D-443

CDC
Centers for Disease Control
and Prevention

INFORMATION FOR THE VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

January 30, 2001

Bethesda, Maryland

WHO COLLABORATING CENTER FOR INFLUENZA REFERENCE AND RESEARCH

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

Page

I. U.S. Surveillance 1

II. Influenza A(H1N1) Viruses.....8

III. Influenza A(H3N2) Viruses.....22

IV. Influenza B Viruses.....36

US Surveillance

Methods Used in United States Influenza Surveillance

World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance System (NREVSS) collaborating laboratories

Approximately 120 WHO and NREVSS collaborating laboratories in the United States report the total number of specimens received for respiratory virus testing and the number testing positive for influenza A(H1N1), A(H3N2), A(not subtyped), or influenza B. Participating laboratories are in state or local health departments with a smaller number in universities or hospitals. A subset of the isolates from these laboratories are submitted for complete antigenic characterization and antiviral resistance testing to the WHO Collaborating Center for Reference and Research on Influenza, CDC.

Pneumonia and influenza (P&I) deaths from 122 cities

Each week throughout the year, the vital statistics offices of 122 cities report the total number of death certificates filed each week and the number of death certificates in which pneumonia or influenza is listed in any position on the certificate. A periodic regression model that incorporates a robust regression procedure is applied to produce a seasonal baseline of P&I deaths since 1983 and to calculate "excess" deaths above the baseline. An increase of 1.645 standard deviations above the seasonal baseline of P&I deaths is considered the "epidemic threshold", i.e., the point at which the observed proportion of deaths attributed to pneumonia or influenza is significantly higher than the expected.

Prior to the 1999-2000 season, a new case definition for a P&I death was introduced in the 122 Cities Mortality Reporting System. It was recognized that one potential effect of using this case definition was to increase P&I mortality measurement levels in comparison to previous seasons. During the summer of 2000, the P&I mortality data were analyzed to determine if the modified case definition had affected mortality estimates. On the basis of this analysis, we estimate that there was an upward shift of approximately 0.8% in 1999-2000 mortality estimates. The 0.8% shift did not represent a true increase in mortality. To adjust for this upward shift in mortality estimates, the 122 cities P&I mortality baseline and epidemic threshold for the 2000-01 season have been adjusted upward as well.

Sentinel physician surveillance network

Approximately 500 regularly reporting volunteer physicians throughout the United States provide the total number of patient visits per week and the number of those patients seen for ILI by age group. A subset of the physicians submit nasal and throat swabs to either a contract laboratory or to their state public health laboratory for virus isolation.

State and territorial epidemiologists

State or territory-wide influenza activity, as assessed by the state or territorial epidemiologist, is reported weekly. Levels of influenza activity are classified as:

No activity;

Sporadic - sporadically occurring influenza-like illness (ILI) or culture-confirmed influenza, with no outbreaks detected;

Regional- outbreaks of ILI or culture-confirmed influenza in a county or counties having a combined population <50% of the state's total population;

Widespread- outbreaks of ILI or culture-confirmed influenza in a county or counties having a combined population ≥50% of the state's total population.

Summary of Influenza Surveillance, United States
October 1, 2000 - January 20, 2001

Influenza activity in the United States overall has been low to moderate but is increasing. The percentage of specimens testing positive for influenza increased from 4% at the end of November to 22% for the week ending January 20, 2001. Influenza A viruses have predominated (range 65% to 88%) in 6 surveillance regions (East North Central, Mountain, New England, South Atlantic, West North Central, and West South Central), and influenza B viruses have predominated (range 54% to 62%) in the remaining 3 regions (East South Central, Pacific, and Mid-Atlantic). The percentage of deaths attributed to pneumonia and influenza (P&I) and the percentage of visits to U.S. sentinel physicians for influenza-like illness (ILI) have not exceeded baseline levels this season.

WHO and NREVSS collaborating laboratories

From October 1, 2000 through January 20, 2001, WHO and NREVSS laboratories tested 30,034 specimens for influenza, and 2,239 (7%) were positive. Of the 2,239 influenza viruses reported, 1,640 (73%) were influenza type A, and 599 (27%) were type B. Of the 626 influenza A viruses that have been subtyped, 605 (97%) were A(H1N1) and 21 (3%) were influenza A(H3N2). Influenza isolates have been identified each week of this season but the proportion of specimens testing positive for influenza has been increasing steadily since December. During the week ending January 20, 22% of specimens tested were positive for influenza.

Sentinel physicians network

Nationwide, the percentage of visits to U.S. sentinel physicians for influenza-like illness (ILI) has not exceeded baseline levels (0%-3%) this season. During the week ending January 20, 3% of patient visits in the U.S. overall were due to ILI, however, the percentage of patient visits for ILI was above baseline levels in 3 of the 9 surveillance regions (Mountain [4%], Pacific [6%], and West South Central [7%]).

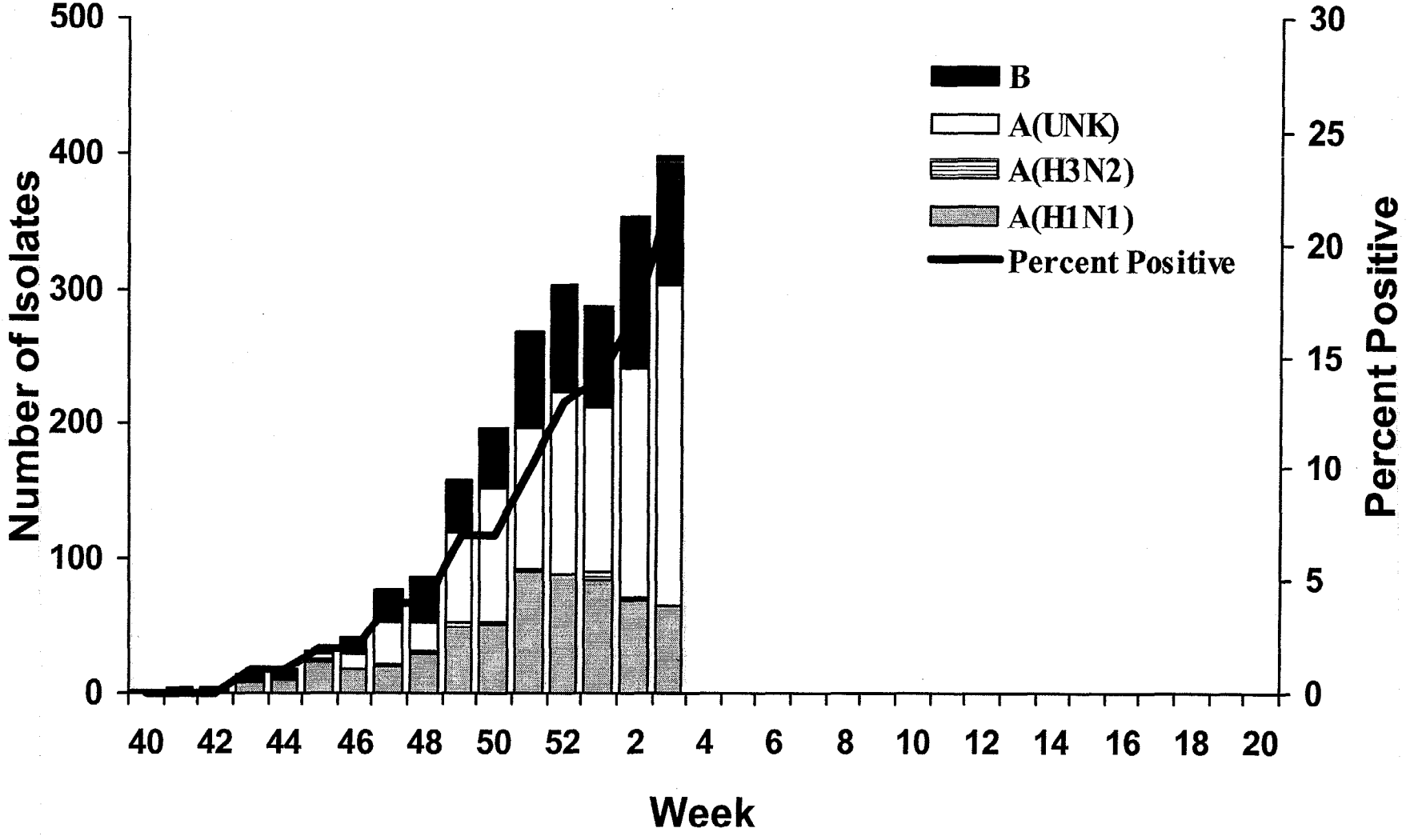
State and territorial epidemiologists

Regional activity has been reported by at least one state each week since the week ending November 18, 2000. Widespread activity was first reported the week ending December 16, 2000. For the week ending January 20, with 49 states reporting, 12 states reported widespread activity, 18 states reported regional activity, and 19 states reported sporadic activity.

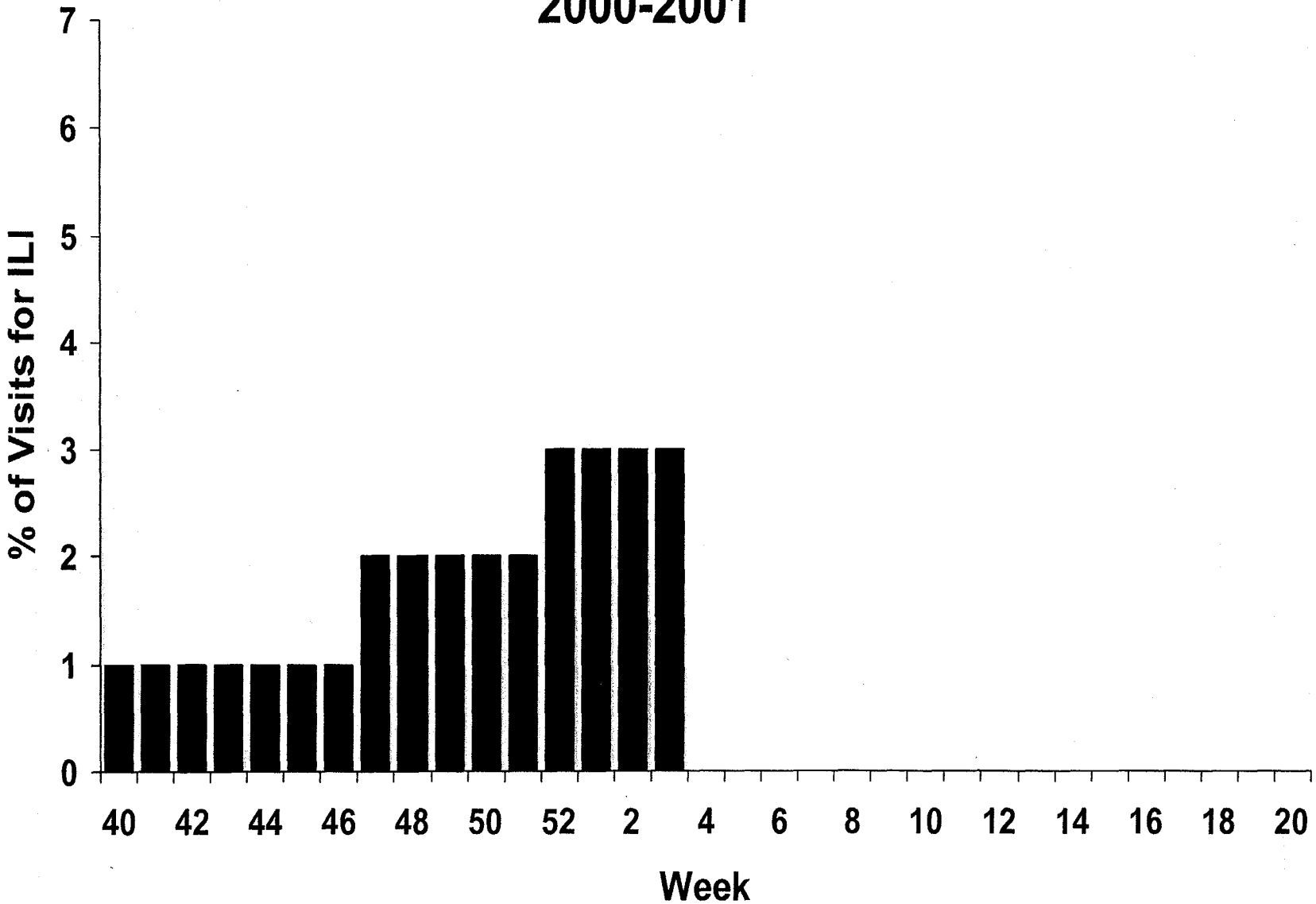
P&I deaths from 122 cities

The percentage of deaths attributed to pneumonia and influenza (P&I) has remained below the epidemic threshold for each week since October 1. During the week ending January 20, 7.9% of deaths were due to pneumonia or influenza. This was below the epidemic threshold of 8.6% for that week

Influenza Viruses Isolated by WHO/NREVSS Collaborating Laboratories 2000-2001

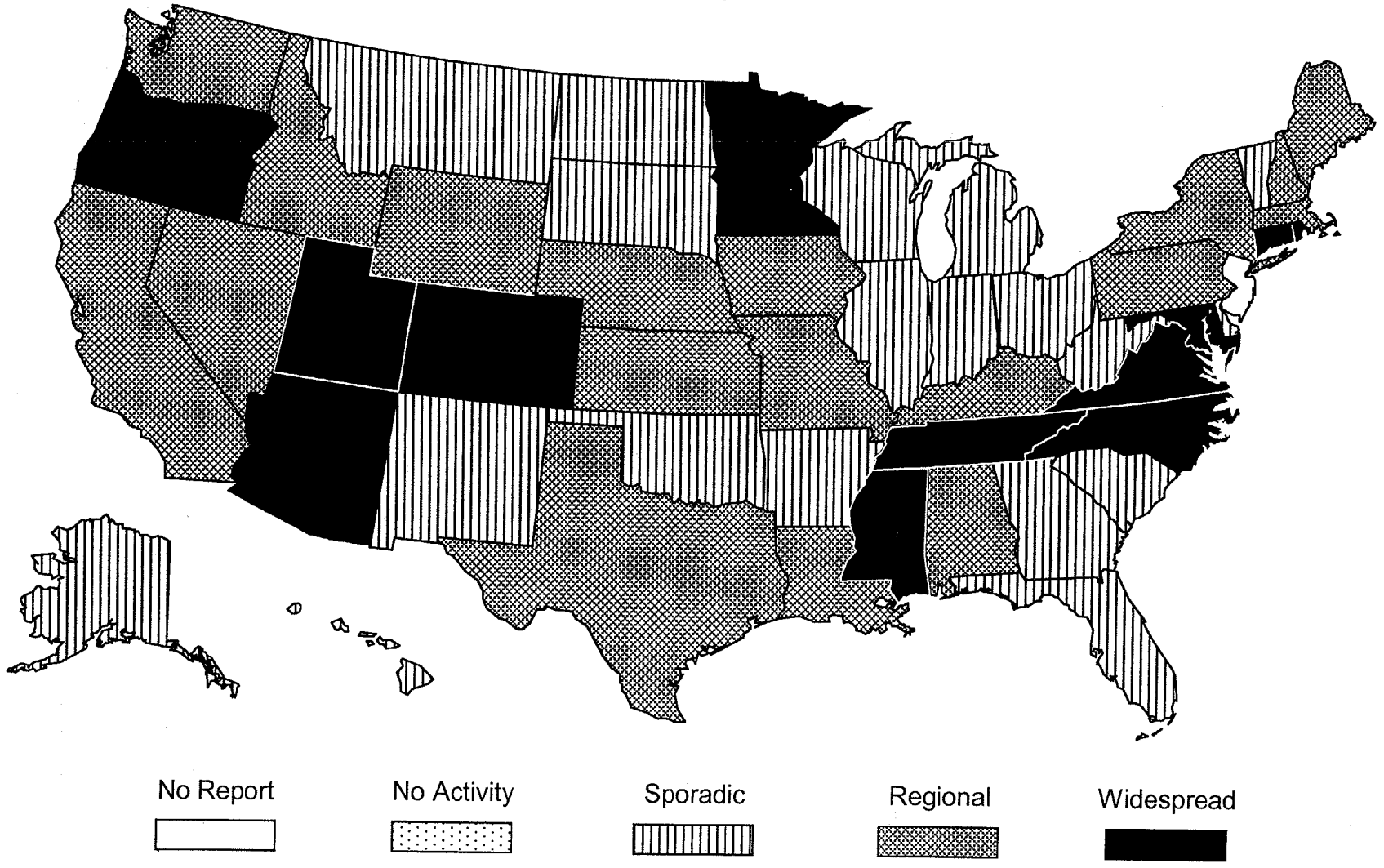


Percentage of Visits for Influenza-like Illness Reported by Sentinel Physicians 2000-2001



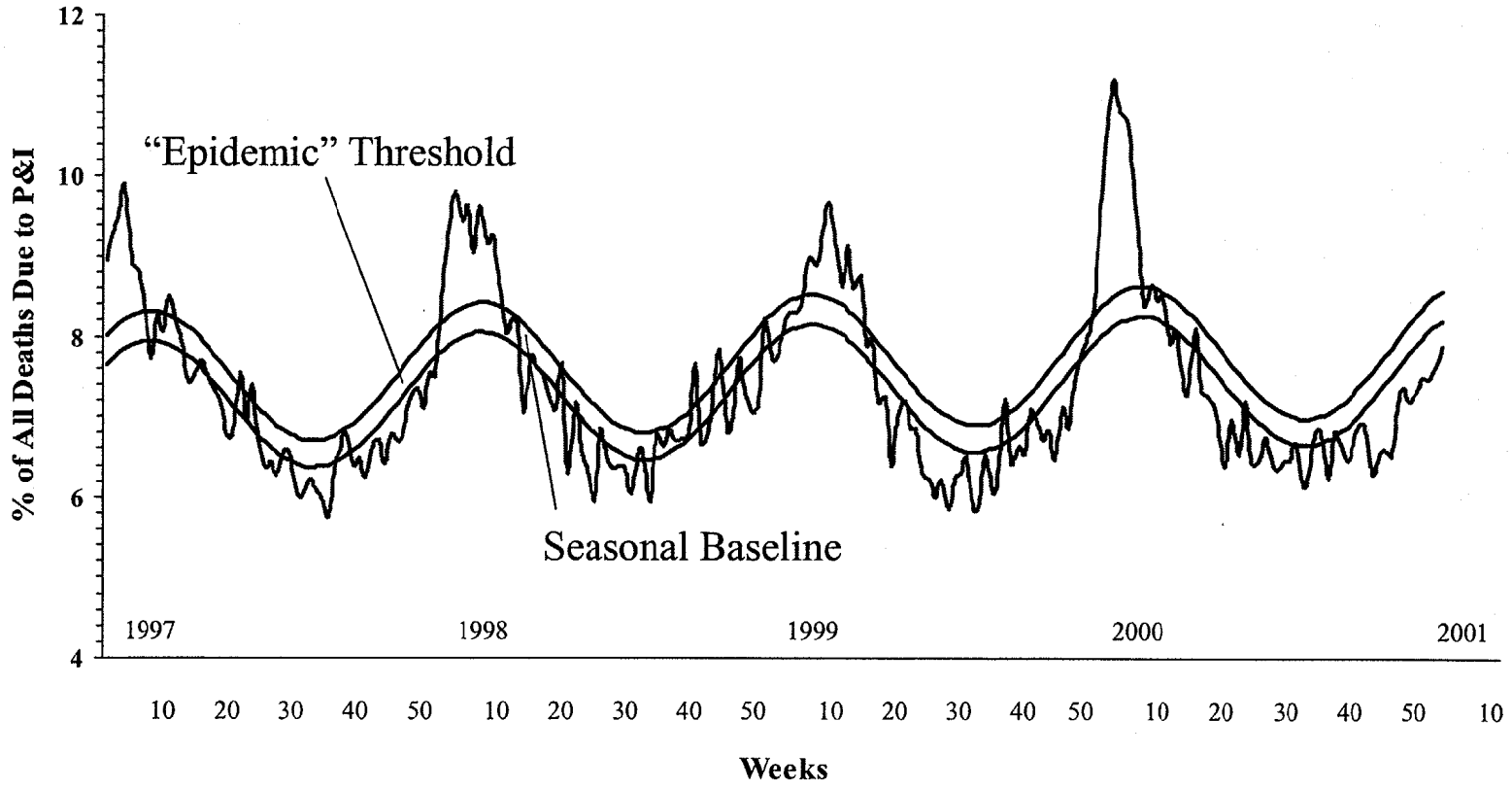
Weekly Influenza Activity Estimates Reported by State & Territorial Epidemiologists

Week ending January 20, 2001 - Week 3



Pneumonia and Influenza Mortality for 122 U.S. Cities

Week Ending 1/20/01



Influenza A(H1N1) Viruses

Page

A. Antigenic Characterization.....10

B. Molecular Genetics.....14

C. Serological Responses.....18

INFLUENZA A(H1N1) WORLDWIDE ACTIVITY[1]

Geographical Region	***October 1999 - March 2000***						***Most Frequently Isolated Strain***[2]
	Oct-99	Nov-99	Dec-99	Jan-00	Feb-00	Mar-00	
United States		+	+	+	+	+	A/Beijing/262/95-like A/New Caledonia/20/99-like
Canada		+	+	+	+	+	A/New Caledonia/20/99-like
Europe		+	+	+	+	+	A/Beijing/262/95-like A/New Caledonia/20/99-like
SoAf/Aus/NZ		+				+	A/New Caledonia/20/99-like
Cen/So America			+				A/New Caledonia/20/99-like
Asia	+	+	+++	++	++	+	A/New Caledonia/20/99-like

Geographical Region	***April 2000 - September 2000***						***Most Frequently Isolated Strain***[2]
	Apr-00	May-00	Jun-00	Jul-00	Aug-00	Sep-00	
United States	+	+	+	++		+	A/New Caledonia/20/99-like
Canada	+	+	+				A/New Caledonia/20/99-like
Europe	+					+	A/New Caledonia/20/99-like
SoAf/Aus/NZ		+	+	+	+		A/New Caledonia/20/99-like
Cen/So America	++	++	+++	+++	++	+	A/New Caledonia/20/99-like
Asia	+	+	+	+	+	+	A/New Caledonia/20/99-like

Geographical Region	***October 2000 - January 2001***						***Most Frequently Isolated Strain***[2]
	Oct-00	Nov-00	Dec-00	Jan-01	Feb-01	Mar-01	
United States	+	++	++	++			A/New Caledonia/20/99-like
Canada	+	+	+				A/New Caledonia/20/99-like
Europe	+	++	++	++			A/New Caledonia/20/99-like
SoAf/Aus/NZ							
Cen/So America	+						A/New Caledonia/20/99-like
Asia	+	+	++	+			A/New Caledonia/20/99-like

[1] Activity level. + = Sporadic, ++ = Outbreak, +++ = Epidemic

[2] Strain data based on characterization tests performed at CDC and other WHO Collaborating Centers.

Preliminary Data 1/22/01

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA A(H1N1) VIRUSES (12/20/00)

STRAIN DESIGNATION	REFERENCE FERRET ANTISERA						
	A	B	C	D	E	Date	Passage
REFERENCE ANTIGENS	BJ/262	NC/20	HK/1252	JOH/82	CI/4795	collected	
1. A/BEIJING/262/95	**640**	160	80	20	10	01/09/95	E3/E3
2. A/NEW CALEDONIA/20/99*	160	**320**	160	10	20	06/09/99	E4/E1
3. A/HK/1252/20000	40	80	**640**	5	10	02/21/00	C2/C1
4. A/JOHANNESBURG/82/96	40	40	20	**1280**	1280	1996	E4/E3
5. A/CHILE/4795/2000	20	20	20	320	**1280**	05/29/00	E2/E1
TEST ANTIGENS							
6. A/TEXAS/73/2000	80	320	160	5	5	11/13/00	X/C1
7. A/TEXAS/79/2000	160	320	320	10	10	11/21/00	X/C1
8. A/TEXAS/80/2000	80	320	160	20	20	11/22/00	X/C1
9. A/TEXAS/85/2000	160	160	160	10	10	11/28/00	M1/C1
10. A/TEXAS/87/2000*	160	320	320	10	20	11/30/00	M1/C1
11. A/TEXAS/89/2000	160	160	320	10	10	11/27/00	M1/C1
12. A/TENNESSEE/05/2000	160	160	160	5	5	11/30/00	C1/C1
13. A/BRAZIL/30/2000	160	160	320	20	10	8/29/00	E1/E1
14. A/ARGENTINA/6023/2000	160	320	320	20	40	6/17/00	X/C1
15. A/ARGENTINA/6032/2000	80	160	320	10	20	6/21/00	X/C1
16. A/ARGENTINA/6048/2000	160	320	320	20	40	6/17/00	X/C1
17. A/ARGENTINA/6049/2000	160	160	320	10	10	6/3/00	X/C1
18. A/ARGENTINA/6051/2000	80	320	320	10	10	6/10/00	X/C1
19. A/TEXAS/90/2000	40	20	20	1280	2560	11/14/00	M1/C1
20. A/ALASKA/32/2000	40	20	20	640	1280	11/13/00	X/C1

* Used in serology tests

Preliminary

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA A(H1N1) VIRUSES (01/04/01)

STRAIN DESIGNATION	REFERENCE FERRET ANTISERA						
	A	B	C	D	E	Date	Passage
REFERENCE ANTIGENS	BJ/262	NC/20	FUJ/156	JOH/82	CI/4795	collected	
1. A/BEIJING/262/95	**320**	160	320	20	10	01/09/95	E3/E3
2. A/NEW CALEDONIA/20/99*	160	**320**	1280	10	40	06/09/99	E4/E1
3. A/FUJIAN/156/2000*	40	80	**640**	5	10	08/25/00	E2/E1
4. A/JOHANNESBURG/82/96	80	40	20	**640**	1280	1996	E4/E3
5. A/CHILE/4795/2000	40	20	10	320	**640**	05/29/00	E2/E1
TEST ANTIGENS							
6. A/S. DAKOTA/02/2000	80	160	320	5	10	12/05/00	M3/C1
7. A/S. DAKOTA/03/2000	80	160	320	5	10	12/04/00	M3/C1
8. A/S. DAKOTA/04/2000	80	160	640	5	10	12/04/00	M3/C1
9. A/IOWA/02/2000	80	160	320	5	10	12/12/00	X/C1
10. A/IOWA/03/2000	80	160	320	5	10	11/29/00	X/C1
11. A/S. CAROLINA/06/2000	80	160	320	5	5	~12/01/00	X/C1
12. A/TEXAS/92/2000	80	160	640	10	10	~12/01/00	X/C1
13. A/MISSOURI/06/2000	40	80	320	10	5	12/6/200	MX/C1
14. A/MISSOURI/03/2000	80	160	640	5	5	UNKN	X/C1
15. A/ENGLAND/191/2000	160	160	640	10	40	11/22/00	C2E1/E1
16. A/HONG KONG/1924/2000*	160	160	640	10	20	10/30/00	C2/C1
17. A/WUHAN/292/2000*	160	160	1280	10	20	09/29/00	E2/E2
18. A/WISCONSIN/07/2000	80	40	20	640	1280	11/28/00	M2/C1
19. A/CANADA/576/2000	40	20	20	640	1280	10/30/00	X/C1
20. A/ENGLAND/192/2000*	20	20	10	320	640	11/07/00	C2E1/E1

* Used in serology tests

Preliminary data

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA A(H1N1) VIRUSES (01/24/01)

STRAIN DESIGNATION	REFERENCE FERRET ANTISERA						
	A	B	C	D	E	Date	Passage
REFERENCE ANTIGENS	BJ/262	NC/20	HK/1252	JOH/82	CI/4795	collected	
1. A/BEIJING/262/95	**320**	80	40	10	10	01/09/95	E3/E3
2. A/NEW CALEDONIA/20/99*	160	**320**	160	20	20	06/09/99	E4/E1
3. A/HK/1252/20000	20	80	**320**	5	5	02/21/00	C2/C2
4. A/JOHANNESBURG/82/96	80	40	40	**1280**	1280	1996	E4/E3
5. A/CHILE/4795/2000	10	10	10	160	**640**	05/29/00	E2/E1
TEST ANTIGENS							
6. A/NEW YORK/16/2000	320	640	640	40	40	12/31/00	M1/C1
7. A/DIST. OF COLOMBIA/01/2001	160	320	320	10	20	01/02/01	X/C1
8. A/TEXAS/93/2000	160	320	320	10	20	12/29/00	X/C1
9. A/MASSACHUSETTS/04/2000	160	320	320	10	20	12/06/00	X2/C1
10. A/IDAHO/02/2000	160	320	320	10	20	12/17/00	X/C1
11. A/N. CAROLINA/12/2000	160	320	160	10	10	12/27/00	M1/C1
12. A/CALIFORNIA/01/2001	160	320	320	10	20	01/04/01	X/C2
13. A/NEW MEXICO/02/2000	80	320	160	10	20	12/13/00	X2/C1
14. A/WYOMING/01/2001	160	320	640	20	40	01/04/01	X/C1
15. A/NEVADA/01/2001	160	160	160	10	10	01/02/01	X/C1
16. A/WASHINGTON/01/2001	80	160	80	10	5	01/03/01	M1/C1
17. A/IOWA/02/2000	80	160	80	10	10	12/12/00	X/C1
18. A/VIRGINIA/12/2000	80	160	80	5	5	12/14/00	M2/C1
19. A/ARKANSAS/01/2001	80	160	160	10	10	01/04/01	X/C1
20. A/LYON/1364/2000	80	160	80	10	5	12/05/00	C2/1/C1
21. A/HONG KONG/1924/2000*	320	320	320	20	20	10/30/00	C2/1/C1
22. A/NEW JERSEY/07/2000	80	80	40	1280	2560	12/24/00	MX/C1
23. A/TEXAS/94/2000	40	40	20	1280	1280	12/29/00	X/C1
24. A/MASSACHUSETTS/05/2000	40	20	20	640	1280	12/04/00	X1/C1

* Used in serology tests

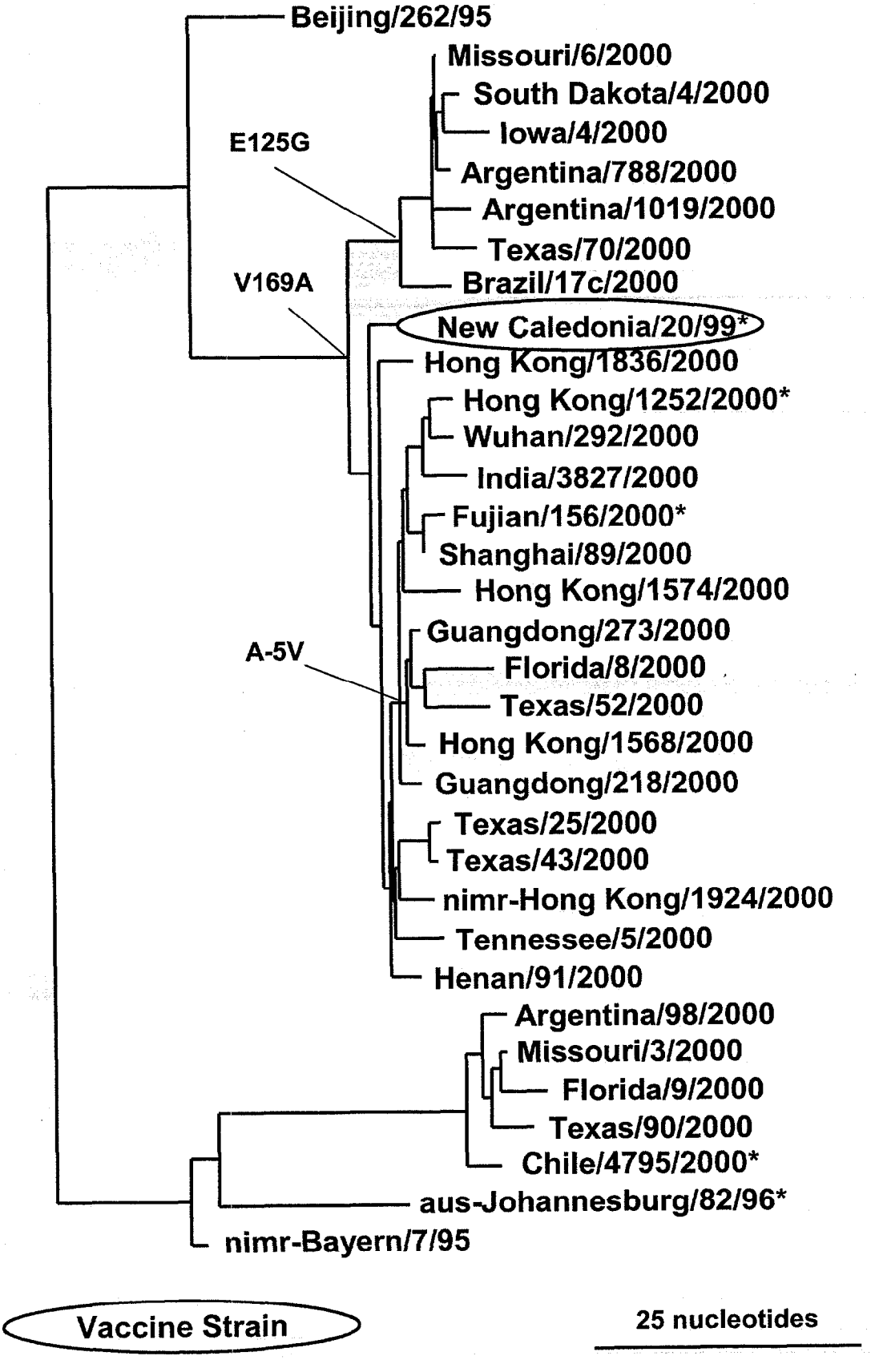
Preliminary data

Influenza A(H1N1) Isolates Characterized by CDC

	U.S.A.	North	Europe	Asia	Cent/So	Africa,	Total
April 1999 - September 1999							
A/Beijing/262/95-like					2	2	4 (10%)
A/Beijing/262/95-like (low)				1	1		2 (5%)
A/New Caledonia/20/99-like				1		5	6 (15%)
A/Johannesburg/82/96-like					27		27 (70%)
						Total	39
October 1999 - March 2000							
A/Beijing/262/95-like	1			2			3 (1.5%)
A/New Caledonia/20/99-like	71	8	2	76	6		163 (79%)
A/New Caled./20/99-like (low)					1		1 (0.5%)
A/Johannesburg/82/96-like	30		4	3	2		39 (19%)
						Total	206
April 2000 - September 2000							
A/New Caledonia/20/99-like	36	1		39	138	7	221 (87%)
A/New Caled./20/99-like (low)				1	1		2 (1%)
A/Johannesburg/82/96-like	7				23	2	32 (12%)
						Total	255
October 2000 - December 2000							
A/New Caledonia/20/99-like	113		3	2			118 (89%)
A/New Caled./20/99-like (low)	4		1				5 (3%)
A/Johannesburg/82/96-like	8	1	1				10 (8%)
						Total	133
Total	270	10	11	125	201	16	633

Preliminary Data 01/24/01

Evolutionary Relationships Among Influenza H1 Hemagglutinin (HA1) Genes



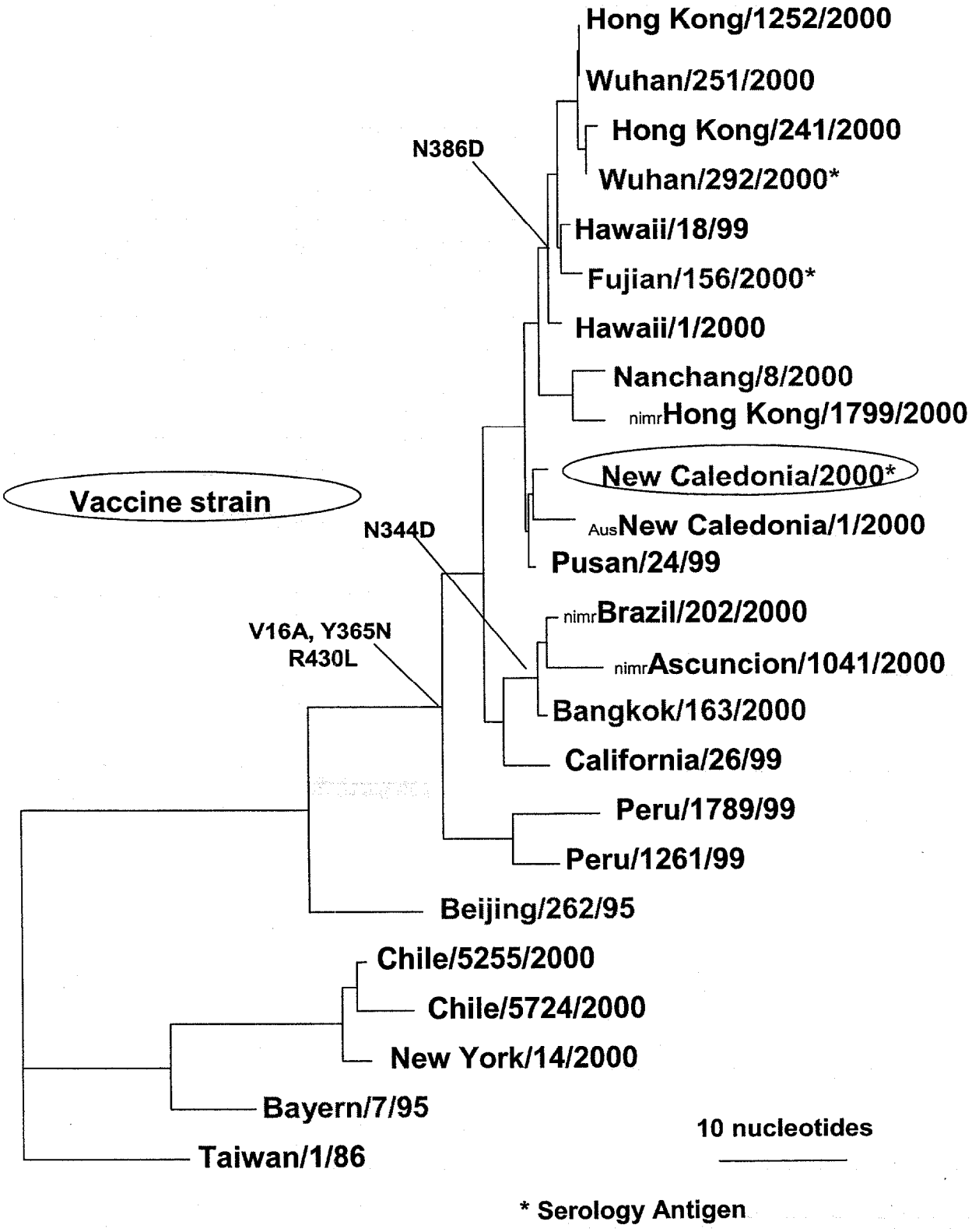
* Serology Antigen

Number of Amino Acid Differences from A/New Caledonia/20/99-like Consensus HA1 Sequence

Isolate	Passage	No. of differences
New Caledonia/20/99*	e4/e1	1
Henan/91/2000	e2/e2	2
Shanghai/89/2000	e2/e1	3
Guangdong/218/2000	e3/e1	3
Fujian/156/2000*	e2/e1	4
Wuhan/292/2000*	e2/e1	4
Beijing/262/95	e3/e4	10

* Serology Antigens

Evolutionary Relationships Among Influenza A N1 Neuraminidase Genes



* Serology Antigen

Number of Amino Acid Differences from Consensus N1 Neuraminidase Sequence

Isolate	Passage	No. of Differences	Position
A/Nanchang/8/2000	X/E1	0	
A/Wuhan/251/2000	E3/E1	1	386
A/Fujian/156/2000	E2/E1	1	386
A/Wuhan/292/2000	E2/E1	2	48, 386
A/New Caledonia/20/99	E4/E1	3	48, 461, 465
A/Bangkok/163/2000	E3/E1	4	48, 222, 344, 465

Hemagglutination Inhibition Antibody Responses to the H1* Component of the 2000-2001 Influenza Vaccine

ADULT POPULATIONS

					% with HI titer ≥ 40	
N	Antigen	% Rise	Pre GMT	Post GMT	Pre Vaccine	Post Vaccine
22[1]	A/New Caledonia/20/99 IVR-116*	77	8	44	14	64
22	A/Hong Kong/1252/2000	55	8	31	18	55
22	A/Brazil/74200/2000	59	7	27	5	64
22	A/Madagascar/57794/2000	77	7	40	14	64
22	A/Texas/26/2000	64	9	44	18	68
22	A/Chile/4795/2000 (A/Bayern-like)	18	18	32	41	55
24[2]	A/New Caledonia/20/99 IVR-116*	42	15	57	29	75
24	A/Hong Kong/1252/2000	46	13	40	21	58
24	A/Brazil/74200/2000	46	13	44	29	67
24	A/Madagascar/57794/2000	42	16	64	29	75
24	A/Texas/26/2000	50	16	69	33	83
24	A/Chile/4795/2000 (A/Bayern-like)	25	38	65	58	75
24[3]	A/New Caledonia/20/99 IVR-116*	96	5	116	0	88
24	A/Hong Kong/1252/2000	88	5	87	0	79
24	A/Brazil/74200/2000	88	5	71	0	75
24	A/Madagascar/57794/2000	96	5	116	0	92
24	A/Texas/26/2000	96	6	160	0	96
24	A/Chile/4795/2000 (A/Bayern-like)	75	9	76	4	63

Preliminary Data 09/06/00

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
3. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

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

Hemagglutination Inhibition Antibody Responses to the H1* Component of the 2000-2001 Influenza Vaccine

ELDERLY POPULATIONS

					% with HI titer ≥ 40	
N	Antigen	% Rise	Pre GMT	Post GMT	Pre Vaccine	Post Vaccine
25[1]	A/New Caledonia/20/99 IVR-116*	52	8	28	0	52
25	A/Hong Kong/1252/2000	36	7	16	0	32
25	A/Brazil/74200/2000	44	7	16	0	32
25	A/Madagascar/57794/2000	52	7	24	0	44
25	A/Texas/26/2000	40	8	21	4	36
25	A/Chile/4795/2000 (A/Bayern-like)	0	15	24	24	44
24[2]	A/New Caledonia/20/99 IVR-116*	33	9	21	17	38
24	A/Hong Kong/1252/2000	21	8	15	17	29
24	A/Brazil/74200/2000	38	8	18	13	29
24	A/Madagascar/57794/2000	38	10	23	17	42
24	A/Texas/26/2000	25	12	24	17	38
24	A/Chile/4795/2000 (A/Bayern-like)	0	19	24	33	54
24[3]	A/New Caledonia/20/99 IVR-116*	75	6	50	4	67
24	A/Hong Kong/1252/2000	58	6	26	8	46
24	A/Brazil/74200/2000	63	5	30	0	50
24	A/Madagascar/57794/2000	75	6	50	0	67
24	A/Texas/26/2000	79	7	62	4	71
24	A/Chile/4795/2000 (A/Bayern-like)	58	12	47	21	58

Preliminary Data 09/06/00

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
3. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

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

Hemagglutination Inhibition Antibody Responses to the H1* Component of the 2000-2001 Influenza Vaccine

ADULT POPULATIONS

N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer ≥ 40 Pre Vaccine	Post Vaccine
24[1]	A/New Caledonia/20/99 IVR-116*	42	15	52	29	71
24	A/Fujian/156/2000	38	10	30	17	58
24	A/Wuhan/292/2000	46	19	73	33	88
24	A/Hong Kong/1924/2000	38	15	53	29	75
24	A/Texas/87/2000	46	17	65	29	83
24	A/England/192/2000	29	23	44	33	58
24[2]	A/New Caledonia/20/99 IVR-116*	96	5	143	0	88
24	A/Fujian/156/2000	88	5	76	0	79
24	A/Wuhan/292/2000	96	6	170	0	92
24	A/Hong Kong/1924/2000	96	6	151	0	88
24	A/Texas/87/2000	96	5	123	0	88
24	A/England/192/2000	67	8	62	4	58

Preliminary Data 01/10/01

1. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

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

Hemagglutination Inhibition Antibody Responses to the H1* Component of the 2000-2001 Influenza Vaccine

ELDERLY POPULATIONS

N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer ≥ 40 Pre Vaccine	Post Vaccine
24[1]	A/New Caledonia/20/99 IVR-116*	29	8	17	13	29
24	A/Fujian/156/2000	25	6	12	4	21
24	A/Wuhan/292/2000	29	13	28	17	58
24	A/Hong Kong/1924/2000	38	11	26	13	46
24	A/Texas/87/2000	29	13	28	21	50
24	A/England/192/2000	4	13	17	17	25
24[2]	A/New Caledonia/20/99 IVR-116*	75	6	49	4	63
24	A/Fujian/156/2000	67	5	28	0	42
24	A/Wuhan/292/2000	88	6	76	0	75
24	A/Hong Kong/1924/2000	75	6	58	4	71
24	A/Texas/87/2000	79	6	65	0	71
24	A/England/192/2000	63	8	42	13	58

Preliminary Data 01/10/01

1. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
* A/New Caledonia/20/99 is the H1N1 component of the vaccine.

Influenza A(H3N2) Viruses

Page

A. Antigenic Characterization.....24

B. Molecular Genetics.....28

C. Serological Responses.....32

INFLUENZA A(H3N2) WORLDWIDE ACTIVITY[1]

Geographical Region	***October 1999 - March 2000***						***Most Frequently Isolated Strain***[2]
	Oct-99	Nov-99	Dec-99	Jan-00	Feb-00	Mar-00	
United States	+	++	+++	+++	++	+	A/Sydney/05/97-like
Canada	+	+	+++	+++	+	+	A/Sydney/05/97-like
Europe	+	+	++	+++	+++	+	A/Sydney/05/97-like
SoAf/Aus/NZ	+			+			A/Sydney/05/97-like
Cen/So America	+	+	+	+	+	+	A/Sydney/05/97-like
Asia	+	++	++	+++	+	+	A/Sydney/05/97-like

Geographical Region	***April 2000 - September 2000***						***Most Frequently Isolated Strain***[2]
	Apr-00	May-00	Jun-00	Jul-00	Aug-00	Sep-00	
United States	+		+		+		A/Panama/2007/99
Canada	+	+					
Europe	+	+				+	
SoAf/Aus/NZ	+	+	+	+	+++	++	A/Panama/2007/99
Cen/So America	+	+	++	+++	+		A/Panama/2007/99
Asia	+	+	++	++	+	+	A/Panama/2007/99

Geographical Region	***October 2000 - January 2001***						***Most Frequently Isolated Strain***[2]
	Oct-00	Nov-00	Dec-00	Jan-01	Feb-01	Mar-01	
United States	+	+	+	+			A/Panama/2007/99
Canada	+						
Europe	+	+	+	+			A/Panama/2007/99
SoAf/Aus/NZ	+						A/Panama/2007/99
Cen/So America							
Asia	+	+	+	+			

[1] Activity level. + = Sporadic, ++ = Outbreak, +++ = Epidemic

[2] Strain data based on characterization tests performed at CDC and other WHO Collaborating Centers.

Preliminary Data 1/22/01

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA A(H3N2) VIRUSES (11/09/00)

STRAIN DESIGNATION	REFERENCE FERRET ANTISERA						
	A	B	C	D	E	Date	Passage
REFERENCE ANTIGENS	SYD/5	MOS/10	PN/2007	U.UDE	MOS/02	collected	
1. A/SYDNEY/05/97	**320**	1280	160	1280	1280	06/23/97	CK2E2/E2
2. A/MOSCOW/10/99	160	**640**	160	640	640	01/15/99	E2/E3
3. A/PANAMA/2007/99*	160	640	**320**	640	640	07/12/99	E4
4. A/ULAN UDE/01/2000	160	320	80	**320**	640	02/28/00	E3/E2
5. A/MOSCOW/02/2000	320	640	160	640	**1280**	01/13/00	E2/E1
TEST ANTIGENS							
6. A/BRAZIL/22/2000	160	640	160	640	1280	07/10/00	C2/C1
7. A/BRAZIL/23/2000	160	640	160	640	640	07/24/00	C2/C1
8. A/BRAZIL/07/2000	320	640	160	640	1280	07/21/00	C2/C1
9. A/BRAZIL/23A/2000	160	640	160	640	640	07/24/00	C2/C1
10. A/BRAZIL/23POA/2000	320	1280	160	640	1280	08/23/00	E1/C1
11. A/GUANGZHOU/253/2000	320	1280	320	1280	1280	03/23/00	C3/C2
12. A/GUANGZHOU/375/2000	320	1280	320	640	1280	04/20/00	C3/C2
13. A/GUANGZHOU/443/2000	160	640	160	640	640	05/19/00	C3/C1
14. A/GUANGZHOU/81/2000	320	640	160	1280	2560	03/09/00	C2/C1
15. A/HONG KONG/1775/2000	160	1280	320	640	1280	08/31/00	C2/C1
16. A/HONG KONG/1789/2000	320	1280	320	1280	1280	09/05/00	C2/C1
17. A/HONG KONG/1805/2000	160	1280	160	640	640	09/06/00	C2/C1
18. A/HONG KONG/1782/2000	160	1280	160	640	640	09/01/00	C2/C1

* Used in serology tests

Preliminary data

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA A(H3H2) VIRUSES (12/13/00)

REFERENCE ANTIGENS	REFERENCE FERRET ANTISERA						
	A	B	C	D	E	Date	Passage
STRAIN DESIGNATION	SYD/5	MOS/10	PN/2007	U. UDE	MOS/02	collected	
1. A/SYDNEY/05/97	**320**	320	80	320	640	06/23/97	CK2E2/E2
2. A/MOSCOW/10/99	320	**640**	160	640	640	01/15/99	E2/E3
3. A/PANAMA/2007/99*	160	640	**320**	640	320	07/12/99	E4
4. A/ULAN UDE/01/2000	160	320	80	**320**	640	02/28/00	E2/E2
5. A/MOSCOW/02/2000	640	1280	640	1280	**1280**	01/13/00	E2/E1
TEST ANTIGENS							
6. A/CALIFORNIA/10/2000	160	640	160	320	640	11/15/00	X/C1
7. A/KENTUCKY/18/2000	320	1280	320	640	320	10/23/00	X2/C1
8. A/HAWAII/13/2000	640	1280	640	1280	1280	10/26/00	M3/C1
9. A/HAWAII/14/2000	320	1280	320	640	640	10/20/00	M3/C1
10. A/HAWAII/15/2000	320	1280	640	1280	1280	10/25/00	M3/C1
11. A/ARGENTINA/5995/2000	320	1280	320	640	640	10/03/00	X/C1

* Used in serology tests

Preliminary data

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA A(H3N2) VIRUSES (01/12/01)

REFERENCE ANTIGENS	REFERENCE FERRET ANTISERA						
	A	B	C	D	E	Date	Passage
STRAIN DESIGNATION	SYD/5	MOS/10	PN/2007	U. UDE	MOS/02	collected	
1. A/SYDNEY/05/97	**320**	640	160	640	640	06/23/97	CK2E2/E2
2. A/MOSCOW/10/99	320	**1280**	320	1280	1280	01/15/99	E2/E3
3. A/PANAMA/2007/99*	160	640	**320**	640	320	07/12/99	E4
4. A/ULAN UDE/01/2000	160	320	80	**320**	640	02/28/00	E2/E2
5. A/MOSCOW/02/2000	320	640	160	640	**1280**	01/13/00	E2/E1
TEST ANTIGENS							
6. A/MISSOURI/05/2000*	320	2560	320	640	640	11/21/00	MX/C1
7. A/NEW YORK/15/2000	320	1280	320	640	640	~12/01/00	M2/C1
8. A/WASHINGTON/05/2000	160	1280	160	320	640	12/08/00	X/C1
9. A/WASHINGTON/04/2000	160	320	160	160	320	12/04/00	X/C1
10. A/CANADA/574/2000	320	2560	640	1280	1280	10/25/00	X/C1
11. A/HONG KONG/1923/2000*	640	2560	640	1280	2560	10/24/00	C2/C1
12. A/BRAZIL/32/2000	640	1280	320	1280	2560	08/11/00	C2/C2
13. A/FUJIAN/140/2000*	160	320	80	160	320	07/30/00	C3/C1

* Used in serology tests

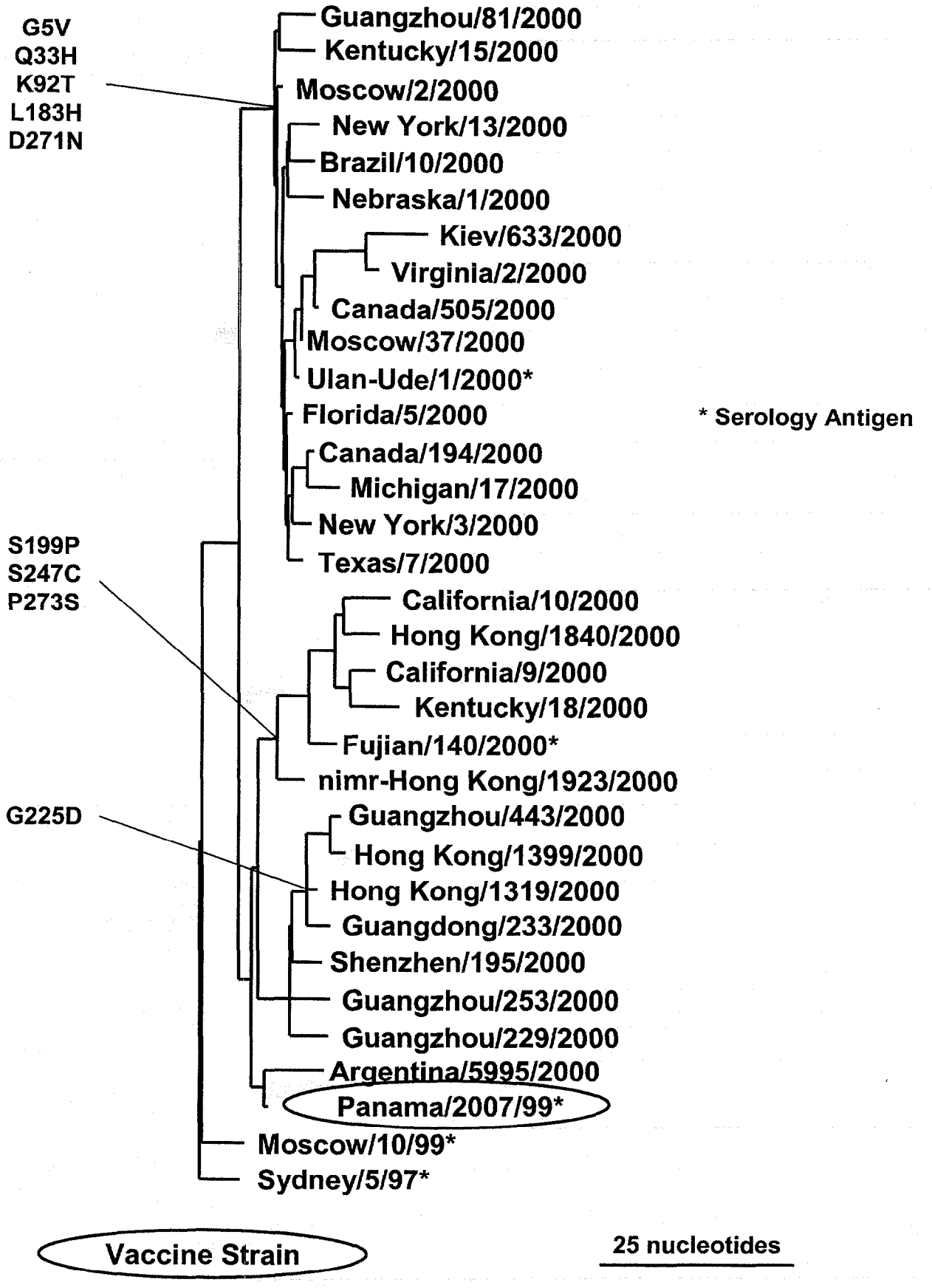
Preliminary data

Influenza A(H3N2) Isolates Characterized by CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 1999 - September 1999							
A/Sydney/05/97-like	115			79	130	37	361 (92%)
A/Syd/05/97-like (low)	4			1	22	4	31 (8%)
						Total	392
October 1999 - March 2000							
A/Sydney/05/97-like	479	19	58	64	11	8	639 (97%)
A/Panama/2007/99-like			6	8	1		15 (2.5%)
A/Pan/2007/99-like (low)	1					1	2 (0.5%)
						Total	656
April 2000 - September 2000							
A/Sydney/05/97-like	3			17	35	9	64 (64%)
A/Panama/2007/99-like				13	15	4	32 (32%)
A/Pan/2007/99-like (low)			1	1	1	1	4 (4%)
						Total	100
October 2000 - December 2000							
A/Panama/2007/99-like	10	1		1	1		13 (100%)
A/Pan/2007/99-like (low)							
						Total	13
Total	612	20	65	184	216	64	1161

Preliminary Data 01/24/01

Evolutionary Relationships Among Influenza H3 Hemagglutinin (HA1) Genes

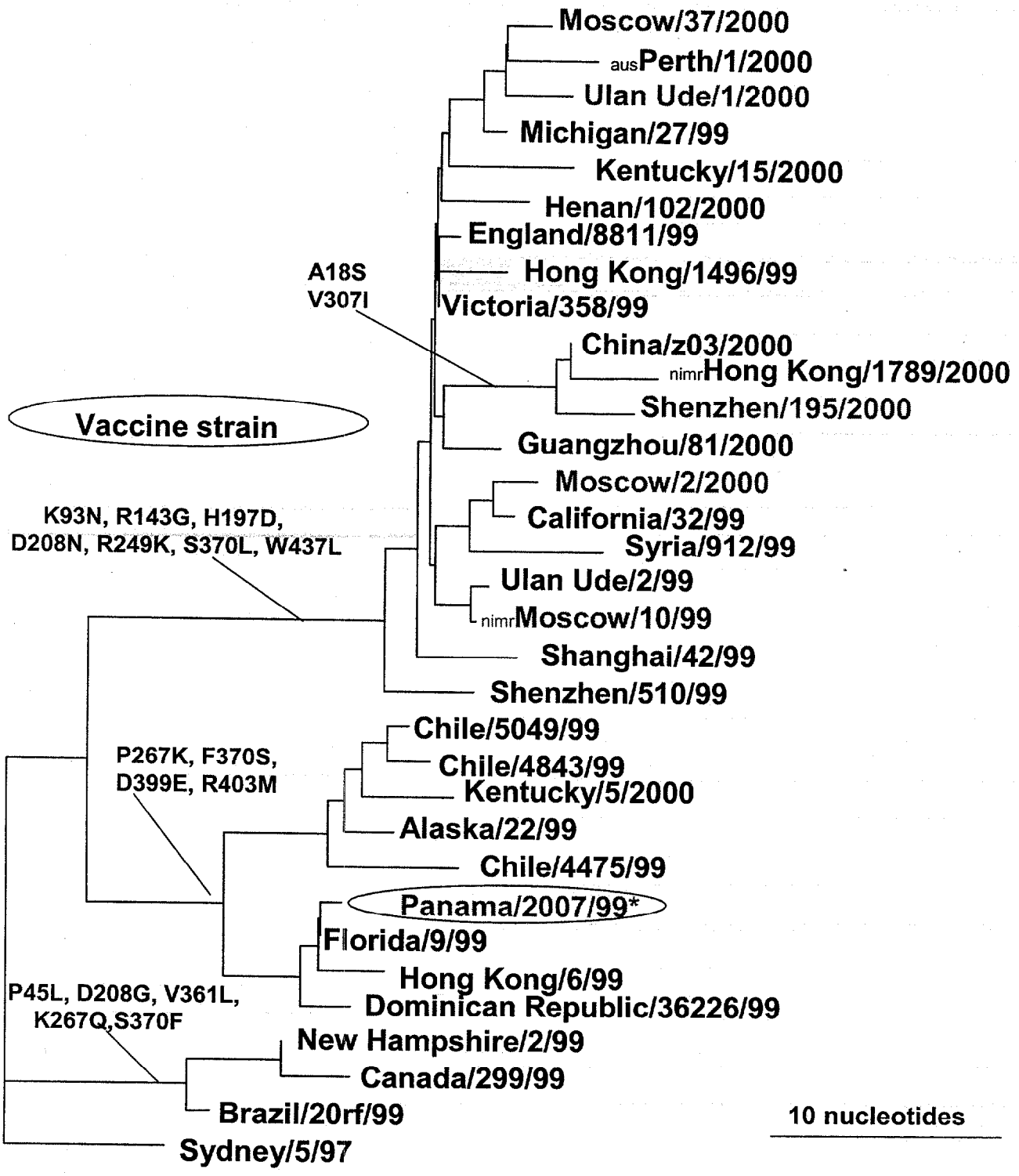


Number of Amino Acid Differences from A/Panama/2007/99-like Consensus HA1 Sequence

Isolate	Passage	No. of Differences
Panama/2007/99*	e3	2
Shenzhen/195/2000	e2/e1	3
Moscow/10/99	e2/e1	6
Kiev/633/2000	e5/e1	7
Moscow/37/2000	e3/e1	7
Ulan-Ude/1/2000	e2/e1	7
Fujian/140/2000*	e2/e2	8
Sydney/5/97	ck2e/e1	10

* Serology Antigens

Evolutionary Relationships Among Influenza A N2 Neuraminidase Genes



* Serology Antigen

Number of Amino Acid Differences from Consensus N2 Neuraminidase Sequence

Isolate	Passage	No. of Differences	Position
nimrA/Moscow/10/99	EX/E3	0	
A/Moscow/2/2000	E2	1	267
A/Ulan Ude/1/2000	E2/E1	1	267
A/Moscow/37/2000	E3	2	267, 430
A/Shenzhen/195/2000	E2/E1	4	18, 23, 267, 307
A/Panama/2007/99	E3	10	93, 143, 197, 208, 249, 267, 360, 399, 403, 437

Hemagglutination Inhibition Antibody Responses to the H3* Component of the 2000-2001 Influenza Vaccine

ADULT POPULATIONS

					% with HI titer ≥ 40	
N	Antigen	% Rise	Pre GMT	Post GMT	Pre Vaccine	Post Vaccine
22[1]	A/Sydney/05/97 Resvir-13*	64	14	53	27	73
22	A/Panama/2007/99 Resvir-17	59	11	38	23	50
22	A/Ulan Ude/01/2000	50	10	27	18	41
22	A/Brazil/991/2000	36	10	27	18	41
22	A/Sydney/203/2000	45	9	26	18	36
22	A/Victoria/509/2000	32	9	24	18	41
24[2]	A/Sydney/05/97 Resvir-13	33	27	78	54	88
24	A/Panama/2007/99 Resvir-17*	46	17	57	33	71
24	A/Ulan Ude/01/2000	42	17	42	25	58
24	A/Brazil/991/2000	42	14	33	17	54
24	A/Sydney/203/2000	42	13	37	25	58
24	A/Victoria/509/2000	42	14	40	25	63
24[3]	A/Sydney/05/97 Resvir-13	92	9	120	13	96
24	A/Panama/2007/99 Resvir-17*	96	6	95	4	96
24	A/Ulan Ude/01/2000	96	6	71	4	92
24	A/Brazil/991/2000	92	6	58	0	79
24	A/Sydney/203/2000	96	5	55	0	71
24	A/Victoria/509/2000	92	6	55	0	75

Preliminary Data 09/07/00

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
3. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

* Vaccine component

Hemagglutination Inhibition Antibody Responses to the H3* Component of the 2000-2001 Influenza Vaccine

ELDERLY POPULATIONS

N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer ≥ 40 Pre Vaccine	Post Vaccine
22[1]	A/Sydney/05/97 Resvir-13*	56	12	43	16	60
22	A/Panama/2007/99 Resvir-17	52	10	32	12	48
22	A/Ulan Ude/01/2000	48	8	22	8	36
22	A/Brazil/991/2000	40	7	19	8	36
22	A/Sydney/203/2000	40	8	21	12	44
22	A/Victoria/509/2000	36	7	20	8	44
24[2]	A/Sydney/05/97 Resvir-13	38	22	52	42	79
24	A/Panama/2007/99 Resvir-17*	33	14	34	21	58
24	A/Ulan Ude/01/2000	33	12	27	21	46
24	A/Brazil/991/2000	42	9	20	17	38
24	A/Sydney/203/2000	33	10	22	17	38
24	A/Victoria/509/2000	42	10	24	17	46
24[3]	A/Sydney/05/97 Resvir-13	75	14	98	29	83
24	A/Panama/2007/99 Resvir-17*	83	11	87	17	75
24	A/Ulan Ude/01/2000	75	10	62	8	75
24	A/Brazil/991/2000	71	9	48	13	67
24	A/Sydney/203/2000	67	8	52	13	71
24	A/Victoria/509/2000	63	9	52	13	75

Preliminary Data 09/07/00

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
3. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

* Vaccine component

Hemagglutination Inhibition Antibody Responses to the H3* Component of the 2000-2001 Influenza Vaccine

ADULT POPULATIONS

					% with HI titer ≥ 40	
N	Antigen	% Rise	Pre GMT	Post GMT	Pre Vaccine	Post Vaccine
22[1]	A/Panama/2007/99 Resvir-17*	50	9	28	14	50
22	A/Fujian/140/2000	18	7	13	9	27
22	A/Hong Kong/1923/2000	32	7	15	0	27
22	A/Missouri/05/2000	50	11	34	14	55
24[2]	A/Panama/2007/99 Resvir-17*	50	18	58	38	75
24	A/Fujian/140/2000	35	9	21	13	42
24	A/Hong Kong/1923/2000	42	12	32	21	54
24	A/Missouri/05/2000	50	14	48	25	67
24[3]	A/Panama/2007/99 Resvir-17*	96	6	80	0	92
24	A/Fujian/140/2000	79	5	34	0	50
24	A/Hong Kong/1923/2000	96	6	46	0	79
24	A/Missouri/05/2000	96	7	87	8	88

Preliminary Data 01/17/2001

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
3. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

* Vaccine component

Hemagglutination Inhibition Antibody Responses to the H3* Component of the 2000-2001 Influenza Vaccine

ELDERLY POPULATIONS

					% with HI titer ≥ 40	
N	Antigen	% Rise	Pre GMT	Post GMT	Pre Vaccine	Post Vaccine
25[1]	A/Panama/2007/99 Resvir-17*	52	10	36	16	52
25	A/Fujian/140/2000	40	7	16	8	24
25	A/Hong Kong/1923/2000	32	8	19	12	36
25	A/Missouri/05/2000	68	11	49	16	56
24[2]	A/Panama/2007/99 Resvir-17*	33	14	35	17	58
24	A/Fujian/140/2000	38	8	16	0	21
24	A/Hong Kong/1923/2000	29	12	24	17	42
24	A/Missouri/05/2000	46	16	41	25	79
24[3]	A/Panama/2007/99 Resvir-17*	83	11	95	17	88
24	A/Fujian/140/2000	67	7	31	4	46
24	A/Hong Kong/1923/2000	63	8	37	13	58
24	A/Missouri/05/2000	75	11	67	17	79

Preliminary Data 01/17/2001

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
3. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

* Vaccine component

Influenza B Viruses

Page

A. Antigenic Characterization.....38

B. Molecular Genetics.....43

C. Serological Responses.....48

INFLUENZA B WORLDWIDE ACTIVITY[1]

Geographical Region	*October 1999 - March 2000*						*Most Frequently Isolated Strain*[2]
	Oct-99	Nov-99	Dec-99	Jan-00	Feb-00	Mar-00	
United States	+	+	+	+	+	+	B/Beijing/184/93-like
Canada	+	+	+	+	+	+	B/Beijing/184/93-like
Europe	+	+	+	+	+	+	B/Beijing/184/93-like
SoAf/Aus/NZ	+		+				B/Beijing/184/93-like
Cen/So America	+				+		B/Beijing/184/93-like
Asia	+	++	++	+	+	+	B/Beijing/184/93-like

Geographical Region	*April 2000 - September 2000*						*Most Frequently Isolated Strain*[2]
	Apr-00	May-00	Jun-00	Jul-00	Aug-00	Sep-00	
United States	+	+	+		+	+	B/Beijing/184/93-like
Canada	+	+	+	+		+	B/Beijing/184/93-like
Europe	+	+	+				B/Beijing/184/93-like
SoAf/Aus/NZ			+	+	++	+	B/Beijing/184/93-like
Cen/So America		+	+	+	+	+	B/Beijing/184/93-like
Asia	+	+	+	+	+	+	B/Beijing/184/93-like

Geographical Region	*October 2000 - January 2001*						*Most Frequently Isolated Strain*[2]
	Oct-00	Nov-00	Dec-00	Jan-01	Feb-01	Mar-01	
United States	+	+	+	+			B/Beijing/184/93-like
Canada	+	+	++	++			B/Beijing/184/93-like
Europe	+	+	+	++			B/Beijing/184/93-like
SoAf/Aus/NZ	+	+					B/Beijing/184/93-like
Cen/So America							
Asia	+	++	+	+			B/Beijing/184/93-like

[1] Activity level. + = Sporadic, ++ = Outbreak, +++ = Epidemic

[2] Strain data based on characterization tests performed at CDC and other WHO Collaborating Centers.

Preliminary Data 1/22/01

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA TYPE B VIRUSES (11/17/00)

STRAIN DESIGNATION	REFERENCE FERRET ANTISERA					
	A	B	C	D	Date	
REFERENCE ANTIGENS	BJ/184	B/YAM	B/JOH/5	B/SICH	collected	Passage
1. B/BEIJING/184/93	**160**	160	160	80	11/09/93	E2/E4
2. B/YAMANASHI/166/98*	160	**160**	320	160	02/21/98	E2/E3
3. B/JOHANNESBURG/5/99	80	80	**320**	160	04/16/99	E6/E4
4. B/SICHUAN/379/99*	80	49	160	**320**	12/02/99	E2/E3
TEST ANTIGENS						
5. B/WASHINGTON/02/2000	160	160	160	320	09/25/00	X/C1
6. B/ALASKA/04/2000	80	80	320	160	09/15/00	M1/C1
7. B/ALASKA/05/2000	80	80	320	320	10/18/00	M1/C1
8. B/MOSCOW/4/2000	80	80	160	160	06/04/00	C1/C1
9. B/MEXICO/14/2000	160	80	160	320	UNKN	X/C1
10. B/TIANJIN/127/2000	80	80	80	80	UNKN	C2/C1
11. B/HONG KONG/538/2000	80	80	80	80	07/31/00	C2/C1
12. B/HONG KONG/557/2000*	160	80	160	160	10/04/00	C2/C1
13. B/HONG KONG/558/2000	80	40	80	80	10/10/00	C2/C1
14. B/HONG KONG/548/2000	80	40	160	160	09/08/00	C2/C1

* Used in serology tests

Preliminary data

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA TYPE B VIRUSES (12/23/00)

STRAIN DESIGNATION	REFERENCE FERRET ANTISERA					
	A	B	C	D	Date	
REFERENCE ANTIGENS	BJ/184	YAM/166	JOH/5	SIC/379	collected	Passage
1. B/BEIJING/184/93	**160**	160	160	80	11/09/93	E2/E5
2. B/YAMANASHI/166/98	160	**320**	160	160	02/21/98	E2/E3
3. B/JOHANNESBURG/5/99	40	80	**160**	160	04/16/99	E6/E4
4. B/SICHUAN/379/99	40	80	160	**160**	12/02/99	E2/E4
TEST ANTIGENS						
5. B/ALASKA/19/2000	160	80	160	160	11/22/00	M1/C1
6. B/ALASKA/18/2000	80	40	80	160	11/15/00	M1/C1
7. B/ALASKA/17/2000	40	40	80	80	11/15/00	E3
8. B/ALASKA/16/2000	40	40	80	80	11/22/00	E2
9. B/TEXAS/11/2000	80	40	80	160	11/22/00	M1/C1
10. B/WISCONSIN/03/2000	40	40	80	160	12/02/00	M1/C1
11. B/CALIFORNIA/06/2000	80	40	80	160	11/20/00	X/C1
12. B/CANADA/580/2000	40	40	80	80	11/20/00	X/C1
13. B/CANADA/593/2000	40	40	80	160	11/29/00	X/C1
14. B/CANADA/585/2000	40	40	80	160	11/15/00	X/C1
15. B/INDIA/3347/2000	40	40	80	160	07/12/00	CX/C2
16. B/JAPAN/6309/2000	80	40	80	80	11/02/00	X/C1
17. B/HONG KONG/548/2000	40	40	80	160	09/08/00	C2/C1
18. B/HONG KONG/564/2000	40	40	80	80	10/24/00	C2/C1

* Used in serology tests

Preliminary data

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA TYPE B VIRUSES (01/11/01)

STRAIN DESIGNATION	REFERENCE FERRET ANTISERA							
	A	B	C	D	E	F	Date	
REFERENCE ANTIGENS	BJ/184	YAM/166	JOH/5	SIC/379	VIC/504	SHI/480	collected	Passage
1. B/BEIJING/184/93	**160**	160	160	80	40	80	11/09/93	E2/E5
2. B/YAMANASHI/166/98*	320	**320**	320	320	160	320	02/21/98	E2/E3
3. B/JOHANNESB./5/99	80	80	**320**	160	80	160	04/16/99	E6/E4
4. B/SICHUAN/379/99*	80	80	160	**160**	80	80	12/02/99	E2/E4
5. B/VICTORIA/504/2000	40	40	160	80	**80**	80	03/08/00	CEK1E12/E1
6. B/SHIZUOKA/480/2000	40	40	80	80	80	**160**	2000	E1E5
TEST ANTIGENS								
7. B/CALIFORNIA/07/2000	320	320	320	320	320	320	~12/01/00	E2
8. B/TEXAS/12/2000	80	80	160	160	160	80	~12/01/00	X/C1
9. B/ARKANSAS/01/2000	80	40	80	80	80	80	~12/01/00	X/C1
10. B/ALASKA/16/2000*	40	40	80	80	80	80	11/22/00	E2
11. B/CANADA/16188/2000*	40	40	80	80	40	80	11/23/00	E2
12. B/CANADA/15360/2000	80	40	160	160	80	80	11/09/00	E1
13. B/CANADA/40413/2000	40	40	160	80	80	80	09/04/00	E2
14. B/JAPAN/6566/2000	160	320	320	320	80	160	11/19/00	E1
15. B/GUANGDONG/120/2000*	80	160	320	160	160	160	03/17/00	E3/E1
16. B/HONG KONG/533/2000	40	40	80	80	40	80	06/19/00	E1
17. B/HONG KONG/558/2000	40	40	160	80	80	80	01/10/00	E1
18. B/HONG KONG/542/2000	80	40	160	80	80	80	07/20/00	E2
19. B/HONG KONG/557/2000*	20	20	80	40	40	40	10/04/00	E2

* Used in serology tests

Preliminary data

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA TYPE B VIRUSES (1/25/01)

STRAIN DESIGNATION	REFERENCE FERRET ANTISERA							
	A	B	C	D	E	F	Date	
REFERENCE ANTIGENS	BJ/184	YAM/166	JOH/5	SIC/379	AK/16	VIC/504	collected	Passage
1. B/BEIJING/184/93	**320**	320	640	160	320	160	11/09/93	E2/E5
2. B/YAMANASHI/166/98*	160	**320**	320	320	320	160	02/21/98	E2/E3
3. B/JOHANNESBURG/5/99	40	80	**320**	160	160	80	04/16/99	E6/E4
4. B/SICHUAN/379/99*	40	80	320	**160**	160	160	12/02/99	E2/E4
5. B/ALASKA/16/2000*	40	40	80	80	**160**	80	10/40/00	E2
6. B/VICTORIA/504/2000	40	40	160	80	160	**80**	03/08/00	CEK1E12/E1
TEST ANTIGENS								
7. B/ARIZONA/10/2000	160	160	640	320	640	160	12/10/00	X/C1
8. B/ARIZONA/11/2000	80	80	320	160	640	160	12/19/00	X/C1
9. B/TENNESSEE/01/2000	80	40	160	80	320	160	11/27/00	C2/C1
10. B/MASS/02/2000	40	40	160	80	160	80	12/18/00	X/C1
11. B/VIRGINIA/01/2000	40	40	80	80	320	80	12/17/00	X/C2
12. B/NEW YORK/03/2000	80	40	160	80	320	80	12/12/00	M1/C1
13. B/NEW YORK/04/2000	40	40	160	160	640	80	12/19/00	X/C1
14. B/N. CAROLINA/01/2000	40	40	80	80	320	80	12/28/00	M1/C1
15. B/TEXAS/01/2001	40	40	80	80	320	160	01/04/00	X/C1
16. B/TEXAS/13/2000	40	40	80	80	320	160	12/29/00	X/C1
17. B/VIRGINIA/02/2000	40	40	160	80	160	80	12/13/00	X/C1
18. B/CALIFORNIA/09/2000	40	40	160	160	320	80	12/13/00	X/C1
19. B/WASHINGTON/01/2001	80	40	160	160	320	80	01/04/01	M1/C1
20. B/MARYLAND/01/2000	40	40	160	160	320	80	12/26/00	M1/C1
21. B/NEW MEXICO/02/2000	80	40	320	160	320	80	12/08/00	X2/C1
22. B/ENGLAND/197/2000	40	80	320	160	160	160	12/08/00	C1/E2/E1
23. B/LISBON/3/2000	80	40	160	160	640	160	10/30/00	C1/2/C1
24. B/EGYPT/907089/2000	40	40	80	80	320	80	10/08/00	C2/C1

* Used in serology tests

Preliminary data

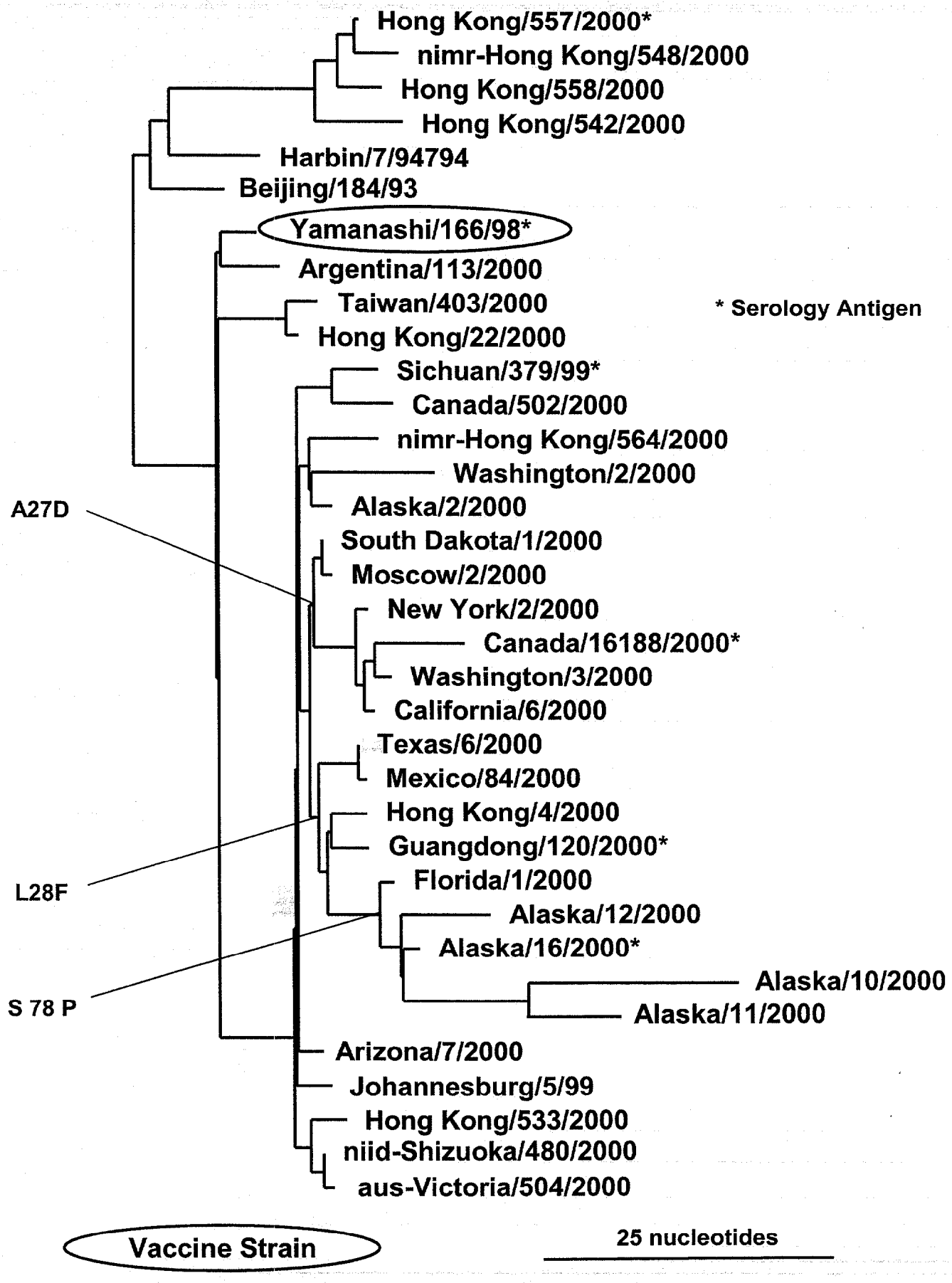
Influenza B Isolates Characterized by CDC

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 1999 - September 1999							
B/Victoria/02/87-like				10			10 (9%)
B/BJ/184/93-B/Yam/166-like*	7	1	1	35	29	22	95 (86%)
B/BJ/184/93-B/Yam-like (low)				5			5 (5%)
						Total	110
October 1999 - March 2000							
B/Victoria/02/87-like				1			1 (1%)
B/BJ/184/93-B/Yam/166-like*	21	3	5	50	2	3	84 (86%)
B/BJ/184/93-B/Yam-like (low)	8			4			12 (12%)
						Total	97
April 2000 - September 2000							
B/Victoria/02/87-like							0
B/BJ/184/93-B/Yam/166-like*	16	1	2	21	15	12	67 (79%)
B/BJ/184/93-B/Yam-like (low)	2	1		7	2	6	18 (21%)
						Total	85
October 2000 - December 2000							
B/Victoria/02/87-like							0
B/BJ/184/93-B/Yam/166-like*	19	2		5			26 (28%)
B/BJ/184/93-B/Yam-like (low)	50	10		1		5	66 (72%)
						Total	92
Total	123	18	8	139	48	48	328

Preliminary Data 01/25/01

*Includes viruses antigenically related to B/Beijing/184/93, the reference strain, or to the equivalent B/Yamanashi/166/98 vaccine strain.

Evolutionary Relationships Among Influenza B Hemagglutinin (HA1) Genes



Number of Amino Acid Differences from B/Yamanashi/166/98-like Consensus HA1 Sequence

Isolate	Passage	No. of Differences
Mexico/84/2000	e2/e1	0
Johannesburg/5/99	e6/e1	1
aus-Victoria/504/2000	cek1e12/e1	2
niid-Shizuoka/480/2000	e1e5	2
Sichuan/379/99*	e2	2
Alaska/16/2000*	e2	3
Guangdong/120/2000*	e3/e1	3
Yamanashi/166/98*	e2/e2	5
Canada/16188/2000*	e2	7
Beijing/184/93	e2/e4	11
Harbin/7/94[1]	e3/e3	14
Hong Kong/557/2000*[1]	e2	14
Hong Kong/542/2000[1]	e2	15

* Serology Antigens
[1] B/Harbin/7/94 genetic lineage

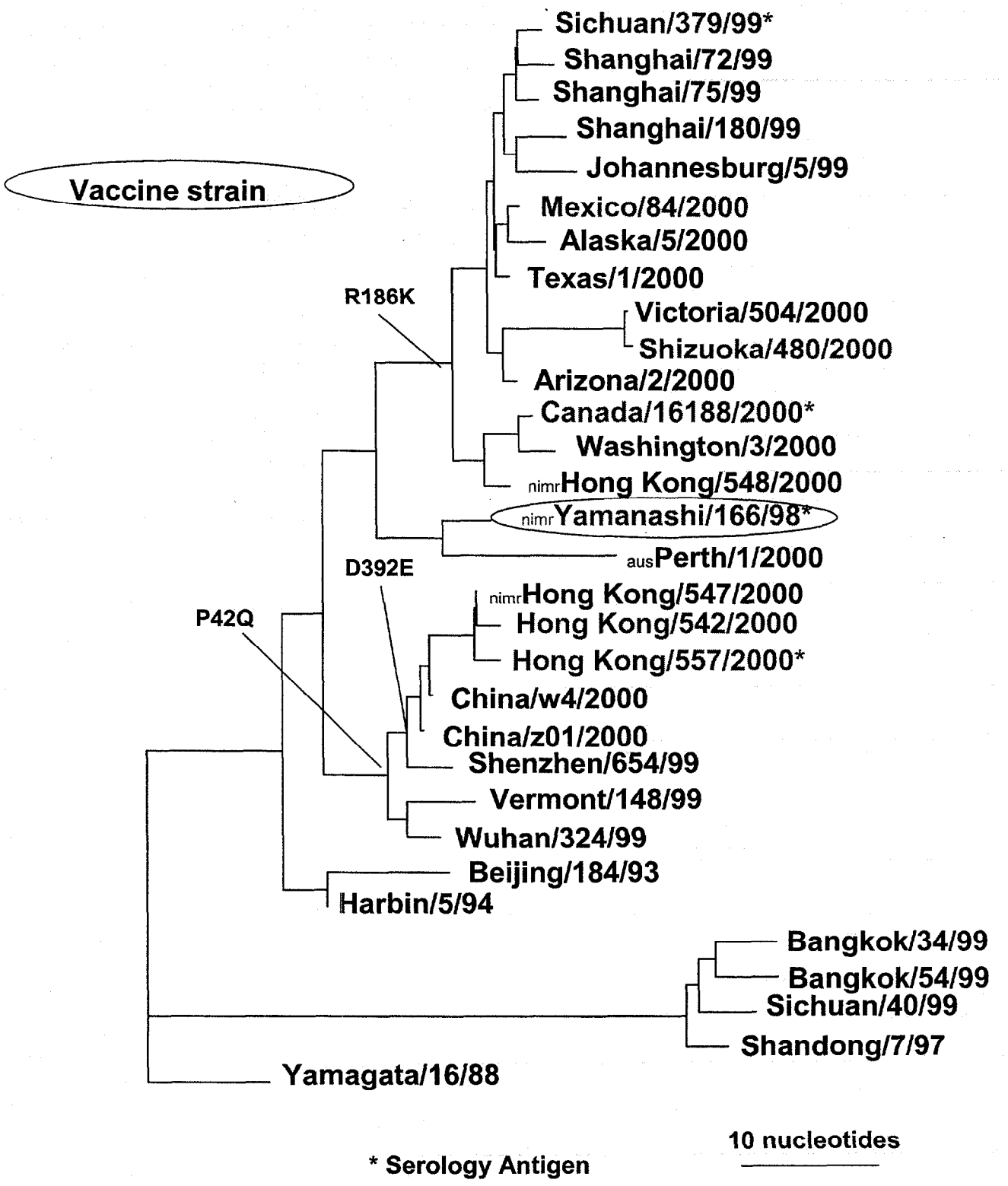
Restriction Analysis of the HA gene of Influenza B Isolates

	U.S.A.	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)
April 1999 - September 1999							
B/Shangdong/7/97*-lineage				10			10 (8%)
B/Beijing/184/93**-lineage	7	1	2	32	39	190	100 (78%)
B/Harbin7/94**-lineage				18			18 (14%)
						Total	128
October 1999 - March 2000							
B/Shangdong/7/97*-lineage				1			1 (1%)
B/Beijing/184/93**-lineage	25	5	7	52	2	10	101 (92%)
B/Harbin7/94**-lineage		1		7			8 (7%)
						Total	110
April 2000 - September 2000							
B/Shangdong/7/97*-lineage							0
B/Beijing/184/93**-lineage	20	1	3	29	18	18	89 (93%)
B/Harbin7/94**-lineage				7			7 (7%)
						Total	96
October 2000 - December 2000							
B/Shangdong/7/97*-lineage							0
B/Beijing/184/93**-lineage	23	1		5			29 (28%)
B/Harbin7/94**-lineage				3			3 (9%)
						Total	32
Total	75	9	12	164	59	47	366

Preliminary Data 01/27/01

* B/Victoria/2/87 genetic group.
** B/Yamagata/16/88 genetic group

Evolutionary Relationships Among Influenza B Neuraminidase Genes



* Serology Antigen

Number of Amino Acid Differences from Consensus B Neuraminidase Sequence

Isolate	Passage	No. of Differences	Position
B/Mexico/84/2000	E2/E1	0	
B/Sichuan/379/99	E2/E2	1	60
Shizuoka/480/2000	E1E4/E1	3	42, 69, 272
B/Canada/16188/2000	E2	3	65, 148, 315
B/Hong Kong/542/2000	E2	7	42, 54, 186, 219, 235, 392, 436
B/Hong Kong/557/2000	E2	8	42, 81, 186, 219, 235, 392, 436, 458
nimrB/Yamanashi/166/98	EX/E3	8	74, 128, 186, 235, 272, 389, 395, 436

Hemagglutination Inhibition Antibody Responses to the B/Yamanashi/166/98* Component of the 2000-2001 Influenza Vaccine

ADULT POPULATIONS

					% with HI titer ≥ 40	
N	Antigen	% Rise	Pre GMT	Post GMT	Pre Vaccine	Post Vaccine
22[1]	B/Yamanashi/166/98* ET	50	34	193	55	100
22	B/Johannesburg/05/99 ET	50	34	170	55	100
22	B/Sichuan/379/99 ET	59	25	137	45	100
22	B/Argentina/64/2000 ET	59	21	103	36	95
22	B/Hong Kong/531/2000 ET	59	23	124	41	100
22	B/Auckland/01/2000 ET	55	24	137	45	100
24[2]	B/Yamanashi/166/98* ET	33	62	185	71	100
24	B/Johannesburg/05/99 ET	33	53	155	75	96
24	B/Sichuan/379/99 ET	38	38	123	63	96
24	B/Argentina/64/2000 ET	33	34	87	54	88
24	B/Hong Kong/531/2000 ET	33	39	127	63	92
24	B/Auckland/01/2000 ET	38	44	143	67	92
24[3]	B/Yamanashi/166/98* ET	100	17	349	38	96
24	B/Johannesburg/05/99 ET	92	18	329	33	96
24	B/Sichuan/379/99 ET	88	14	285	29	96
24	B/Argentina/64/2000 ET	96	18	233	29	100
24	B/Hong Kong/531/2000 ET	92	15	277	38	96
24	B/Auckland/01/2000 ET	92	13	233	33	96

Preliminary Data 09/13/2000

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
3. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

* B/Yamanashi/166/98 is the B/Beijing/184/93-like component of the northern hemisphere vaccine.

Hemagglutination Inhibition Antibody Responses to the B/Yamanashi/166/98* Component of the 2000-2001 Influenza Vaccine

ELDERLY POPULATIONS

N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer ≥ 40 Pre Vaccine	Post Vaccine
25[1]	B/Yamanashi/166/98* ET	40	33	100	56	96
25	B/Johannesburg/05/99 ET	44	29	80	52	88
25	B/Sichuan/379/99 ET	36	24	57	40	80
25	B/Argentina/64/2000 ET	36	19	40	36	72
25	B/Hong Kong/531/2000 ET	36	22	59	40	84
25	B/Auckland/01/2000 ET	48	24	70	44	84
24[2]	B/Yamanashi/166/98* ET	8	58	78	67	88
24	B/Johannesburg/05/99 ET	8	48	69	67	83
24	B/Sichuan/379/99 ET	4	37	49	63	75
24	B/Argentina/64/2000 ET	4	21	29	38	58
24	B/Hong Kong/531/2000 ET	4	35	49	67	83
24	B/Auckland/01/2000 ET	8	40	55	67	79
24[3]	B/Yamanashi/166/98* ET	71	18	226	33	100
24	B/Johannesburg/05/99 ET	75	15	207	29	100
24	B/Sichuan/379/99 ET	79	14	180	25	100
24	B/Argentina/64/2000 ET	79	16	155	33	92
24	B/Hong Kong/531/2000 ET	92	12	180	21	100
24	B/Auckland/01/2000 ET	67	16	155	33	96

Preliminary Data 09/13/2000

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
3. Sera were kindly provided by Dr. John Wood, NIBSC, Hertfordshire, UK. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.

* B/Yamanashi/166/98 is the B/Beijing/184/93-like component of the northern hemisphere vaccine.

Hemagglutination Inhibition Antibody Responses to the B/Yamanashi/166/98* Component of the 2000-2001 Influenza Vaccine

ADULT POPULATIONS

N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer ≥ 40 Pre Vaccine	Post Vaccine
22[1]	B/Yamanashi/166/98 ET	55	24	121	45	100
22	B/Sichuan/379/99 ET	64	21	97	32	95
22	B/Canada/16188/2000 ET	59	36	165	59	100
22	B/Alaska/16/2000 ET	67	17	88	27	95
22	B/Guangdong/120/2000 ET	67	27	150	52	100
22	B/Hong Kong/557/2000 ET	67	12	70	19	81
24[2]	B/Yamanashi/166/98 ET	33	42	160	61	95
24	B/Sichuan/379/99 ET	39	25	78	48	83
24	B/Canada/16188/2000 ET	39	49	160	65	96
24	B/Alaska/16/2000 ET	41	22	71	36	79
24	B/Guangdong/120/2000 ET	30	41	151	65	91
24	B/Hong Kong/557/2000 ET	43	21	73	35	83
24[3]	B/Yamanashi/166/98 ET	96	18	247	42	100
24	B/Sichuan/379/99 ET	96	13	185	25	96
24	B/Canada/16188/2000 ET	88	23	339	54	100
24	B/Alaska/16/2000 ET	92	14	174	21	96
24	B/Guangdong/120/2000 ET	92	13	207	29	96
24	B/Hong Kong/557/2000 ET	88	13	135	21	92

Preliminary Data 01/19/2001

1. Sera were kindly provided by Alan Hampson, WHO Collaborating Center, Melbourne, Australia. The populations were vaccinated with the 2000 trivalent influenza vaccine containing 15 mkg each of A/Sydney/05/97(H3N2)-like, A/New Caledonia/20/99(H1N1), and B/Yamanashi/166/98-like hemagglutinin.
2. Sera were kindly provided by Dr. Roland Levandowski, FDA, Bethesda, MD. The populations were vaccinated with the 2000-20001 trivalent influenza vaccine containing 15 mkg each of A/Panama/2007/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Yamanashi/166/98-like hemagglutinin.
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* B/Yamanashi/166/98 is the B/Beijing/184/93-like component of the northern hemisphere vaccine.

Hemagglutination Inhibition Antibody Responses to the B/Yamanashi/166/98* Component of the 2000-2001 Influenza Vaccine

ELDERLY POPULATIONS

N	Antigen	% Rise	Pre GMT	Post GMT	% with HI titer ≥ 40 Pre Vaccine	Post Vaccine
25[1]	B/Yamanashi/166/98 ET	24	47	97	60	92
25	B/Sichuan/379/99 ET	36	38	85	52	92
25	B/Canada/16188/2000 ET	33	73	160	75	96
25	B/Alaska/16/2000 ET	22	42	74	61	84
25	B/Guangdong/120/2000 ET	30	69	132	74	96
25	B/Hong Kong/557/2000 ET	26	39	64	52	80
24[2]	B/Yamanashi/166/98 ET	4	38	49	67	75
24	B/Sichuan/379/99 ET	4	20	25	42	58
24	B/Canada/16188/2000 ET	4	37	48	67	78
24	B/Alaska/16/2000 ET	8	21	29	42	63
24	B/Guangdong/120/2000 ET	0	49	60	75	79
24	B/Hong Kong/557/2000 ET	4	21	27	33	50
24[3]	B/Yamanashi/166/98 ET	83	14	174	25	96
24	B/Sichuan/379/99 ET	78	13	155	13	91
24	B/Canada/16188/2000 ET	79	22	302	46	100
24	B/Alaska/16/2000 ET	83	11	93	21	83
24	B/Guangdong/120/2000 ET	78	11	105	13	83
24	B/Hong Kong/557/2000 ET	86	9	91	9	81

Preliminary Data 01/19/2001

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