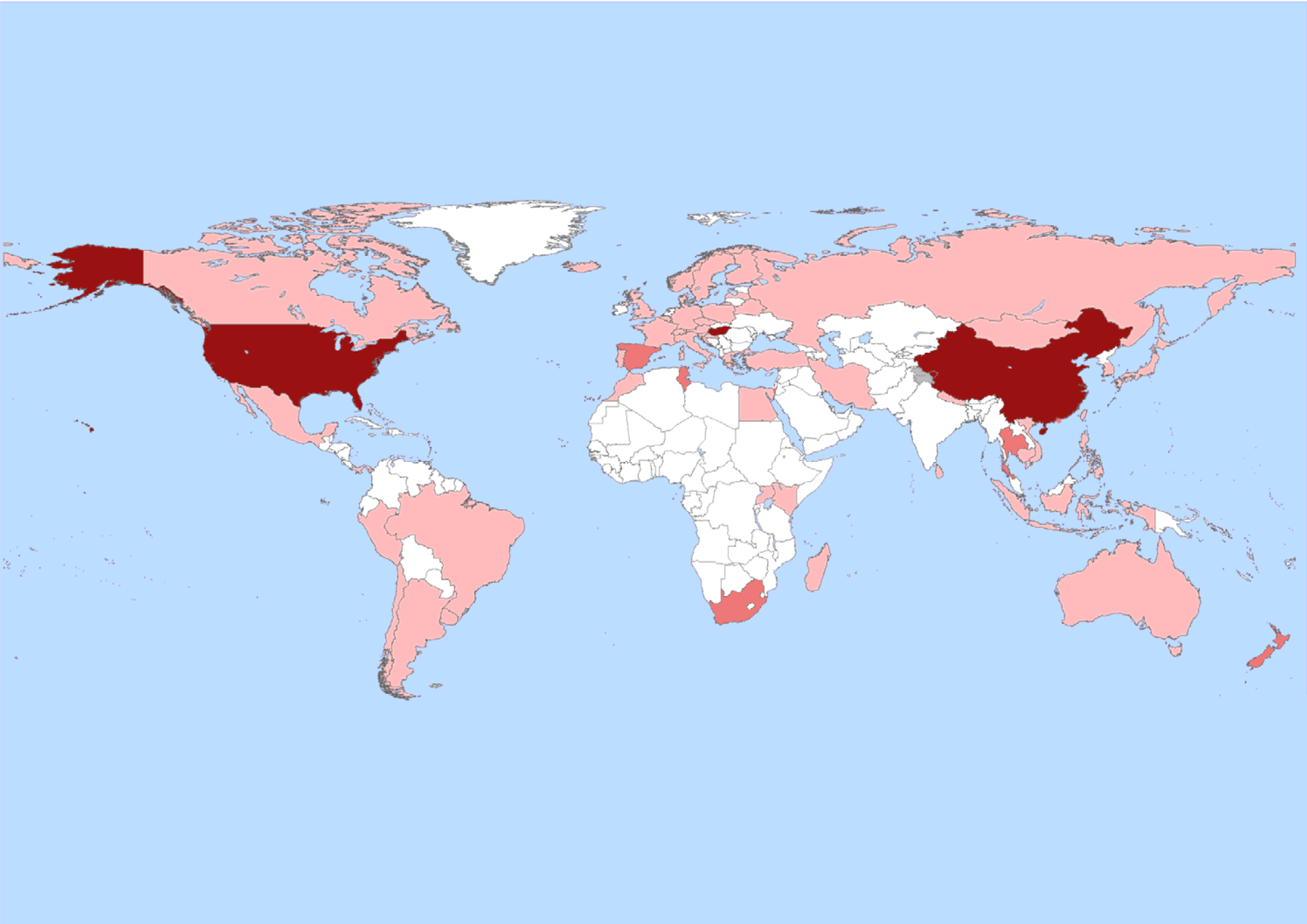
* H3N2 component of the vaccine.

WHO Recommendations

- It is recommended that vaccines for use in the 2008-2009 influenza season contain:
  - an A/Brisbane/10/2007 (H3N2)-like virus.

Influenza B Viruses

B, September 2007 – January 2008



HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA TYPE B VIRUSES (02/12/08)

		REFERENCE FERRET ANTISERA									
REFERENCE ANTIGENS		FL/4	AS/3	BA/3333	JA SENDAI/114	OH/1	MY/2506	PA/5	VI/304	Date Collected	Passage
1	B/FLORIDA/04/2006 *	160	320	320	160	10	80	20	40	11/01/06	E3
2	B/BRISBANE/03/2007	160	320	320	320	10	80	20	40	03/09/07	E2/E1
3	B/BANGLADESH/3333/2007 *	80	320	320	80	5	80	20	40	08/19/07	E4
4	B/SENDAI-H/114/2007*	160	320	160	160	20	80	10	40	UNKNOWN	E1+2/E1
5	B/OHIO/01/2005	5	5	5	5	1280	640	640	2560	02/23/05	E2
6	B/MALAYSIA/2506/2004*	5	5	10	5	2560	1280	1280	2560	06/12/04	E3/E2
7	B/PENNSYLVANIA/05/2007 *	5	5	5	5	640	640	640	1280	03/01/07	E3
8	B/VICTORIA/304/2006	5	5	5	5	640	640	640	2560		E2,2/E1
TEST ANTIGENS											
9	B/NEW YORK/11/2007 TC	640	160	320	320	5	40	5	20	12/24/07	C1
10	B/NEW YORK/11/2007 EGG	640	320	320	320	5	40	10	20	12/24/07	E1
11	B/WISCONSIN/09/2007	320	640	640	640	5	160	10	80	12/27/07	C1
12	B/WISCONSIN/01/2008	320	640	640	320	5	80	10	20	01/01/08	C1
13	B/NEW MEXICO/04/2007	320	320	320	320	5	80	10	40	12/19/07	MX/C1
14	B/WISCONSIN/13/2007	160	160	320	320	5	40	10	20	12/31/07	M1/C1
15	B/WISCONSIN/03/2008	160	640	320	320	10	160	40	160	01/02/08	E3
16	B/NEW MEXICO/01/2008	160	80	320	160	5	20	5	20	01/02/08	MX/C1
17	B/COLORADO/01/2007	80	160	320	80	10	40	20	20	10/28/07	E2
18	B/NEW YORK/10/2007 EGG	80	80	160	80	10	40	10	10	12/21/07	E3
19	B/HONG KONG/1325/2007	640	320	640	640	5	40	10	20	12/05/07	C2/C1
20	B/HONG KONG/1363/2007	640	320	640	320	5	80	10	20	12/24/07	C2/C2
21	B/SINGAPORE/52/2007	640	320	640	640	5	40	10	20	06/29/07	C2/C1
22	B/THAILAND/889/2007	640	320	640	320	5	80	10	20	11/16/07	C1/C1
23	B/THAILAND/872/2007	640	320	320	320	5	40	5	10	11/19/07	C1/C1
24	B/THAILAND/873/2007	640	320	640	640	5	80	10	20	11/14/07	C1/C1
25	B/THAILAND/869/2007	320	160	640	160	5	40	5	20	11/23/07	C1/C1
26	B/HONG KONG/1303/2007	160	160	320	160	5	40	5	10	11/01/07	C2/C2
27	B/CALIFORNIA/20/2007	5	5	10	5	160	80	160	320	11/27/07	C1/C1
28	B/HONG KONG/1362/2007	5	5	10	5	5120	1280	2560	5120	12/24/07	C2/C1
29	B/THAILAND/762/2007	5	5	5	5	2560	1280	2560	5120	10/09/07	C2/C1
30	B/HONG KONG/1327/2007	5	5	20	5	160	160	320	320	12/07/07	C2/C1
31	B/THAILAND/785/2007	5	5	5	5	160	160	320	320	10/18/07	C2/C1
32	B/THAILAND/810/2007	5	5	5	5	160	80	160	320	10/25/07	C2/C1

* = Serology antigen

Influenza B Isolates Characterized by CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 2007 – September 2007							
B/Ohio/01/2005-like	2		2	15	6	7	32 (14%)
B/Ohio/01/2005-like (low)*	1		1	10		2	14 (6%)
B/Ohio/01/2005-like (low)**	6	1	3	16	7	6	39 (17%)
B/Florida/04/2006-like	18	3	2	79	31	3	136 (60%)
B/Florida/04/2006-like (low)				6			6 (3%)
						Total	227
October 2007 – January 2008							
B/Ohio/01/2005-like	2			3			5 (5%)
B/Ohio/01/2005-like (low)*	1						1 (1%)
B/Ohio/01/2005-like (low)**	1			5			6 (6%)
B/Florida/04/2006-like	66	3		15			84 (87%)
B/Florida/04/2006-like (low)	1						1 (1%)
						Total	97
Total	98	7	8	149	44	18	324

* 4-fold down to B/Ohio/01/2005
** 8-fold or greater down to B/Ohio/01/2005

Preliminary Data 02/14/2008

TABLE 5.3

	January 31, 2008	Haemagglutination Inhibition Assay - WHO influenza Centre, Melbourne													
		Reference Antisera													
		A	B	C	D	E	F	G	H	I	J	K	L		
		F865	F884	F898	F899	CDC	F874	F875	F967	F982	CDC	F997	NIID	Passage	
	Reference Strains	MAL/2506	MAL/174	NC/5	VIC/304	PENS/5	SHAN/361	FLOR/7	THAI/369	BRIS/3	BRIS/3	FLOR/4	SENDI-H/114	History	Date
A	B/MALAYSIA/2506/2004	1280	640	1280	1280	1280	<20	<20	<20	<20	<20	<20	<20	E5	
B	B/MALAYSIA/174/2006	1280	320	1280	1280	>2560	<20	<20	<20	<20	<20	<20	<20	X,MDCK3	
C	B/NEW CALEDONIA/5/2006	640	320	1280	1280	1280	<20	<20	<20	<20	<20	<20	<20	E5	
D	B/VICTORIA/304/2006	640	320	320	640	640	<20	<20	<20	<20	<20	<20	<20	E4	
E	B/PENNSYLVANIA/5/2007	640	320	640	640	640	<20	<20	<20	<20	<20	<20	<20	E4	
F	B/SHANGHAI/361/2002	80	<20	80	80	40	320	640	20	1280	>2560	1280	640	E7	
G	B/FLORIDA/7/2004	40	<20	40	40	40	320	640	20	640	1280	640	640	E7	
H	B/THAILAND/369/2007	<20	<20	20	<20	<20	80	640	320	640	1280	640	640	MDCK8	
I	B/BRISBANE/3/2007	80	<20	40	40	40	160	640	20	640	1280	640	640	E3	
J	B/BRISBANE/3/2007	<20	<20	20	<20	<20	40	640	80	320	640	320	640	MDCKX,MDCK2	
K	B/FLORIDA/4/2006	40	<20	20	40	40	160	320	160	320	640	320	320	E4	
L	B/SENDI-H/114/2007	40	<20	40	40	20	160	640	20	640	640	320	320	E4	
	Antigens														
1	B/SINGAPORE/207/2007	<20	<20	<20	<20	<20	40	640	80	320	640	320	320	MDCKX,MDCK1	19/11/2007
2	B/MALAYSIA/3/2007	<20	<20	<20	<20	<20	40	320	40	320	320	320	320	MDCKX,MDCK1	6/07/2007
3	B/SINGAPORE/205/2007	<20	<20	<20	<20	<20	40	640	160	640	640	320	640	MDCKX,MDCK1	9/11/2007
4	B/MALAYSIA/1679/2007	<20	<20	<20	<20	<20	40	320	20	320	320	320	320	MDCKX,MDCK1	6/11/2007
5	B/MALAYSIA/8/2007	<20	<20	<20	<20	<20	40	320	160	320	640	320	320	MDCKX,MDCK1	20/07/2007
6	B/SINGAPORE/59/2007	<20	<20	<20	<20	<20	20	320	40	320	320	160	320	MDCK2	13/09/2007
7	B/SINGAPORE/202/2007	<20	<20	20	<20	<20	20	160	80	160	320	160	320	MDCKX,MDCK1	2/11/2007
8	B/MALAYSIA/2/2007	<20	<20	20	<20	<20	40	160	160	160	320	160	320	MDCKX,MDCK1	11/06/2007
9	B/MALAYSIA/5/2007	<20	<20	<20	<20	<20	20	320	20	320	320	160	320	MDCKX,MDCK1	13/07/2007
10	B/MALAYSIA/6/2007	<20	<20	<20	<20	<20	20	640	20	320	320	160	320	MDCKX,MDCK1	16/07/2007
11	B/MALAYSIA/7/2007	<20	<20	<20	<20	<20	40	320	40	320	320	160	320	MDCKX,MDCK1	17/07/2007
12	B/MALAYSIA/1726/2007	<20	<20	20	<20	<20	20	640	40	320	320	160	320	MDCKX,MDCK1	29/11/2007
13	B/MALAYSIA/1756/2007	<20	<20	<20	<20	<20	20	320	40	320	320	160	320	MDCKX,MDCK1	3/12/2007
14	B/MALAYSIA/1762/2007	<20	<20	<20	<20	<20	40	320	80	320	320	160	320	MDCKX,MDCK1	12/11/2007
15	B/MALAYSIA/1735/2007	<20	<20	<20	<20	<20	40	320	80	320	320	160	320	MDCKX,MDCK1	6/11/2007
16	B/MALAYSIA/1841/2007	<20	<20	20	<20	<20	20	160	40	80	320	80	320	MDCKX,MDCK1	28/12/2007
17	B/MALAYSIA/9/2007	<20	<20	<20	<20	<20	20	320	20	160	320	80	320	MDCKX,MDCK1	2/08/2007
18	B/SINGAPORE/208/2007	320	160	320	640	640	<20	<20	<20	<20	<20	<20	<20	MDCKX,MDCK1	27/11/2007
19	B/MALAYSIA/1/2007	80	320	160	640	640	<20	<20	<20	<20	<20	<20	<20	MDCKX,MDCK1	29/05/2007
20	B/MALAYSIA/10/2007	40	640	80	640	160	<20	<20	<20	<20	<20	<20	<20	MDCKX,MDCK1	17/10/2007

B viruses tested in HI assays in WHOCCs

(Sep 2007 – present)

	Victoria	Yamagata
• Australia	15 [16%]	78 [84%]
Low reactors		(17%)
• CDC	12 [12%]	85 [88%]
Low reactors		(1%)
• Japan	4 [33%]	8 [67%]
Low reactors		(0%)
• UK	15 [19%]	63 [81%]
Low reactors		(27%)
Total	46 [16%]	234 [84%]
Low reactors		(16%)

Evolutionary Relationships Among Influenza B Yamagata Lineage HA (HA1) Genes, 2007-08

LR- low reactor in HI to A/Florida/04/2006

Egg isolate

Serology Antigen in Boldface

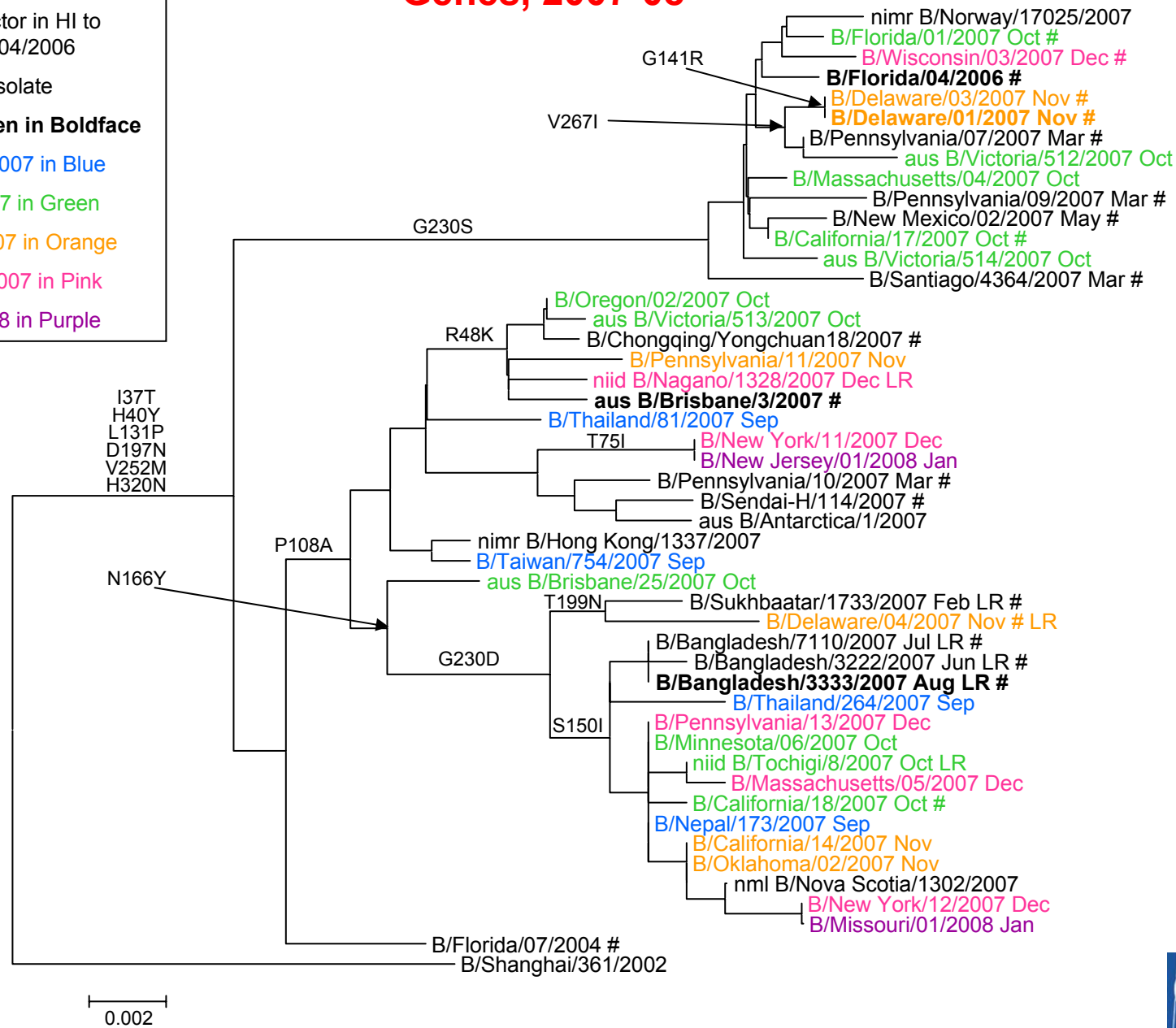
September 2007 in Blue

October 2007 in Green

November 2007 in Orange

December 2007 in Pink

January 2008 in Purple



Evolutionary Relationships Among Influenza B Victoria Lineage HA (HA1) Genes, 2007-08

LR- low reactor in HI to A/Malaysia/2506/2004

Vaccine Strain

Egg isolate

Serology Antigen in Boldface

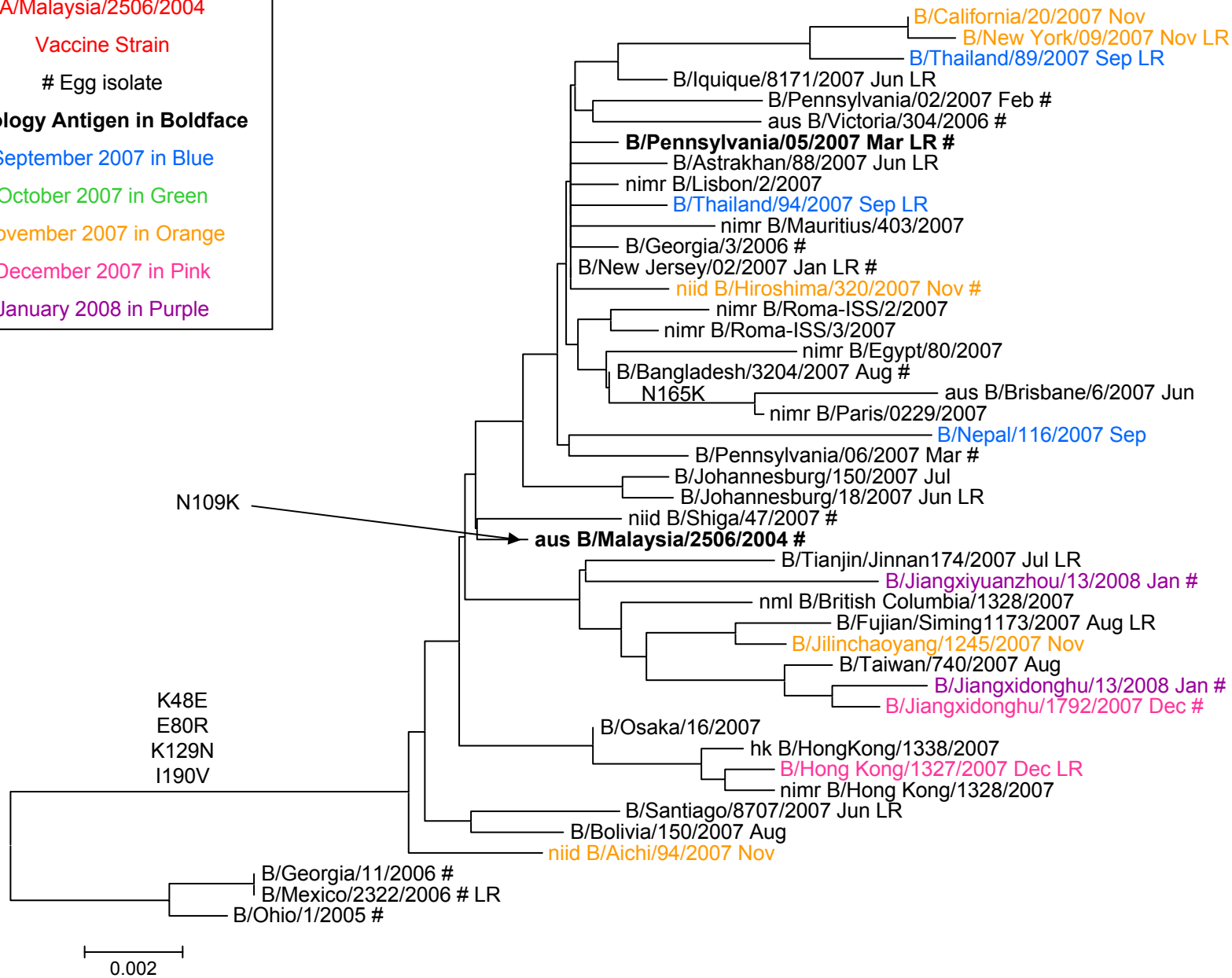
September 2007 in Blue

October 2007 in Green

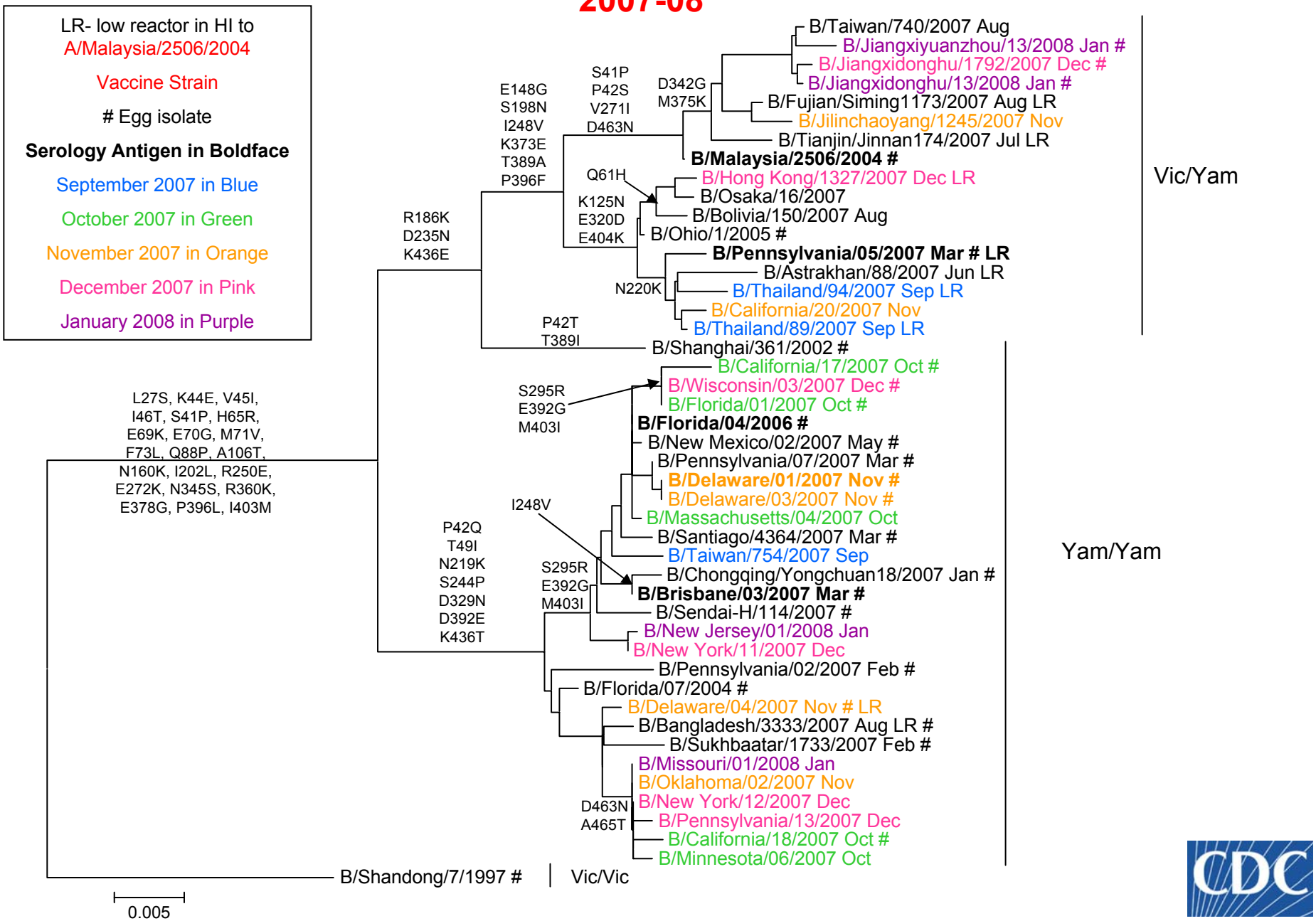
November 2007 in Orange

December 2007 in Pink

January 2008 in Purple



Evolutionary Relationships Among Influenza B Neuraminidase (NA) Genes, 2007-08



HI Antibody Responses to the B Component of the 2007 - 2008 Influenza Vaccine

PEDIATRIC POPULATIONS

									% with HI titer ≥ 40			% with HI titer ≥ 160		
Population	N	Antigen		% Rise 1st	% Rise 2nd	Pre GMT	Post GMT 1st	Post GMT 2nd	Pre	Post 1st	Post 2nd	Pre	Post 1st	Post 2nd
USA[1]	15	B/Florida/4/2006	Yam	15	15	5	7	9	0	15	15	0	0	0
	14	B/Sendai-H/114/2007	Yam	7	21	5	6	10	0	7	14	0	0	0
	15	B/Bangladesh/3333/2007	Yam	15	15	5	6	6	0	8	8	0	0	0
	15	B/Malaysia/2506/2004*	Vic	23	77	5	11	55	0	23	77	0	13	33
	15	B/Pennsylvania/5/2007	Vic	15	69	5	10	58	0	23	77	0	13	33
USA[2]	29	B/Florida/4/2006	Yam	N/A	31	5	N/A	12	0	N/A	24	0	N/A	7
	29	B/Sendai-H/114/2007	Yam	N/A	34	5	N/A	13	0	N/A	28	0	N/A	7
	29	B/Bangladesh/3333/2007	Yam	N/A	14	5	N/A	7	0	N/A	7	0	N/A	0
	29	B/Malaysia/2506/2004*	Vic	N/A	72	8	N/A	65	14	N/A	72	0	N/A	28
	29	B/Pennsylvania/5/2007	Vic	N/A	66	8	N/A	63	14	N/A	69	0	N/A	28

Preliminary Data 02/01/08

1. Sera were kindly provided by Virginia Commonwealth University, Medical Center, Department of Pediatrics. The populations were vaccinated with 2 doses of the 2007-2008 trivalent influenza vaccine containing 7.5ug each of A/Wisconsin/67/2005 X161B (H3N2)-like, A/Solomon Islands/03/2007(H1N1)-like, and B/Malaysia/2506/2004-like hemagglutinin.
2. Sera were kindly provided by Dr. Zhiping Ye, FDA, Bethesda, MD. The populations were vaccinated with the 2007-2008 trivalent influenza vaccine containing 15ug each of A/Wisconsin/67/2005 X161B (H3N2)-like, A/Solomon Islands/03/2006 (H1N1)-like, and B/Malaysia/2506/2004-like hemagglutinin.

* B component of the vaccine.

Note: All B serology antigens were ether treated.

Summary of influenza B

- Influenza B outbreaks were reported in several countries.
- Viruses of both B/Victoria/2/87 and B/Yamagata/16/88 lineages were reported in many countries but B/Yamagata/16/88 lineage viruses predominated.
- For the B/Victoria/2/87 lineage viruses, the majority of recent isolates were antigenically similar to B/Malaysia/2506/2004 or B/Ohio/1/2005 (B/Malaysia/2506/2004-like reference virus).
- Most of the recent B/Yamagata/16/88 lineage viruses were antigenically similar to B/Florida/4/2006.