



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

February 18-19, 2004

Bethesda, MD

**WHO COLLABORATING CENTER FOR SURVEILLANCE,
EPIDEMIOLOGY AND CONTROL OF INFLUENZA**

**Influenza Branch
Division of Viral and Rickettsial Diseases
National Center for Infectious Diseases
Centers for Disease Control and Prevention
Atlanta, GA 30333**

US Surveillance

Summary of Influenza Surveillance, United States September 28, 2003 – January 31, 2004*

Influenza activity in the United States began uncommonly early and has been moderately severe. Influenza A viruses have predominated (99.4%) in all 9 surveillance regions during the 2003-04 season. The majority of influenza viruses subtyped were influenza A (H3N2). Influenza B viruses have been isolated in all 9 surveillance regions, but only the South Atlantic and Mountain regions have reported more than 10 influenza B viruses for the season. The percentage of specimens testing positive for influenza peaked at 36.0% during the week ending December 6, 2003. The percentage of outpatient visits for influenza-like illness (ILI) peaked at 7.8% during the week ending December 27, 2003 and pneumonia and influenza mortality peaked at 10.3% during the weeks ending January 10 and January 17.

WHO and NREVSS Collaborating Laboratories

Since September 28, WHO and NREVSS laboratories have tested 87,333 specimens for influenza viruses, of which 22,199 (25.4%) were positive. Of these, 22,067 (99.4%) were influenza A viruses, and 132 (0.6%) were influenza B viruses. Of the 22,067 influenza A viruses, 5,782 (26.2%) have been subtyped; 5,780 (99.9%) were influenza A (H3N2) viruses and two (0.1%) was an influenza A (H1) virus. The percentage of specimens testing positive for influenza first exceeded 10% during the week ending October 25, 2003 (19.1%), peaked at 36.0% during the week ending December 6, and remained above 10% until the week ending January 17, 2004 (8.9%). For the week ending January 31, WHO and NREVSS laboratories reported 1,213 specimens tested for influenza viruses, and 76 (6.3%) were positive.

Pneumonia and Influenza Mortality (122 Cities)

The percentage of deaths attributed to pneumonia and influenza (P&I) peaked at 10.3% during the weeks ending January 10 and 17. Although the percentage of deaths due to pneumonia and influenza has declined in recent weeks, the percentage during the week ending January 31 (9.3%) remains above the national baseline (8.2%).

Sentinel Provider Network

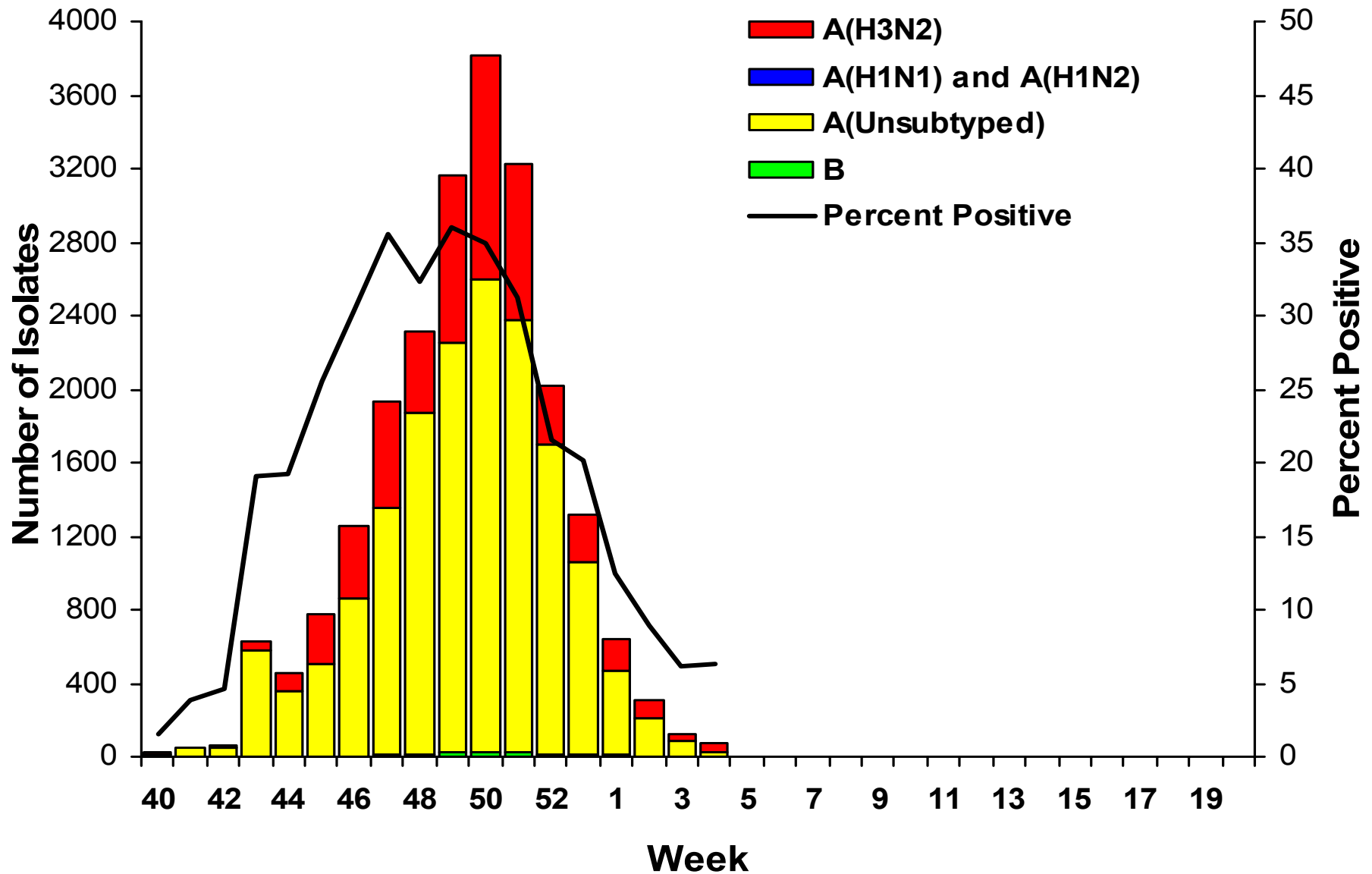
The national percentage of patient visits for ILI first exceeded the national baseline of 2.5% during the week ending November 15, 2003 and remained above the baseline for 9 consecutive weeks before declining to 2.0% during the week ending January 17, 2004. The peak occurred during the week ending December 27, 2003 (7.8%). On a regional level the timing of peak ILI activity ranged from the week ending November 22 in the West South Central region to the week ending December 27 in the New England, Mid Atlantic, East North Central and South Atlantic regions. For the week ending January 31, 2004, the national percentage of patient visits for ILI was 1.9%. This is the third consecutive week below the national baseline of 2.5%.

State and Territorial Epidemiologists

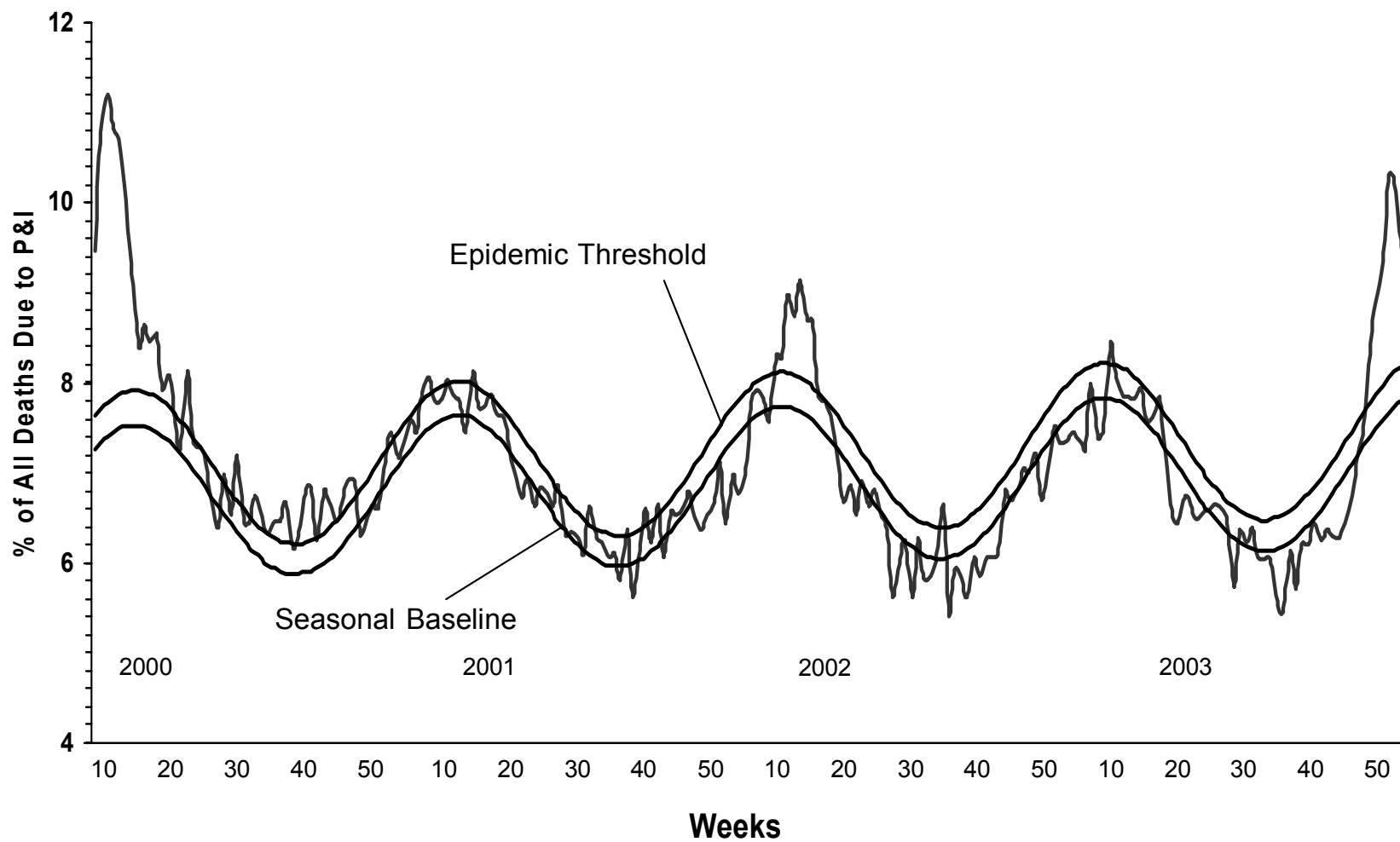
Nationally, influenza activity as reported by state and territorial epidemiologists peaked during the week ending December 20 when 45 states reported widespread activity. Widespread activity was first reported by Texas during the week ending October 11, 2003 and remained widespread for 10 consecutive weeks. During the week ending January 31, no states reported widespread activity and 11 states reporting regional activity.

Report prepared: January 31, 2004

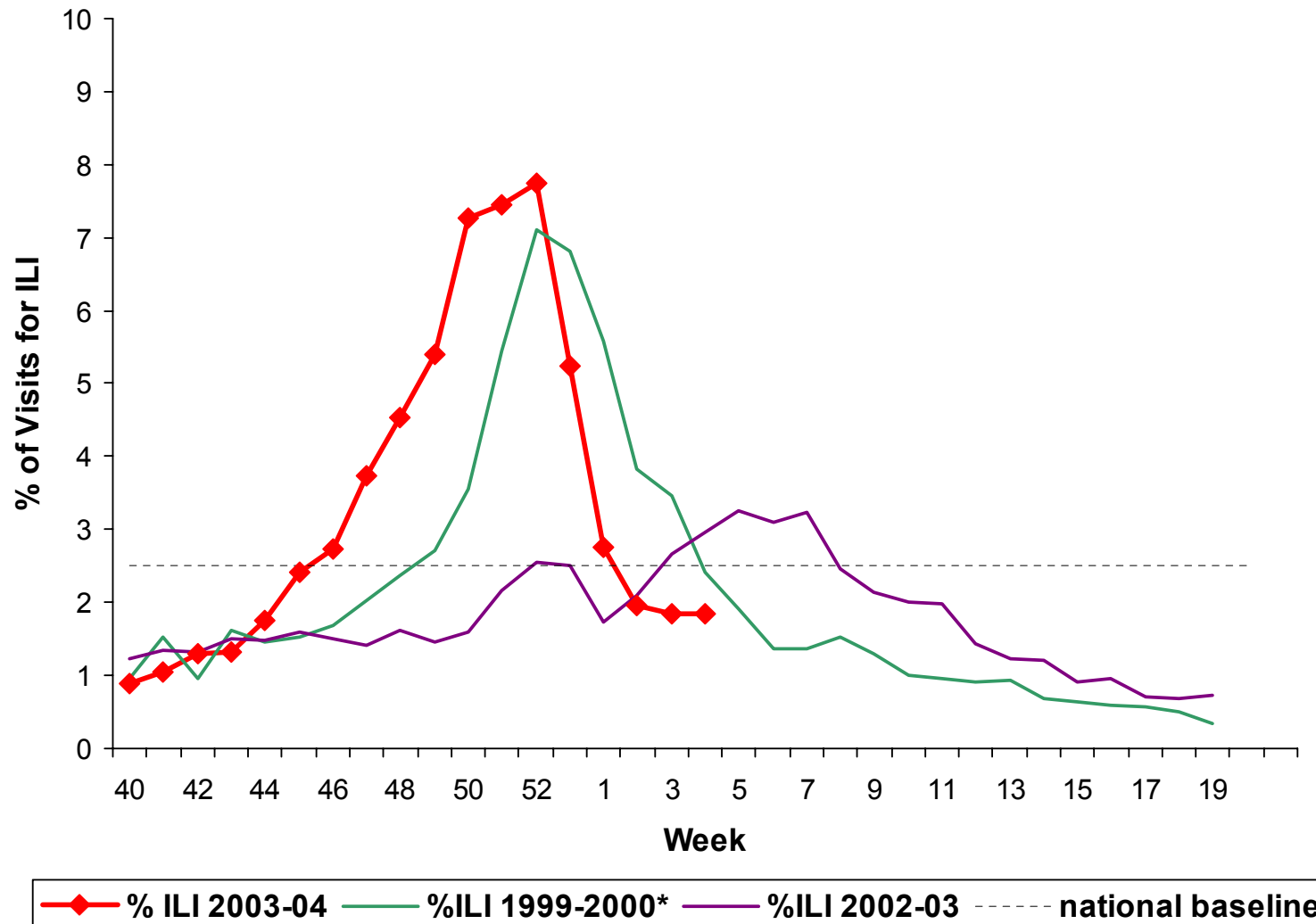
WHO/NREVSS Collaborating Laboratories National Summary, 2003-04



Pneumonia and Influenza Mortality for 122 U.S. Cities Week Ending 01/31/2004



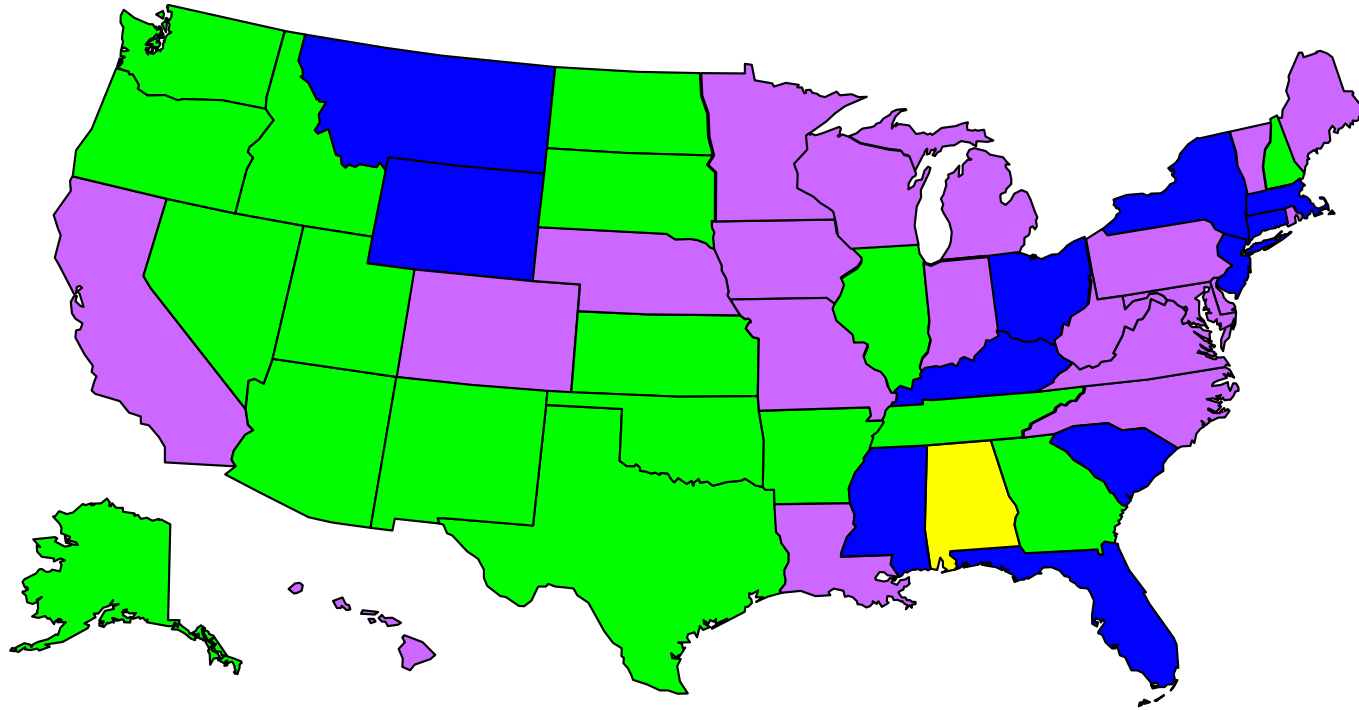
Percentage of Visits for Influenza-like Illness Reported by Sentinel Providers National Summary, 2003-04



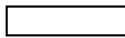
* The 1999-2000 season was selected for comparison because it was the most recent A(H3N2) season of moderate severity.

Weekly Influenza Activity Estimates Reported by State & Territorial Epidemiologists

Week ending January 31, 2004 - Week 4



No Report



No Activity



Sporadic



Local Activity



Regional



Widespread



Influenza A(H1) Viruses

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA H1 VIRUSES (02/06/04)

STRAIN DESIGNATION		REFERENCE FERRET ANTISERA									Date collected	Passage	NA
		A	B	C	D	E	F	G	H	I			
REFERENCE ANTIGENS		BJ/262	NC/20	FU/156	CI/8885	HI/10	CI/9848	PE/3135	NE/52	HI/15			
1	A/BEIJING/262/95	640	640	320	320	320	160	80	320	80	01/09/95	E3/E3	N1
2	A/NEW CALEDONIA/20/99*	160	1280	320	320	160	160	160	320	80	06/09/99	E4/E2	N1
3	A/FUJIAN/156/2000	80	640	320	160	160	80	80	640	80	08/25/00	E2/E2	N1
4	A/CHILE/8885/2002	80	640	160	160	80	80	20	160	80	07/03/02	E1/E4	N1
5	A/HAWAII/10/2002	160	640	160	160	320	80	20	320	40	03/22/02	E3	N2
6	A/CHILE/9848/2002	40	320	80	160	80	80	20	160	40	07/17/02	E4/E2	N1
7	A/PERU/3135/2003	160	80	160	10	20	20	640	40	160	04/09/03	X/C3	N1
8	A/NEIMENGGU/52/2002	40	640	320	80	80	80	40	320	80	01/25/02	E2/E4	N1
9	A/HAWAII/15/2001	40	40	80	20	20	20	320	5	160	02/17/01	M2/C3	N1
TEST ANTIGENS													
10	A/VIRGINIA/20/2003	160	640	160	640	320	80	80	320	40	11/05/03	XC/C1	N2
11	A/BELEM/84038/2003	640	1280	320	320	640	160	80	640	80	05/08/03	X2/C2	n.d.
12	A/COLOMBIA/3664/2003	320	1280	320	320	160	320	320	640	80	08/14/02	X3/C1	n.d.
13	A/COLOMBIA/3736/2003	320	1280	640	320	320	160	320	1280	160	10/02/02	X3/C1	n.d.
14	A/COLOMBIA/3745/2003	320	1280	640	160	160	160	320	1280	80	10/04/02	X3/C1	n.d.
15	A/DAKAR/85/2003	320	1280	640	320	320	160	320	1280	160	10/09/03	C2\1/C1	n.d.
16	A/NAGANO/1328/2003	160	1280	640	160	160	160	160	640	80	UNKN	C2/C1	n.d.
17	A/CANADA/657/03	320	1280	640	160	160	160	640	1280	160	10/24/03	X1/C1	n.d.
18	A/SINGAPORE/66/2003	320	640	320	160	160	80	160	1280	80	09/02/03	C2/C1	n.d.
19	A/ICELAND/122/2003	320	640	160	320	320	160	40	320	80	12/06/03	C3\1/C1	n.d.
20	A/CANADA/740/2003	320	640	160	320	320	80	40	320	80	11/16/03	X1/C1	n.d.
21	A/PERU/5003/2003	80	640	160	320	80	160	40	320	80	09/19/03	X/C1	n.d.

* Serology antigens

Influenza A(H1) Isolates Characterized by CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 2002 - September 2002							
A/N.Caledonia/20/99-like	4	2		7	40	1	54 (77%)
A/N.Caledon./20/99-like (low)	2				14		16 (23%)
						Total	70
October 2002 - March 2003							
A/N.Caledonia/20/99-like	281	34	9	8	17	1	350 (98%)
A/N.Caledon./20/99-like (low)	4	1			2		7 (2%)
						Total	357
April 2003 – September 2003							
A/N.Caledonia/20/99-like	10	4	3		105	2	124 (95%)
A/N.Caledon./20/99-like (low)					6		6 (5%)
						Total	130
October 2003 – February 2004							
A/N.Caledonia/20/99-like	2	2	1	1	2	1	9 (90%)
A/N.Caledon./20/99-like (low)			1				1 (10%)
						Total	10
Total	303	43	14	16	186	5	567

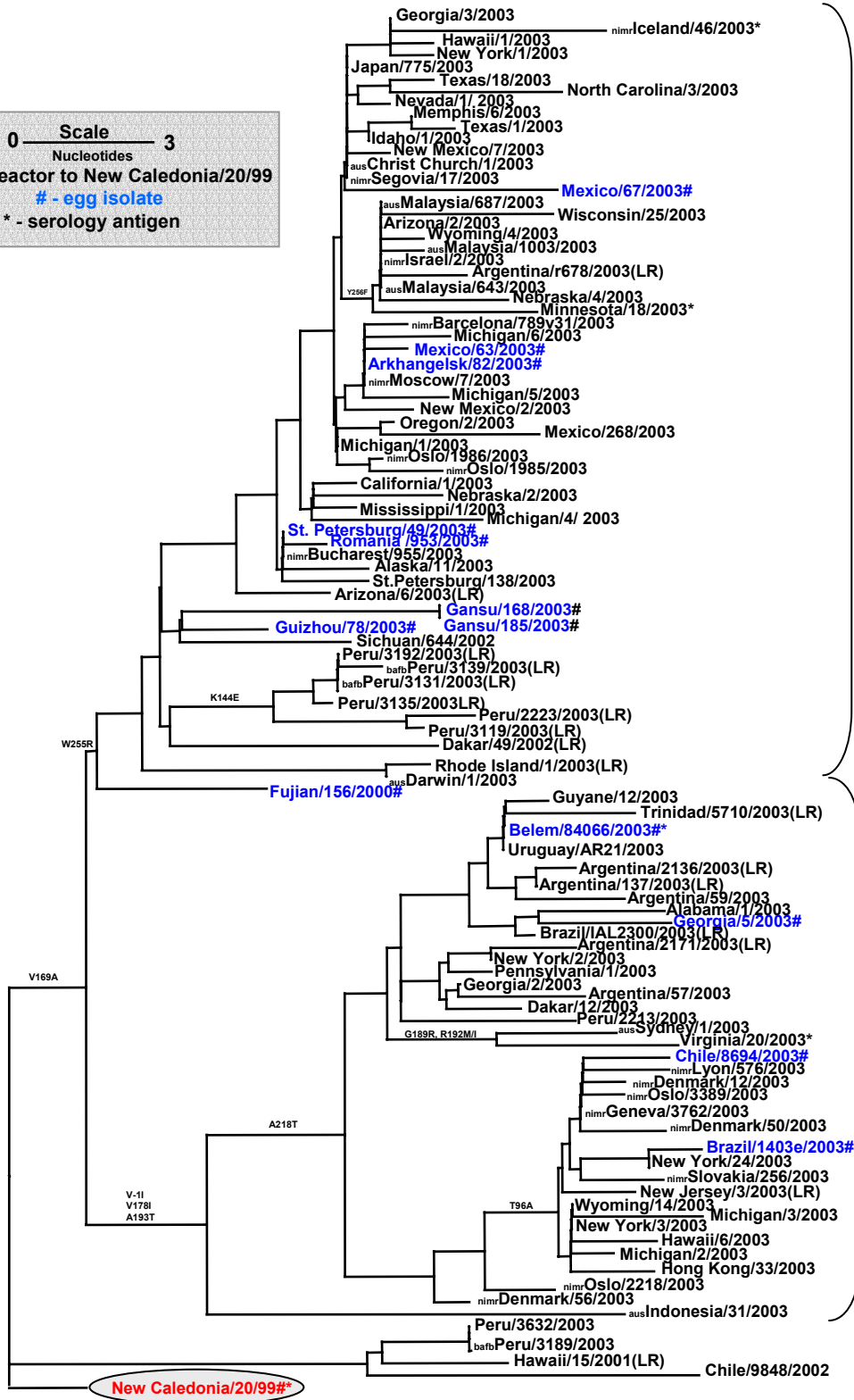
Influenza A(H1N1) & A(H1N2) Isolates Identified by CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 2002 - September 2002							
H1N1	5	2		7	51	1	66 (94%)
H1N2	1				3		4 (6%)
						Total	70
October 2002 - March 2003							
H1N1	209	24	9	7	3	1	253 (71%)
H1N2	76	11		1	16		104 (29%)
						Total	357
April 2003 - September 2003							
H1N1	8	4	3		43	1	59 (47%)
H1N2	2				64	1	67 (53%)
						Total	126
October 2003 – February 2004							
H1N1	1					1	2 (40%)
H1N2	1	2					3 (60%)
						Total	5
Total	303	43	12	15	180	5	558

Evolutionary Relationships Among Influenza A (H1 subtype) Hemagglutinin Genes (HA1 domain), 2004

0 — Scale — 3
Nucleotides

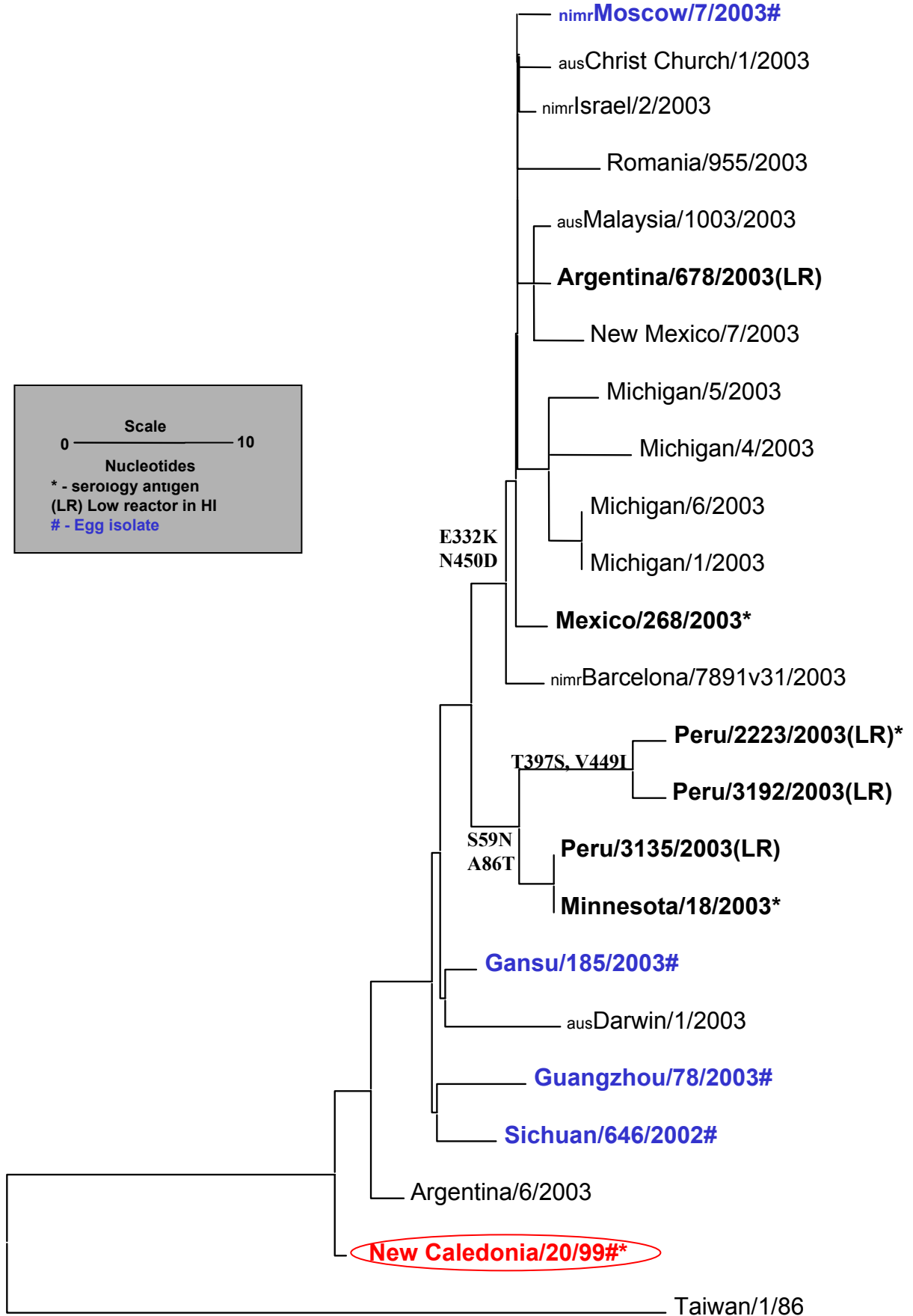
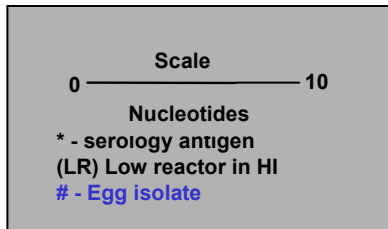
LR - low reactor to New Caledonia/20/99
- egg isolate
* - serology antigen



H1N1

H1N2

Evolutionary Relationships Among Influenza A N1 Neuraminidase Genes



**HI Antibody Responses to the H1* Component of the 2003 -2004 Influenza Vaccine
ADULT POPULATIONS**

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
US ¹	24						
		A/New Caledonia/20/99 IVR-116*	35	11	36	13	58
		A/Minnesota/18/2003	26	25	76	52	79
		A/Virginia/20/2003**	43	10	29	13	50
		A/Belem/84066/2003**	39	7	23	0	42
UK ²	24						
		A/New Caledonia/20/99 IVR-116*	58	5	27	0	54
		A/Minnesota/18/2003	67	7	44	8	63
		A/Virginia/20/2003**	63	5	22	0	42
		A/Belem/84066/2003**	50	5	17	0	29
Japan ³	25						
		A/New Caledonia/20/99 IVR-116*	44	8	19	8	32
		A/Minnesota/18/2003	48	10	30	20	52
		A/Virginia/20/2003**	48	6	16	4	32
		A/Belem/84066/2003**	36	6	13	0	20

1. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

2. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Shangdong/07/97-like hemagglutinin.

3. Sera were kindly provided by Dr. Takato Odagiri, WHO Collaborating Center, Tokyo, Japan. The populations were vaccinated with the 2003-2004 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

* A/New Caledonia/20/99 is the H1N1 component of the vaccine.

** H1N2

**HI Antibody Responses to the H1* Component of the 2003 -2004 Influenza Vaccine
ELDERLY POPULATIONS**

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
US ¹	23						
		A/New Caledonia/20/99 IVR-116*	19	9	14	10	22
		A/Minnesota/18/2003	14	13	23	19	39
		A/Virginia/20/2003**	10	10	15	10	26
		A/Belem/84066/2003**	10	7	9	5	9
UK ²	24						
		A/New Caledonia/20/99 IVR-116*	25	5	12	0	21
		A/Minnesota/18/2003	42	5	15	0	21
		A/Virginia/20/2003**	33	5	12	5	21
		A/Belem/84066/2003**	25	5	8	0	13
Japan ³	30						
		A/New Caledonia/20/99 IVR-116*	20	8	13	7	20
		A/Minnesota/18/2003	27	9	16	13	30
		A/Virginia/20/2003**	27	8	16	7	30
		A/Belem/84066/2003**	27	6	11	7	17

1. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

2. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Shangdong/07/97-like hemagglutinin.

3. Sera were kindly provided by Dr. Takato Odagiri, WHO Collaborating Center, Tokyo, Japan. The populations were vaccinated with the 2003-2004 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

* A/New Caledonia/20/99 is the H1N1 component of the vaccine.

** H1N2

**Hemagglutination Inhibition Antibody Responses to the
H1* Component of the 2003 -2004 Influenza Vaccine
PEDIATRIC POPULATION**

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
US ¹	25						
		A/New Caledonia/20/99 IVR-116*	56	5	18	0	32
		A/Minnesota/18/2003	22	6	10	4	16
		A/Virginia/20/2003**	63	5	35	0	48
		A/Belem/84066/2003**	41	5	13	0	20

1. Sera were kindly provided by Dr. Christine Turley, UTMB, Galveston, TX. Children 6-23 months of age were vaccinated twice with the 2003-2004 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

* A/New Caledonia/20/99 is the H1N1 component of the vaccine.

** H1N2

Influenza A(H3N2) Viruses

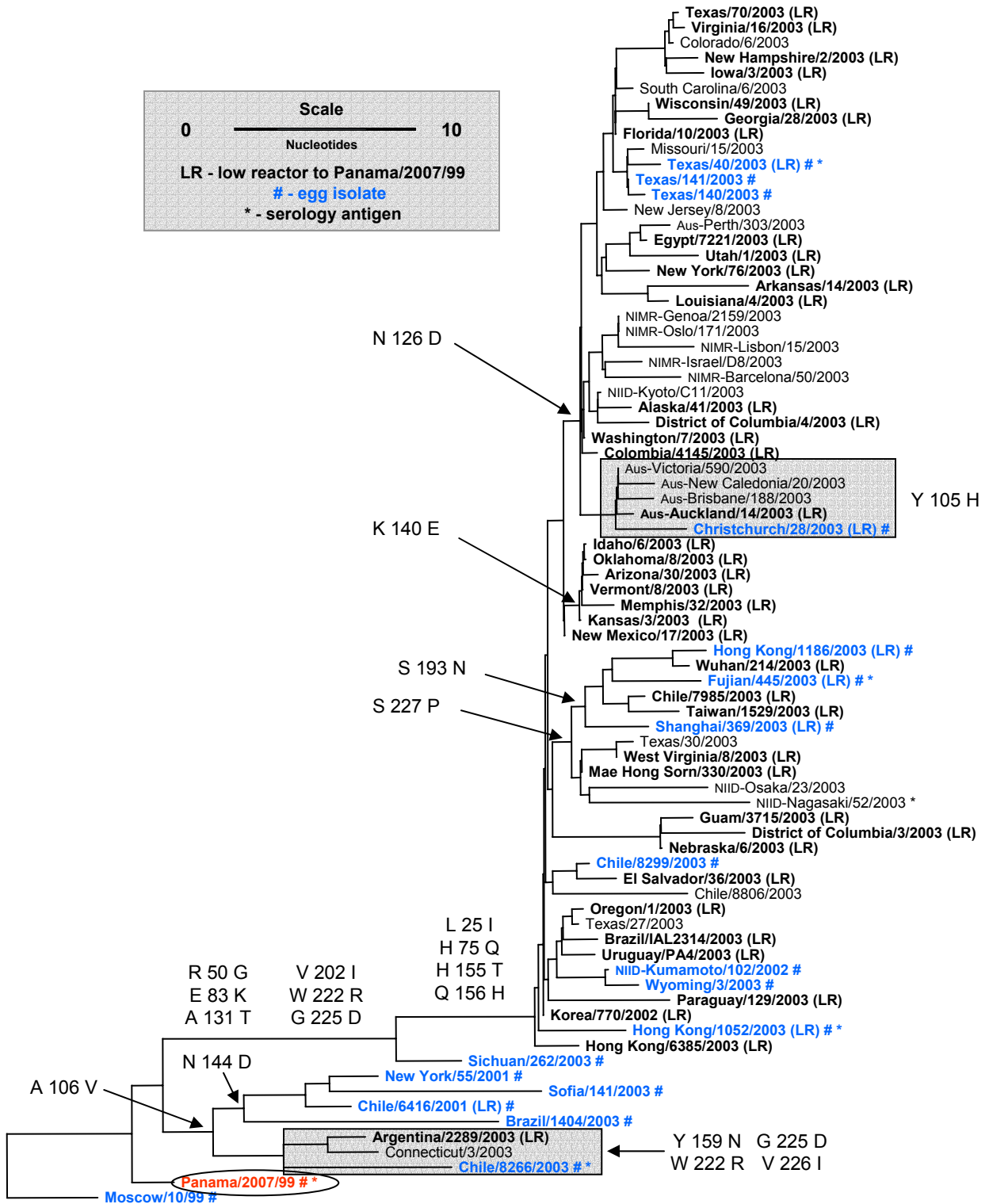
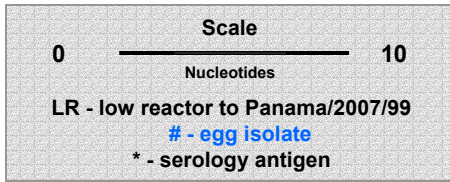
HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA H3 VIRUSES (01/30/04)

		REFERENCE FERRET ANTISERA										Date collected	Passage
REFERENCE ANTIGENS		A PN/2007	B FJ/411	C KO/770	D WY/03	E KUM/102	F LA/04	G TX/40	H SH/369	I HK/1186	J TW/1529		
1	A/PANAMA/2007/99*	1280	160	160	320	160	160	640	40	160	160	07/12/99	E6
2	A/FUJIAN/411/2002	320	2560	2560	2560	1280	2560	2560	640	1280	640	08/11/02	X/C4
3	A/KOREA/770/2002	160	1280	1280	2560	1280	1280	1280	320	1280	640	12/02/02	X/C4
4	A/WYOMING/3/2003	320	1280	1280	2560	1280	2560	2560	320	640	640	02/13/03	SpfCK2/E2
5	A/KUMAMOTO/102/2002	320	1280	1280	2560	1280	2560	2560	320	1280	640	12/25/02	E4/E1
6	A/LOUISIANA/04/2003	160	320	320	640	160	640	1280	160	320	160	10/21/03	X/C2
7	A/TEXAS/40/2004*	640	2560	2560	2560	1280	2560	2560	320	1280	1280	10/02/03	SpfCKE3
8	A/TEXAS/141/2004	640	1280	1280	2560	640	1280	2560	160	640	640	10/06/03	SpfCKE3
9	A/SHANGHAI/369/2003	160	160	320	320	160	80	640	320	160	320	04/16/03	E2/E3
10	A/HONG KONG/1186/2003	40	160	320	320	160	160	640	80	320	160	04/04/03	SPFCK3E4
11	A/TAIWAN/1529/2003	80	320	320	640	320	160	640	160	320	320	09/07/03	M2/C3
TEST ANTIGENS													
12	A/IOWA/06/2003	320	1280	1280	1280	1280	1280	2560	320	640	320	12/12/03	X1/C2
13	A/VERMONT/09/2003	320	640	640	1280	640	640	1280	160	320	160	12/18/03	C2
14	A/WYOMING/55/2003	80	160	320	320	160	320	640	80	160	80	12/01/03	X1/C2
15	A/RHODE ISL./04/2003	160	320	320	320	160	320	640	80	80	80	12/09/03	X1/C2
16	A/VERMONT/10/2003	160	320	320	640	320	320	640	80	80	80	12/19/03	C2
17	A/NEW YORK/103/2003	160	160	320	320	320	320	640	80	80	80	12/22/03	M1/C1
18	A/ARIZONA/47/2003	40	160	160	320	160	320	640	40	80	80	12/14/03	MX/C1
19	A/VERMONT/06/2003	80	160	160	320	160	160	320	40	80	40	12/18/03	C1
20	A/PERU/5004/2003	80	320	640	640	320	80	320	160	320	160	09/20/03	X/C1
22	A/PERU/5035/2003	160	640	640	1280	320	160	320	320	320	160	10/11/03	X/C1
23	A/PERU/5049/2003	160	320	640	320	160	160	320	160	160	160	11/20/03	X/C1
24	A/NAGASAKI/52/2003	320	1280	2560	2560	1280	640	2560	320	640	640	UNKN	C5/C1
25	A/THAILAND/0282/2003	320	1280	2560	5120	2560	640	1280	640	1280	640	UNKN	X/C1
27	A/HEBEI/187/2003	160	1280	1280	1280	1280	640	2560	640	1280	640	12/08/03	C1/C1
28	A/HEBEI/191/2003	160	1280	1280	2560	1280	1280	1280	320	640	320	12/09/03	C1/C1
29	A/QATAR/5681/2003	80	1280	1280	2560	1280	1280	2560	160	640	640	12/18/03	X/C2
31	A/KOREA/5834/2003	320	1280	1280	2560	640	1280	1280	320	320	640	12/18/03	X/C1
32	A/THAILAND/0332/2003	320	1280	1280	1280	640	640	1280	320	1280	640	UNKN	X/C1
33	A/THAILAND/0812/2003	320	640	1280	1280	640	320	1280	320	640	640	UNKN	X/C1
34	A/HEBEI/152/2003	80	640	640	1280	640	320	320	320	640	160	11/02/03	C1/C1
36	A/LIAONING/8/2003	80	640	640	1280	640	640	640	160	320	320	11/23/03	C3/C1
37	A/JAPAN/5684/2003	160	640	640	1280	640	1280	1280	160	320	320	12/19/03	X/C1
38	A/KOREA/5297/2003	80	320	640	640	320	320	640	160	160	160	11/22/03	X/C1
39	A/KOREA/5624/2003	80	640	640	640	320	320	320	80	160	80	12/14/03	X/C1
40	A/FANGSHAN/4/2003	80	320	320	640	320	160	320	160	320	160	12/04/03	C2/C1
41	A/BEIJING/170/2003	80	320	320	640	320	320	640	160	160	160	12/05/03	C2/C1
42	A/ANHUI/546/2003	80	320	320	320	320	80	160	160	160	160	11/05/03	C3/C1
43	A/JAPAN/5685/2003	20	160	320	320	160	80	80	80	160	80	12/19/03	X/C1
44	A/KOREA/5842/2003	80	160	320	160	160	160	320	80	160	80	12/22/03	X/C1
45	A/KYRGYZTAN/5863/2003	160	320	320	640	320	640	1280	80	160	160	12/18/03	X/C1

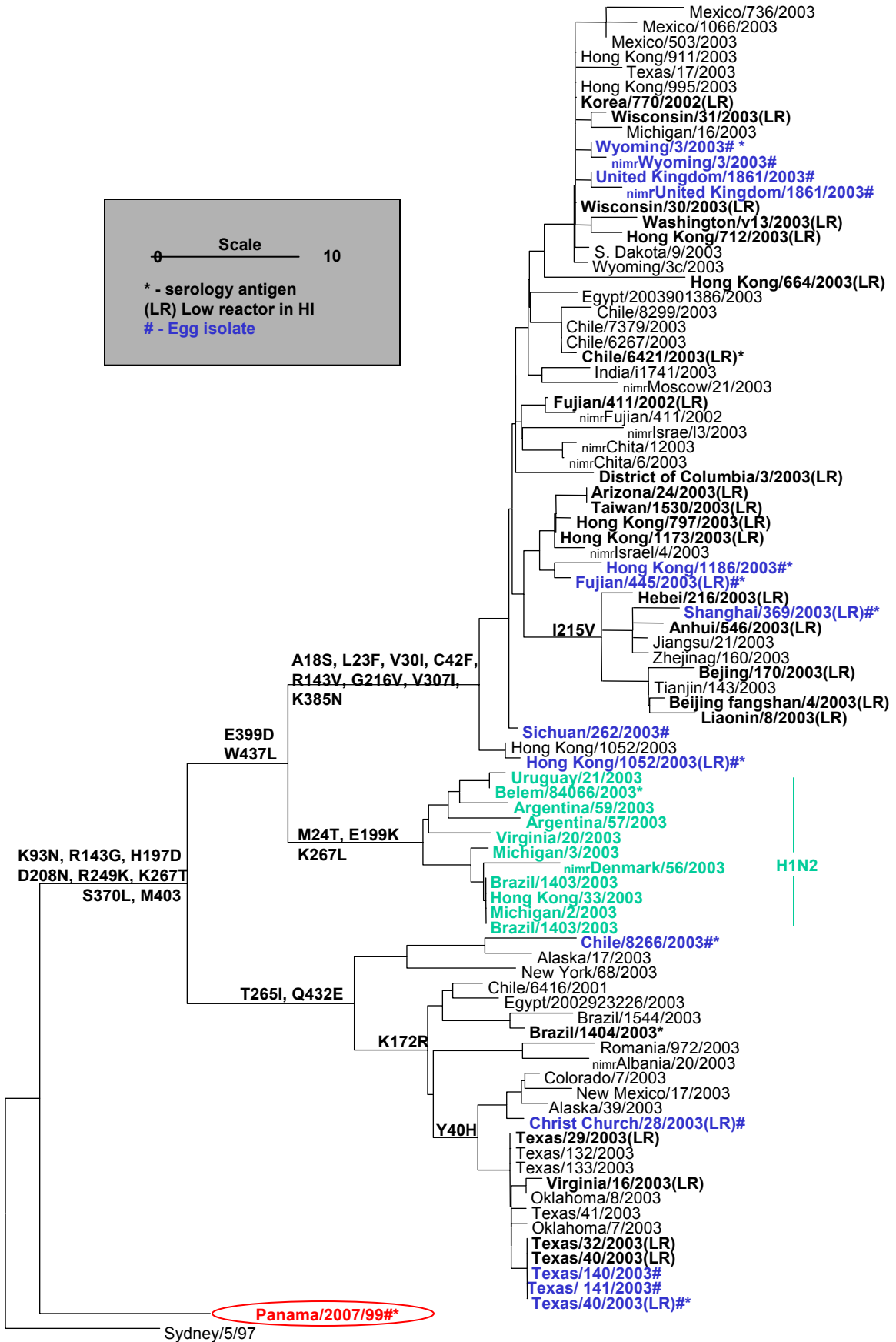
Influenza A(H3N2) Isolates Characterized by CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 2002 - September 2002							
A/Panama/2007/99-like	15	1	3	108	28	12	167 (89%)
A/Panama/2007/99-like (low)				8	3	9	20 (11%)
						Total	187
October 2002 - March 2003							
A/Panama/2007/99-like	101	8	22	128	7	16	282 (72%)
A/Panama/2007/99-like (low)	3			19		1	23 (6%)
A/Fujian/411/2002-like	16	7	8	47	5	2	85 (22%)
						Total	390
April 2003 – September 2003							
A/Panama/2007/99-like	41	13		29	171	1	255 (58%)
A/Panama/2007/99-like (low)	1		1		3		5 (1%)
A/Fujian/411/2002-like	31	10		79	48	14	170 (40%)
						Total	429
October 2003 – February 2004							
A/Panama/2007/99-like	106	1	3	7	1		118 (16%)
A/Fujian/411/2002-like	480	3	18	76	10	15	602 (81%)
						Total	720
Total	662	43	55	501	276	70	1739

Evolutionary Relationships Among Influenza A (H3 subtype) Hemagglutinin Genes (HA1 domain), 2004



Evolutionary Relationships Among Influenza A N2 Neuraminidase Genes



**HI Antibody Responses to the H3* Component of the 2003 -2004 Influenza Vaccine
ADULT POPULATIONS**

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
USA ¹	24	A/Panama/2007/99 Resvir-17*	26	51	116	74	92
		A/Texas/40/2003	35	26	64	48	75
		A/Fujian/445/2003	43	20	60	35	75
		A/Chile/82660/2003	30	9	22	9	33
		A/Nagasaki/52/2003	26	18	38	35	63
UK ²	24	A/Panama/2007/99 Resvir-17*	71	7	36	8	42
		A/Texas/40/2003	46	6	16	0	33
		A/Fujian/445/2003	54	5	18	0	25
		A/Chile/82660/2003	21	5	9	0	21
		A/Nagasaki/52/2003	42	5	15	0	25
Japan ³	25	A/Panama/2007/99 Resvir-17*	24	26	50	36	72
		A/Texas/40/2003	16	21	35	28	64
		A/Fujian/445/2003	12	16	27	28	56
		A/Chile/82660/2003	12	6	9	0	4
		A/Nagasaki/52/2003	20	14	21	28	48
Australia ⁴	24	A/Panama/2007/99 Resvir-17*	71	16	110	25	92
		A/Texas/40/2003	79	12	80	17	96
		A/Fujian/445/2003	75	10	76	13	92
		A/Chile/82660/2003	57	6	27	0	39
		A/Nagasaki/52/2003	78	10	65	17	87

1. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

2. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Shangdong/07/97-like hemagglutinin.

3. Sera were kindly provided by Dr. Takato Odagiri, WHO Collaborating Center, Tokyo, Japan. The populations were vaccinated with the 2003-2004 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

4. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2003 trivalent influenza vaccine containing 15: g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Shangdong/07/97-like hemagglutinin.

* A/Panama/2007/99 is the H3N2 component of the vaccine.

**HI Antibody Responses to the H3* Component of the 2003 -2004 Influenza Vaccine
ELDERLY POPULATIONS**

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
USA ¹	23	A/Panama/2007/99 Resvir-17*	24	43	93	76	100
		A/Texas/40/2003	14	27	40	62	74
		A/Fujian/445/2003	24	18	32	38	57
		A/Chile/82660/2003	24	8	12	5	9
		A/Nagasaki/52/2003	19	18	27	38	52
UK ²	24	A/Panama/2007/99 Resvir-17*	54	9	30	13	54
		A/Texas/40/2003	46	7	20	8	42
		A/Fujian/445/2003	46	7	20	4	42
		A/Chile/82660/2003	38	6	11	0	17
		A/Nagasaki/52/2003	42	7	16	13	33
Japan ³	30	A/Panama/2007/99 Resvir-17*	20	30	53	57	73
		A/Texas/40/2003	13	27	42	47	73
		A/Fujian/445/2003	10	30	41	60	73
		A/Chile/82660/2003	3	9	10	13	17
		A/Nagasaki/52/2003	10	18	24	30	40
Australia ⁴	24	A/Panama/2007/99 Resvir-17*	25	34	92	54	75
		A/Texas/40/2003	33	20	60	38	63
		A/Fujian/445/2003	29	16	49	29	63
		A/Chile/82660/2003	25	8	18	8	29
		A/Nagasaki/52/2003	46	16	50	29	67

1. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

2. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Shangdong/07/97-like hemagglutinin.

3. Sera were kindly provided by Dr. Takato Odagiri, WHO Collaborating Center, Tokyo, Japan. The populations were vaccinated with the 2003-2004 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

4. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2003 trivalent influenza vaccine containing 15: g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Shangdong/07/97-like hemagglutinin.

* A/Panama/2007/99 is the H3N2 component of the vaccine.

**HI Antibody Responses to the H3* Component of the 2003 -2004 Influenza Vaccine
PEDIATRIC POPULATION**

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
USA ¹	25						
		A/Panama/2007/99 Resvir-17	63	5	50	0	64
		A/Texas/40/2003	44	5	33	0	48
		A/Fujian/445/2003	44	5	31	0	48
		A/Chile/82660/2003	41	5	13	0	24
A/Nagasaki/52/2003	44	5	29	0	48		

1. Sera were kindly provided by Dr. Christine Turley, UTMB, Galveston, TX. Children 6-23 months of age were vaccinated twice with the 2003-2004 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

* A/Panama/2007/99 is the H3N2 component of the vaccine.

**Hemagglutination Inhibition Antibody Responses to the H3* Component
Among Students Vaccinated with 2003-2004 Inactivated Vaccine**

Vaccine	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vacc.	Post Vacc.
Inactivated Vaccine ¹	49	A/Panama/2007/99 Resvir-17*	68	13	98	24	86
		A/Wyoming/3/2003	64	10	61	36	76
		A/Fujian/445/2003	64	8	42	10	63
		A/Christchurch/28/2003	36	6	14	4	31

Preliminary Data 12/17/03

1. Sera were kindly provided by Arnold Monto, University of Michigan School of Public Health, Ann Arbor, Michigan. The students were vaccinated with the 2003-2004 trivalent influenza vaccine containing 15: g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Shangdong/07/97-like hemagglutinin.

* = Vaccine Component

Influenza B Viruses

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA TYPE B VIRUSES (01/22/04; 01/29/04)

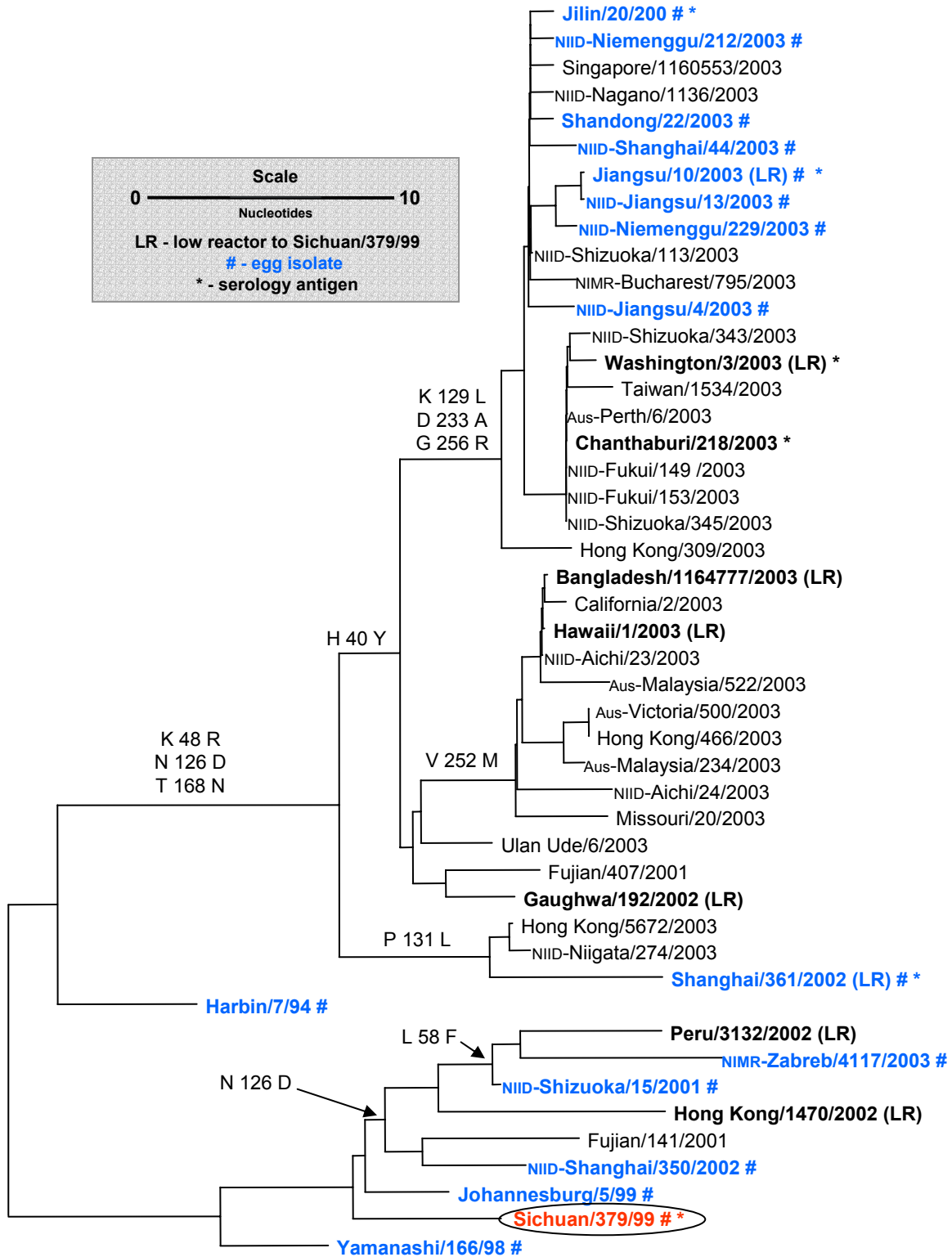
STRAIN DESIGNATION	REFERENCE FERRET ANTISERA									Date collected	Passage
	A SIC/379	B SHI/15	C SHA/07	D HK/330	E HK/1434	F BRI/32	G SC/04	H HK/553	I FUJ/203		
1 B/SICHUAN/379/99	640	320	10	10	10	20	10	5	20	12/2/1999	E2/E2
2 B/SHIZUOKA/15/2001	640	640	20	20	20	20	20	5	40	1/17/2001	E3/E3
3 B/SHANDONG/7/97	20	10	640	1280	320	1280	320	320	1280	11/3/1997	E4/E3
4 B/HONG KONG/330/2001	10	10	640	640	640	1280	320	320	1280	4/9/2001	E3
5 B/HONG KONG/1434/2002*	10	10	320	640	640	1280	160	160	1280	1/15/2002	E5
6 B/BRISBANE/32/2002	10	10	320	640	160	640	160	160	640	7/2/2002	E2/E4
7 B/S.CAROLINA/04/2003	5	5	160	80	80	320	320	160	160	2/6/2003	X1/C2
8 B/HONG KONG/553/03	5	5	160	160	80	320	320	640	320	3/31/2003	C2/C2
9 B/FUJIAN/203/2003	5	5	320	640	320	640	160	160	1280	4/12/2003	E3/E4
TEST ANTIGENS											
10 B/OMAN/3982/2003	160	160	5	5	5	5	5	5	5	6/24/2003	C2/C1
11 B/OMAN/6749/2003	160	160	5	5	5	5	5	5	5	8/13/2003	C2/C1
12 B/HAWAII/04/2003	160	160	5	5	5	5	5	5	5	10/1/2003	M2/C1
13 B/JIANGSU/10/2003	80	160	5	5	5	5	5	5	5	9/11/2003	E3/E1
14 B/NEBRASKA/05/2003	80	80	5	5	5	5	5	5	5		X1/C1
15 B/JIANGSU/10/2003*	80	160	5	5	5	5	5	5	10	9/11/2003	E3/E1
10 B/GUANGDONG/657/2003	80	160	5	5	5	5	5	5	5	9/15/2003	C2/C1
11 B/CHANTABURI/218/03	160	160	5	5	5	5	5	5	5	7/26/2003	CX/E1
12 B/HAWAII/08/2003	5	5	80	80	80	160	320	160	160	7/28/2003	M2/C1
13 B/HAWAII/09/2003	5	5	40	40	40	80	160	80	160	4/25/2003	M2/C2
14 B/HAWAII/11/2003	5	5	80	40	80	160	320	160	160	4/17/2003	M2/C1

* Serology antigens

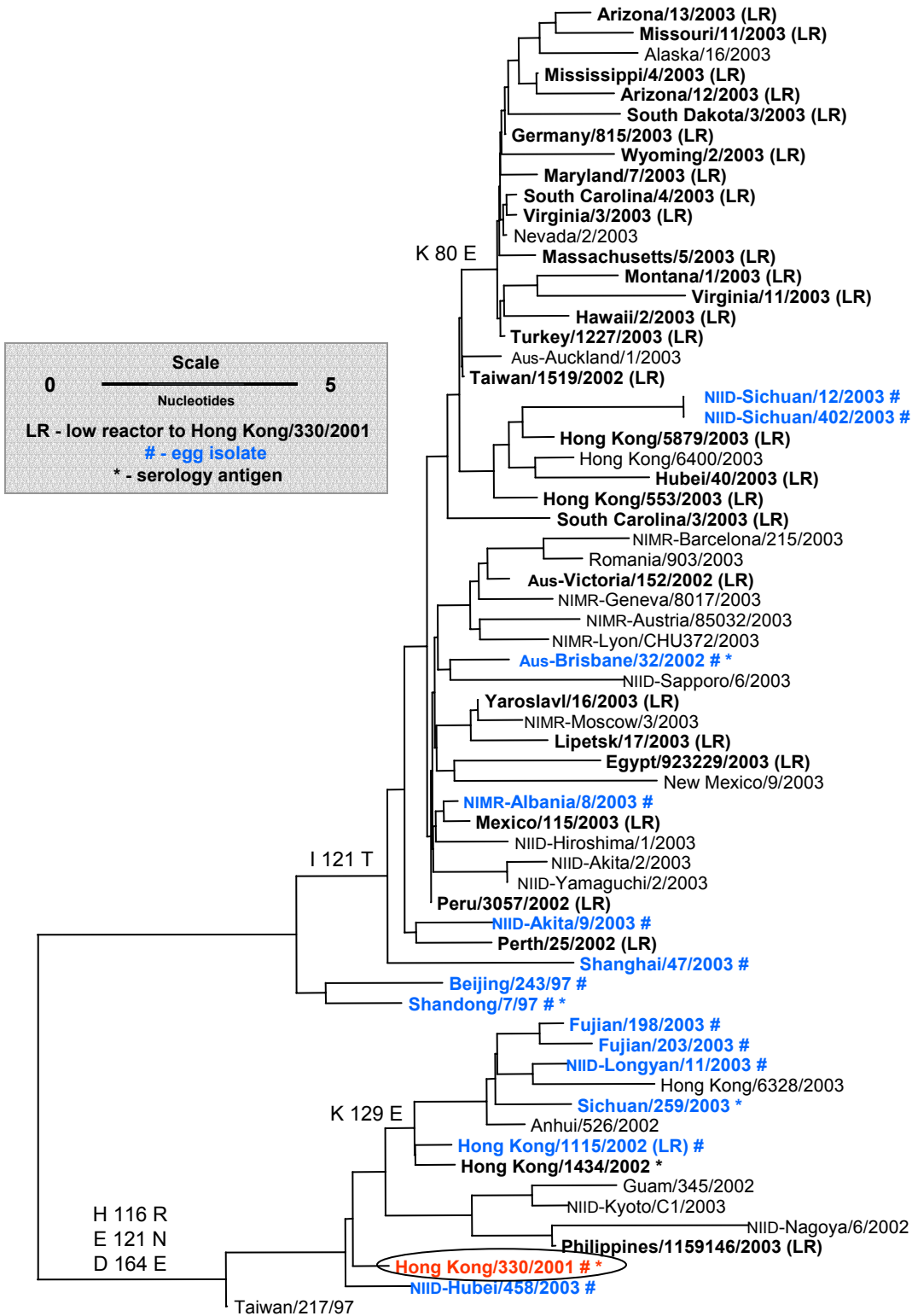
Influenza B Isolates Characterized by CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 2002 - September 2002							
B/Hong Kong/330/2001-like	56			22	59	17	154 (43%)
B/HK/330/2001-like (low)	41			68	49	16	174 (49%)
B/Sichuan/379/99-like	2			10	2		14 (4%)
B/Sichuan/379/99 (low)	1			6	8		15 (4%)
						Total	357
October 2002 - March 2003							
B/Hong Kong/330/2001-like	130		12	95	5	1	243 (52%)
B/HK/330/2001-like (low)	135	2	8	52	5	6	208 (44%)
B/Sichuan/379/99-like				10			10 (1%)
B/Sichuan/379/99 (low)	1		1	7			9 (2%)
						Total	470
April 2003 – September 2003							
B/Hong Kong/330/2001-like	5	3		4		1	13 (30%)
B/HK/330/2001-like (low)	11				1	5	17 (40%)
B/Sichuan/379/99-like				1			1 (2%)
B/Sichuan/379/99 (low)	1			10		1	12 (28%)
						Total	43
October 2003 – February 2004							
B/Hong Kong/330/2001-like	1						1 (9%)
B/HK/330/2001-like (low)					1		1 (9%)
B/Sichuan/379/99-like	2						2 (18%)
B/Sichuan/379/99 (low)	5			2			7 (64%)
						Total	11
Total	391	5	21	287	130	47	881

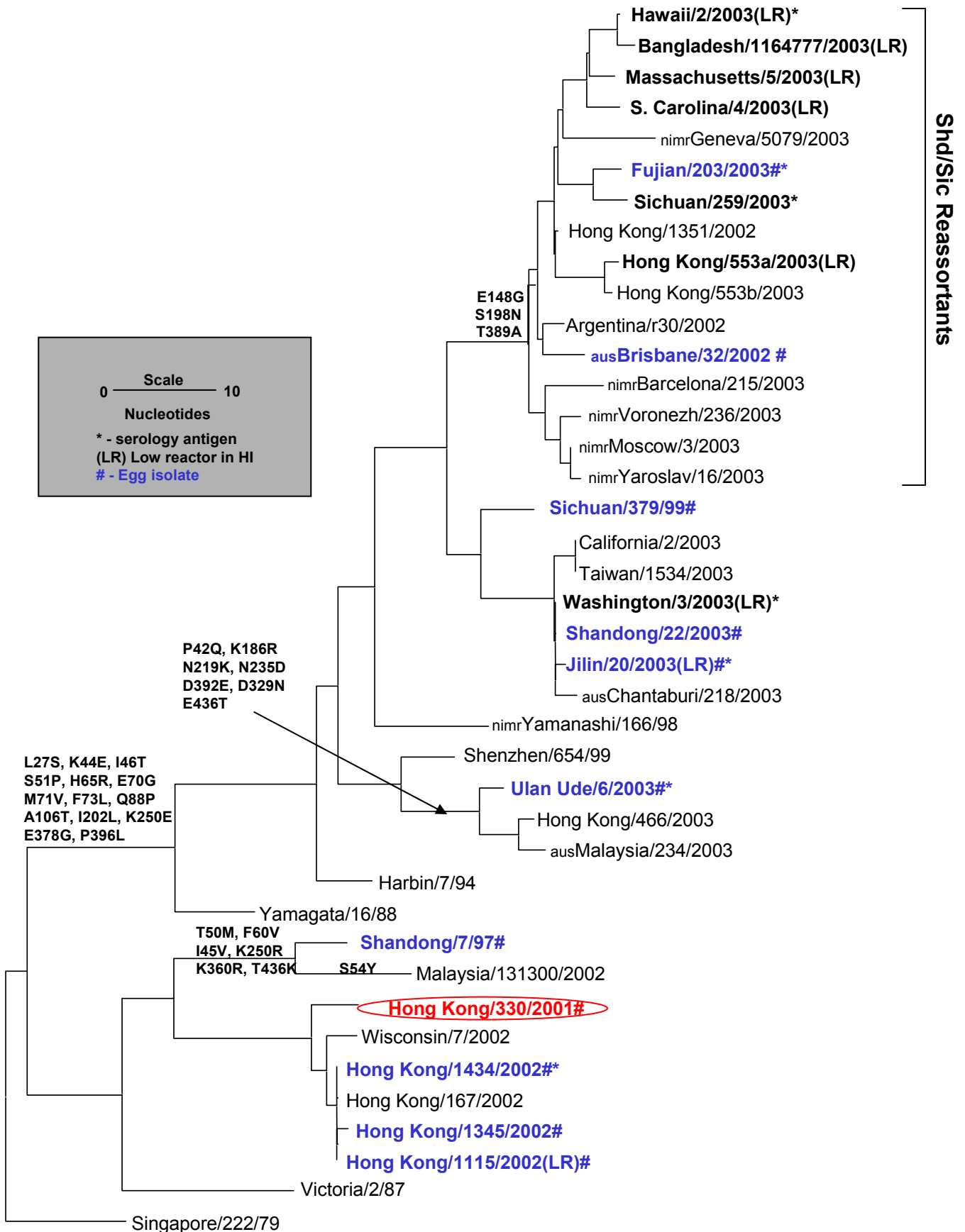
Evolutionary Relationships Among Influenza B (Yamagata lineage) Hemagglutinin Genes (HA1 domain), 2004



Evolutionary Relationships Among Influenza B (Victoria lineage) Hemagglutinin Genes (HA1 domain), 2004



Evolutionary Relationships Among Influenza B Neuraminidase Genes



HI Antibody Responses to the B* Component of the 2003 -2004 Influenza Vaccine ADULT POPULATIONS

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
USA ¹	24	B/Hong Kong/1434/2002* ET	78	10	82	9	79
		B/Sichuan/259/2003 ET	74	8	67	9	75
		B/Jilin/20/2003** ET	48	17	52	30	79
		B/Washington/03/2003** ET	39	17	44	30	75
		B/Jiangsu/10/2003** ET	22	10	19	0	33
UK ²	24	B/Hong Kong/1434/2002* ET	71	5	28	0	54
		B/Sichuan/259/2003 ET	67	5	22	0	46
		B/Jilin/20/2003** ET	42	6	15	8	29
		B/Washington/03/2003** ET	38	6	14	8	21
		B/Jiangsu/10/2003** ET	17	6	12	4	21
Japan ³	30	B/Hong Kong/1434/2002* ET	24	13	24	32	52
		B/Sichuan/259/2003 ET	28	10	18	16	32
		B/Jilin/20/2003** ET	12	14	19	36	48
		B/Washington/03/2003** ET	12	14	17	36	40
		B/Jiangsu/10/2003** ET	20	8	11	4	8
Australia ⁴	19	B/Hong Kong/1434/2002* ET	68	7	70	5	80
	10	B/Sichuan/259/2003 ET	40	8	106	0	90
	16	B/Jilin/20/2003** ET	38	15	48	31	63
	17	B/Washington/03/2003** ET	41	14	58	35	76

1. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

2. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Shangdong/07/97-like hemagglutinin.

3. Sera were kindly provided by Dr. Takato Odagiri, WHO Collaborating Center, Tokyo, Japan. The populations were vaccinated with the 2003-2004 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

4. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2003 trivalent influenza vaccine containing 15: g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Shangdong/07/97-like hemagglutinin.

* B/Hong Kong/1434/2002 is closely related to the vaccine component.

** B/Sichuan/379/99 lineage viruses

**HI Antibody Responses to the B* Component of the 2003 -2004 Influenza Vaccine
ELDERLY POPULATIONS**

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
USA ¹	23	B/Hong Kong/1434/2002* ET	67	11	57	19	78
		B/Sichuan/259/2003 ET	67	10	51	10	74
		B/Jilin/20/2003** ET	24	15	33	24	43
		B/Washington/03/2003** ET	24	17	38	38	52
		B/Jiangsu/10/2003** ET	14	15	28	19	43
UK ²	24	B/Hong Kong/1434/2002* ET	54	6	23	4	42
		B/Sichuan/259/2003 ET	54	6	19	4	38
		B/Jilin/20/2003** ET	13	7	11	4	13
		B/Washington/03/2003** ET	21	7	12	4	13
		B/Jiangsu/10/2003** ET	25	6	11	0	13
Japan ³	30	B/Hong Kong/1434/2002* ET	0	18	22	30	40
		B/Sichuan/259/2003 ET	13	14	20	30	43
		B/Jilin/20/2003** ET	0	9	10	17	20
		B/Washington/03/2003** ET	0	9	10	13	20
		B/Jiangsu/10/2003** ET	7	8	10	10	13
Australia ⁴	22	B/Hong Kong/1434/2002* ET	73	8	45	5	68
	18	B/Sichuan/259/2003 ET	78	7	43	6	67
	20	B/Jilin/20/2003** ET	30	19	46	30	65
	18	B/Washington/03/2003** ET	42	14	43	21	50
	12	B/Jiangsu/10/2003** ET	20	12	21	7	33

1. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

2. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2002-2003 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Shangdong/07/97-like hemagglutinin.

3. Sera were kindly provided by Dr. Takato Odagiri, WHO Collaborating Center, Tokyo, Japan. The populations were vaccinated with the 2003-2004 trivalent influenza vaccine containing 15ug each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

4. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2003 trivalent influenza vaccine containing 15: g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Shangdong/07/97-like hemagglutinin.

* B/Hong Kong/1434/2002 is closely related to the vaccine component.

** B/Sichuan/379/99 lineage viruses

**HI Antibody Responses to the B* Component of the 2003 -2004 Influenza Vaccine
PEDIATRIC POPULATION**

Population	N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer \geq 40	
						Pre Vaccine	Post Vaccine
USA ¹	25	B/Hong Kong/1434/2002* ET	41	6	15	4	24
		B/Sichuan/259/2003 ET	30	5	14	0	28
		B/Jilin/20/2003** ET	7	5	6	0	4
		B/Washington/03/2003** ET	7	5	6	4	8
		B/Jiangsu/10/2003** ET	0	5	5	0	0

1. Sera were kindly provided by Dr. Christine Turley, UTMB, Galveston, TX. Children 6-23 months of age were vaccinated twice with the 2003-2004 trivalent influenza vaccine containing 15:g each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Hong Kong/330/2001-like hemagglutinin.

* B/Hong Kong/1434/2002 is closely related to the vaccine component.

** B/Sichuan/379/99 lineage viruses