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FOR REFERENCE AND RESEARCH ON INFLUENZA**

**REPORT**

**August 2001 to July 2002**

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During the past year, the Influenza Centre characterized approximately 1300 influenza viruses from 47 countries. Fifty six per cent were type A, of which 75% were H3N2, 11% were H1N1 and 14% were H1N2, and 44% were influenza B (Table 1). Although similar numbers of AH3N2 and B viruses were isolated during October to April (Table 2), H3N2 viruses were predominant among isolates received from countries such as Denmark, Finland, Iceland, Mauritania, Norway, and Sweden, whereas B viruses predominated among those received from Italy and Yugoslavia. The H1N2 subtype was prominent among viruses isolated in several countries, Egypt, Ireland, Israel, Romania and the UK, where they accounted for the majority of H1 isolates; in contrast H1 viruses isolated in Spain and Japan were almost exclusively H1N1. Sporadic cases of human infection by swine H1N1 viruses were detected in Hong Kong in November and in Switzerland in February. Swine viruses of H1N1, H1N2 and H3N2 subtypes from France and Italy were also characterized.

Noteable changes in the circulating viruses included the emergence of the H1N2 subtype, a reassortant between recently circulating H1N1 and H3N2 viruses, and the increasing prevalence of B/Victoria-lineage viruses worldwide, necessitating a change in vaccine composition to include a B/Hong Kong/330/2001-like (Victoria lineage) strain (WER 8, 62-66,2002).

#### **A H1N1 viruses**

Most of the H1N1 viruses were antigenically closely related to A/New Caledonia/20/99 (Table 3) and similar to viruses circulating during the previous year. None were A/Bayern/7/95-like and few gave reduced HI titres (4 fold or greater) with antisera to A/New Caledonia/20/99-like reference viruses.

As previously, the A/New Caledonia/20/99-like viruses separated into two phylogenetic groups on the basis of their HA and NA sequences (Figures 1 and 3, Table 4), which were indistinguishable in HI tests. Group 1 viruses were more closely related to A/New Caledonia/20/99 and differed in HA1 sequence by the common amino acid changes valine 166 to alanine (V166A) and tryptophan 252 to arginine (W252R) (Figure 2, Table 4). Their NA sequences were similar to that of A/New Caledonia/20/99 (Figure 4). The HA1 sequences of viruses in group 2, represented by A/Madagascar/57794/00, were distinguished by the changes glutamic acid 120 to glycine (E120G), lysine 163 to methionine (K163M) and aspartic acid 273 to glycine (D273G) (Figure 2, Table 4). The principal amino acid differences which distinguish the NA sequences of the latter viruses from those of group 1 include isoleucine 48 to valine (I48V), valine 75 to isoleucine (V75I), arginine 22 to glutamine (R222Q) and aspartic acid 344 to asparagine (D344N) (Figure 4, Table 4).

A H1N1 virus, A/Hong Kong/1308/01, isolated from a 3 month old child in Hong Kong was antigenically and genetically (data from W. Lim) closely related to classical H1N1 swine viruses represented by A/New Jersey/8/76 (Table 5).

A single H1N1 isolate, A/Switzerland/8808/02, from a farmer in Switzerland was antigenically and genetically similar to contemporary A/swine/IV/1455/99-like viruses circulating in European pigs (Tables 6 and 7).

### **A H1N2 viruses**

This subtype, which emerged during 2000-2001 and was identified among viruses isolated in Saudi Arabia in March 2001, circulated in many countries around the world. The HAs of the H1N2 viruses were antigenically closely related to those of A/New Caledonia/20/99 (H1N1) -like viruses (Table 3) and the NAs were antigenically closely related to those of A/Moscow/10/99(H3N2)-like viruses (Table 8). The HA1 sequences were more closely related to those of group 1 A/New Caledonia/20/99(H1N1)-like viruses (Figure 1) and were distinguished by the amino acid changes, alanine 190 to threonine (A190T) and histidine 193 to asparagine (H193N) or alanine 215 to threonine (A215T) (plus valine 175 to isoleucine (V175I) in some isolates)(Figure 2). Their NA sequences were similar to those of recent A/Moscow/10/99(H3N2)-like viruses, such as A/Singapore/15/01(Figure 7); many were distinguished by two amino acid changes, glutamic acid 199 to lysine (E199K) and lysine 431 to asparagine (K431N) (Figure 8). The six internal genes of representative H1N2 viruses, such as A/Saudia Arabia/2231/01 were also closely related to those of contemporary A/Moscow/10/99 (H3N2)-like viruses and distinct from the genes of recent H1N1 viruses, such as A/Saudi Arabia/7971/00 or A/New Caledonia/20/99 (Table 9).

### **A H3N2 viruses**

Many H3N2 viruses were closely related antigenically to A/Panama/2007/99 (Table 10). Of recent isolates which gave reduced HI titres (4-fold or greater) with ferret antisera to A/Moscow/10/99 and A/Panama/2007/99, most appeared more closely related to A/Toulouse/878/01, A/Singapore/15/01 and/or A/Hong Kong/734/01(or A/Hong Kong/1550/02, not shown), representative of more recent (genetic) variants. These reference viruses were not clearly distinguished from A/Panama/2007/99 in HI tests (Table 10) and no consistent correlation was noted between reduced HI titres and changes in HA sequence.

The HA and NA sequences of viruses, isolated between August 2001 and July 2002, mostly fell within one of two phylogenetic groups, 1c and 1b (see Annual Report, 2001) represented by A/Toulouse/878/01 and A/Hong Kong/1143/02 (or A/Hong Kong/1550/02), respectively (Figures 5 and 7), which emerged during the previous year. The former are characterized by the amino acid changes alanine 106 to valine (A106V), asparagine 144 to aspartic acid (N144D; with the loss of a glycosylation site) and serine 186 to glycine (S186G) from the HA of A/Panama/2007/99 (other frequently observed changes include arginine 220 to glycine (R220G), aspartic acid 219 to glycine (D291G) and alanine 304 to proline (A304P) (Figure 6, Table 11). Amino acid differences (relative to the NA of A/Moscow/10/99) characteristic of the NAs of these viruses include lysine 172 to arginine (K172R), thronine 265 to isoleucine (T265I), proline 267 to threonine (P267T), serine 332 to phenylalanine (S332F), aspartic acid 399 to glutamic acid (D399E), glutamine 432 to glutamic acid (Q432E) and leucine 437 to tryptophan (L437W) (Figure 8, Table 11). The HAs of the A/HK/1143/02 group (1b) are distinguished by the changes arginine 50 to glycine (R50G) , glutamic acid 83 to lysine (E83K), valine 202 to isoleucine (V202I), tryptophan 222 to arginine (W222R) and glycine 225 to aspartic acid (G225D) (most also have alanine 131 to threonine (A131T) and serine 186 to glycine (S186G) changes). The NAs of these viruses are distinguished by the changes alanine 18 to serine (A18S), leucine 23 to phenylalanine (L23F), valine 30 to isoleucine (V30I), cysteine 42 to phenylalanine (C42F), proline 267 to threonine (P267T) and valine 307 to isoleucine (V307I), relative to the NA of A/Moscow/10/99 (Table 11). The latter variant (1b) has been less prominent among more recent isolates.

Influenza viruses associated with a severe outbreak, with high mortality, in Madagascar during July 2002 (WER 77, 294,2002) were antigenically closely related to A/Panama/2007/99 (Table 10) and genetically similar to other contemporary isolates which fall within group 1c (Figures 5 and 7).

## **B viruses**

Although more than three quarters of the B viruses isolated between December and May were antigenically closely related to B/Sichuan/379/99, the proportion of B/Hong Kong/330/01-like (Victoria-lineage) isolates increased from 13% in January to 36% in April (Tables 2 and 12), and these viruses have become predominant among B viruses circulating in many parts of the world.

As previously, the HA and NA sequences of B/Sichuan/379/99-like (Yamagata-lineage) viruses fell into two sublineages (Figures 9 and 11). Sequences within the Sichuan-lineage were similar to those of viruses circulating earlier during 2001 and were close to those of B/Sichuan/379/99. Common changes in the HAs include leucine 58 to phenylalanine (L58F) and asparagine 126 to aspartic acid (N126D) and in the NAs, glutamic acid 148 to glycine (E148G) (Table 13). A divergent group, composed mainly of Japanese isolates (not shown), was characterized by several changes in HA sequence, arginine 69 to glycine (R69G), threonine 121 to alanine (T121A), arginine 136 to lysine (R136K), asparagine 164 to aspartic acid (N164D), threonine 181 to alanine (T181A) and lysine 182 to asparagine (K182N). The HA and NA sequences of an increasing proportion of viruses fell within the Harbin-lineage and were similar to those of viruses circulating during the previous year. Their HAs were distinguishable from those of earlier isolates, such as B/Hong Kong/557/00 by the change histidine 40 to tyrosine (H40Y) (Table 13). The NAs of the B/Harbin-lineage viruses are distinguished from those of recent B/Sichuan-lineage viruses by 8 principal differences, proline 42 to glutamine (P42Q), glycine 148 to glutamic acid (G148E), lysine 186 to arginine (K186R), asparagine 219 to lysine (N219K), asparagine 235 to aspartic acid (N235D), aspartic acid 329 to asparagine (D329N), aspartic acid 392 to glutamic acid (D392E) and glutamic acid 436 to threonine (E436T) (Figure 12). B/Harbin-lineage viruses were not distinguished from B/Sichuan-lineage viruses in HI tests.

Most B/Victoria-lineage viruses were antigenically closely related to B/Hong Kong/330/01 or B/Hong Kong/335/01 (Table 12). They were separated into two groups on the basis of their HA and NA sequences. The HAs of viruses in group 1, represented by B/Hong Kong/330/01 or B/Hong Kong/335/01, were distinguished from those of previous isolates, such as B/Shandong/7/97, by the amino acid changes histidine 116 to arginine (H116R), isoleucine 121 to asparagine (I121N) and aspartic acid 164 to glutamic acid (D164E) (Figures 9 and 10, Table 13). As for some Yamagata-lineage viruses, differences in residues 197 (N197S/T) and 199 (T199I/A)) altered glycosylation of asparagine 197 in HA (Figure 10). Changes in the neuraminidase sequences of these viruses relative to those of earlier isolates, such as B/Shandong/7/97, include methionine 50 to threonine (M50T), cysteine 54 to serine (C54S), valine 60 to phenylalanine (V60F), glutamic acid 69 to lysine (E69K), asparagine 345 to serine (N345S), arginine 360 to lysine (R360K), and lysine 436 to threonine (K436T) (Figure 12, Table 13). The HAs of group 2 viruses, represented by B/Tehran/80/02 were more closely related in sequence to the HA of B/Shandong/7/97 (Figures 9 and 10, Table 13). The NAs of many of these viruses were, however, similar to those of recent B/Sichuan/379/99-like viruses (Figures

11 and 12, Table 13). These reassortant viruses, containing a Shandong-like HA and a Sichuan-like NA, therefore represent a 4th group of genetically distinguishable B viruses.

### **Swine Influenza Viruses**

Of 60 viruses characterized (12 isolated in France and 48 in Italy), 27 were of the H1N1 subtype, 7 were H1N2 and 26 were H3N2. Most H1N1 isolates were antigenically closely related, in HI and NI tests, to the reference viruses A/swine/Ille et Vilaine/1455/99 (Sw/IV/1455/99) or A/swine/Côtes d'Armor/1482/99 (Sw/CA/1482/99) (Table 14, A and B). The H1N2 viruses, isolated in France, were antigenically most closely related to the reference swine virus Sw/CA/790/97 (Table 15, A and B). The H3N2 viruses, isolated in Italy, were antigenically closely related to the recent reference strain A/Italy/1523/98 (Table 16, A and B).

### **Reagents**

Influenza viruses and antisera sent to National Influenza Centres and other Collaborating Centres are listed in Tables 17 and 18.

### **Acknowledgements**

We specifically acknowledge the collaborative efforts of the staff of the many National Influenza Centres who submitted viruses for characterization. Conclusions regarding HA and NA sequences are based on sequence data shared among the four WHO Collaborating Centres and data received from the Influenza Centres in Hong Kong, Italy, Norway, South Africa and the U.K. (indicated by suffixes).

## Publications (2001 - )

Coiras, M.T., Aguilar, J.C., Galiano, M., Carlos, S., Gregory, V., Lin, Y.P. Hay, A. and Peres-Brena, P. (2001). Rapid molecular analysis of the haemagglutinin gene of human influenza A H3N2 viruses isolated in Spain from 1996 to 2000. *Arch. Virol.*, **146**, 2133-2147.

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Marozin, S., Gregory, V., Cameron, K., Bennett, M., Valette, M., Aymard, M., Foni, E., Barigazzi, G., Lin, Y. and Hay, A. (2001). Antigenic and genetic diversity among swine influenza viruses in Europe. In *Options for the Control of Influenza IV*. Eds. A.D.M.E. Osterhaus, N. Cox and A.Hampson. Elsevier Science B.V., Amsterdam, pp 233-240.

Marozin, S., Gregory, V., Cameron, K., Bennett, M., Valette, M., Aymard, M., Foni, E., Barigazzi, G., Lin, Y. and Hay, A. (2002). Antigenic and genetic diversity among swine influenza A H1N1 and H1N2 viruses in Europe. *J. Gen. Virol.* **83**, 735-745.

Van Reeth, K., Gregory, V., Hay, A. and Pensaert, M. (2002). Protection against a European H1N2 swine influenza virus in pigs previously infected with H1N1 and/or H3N2 subtypes. *Vaccine*, in press.

## **Submitted for Publication**

Ellis, J.S., Alvarez-Aguero, A., Lin, Y.P., Gregory, V., Hay, A. and Zambon, M.C. Impact of influenza AH1N2 viruses during the 2001-02 influenza season in the United Kingdom. Submitted for publication.

Marx, A., Tavernini, M., Gregory, V., Lin, Y.P., Hay, A., Tschopp, A. and Steffen, R. Influenza virus infection in travellers to developing countries. Submitted for publication.

Ansaldi, F., D'Agaro, P., de Florentiis, D., Crovari, P., Gasparini, R., Donatelli, I., Puzzelli, S., Gregory, V., Bennett, M., Lin, Y., Hay, A., and Campello, C. Molecular characterization of influenza B viruses circulating in Northern Italy during the 2001-2002 epidemic season. Submitted for publication.

**Table 1: Human influenza isolates characterized August 2001 - July 2002**

<b>Country</b>	<b>H1N1*</b> <b>A/New Caledonia</b> <b>20/99</b>	<b>H1N2</b> <b>A/Egypt</b> <b>96/02</b>	<b>H3N2</b> <b>A/Moscow</b> <b>10/99</b>	<b>B</b> <b>B/Sichuan</b> <b>379/99</b>	<b>B/HK</b> <b>335/01</b>
Albania				3	
Argentina			1		
Australia	3		7	1	
Belgium		1	4	1	
Brazil	1			3	
Chile			1		
Czech Republic			5		
Denmark			30	1	1
Egypt		20			1
Finland	2		15	5	
France	1	7	48	53	12
Germany		1	43	37	14
Greece			2		
Hawaii					8
Hong Kong SAR China	8		8	4	16
Iceland			26		
Iran					2
Ireland		8	7	1	
Israel		39	34	7	14
Italy	7		17	100	31
Japan	9		2	8	4
Latvia		2	16	19	
Madagascar			5	12	
Malaysia				1	
Mauritania			13	1	
Mauritius			4	7	2
Netherlands		1	1	1	3
New Caledonia	1				
New Zealand	3		3	1	
Norway			18	2	5
Paraguay			2		
Philippines	1				3
Poland	3		7		
Portugal	2	1	1		
Reunion			5		
Romania		8	20	11	
Russia	4		3	9	1
Senegal			23	20	
Slovakia			1	4	
Slovenia				6	
South Africa			3	5	
Spain	22		91	87	
Sweden	1	1	36	2	
Switzerland		1	8	3	1
Thailand	2		4	1	
United Kingdom		9	8		
Yugoslavia	3			22	
<b>Total = 1250</b>	<b>73</b> <b>(6%)</b>	<b>99</b> <b>(8%)</b>	<b>522</b> <b>(42%)</b>	<b>438</b> <b>(35%)</b>	<b>118</b> <b>(9%)</b>

\* NA subtype of some 2001 isolates of H1 was not determined

**Table 2. Human influenza viruses isolated August 2001 - July 2002**

<b>Month of isolation</b>	<b>H1N1* A/New Caledonia 20/99</b>	<b>H1N2 A/Egypt 96/02</b>	<b>H3N2 A/Panama 2007/99</b>	<b>B</b>	
				<b>B/Sichuan 379/99</b>	<b>B/HK 335/01</b>
<b>2001</b>					
<b>August</b>	3	1	3	10	5
<b>September</b>	1		5	9	
<b>October</b>	3		5	4	
<b>November</b>		1	4	3	1
<b>December</b>		16	47	29	6
<b>2002</b>					
<b>January</b>	20	48	178	161	25
<b>February</b>	18	15	145	132	38
<b>March</b>	9	17	57	54	22
<b>April</b>	1	5	33	18	10
<b>May</b>			10	1	3
<b>June</b>			2		
<b>July</b>			4		
<b>Total = 1182</b>	55 (5%)	103 (9%)	493 (42%)	421 531 (45%)	110

\* NA subtype of some 2001 isolates of H1 was not determined

**Table 3. Antigenic analyses of the HAs of H1N1 and H1N2 viruses**

Viruses	Isolation Date	Haemagglutination inhibition titre <sup>1</sup>					
		Post-infection ferret sera					
		A/Bay 7/95	A/Beij 262/95	A/NC 20/99	A/HK 1252/00	A/Mad 57794/00	A/Eg 96/02
<b>A/Bayern/7/95 (H1N1)</b>		<b>2560</b>	320	40	<	40	40
<b>A/Beijing/262/95 (H1N1)</b>		80	<b>2560</b>	320	40	640	640
<b>A/New Caledonia/20/99 (H1N1)</b>		40	320	<b>1280</b>	160	1280	1280
<b>A/Hong Kong/1252/00 (H1N1)</b>		<	40	160	<b>640</b>	160	160
<b>A/Madagascar/57794/00 (H1N1)</b>		40	320	1280	160	<b>1280</b>	640
<b>A/Egypt/96/02 (H1N2)</b>		<	320	640	80	1280	<b>1280</b>
<b>H1N1</b>							
A/Philippines/637/01 <sup>2</sup>	10.8.01	<	80	640	80	1280	—
A/Hong Kong/1273/01 <sup>2</sup>	29.8.01	40	320	1280	160	1280	—
A/New Caledonia/10/01 <sup>2</sup>	4.9.01	<	320	1280	80	1280	—
A/Bangkok/544/01 <sup>2</sup>	9.10.01	<	160	640	80	1280	—
A/Darwin/18/01 <sup>2</sup>	11.10.01	<	80	640	40	1280	—
A/Palencia/5/02	8.1.02	<	160	640	160	640	—
A/Madrid/RR1045/02	11.1.02	40	160	1280	160	1280	1280
A/Barcelona/90/02	17.1.02	40	320	640	40	640	—
A/Akita/25/02	29.1.02	<	80	1280	40	1280	640
A/Kaliningrad/2187/02	12.2.02	<	80	1280	80	1280	1280
A/Lisbon/4/02	14.2.02	80	80	640	80	320	640
A/Poland/8/02	23.2.02	<	40	1280	80	1280	1280
A/Finland/108/02	6.3.02	<	80	640	80	640	640
A/Hong Kong/841/02	25.4.02	<	80	320	160	1280	640
<b>H1N2</b>							
A/Israel/152/01	13.8.01	<	160	640	80	640	—
A/Stockholm/13/02	Jan-02	40	160	640	80	640	640
A/England/2/02	3.1.02	<	160	1280	160	1280	—
A/Belgium/338/02	14.1.02	<	160	1280	80	1280	1280
A/Latvia/686/02	18.1.02	<	80	640	80	1280	—
A/Lisbon/2/02	14.2.02	<	80	640	80	640	1280
A/Ireland/3407/02	Mar-02	<	80	640	80	1280	1280
A/Netherlands/352/02	Mar-02	<	80	1280	80	1280	1280
A/Switzerland/3100/02	Mar-02	40	160	1280	160	1280	1280
A/Lyon/807/02	4.3.02	<	80	320	80	640	1280
A/Sachsen/32/02	5.3.02	<	160	640	80	640	1280
A/Constanta/879/02	20.3.02	<	80	640	<	640	640
A/Inverness/5824106/02	1.4.02	<	160	640	80	1280	1280
A/Montpellier/1120/02	18.4.02	<	160	1280	80	640	1280
A/Auckland/2/02	June-02	<	80	640	80	320	640
A/Johannesburg/5/02	2.7.02	40	160	1280	80	1280	1280

1. <, <40; 2. NA subtype not determined

**Table 4. Amino acid changes characteristic of H1N1 sequence variants**

Variant group	Representative strain	Amino acid changes <sup>1</sup>	
		HA	NA
1	A/Hong Kong/437/02	V166A W252R	
2	A/Madagascar/57794/00	E120G K163M D273G	V75I R222Q D344N (R432K)

<sup>1</sup> relative to A/New Caledonia/20/99

**Table 5. Antigenic analysis of A/Hong Kong/1308/01**

Viruses	Haemagglutination inhibition titre <sup>1</sup>								
	Hyperimmune rabbit sera			Post-infection ferret sera					
	A/Braz 11/78	Sw/Fin 2899/82	Sw/Wis 67	A/Bay 7/95	A/NC 20/99	Sw/Iowa 15/30	Sw/Wis 67	A/NJ 8/76	Sw/Fin 2899/82
A/Brazil/11/78	<b>5120</b>	640	80	40	40	<	<	<	<
A/Bayern/7/95	1280	160	40	<b>2560</b>	80	<	<	<	<
A/New Caledonia/20/99	<	160	<	40	<b>1280</b>	<	<	<	<
Sw/Iowa/15/30	160	5120	2560	<	<	<b>320</b>	<	<	<
Sw/Wisconsin/67	80	5120	<b>5120</b>	40	<	320	<b>320</b>	640	<
A/New Jersey/8/76	80	5120	5120	40	<	160	160	<b>1280</b>	320
Sw/Finistere/2899/82	80	<b>5120</b>	5120	<	<	160	<	160	<b>640</b>
A/Hong Kong/1308/01	40	5120	5120	<	<	<	80	640	320

1. <, <40

**Table 6. Antigenic analysis of A/Switzerland/8808/02 (H1N1)**

Viruses	Subtype	Haemagglutination inhibition titre <sup>1</sup>							
		Post-infection ferret sera							
		A/Braz <sup>2</sup> 11/78	Sw/Fin <sup>2</sup> 2899/82	Sw/Fin 2899/82	Sw/It 513-1/98	Sw/CA 1482/99	Sw/IV 1455/99	Sw/CA 790/97	Sw/CA 604/99
A/Brazil/11/78	H1N1	5120	320	<	<	40	80	<	<
Sw/Finistere/2899/82	H1N1	<	5120	1280	80	1280	160	<	<
Sw/Italy/1513-1/98	H1N1	40	5120	1280	320	1280	160	<	<
Sw/CA/1482/99	H1N1	80	5120	1280	320	2560	320	<	<
Sw/IV/1455/99	H1N1	<	1280	640	40	640	1280	<	<
Sw/CA/790/97	H1N2	5120	320	<	<	<	<	320	320
Sw/CA/604/99	H1N2	5120	320	<	<	<	<	160	640
A/Switzerland/8808/02	H1N1	<	2560	320	40	320	320	<	<

1. <, <40; 2. Hyperimmune rabbit serum

**Table 7. Genetic relationships between A/Switzerland/8808/02 and viruses representative of European swine H1N1 and human H1N1 and H3N2 subtypes**

Gene	Percent similarity with A/Switzerland/8808/02 <sup>1</sup>			
	Sw/IV/1455/99	Sw/CA/1482/99	A/NC/20/99	A/Moscow/10/99
PB2	97.7	96	83.2	83.6
PB1	98.8	94.2	78.9	84.6
PA	98.2	95.2	83.4	84.5
H1	98.3	90.4	70.3	-
NP	98.8	96.5	83.1	81.5
N1	99.1	91.5	79.6	-
M	99.2	95.9	85.5	85.2
NS	98.3	93.5	83.4	82.5

<sup>1</sup> Based on comparisons of the sequences (coding) of nucleotides 1-871 (PB2), 55-860 (PB1), 36-861 (PA), 229-1019 (H1), 1038-1371 (NP), 73-1352 (N1), 153-884 (M) and 55-774 (NS).

**Table 8. Antigenic analyses of the NAs of H1N2 viruses**

Viruses	Neuraminidase inhibition titre			
	Hyperimmune rabbit sera <sup>1</sup>		Post-infection ferret sera <sup>2</sup>	
	A/Bz 11/78	A/Bj 32/92	A/Mos 10/99	A/Eg 96/02
A/Brazil/11/78 (H1N1)	<b>1000</b>	<	<	<
A/Beijing/32/92 (H3N2)	<	<b>10000</b>	<	<
A/Moscow/10/99 (H3N2)	<	100	<b>640</b>	320
A/Egypt/96/02 (H1N2)	<	100	160	<b>640</b>
A/Egypt/84/01	<	100	40	640
A/Sachsen/32/02	<	50	80	640
A/Lyon/CHU/1575/02	<	50	80	640
A/Lisbon/2/02	<	50	80	640
A/Latvia/688/02	<	100	80	640
A/Israel/7/02	<	100	160	640
A/Inverness/5823740/02	<	100	160	640

1. <, <10; 2. <, <40

**Table 9. Genetic relationships between H1N2, H1N1 and H3N2 viruses**

Gene	Percent similarity with A/Saudi Arabia/2231/01 <sup>1</sup>		
	A/Saudi Arabia/7971/00	A/New Caledonia/20/99	A/Moscow/10/99
PB2	86.8	86.4	98.6
PB1	78.1	78.7	100
PA	89.9	90	99
H1	98.7	98.5	-
NP	88.2	88.2	99.7
N2	-	-	99
M	91.6	91.8	98.4
NS	88.6	88.9	99.9

1. Based on comparisons of the sequences of nucleotides 463-809 (PB1), 60-492 (PB2), 60-893 (PA), 99-974 (H1), 1037-1409 (NP), 395-1395 (N2), 154-856 (M) and 81-800 (NS).

**Table 10. Antigenic analyses of the HAs of H3N2 viruses**

Viruses	Isolation Date	Haemagglutination inhibition titre*					
		Post-infection ferret sera					
		A/Syd 5/97	A/Mosc 10/99	A/Pan 2007/99	A/Toul 878/01	A/Sing 15/01	A/HK 734/01
<b>A/Sydney/5/97</b>		<b>5120</b>	1280	2560	640	640	1280
<b>A/Moscow/10/99</b>		2560	<b>2560</b>	2560	1280	640	1280
<b>A/Panama/2007/99</b>		5120	1280	<b>5120</b>	1280	1280	1280
<b>A/Toulouse/878/01</b>		1280	640	1280	<b>1280</b>	640	1280
<b>A/Singapore/15/01</b>		1280	640	2560	1280	<b>640</b>	1280
<b>A/Hong Kong/734/01</b>		1280	1280	640	640	640	<b>1280</b>
A/Asuncion/918/01	16.8.01	2560	1280	2560	—	—	—
A/Auckland/142/01	2.10.01	2560	1280	2560	2560	1280	1280
A/Tak/547/01	9.10.01	1280	1280	2560	1280	1280	640
A/England/688/01	Oct-01	640	640	1280	2560	2560	640
A/Paris/220/01	Nov-01	1280	1280	1280	1280	1280	640
A/Perth/270/01	13.11.01	1280	1280	2560	2560	1280	640
A/Hong Kong/1307/01	21.11.01	1280	2560	2560	1280	2560	1280
A/Switzerland/6493/01	14.12.01	1280	1280	2560	2560	2560	1280
A/Valladolid/4/01	15.12.01	1280	640	1280	2560	1280	640
A/Lyon/1413/01	26.12.01	1280	1280	2560	1280	2560	640
A/Israel/4/02	1.1.02	1280	1280	2560	2560	2560	640
A/Madrid/G1222/02	9.1.02	1280	640	2560	1280	2560	640
A/Netherlands/001/02	7.1.02	640	2560	1280	1280	640	1280
A/Salamanca/8/02	9.1.02	640	1280	5120	640	640	1280
A/Ireland/999/02	23.1.02	1280	2560	2560	2560	640	2560
A/Prague/3/02	25.1.02	640	640	1280	640	320	640
A/Nouakchott/7/02	18.2.02	640	640	320	640	320	640
A/Bucharest/423/02	19.2.02	160	160	320	160	160	160
A/Genoa/4/02	19.2.02	640	320	1280	1280	320	320
A/Lyon/CHU/4584/02	21.2.02	640	640	640	320	320	640
A/Fukouka/15/02	23.2.02	640	320	640	320	320	640
A/Lisbon/5/02	1.3.02	1280	1280	2560	1280	640	1280
A/Dakar/7/02	6.3.02	1280	1280	1280	1280	320	640
A/Denmark/21/02	12.3.02	1280	640	1280	640	320	640
A/Lazio/2/02	16.3.02	1280	640	1280	640	320	640
A/Iceland/87/02	18.3.02	640	320	1280	1280	320	640
A/Reunion/1017/02	18.3.02	1280	1280	2560	1280	640	1280
A/Finland/135/02	1.4.02	1280	1280	1280	2560	640	2560
A/Belgium/969/02	2.4.02	1280	1280	2560	1280	1280	2560
A/Berlin/59/02	4.4.02	1280	1280	1280	1280	640	1280
A/Mauritius/175/02	5.4.02	2560	2560	2560	2560	640	2560
A/Inverness/5824157/02	6.4.02	1280	640	2560	2560	640	2560
A/Bratislava/134/02	18.4.02	320	640	1280	1280	320	640
A/Latvia/4882/02	23.4.02	320	320	320	160	160	320
A/Oslo/2650/02	24.4.02	1280	1280	2560	1280	640	1280
A/Lipetsk/14/02	26.4.02	320	320	640	160	160	320
A/Malmo/5/02	2.5.02	2560	1280	2560	2560	640	2560
A/Hong Kong/1143/02	6.6.02	160	160	320	80	80	160
A/Madagascar/66220/02	19.7.02	2560	2560	5120	—	—	—
A/Madagascar/66222/02	19.7.02	2560	2560	5120	—	—	—

\* <, <40

**Table 11. Amino acid changes characteristic of H3N2 sequence variants**

Variant group <sup>1</sup>	Representative strain	Amino acid changes	
		HA <sup>2</sup>	NA <sup>3</sup>
1b	A/Hong Kong/1143/02	R50G E83K S186G V202I W222R G225D (A131T)	A18S L23F V30I C42F P267T V307I
1c	A/Toulouse/878/01	A106V N144D S186G (R220G) (D291G) (A304P)	K172R T265I P267T S332F D399E Q432E L437W

1. designation based on previously distinguished groups (Annual Report, 2001); 2. Relative to A/Panama/2007/99; 3. Relative to A/Moscow/10/99

**Table 12. Antigenic analyses of the HAs of B viruses**

Viruses	Isolation date	Haemagglutination inhibition titre <sup>1</sup>					
		B/Shan <sup>2</sup> 7/97	Post-infection ferret sera				
			B/HK 330/01	B/HK 335/01	B/Sich 379/99	B/Gd 120/00	B/Shiz 15/01
<b>B/Shandong/7/97</b>		<b>2560</b>	80	160	<	<	<
<b>B/Hong Kong/330/01</b>		2560	<b>160</b>	320			
<b>B/Hong Kong/335/01</b>		2560	160	<b>320</b>	<	<	<
<b>B/Sichuan/379/99</b>		<	<	<	<b>320</b>	640	640
<b>B/Guandong/120/00</b>		80	<	<	320	<b>640</b>	640
<b>B/Shizuoka/15/01</b>		<	<	<	80	160	<b>160</b>
B/Hong Kong/672/01	10.9.01	<	<	<	320	320	320
B/Dakar/63/01	22.9.01	<	<	<	160	320	320
B/Auckland/76/01	24.9.01	<	<	<	320	320	320
B/Tak/549/01	9.10.01	<	<	<	160	160	160
B/Lyon/999/01	19.10.01	<	<	<	320	320	320
B/Switzerland/5384/01	Nov.01	<	<	<	160	160	320
B/Trieste/1/02	Dec-01	<	<	<	320	320	640
B/Israel/5501	25.12.01	<	<	<	320	640	640
B/Lazio/3/01	Jan-02	40	<	<	320	640	640
B/Caen/2212/02	3.1.02	40	<	<	320	320	640
B/Leon/2/02	7.1.02	<	<	<	320	320	320
B/Belgium/228/02	9.1.02	<	<	<	160	320	640
B/St. Petersburg/15/02	30.1.02	<	<	<	160	320	640
B/Yugoslavia/8/02	7.2.02	<	<	<	320	320	320
B/Nouakchott/4/02	17.2.02	80	<	<	160	640	640
B/Stockholm/02/01	19.2.02	<	<	<	160	640	320
B/Perm/3/02	22.2.02	<	<	<	160	320	640
B/Bucharest/820/02	20.3.02	<	<	<	320	320	320
B/Slovenia/253/02	22.3.02	<	<	<	320	320	640
B/Barcelona/460/02	23.3.02	<	<	<	160	320	640
B/Ireland/4889/02	Apr-02	80	<	<	160	320	640
B/Hannover/67/02	2.4.02	<	<	<	160	640	640
B/Albania/34/02	4.4.02	<	<	<	160	160	320
B/Bratislava/131/02	6.4.02	<	<	<	320	640	640
B/Finland/143/02	17.4.02	<	<	<	40	160	160
B/Latvia/4998/02	25.4.02	<	<	<	320	320	640
B/Madagascar/65494/02	3.5.02	40	<	<	160	160	320
B/Philippines/633/01	10.8.01	2560	80	320	<	<	<
B/Hong Kong/652/01	22.8.01	1280	40	160	<	<	<
B/Genoa/20/01	27.11.01	1280	40	160	<	<	<
B/Omsk/2/02	21.1.02	1280	<	80	<	<	<
B/Netherlands/23/02	25.1.02	2560	40	160	<	<	<
B/Switzerland/8329/02	30.1.02	1280	40	80	<	<	<
B/Tehran/80/02	9.2.02	2560	40	160	<	<	<
B/Baden-Wuerttemberg/66/02	14.3.02	2560	<	160	<	<	<
B/Denmark/2/02	22.3.02	2560	<	160	<	<	<
B/Paris/2209/02	Apr-02	2560	—	160	<	<	<
B/Egypt/245/02	10.4.02	1280	40	160	<	<	<
B/Lyon/328/02	10.4.02	2560	160	160	<	<	<
B/Sendai-H/1695/02	15.4.02	1280	—	160	<	<	<
B/Israel/82/02	23.4.02	2560	<	160	<	<	<
B/Oslo/2535/02	27.4.02	1280	40	160	<	<	<
B/Mauritius/219/02	6.5.02	2560	40	320	<	<	<
B/Johannesburg/3/02	25.6.02	2560	—	160	<	<	<

1. <, <40; 2. Hyperimmune sheep serum (supplied by NIBSC)

**Table 13. Amino acid changes characteristic of B sequence variants**

Lineage	Representative strain	Amino acid changes	
		HA	NA
Sichuan <sup>1</sup>	B/Lyon/246/02	L58F N126D	E148G
Harbin <sup>2</sup>	B/Finland/141/02	H40Y	D329N A358E
Victoria <sup>3</sup>	B/Tehran/80/02	I121T	E148G <sup>1</sup> S198N T389A
	B/Hong Kong/330/01	H116R I121N D164E	M50T C54S V60F E69K N345S R360K K436T (M369I)

1. relative to B/Sichuan/379/99; 2. Relative to B/Hong Kong/557/00; 3. Relative to B/Shandong/7/97

**Table14. Antigenic analyses of swine H1N1 viruses**

**(A)**

Viruses	Haemagglutination inhibition titre <sup>1</sup>				
	Hyperimmune rabbit sera		Post-infection ferret sera		
	A/Braz 11/78	Sw/Fin 2899/82	Sw/Fin 2899/82	Sw/CA 1482/99	Sw/IV 1455/99
<b>A/Brazil/11/78</b>	<b>5120</b>	640	<	<	<
<b>Sw/Fin/2899/82</b>	<	<b>5120</b>	<b>5120</b>	5120	320
<b>Sw/CA/1482/99</b>	40	5120	5120	<b>5120</b>	640
<b>Sw/IV/1455/99</b>	<	2560	640	640	<b>2560</b>
Sw/Italy/15100/01	<	5120	2560	5120	1280
Sw/Italy/15299-3/01	<	5120	1280	2560	640
Sw/Italy/15338/01	<	2560	1280	1280	320
Sw/Italy/15339-4/01	<	5120	1280	1280	640
Sw/Italy/524-4/02	<	5120	1280	1280	640
Sw/Italy/537-3/02	<	5120	1280	1280	640
Sw/Italy/5669-5/02	<	5120	640	1280	640
Sw/Italy/47214-1/02	<	5120	1280	1280	320
Sw/CA/910/02	<	2560	1280	1280	320
Sw/CA/1101/02	<	1280	640	640	320
Sw/CA/1103/02	<	2560	640	1280	640

1. <, <40

**(B)**

Viruses	Neuraminidase inhibition titre			
	Hyperimmune rabbit sera <sup>1</sup>		Post-infection ferret sera <sup>2</sup>	
	Sw/CA 3633/84	Sw/Fin 2899/82	Sw/Fin 2899/82	Sw/IV 1455/99
<b>Sw/CA/3633/84 (H3N2)</b>	<b>10000</b>	<	<	<
<b>Sw/Finistere/2899/82</b>	<	<b>10000</b>	<b>640</b>	160
<b>Sw/Italy/1513-1/98</b>	<	10000	640	640
<b>Sw/IV/1455/99</b>	<	10000	80	<b>640</b>
Sw/Italy/15100/01	<	10000	320	640
Sw/Italy/15338/01	<	10000	80	640
Sw/Italy/524-4/02	<	1000	<	320
Sw/Italy/5669-5/02	<	10000	320	640
Sw/Italy/47214-1/02	<	10000	320	640
Sw/CA/910/02	<	10000	320	640
Sw/CA/1101/02	<	10000	320	640
Sw/CA/1103/02	<	1000	80	640

1. <, <10; 2. <, <40

**Table15. Antigenic analyses of swine H1N2 viruses**

**(A)**

Viruses	Subtype	Haemagglutination inhibition titre <sup>1</sup>					
		Hyperimmune rabbit sera		Post-infection ferret sera			
		A/Braz 11/78	Sw/Fin 2899/82	A/Braz 11/78	Sw/CA 790/97	Sw/It 1521/98	Sw/CA 800/00
<b>A/Brazil/11/78</b>	<b>H1N1</b>	<b>5120</b>	640	<b>640</b>	40	40	40
<b>Sw/Fin/2899/82</b>	<b>H1N1</b>	<	<b>5120</b>	<	<	<	<
<b>Sw/CA/790/97</b>	<b>H1N2</b>	5120	320	320	<b>5120</b>	320	320
<b>Sw/Italy/1521/98</b>	<b>H1N2</b>	1280	<	<	160	<b>320</b>	<
<b>Sw/CA/800/00</b>	<b>H1N2</b>	5120	320	320	2560	320	<b>1280</b>
Sw/CA/1271/01		2560	80	40	640	40	80
Sw/CA/1374/01		5120	160	160	640	40	80
Sw/CA/906/01		5120	40	160	320	40	80

1 < = <40

**(B)**

Viruses	Subtype	Neuraminidase inhibition titre					
		Hyperimmune rabbit sera <sup>1</sup>		Post-infection ferret sera <sup>2</sup>			
		Sw/Fin 2899/92	A/PC 1/73	Sw/CA 3633/84	Sw/It 1523/98	Sw/CA 790/97	Sw/It 1521/98
<b>Sw/Finistere/2899/82</b>	<b>H1N1</b>	<b>10000</b>	10	<	<	<	<
<b>A/Port Chalmers/1/73</b>	<b>H3N2</b>	<	<b>10000</b>	640	80	<	<
<b>Sw/CA/3633/84</b>	<b>H3N2</b>	<	10000	<b>640</b>	80	<	<
<b>Sw/Italy/1523/98</b>	<b>H3N2</b>	<	1000	160	<b>640</b>	<	<
<b>Sw/CA/790/97</b>	<b>H1N2</b>	<	1000	40	<	<b>640</b>	640
<b>Sw/Italy/1521/98</b>	<b>H1N2</b>	<	1000	<	<	320	<b>640</b>
Sw/CA/1271/01		<	1000	80	80	320	160
Sw/CA/906/01		<	1000	40	<	80	80

1. <, <10; 2. <, <40

**Table 16. Antigenic analyses of swine H3N2 viruses**

(A)

Viruses	Haemagglutination inhibition titre <sup>1</sup>				
	Post-infection ferret sera				
	Sw/CA 3633/84	Sw/It 1407-2/95	Sw/Eire 471/96	Sw/It 1477/96	Sw/It 1523/98
<b>Sw/CA/3633/84</b>	<b>5120</b>	<	1280	1280	640
<b>Sw/Italy/1407-2/95</b>	40	<b>2560</b>	<	80	40
<b>Sw/Eire/471/96</b>	640	<	<b>1280</b>	80	160
<b>Sw/Italy/1477/96</b>	320	<	40	<b>5120</b>	320
<b>Sw/Italy/1523/98</b>	320	<	80	1280	<b>1280</b>
Sw/Italy/12178/01	320	<	80	2560	1280
Sw/Italy/14607/01	640	<	160	2560	1280
Sw/Italy/14608/01	320	<	80	1280	640
Sw/Italy/15403/01	320	<	80	1280	1280
Sw/Italy/22491-1/02	160	<	80	1280	640
Sw/Italy/22714-3/02	160	<	80	1280	1280

< = < 40

(B)

Viruses	Neuraminidase inhibition titre					
	Hyperimmune rabbit sera <sup>1</sup>		Post-infection ferret sera <sup>2</sup>			
	Sw/Fin 2899/92	A/PC 1/73	Sw/CA 3633/84	Sw/It 1523/98	Sw/CA 790/97	Sw/It 1521/98
<b>Sw/Finistere/2899/82 (H1N1)</b>	<b>10000</b>	10	<	<	<	<
<b>A/Port Chalmers/1/73</b>	<	<b>10000</b>	640	80	<	<
<b>Sw/CA/3633/84</b>	<	10000	<b>640</b>	80	<	<
<b>Sw/Italy/1523/98</b>	<	1000	160	<b>640</b>	<	<
<b>Sw/CA/790/97 (H1N2)</b>	<	1000	40	<	<b>640</b>	640
<b>Sw/Italy/1521/98 (H1N2)</b>	<	1000	<	<	320	<b>640</b>
Sw/Italy/12178/01	<	1000	160	640	<	<
Sw/Italy/14607/01	<	1000	160	640	<	<
Sw/Italy/14608/01	<	1000	160	640	<	<
Sw/Italy/15403/01	<	1000	160	640	<	<
Sw/Italy/22491-1/02	<	1000	80	320	<	<

1. <, <10; 2. <, <40

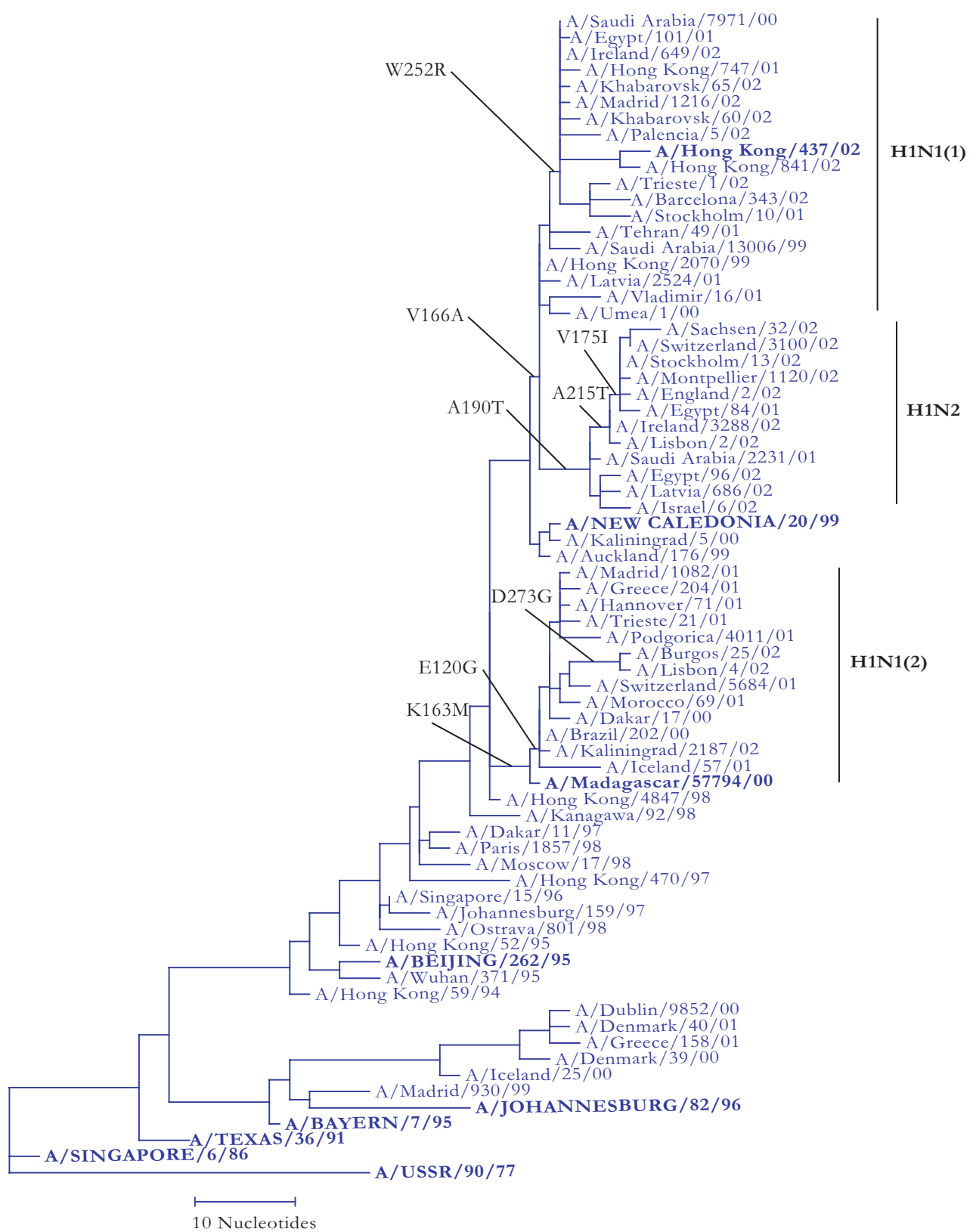
**Table 17. Viruses despatched August 2001 - July 2002**

<b>Country</b>	<b>A</b>	<b>B</b>	<b>Swine</b>	<b>Avian</b>
Australia	5	6		
Austria	1	2		
Belgium		8	11	
Bulgaria	1	1		
China				20
Czech Republic	1	4		
Denmark	10	6	2	
Finland		4		
France	1	4	11	
Germany		3		
Hong Kong				20
Hungary		2		
Ireland			1	
Israel	1	3		
Italy		2	11	
Japan	5	6		20
Latvia	2	1		
Netherlands	7	6	2	
Norway		1		
Poland	2			
Switzerland	2	6		
United Kingdom	17	19	11	20
United States	92	46		40
<b>Total = 446</b>	<b>147</b>	<b>130</b>	<b>49</b>	<b>120</b>

**Table 18. Antisera despatched August 2001 - July 2002**

<b>Country</b>	<b>A</b>	<b>B</b>	<b>Swine</b>	<b>Avian</b>
Argentina	3	1		
Belgium			11	
China				20
Czech Republic	1	3		
Denmark	2	3	1	
Finland				
France		5	15	
Germany		2		
Hong Kong				20
Ireland			1	
Israel	1	4		
Italy		4	11	
Japan				20
Latvia	2	1		
Morocco	2	1		
Netherlands			2	
Norway		1		
Poland	2	1		
South Africa		1		
Switzerland	6	6		
United Kingdom	4	5	11	20
United States				40
<b>Total = 233</b>	<b>23</b>	<b>38</b>	<b>52</b>	<b>120</b>

**Figure 1. Phylogenetic comparison of nucleotide sequences encoding H1 haemagglutinins**



**Figure 2. HA sequences (amino acids 1-300) of H1N1 and H1N2 viruses**

	1										100
<b>A/Bayern/7/95</b>					r	t			s	f	a
<b>A/Johannesburg/82/96</b>				n	r	t			s	f	a
<b>A/Beijing/262/95</b>									s		
<b>A/New Caledonia/20/99</b>											
A/Hong Kong/1252/00											
A/Stockholm/10/01									k		
A/Hong Kong/1273/01											
A/Ireland/649/02											
A/Madrid/1216/02							i				
A/Khabarovsk/65/02											
A/Trieste/1/02											
A/Palencia/5/02										s	
A/Hong Kong/841/02											
<b>A/Hong Kong/437/02</b>											
<b>A/Saudi Arabia/7971/00</b>											
<b>A/Egypt/96/02</b>										s	
A/Egypt/84/01											
A/Saudi Arabia/2231/01											
A/Israel/173/01											
A/Ireland/3288/02											
A/England/2/62											
A/Lisbon/2/02	~~~~~										
A/Switzerland/3100/02	~~~~										
A/Latvia/686/02											
A/Sachsen/32/02							w				
A/Montepellier/1120/02											
A/Stockholm/13/02											
<b>A/Madagascar/57794/00</b>											
A/Morocco/69/01											
A/Kaliningrad/2187/02											
A/Lisbon/4/02	~~~~~	~~~~~									
A/Burgos/25/02											
Consensus	DTICIGYHAN	NSTDTVDTVL	EKNVTVTHSV	NLLEDHNGK	LCLLKGIAPL	QLGNCSVAGW	ILGNPECELL	ISKESWSYIV	ETPNPENGTC	YPGYFADYEE	

**Figure 2 (continued)**

	101									200
<b>A/Bayern/7/95</b>				t	k	e	v	s	i	
<b>A/Johannesburg/82/96</b>				t	k	e	v	s	i	
<b>A/Beijing/262/95</b>				t		e	n v	s v	i	
<b>A/New Caledonia/20/99</b>							v			
A/Hong Kong/1252/99					e					
A/Stockholm/10/01					k		k			
A/Hong Kong/1273/01					k				r	
A/Ireland/649/02										
A/Madrid/1216/02										
A/Khabarovsk/65/02							s			
A/Trieste/1/02					k				n	
A/Palencia/5/02										
A/Hong Kong/841/02					r					
<b>A/Hong Kong/437/02</b>				t					n	
<b>A/Saudi Arabia/7971/00</b>										
<b>A/Egypt/96/02</b>				i					n t	
A/Egypt/84/01			a					i	n t	
A/Saudi Arabia/2231/01									t	
A/Israel/173/01			r						t	
A/Ireland/3288/02								i	t	
A/England/2/02								i	n t	
A/Lisbon/2/02							r	i	t	
A/Switzerland/3100/02								i	n t	
A/Latvia/686/02									n t	
A/Sachsen/32/02								i	n t	
A/Montpellier/1120/02								i	n t	
A/Stockholm/13/02								i	n t	
<b>A/Madagascar/57794/00</b>							m v		n	
A/Morocco/69/01			g				m v			
A/Kaliningrad/2187/02			g				m v		n	
A/Lisbon/4/02			g				m v			
A/Burgos/25/02			g				m v		v	
Consensus	LREQLSSVSS	FERFEIFPKE	SSWPNHTVTK	GVSASC SHNG	KSSFYRNLLW	LTGKNGLYPN	LSKSYANNKE	KEVLVLWGVH	HPPNIGDQRA	LYHTENAYVS

**Figure 2 (continued)**

	201									300
<b>A/Bayern/7/95</b>								s_g		
<b>A/Johannesburg/82/96</b>			g					s_g		
<b>A/Beijing/262/95</b>			g					n		
<b>A/New Caledonia/20/99</b>										
A/Hong Kong/1252/00										
A/Stockholm/10/01						r				
A/Hong Kong/1273/01						r				
A/Ireland/649/02						r				
A/Madrid/1216/02						r				
A/Khabarovsk/65/02						r				
A/Trieste/1/02						r	g			
A/Palencia/5/02						r				a
A/Hong Kong/841/02						r				
<b>A/Hong Kong/437/02</b>						r				
<b>A/Saudi Arabia/7971/00</b>						r				
<b>A/Egypt/96/02</b>		t								
A/Egypt/84/01		t								
A/Saudi Arabia/2231/01		t								
A/Israel/173/01		t								
A/Ireland/3288/01		t								
A/England/2/02		t								
A/Lisbon/2/02		t								
A/Switzerland/3100/02		t								
A/Latvia/686/02		t								
A/Sachsen/32/02		kt								
A/Montpellier/1120/02		t								
A/Stockholm/13/02		t								
<b>A/Madagascar/57794/00</b>										
A/Morocco/69/01	m							g		
A/Kaliningrad/2187/02										
A/Lisbon/4/02							l	g		
A/Burgos/25/02							l	g		
Consensus	VVSSHYSRRF	TPEIAKRPKV	RDQEGRINYY	WTLLEPGDTI	IFEANGNLIA	PWYAFALSRG	FGSGIITSNA	PMDECDKQCQ	TPQGAINSSL	PFQNVHPVTI







### Figure 4 (continued)

	401					470	
A/Beijing/262/95			r				
A/New Caledonia/20/99							
A/Oslo/2289/01					x_~~~~	~~~~~	
A/Oslo/1512/01					~	~~~~~	
A/Zagreb/2980/01						~~~	
A/Stockholm/8/01					g		
A/Hong Kong/747/01						~~~~~	
<b>A/Hong Kong/437/02</b>					a		
A/Khabarovsk/65/02		t					
A/Hong Kong/841/02					a		
A/Lyon/651/01	a	f	g		i_~~~~	~~~~~	
A/Iceland/57/01							
A/Lyon/712/01		g					
A/Morocco/69/01		g				~~~~~	
A/Iceland/1/01				k			
A/Finland/131/02				k			
Consensus	GYSGSFVQHP	ELTGLDCIRP	CFWVELVRGL	PRENTTIWTS	GSSISFCGVN	SDTANWSWPD	GAELPFTIDK



**Figure 6. HA sequences (amino acids 1-300) of H3N2 viruses**

	1									100
A/Sydney/5/97	i					r				
A/Moscow/10/99						r				
A/Panama/2007/99			s							
A/Toulouse/878/01								s		
A/Hessen/23/02	e	m								
A/Lipetsk/14/02									d	
A/Asuncion/918/01										
A/Lyon/1193/01										
A/Hong Kong/568/02					n					
A/Latvia/2710/02	i							w		
A/Valladolid/4/01										
A/Oslo/888/02										
A/Iceland/93/02	s				s					
A/Switzerland/6493/01										
A/Trieste/3/02										
A/Reunion/1001/02					a					
A/Mauritius/175/02										
A/Inverness/117/02										
A/Bucharest/423/02										
A/Madagascar/65357/02										
A/Madagascar/66220/02										
A/Nouakchott/7/02										
A/Bratislava/134/02										
A/Finland/135/02										
A/Malmo/3/02										
A/Hong Kong/1269/01	~	k				g				
A/Paris/1315/01	n					g				
A/Madagascar/62645/01	ps					g				
A/Dakar/26/01		k			n	g	n			
A/Hong Kong/1550/02						g			k	s
A/Hong Kong/1143/02			i			g		q	k	
A/Moscow/1/02						g			k	
A/Hong Kong/1537/02			i			g		q	k	
Consensus	QKLPGNDNST	ATLCLGHHAV	PNGTLVKTIT	NDQIEVTNAT	ELVQSSSTGR	ICDSPHQILD	GENCTLIDAL	LGDPHCDGFQ	NKEWDLFVER	SKAYSNCYPY

**Figure 6 (continued)**

	101									200	
<b>A/Sydney/5/97</b>	a			y	s	i		d	s	t	i
<b>A/Moscow/10/99</b>	a				i		r	d	s	t	
<b>A/Panama/2007/99</b>	a				n				l	s	
<b>A/Toulouse/878/01</b>					n			l			
A/Hessen/23/02											
A/Lipetsk/14/02											
A/Asuncion/918/01											
A/Lyon/1193/01											
A/Hong Kong/568/02											
A/Latvia/2710/02											
A/Valladolid/4/01											
A/Oslo/888/02											
A/Iceland/93/02											
A/Switzerland/6493/01											
A/Trieste/3/02									l		
A/Reunion/1001/02											
A/Mauritius/175/02											
A/Inverness/117/02										s	
A/Bucharest/423/02									l		
A/Madagascar/65357/02											
A/Madagascar/66220/02											
A/Nouakchott/7/02											
A/Bratislava/134/02							y			t	
A/Finland/135/02											
A/Malmo/3/02											
A/Hong Kong/1269/01	a				n				s		
A/Paris/1315/01	a				n				s		
A/Madagascar/62645/01	a				n				s		p
A/Dakar/26/01	a				n				s		
A/Hong Kong/1550/02	a				n				v	i	
<b>A/Hong Kong/1143/02</b>	a			t	n		t				
A/Moscow/1/02	a			t	n						
A/Hong Kong/1537/02	a			t	n		t				
Consensus	DVPDYVSLRS	LVASSGTLEF	NNESFNWTGV	AQNGTSSACK	RRSDKSFFSR	LNWLHQLKYK	YPALNVTMPN	NEKFDKLYIW	GVHHPGTDSD	QISLYAQASG	

**Figure 6 (continued)**

	201									300
A/Sydney/5/97			i							
A/Moscow/10/99			i							
<b>A/Panama/2007/99</b>										
<b>A/Toulouse/878/01</b>										
A/Hessen/23/02										
A/Lipetsk/14/02										
A/Asuncion/918/01										
A/Lyon/1193/01										i
A/Hong Kong/568/02										
A/Latvia/2710/02										
A/Valladolid/4/01			g				m			
A/Oslo/888/02			g						g	
A/Iceland/93/02			g							
A/Switzerland/6493/01										g
A/Trieste/3/02										g
A/Reunion/1001/02										g
A/Mauritius/175/02										g
A/Inverness/117/02		k								g
A/Bucharest/423/02										g
A/Madagascar/65357/02										g
A/Madagascar/66220/02										g
A/Nouakchott/7/02			g							g
A/Bratislava/134/02			g							g
A/Finland/135/02			g							g
A/Malmo/3/02			g				v			g
A/Hong Kong/1269/01		i		d						
A/Paris/1315/01				d						
A/Madagascar/62645/01		k		d						v
A/Dakar/26/01		n		i	di					
A/Hong Kong/1550/01		i		r	d					
<b>A/Hong Kong/1143/02</b>		i	a	r	d					
A/Moscow/1/02		i		r	d					
A/Hong Kong/1537/02		i		r	d					
Consensus	RVTVSTKRSQ	QTVIPNIGSR	PWVRGVSSRI	SIYWTIVKPG	DILLINSTGN	LIAPRGYFKI	RSGKSSIMRS	DAPIGKCNSE	CITPNGSIPN	DKPFQNVNRI



**Figure 8. NA sequences of H3N2 and H1N2 viruses**

	1									100
A/Sydney/5/97	_____	_____	_____	_____	s	_____	_____	_____	_____	k
A/Panama/2007/99	_____	_____	_____	_____	_____	_____	_____	_____	_____	k
A/Moscow/10/99	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Singapore/15/01	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
A/Egypt/96/02	_____	_____	t	_____	_____	_____	_____	_____	_____	_____
A/Sachsen/32/02	_____	_____	t	_____	_____	_____	_____	_____	_____	_____
A/Montpellier/1120/02	_____	_____	t	_____	_____	_____	_____	_____	_____	_____
A/Toulouse/878/01	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Denmark/41/00	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Asuncion/918/01	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Valladolid/4/01	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Madagascar/65357/02	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Lipetsk/14/02	_____	l	_____	_____	_____	_____	_____	_____	_____	_____
A/Ireland/1092/02	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
A/Stockholm/24/02	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Iceland/93/02	_____	_____	_____	_____	_____	a	_____	_____	_____	_____
A/Bucharest/423/02	_____	_____	f	_____	_____	_____	_____	_____	_____	_____
A/Mauritius/175/02	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Hong Kong/2/00	_____	s	f	_____	_____	_____	_____	_____	_____	_____
A/Hong Kong/1789/00	_____	s	f	_____	_____	t	_____	_____	_____	_____
A/Hong Kong/1143/02	_____	s	f	i	f	_____	_____	_____	_____	_____
A/Hong Kong/1146/02	~~~~~	~~~~~	_____	i	f	_____	_____	_____	_____	_____
A/Moscow/1/02	_____	s	f	i	f	_____	_____	_____	_____	_____
Consensus	MNPNQKIITI	GSVSLTIATI	CFLMQIAILV	TTVTLHFKQY	ECNSPPNNQV	MLCEPTIER	NITEIVYLTN	TTIEKEICPK	LAEYRNWSKP	QCNIITGFAPF
	101									200
A/Sydney/5/97	_____	_____	_____	_____	r	_____	_____	_____	_____	h
A/Panama/2007/99	_____	_____	_____	_____	r	_____	_____	_____	_____	h
A/Moscow/10/99	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Singapore/15/01	~~~~~	~~~~~	~~~~~	_____	i	_____	_____	_____	_____	_____
A/Egypt/96/02	_____	_____	_____	_____	_____	_____	_____	_____	_____	k
A/Sachsen/32/02	_____	_____	_____	_____	_____	_____	_____	_____	_____	k
A/Montpellier/1120/02	_____	_____	_____	_____	_____	_____	_____	_____	_____	k
A/Toulouse/878/01	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Denmark/41/00	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Asuncion/918/01	_____	_____	_____	_____	_____	n	_____	r	_____	_____
A/Valladolid/4/01	_____	_____	_____	_____	_____	_____	_____	r	_____	_____
A/Madagascar/65357/02	_____	_____	_____	_____	_____	g	_____	r	_____	_____
A/Lipetsk/14/02	_____	_____	_____	_____	_____	g	_____	r	_____	_____
A/Ireland/1092/02	~~~~~	~~~~~	~~~~~	_____	s	_____	_____	r	_____	_____
A/Stockholm/24/02	_____	_____	_____	_____	_____	_____	_____	r	_____	_____
A/Iceland/93/02	_____	_____	_____	_____	_____	_____	_____	r	_____	_____
A/Bucharest/423/02	_____	_____	_____	_____	_____	_____	_____	r	_____	_____
A/Mauritius/175/02	_____	_____	_____	_____	_____	_____	_____	r	_____	_____
A/Hong Kong/2/00	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Hong Kong/1789/02	_____	_____	_____	_____	_____	_____	_____	_____	_____	_____
A/Hong Kong/1143/02	_____	_____	_____	_____	v	_____	_____	_____	_____	_____
A/Hong Kong/1146/02	_____	_____	_____	_____	v	_____	_____	_____	_____	_____
A/Moscow/1/02	_____	_____	_____	_____	v	_____	_____	_____	_____	_____
Consensus	SKDNSIRLSA	GGDIWVTREP	YVSCDPDKCY	QFALGQGTTL	NNGHSNDTVH	DRTPYRTLML	NELGVPFHLG	TKQVCIWSS	SSCHDGKAWL	HVCVTGDDEN

# Figure 8 (continued)

	201									300
<b>A/Sydney/5/97</b>	d				r		p			
<b>A/Panama/2007/99</b>	d				r		t_k			
<b>A/Moscow/10/99</b>							t_p			
A/Singapore/15/01							t_l			
<b>A/Egypt/96/02</b>							t_l			
A/Sachsen/32/02					e		t_l			
<u>A/Montpellier/1120/02</u>							t_l			
<b>A/Toulouse/878/01</b>							s			
A/Denmark/41/00										
A/Asuncion/918/01										
A/Valladolid/4/01					e					
A/Madagascar/65357/02										
A/Lipetsk/14/02										
A/Ireland/1092/02										
A/Stockholm/24/02							k			
A/Iceland/93/02							n			
A/Bucharest/423/02										
A/Mauritius/175/02										
A/Hong Kong/2/00							t			
A/Hong Kong/1789/00							t			
<b>A/Hong Kong/1143/02</b>		v					i_t			
A/Hong Kong/1146/02							t			
A/Moscow/1/02		v					i_t			
Consensus	ATASFIYNGR	LVDSIGSWSK	KILRTQESEC	VCINGTCTVV	MTDGSASGKA	DTKILFIEEG	KIVHISTLSG	SAQHVEECSC	YPRYPGVRCV	CRDNWKGSNR
	301									400
<b>A/Sydney/5/97</b>				n			f			d
<b>A/Panama/2007/99</b>							s			
<b>A/Moscow/10/99</b>										d
A/Singapore/15/01										d
<b>A/Egypt/96/02</b>										d
A/Sachsen/32/02										d
<u>A/Montpellier/1120/01</u>										d
<b>A/Toulouse/878/01</b>				f				a		
A/Denmark/41/00				f						
A/Asuncion/918/01				f			s			
A/Valladolid/4/01				f						
A/Madagascar/65357/02				f						
A/Lipetsk/14/02				f						
A/Ireland/1092/02				f						
A/Stockholm/24/02				f				k		
A/Iceland/93/02				f						
A/Bucharest/423/02	l			f						
A/Mauritius/175/02				f						
A/Hong Kong/2/00	i									d
A/Hong Kong/1789/00	i									d
<b>A/Hong Kong/1143/02</b>	i							n		d
A/Hong Kong/1146/02	i							n		d
A/Moscow/1/02	i							n		d
Consensus	PIVDINVKDY	SIVSSYVCSG	LVGDTPRKND	SSSSSHCLDP	NNEEGGHGK	GWAFDDGNDV	WMGRTISEKL	RSGYETFKVI	EGWSKPNSKL	QINRQVIVER

**Figure 8 (continued)**

	401						469
<b>A/Sydney/5/97</b>	_____	_____	_____	_____	_____	_____	_____
<b>A/Panama/2007/99</b>	_____m_____	_____	_____	_____	_____	_____	_____
<b>A/Moscow/10/99</b>	_____	_____	_____	_____l_____	_____	_____	_____
A/Singapore/15/01	_____	_____	_____	_____l_____	_____	_____	_____
<b>A/Egypt/96/02</b>	_____	_____	_____	_____n_____l_____	_____	_____	_____
A/Sachsen/32/02	_____	_____	_____	_____n_____l_____	_____	_____	_____
<u>A/Montpellier/1120/02</u>	_____	_____	_____	_____nl_____l_____	_____	_____	_____
<b>A/Toulouse/878/01</b>	_____	_____	_____	_____s_____	_____	_____	_____~ ~ ~ ~ ~ ~ ~ ~
A/Denmark/41/00	_____	_____	_____	_____e_____	_____r_____	_____	_____
A/Asuncion/918/01	_____	_____	_____	_____e_____	_____	_____~ ~ ~ ~ ~ ~ ~ ~	_____
A/Valladolid/4/01	_____p_____	_____	_____	_____e_____	_____	_____	_____
A/Madagascar/65357/02	_____	_____	_____	_____e_____	_____	_____	_____
A/Lipetsk/14/02	_____	_____	_____	_____e_____	_____	_____	_____
A/Ireland/1092/02	_____	_____	_____	_____e_____	_____	_____	_____
A/Stockholm/24/02	_____	_____	_____	_____e_____i_____	_____	_____	_____
A/Iceland/93/02	_____	_____	_____	_____e_____	_____	_____	_____
A/Bucharest/423/02	_____	_____	_____	_____e_____	_____	_____	_____
A/Mauritius/175/02	_____	_____	_____	_____e_____	_____	_____	_____
<u>A/Hong Kong/2/00</u>	_____	_____	_____	_____l_____	_____	_____	_____
A/Hong Kong/1789/00	_____	_____	_____	_____l_____	_____g_____	_____	_____
<b>A/Hong Kong/1143/02</b>	_____	_____	_____	_____l_____	_____	_____	_____
A/Hong Kong/1146/02	_____	_____	_____	_____l_____	_____	_____	_____
A/Moscow/1/02	_____	_____	_____	_____l_____	_____	_____	_____
Consensus	GNRSGYSGIF	SVEGKSCINR	CFYVELIRGR	KQETE VVWTS	NSIVVFCGTS	GTYGTGSWPD	GADINLMPI





**Figure 10 (continued)**

	101									200
<b>B/Beijing/184/93</b>			n		r		r.		k	i
<b>B/Harbin/7/94</b>			n		r		r. d		v	a
B/Hong Kong/547/00			y		s		. n		v	d
<b>B/Hong Kong/557/00</b>			d				. n		v	
B/Lyon/862/01			d				. n		hv	
B/Switzerland/6615/01			d		r		. n		v	
B/St. Petersburg/150/02			d				. n		v	
B/Baden-Wuerttemberg/63/02			d				. n		v e	
B/Khabarovsk/155/02			d				. n		v	
B/Ulan Ude/4/02			d		e		. n		v	i
B/Finland/141/02			d		r		. n		v	
<b>B/Sichuan/379/99</b>		k	n				r.		h ke	d
B/Hong Kong/692/01		k	k e				r.		i h ke	
B/Lyon/1342/01		k	d				r.		h ke	
B/Israel/55/01		k	d				r.		h ke	i
B/Lyon/246/02		k	d				r.		h ke	
B/Bratislava/60/02		k	d k				r.		h ke	
B/Latvia/1116/02		k	d		n		r.		h ke	
B/Rome/2/02		k	d				r.		h ke	
B/Barcelona/1460/02		k	d		n		r.		h ke	
<b>B/Shandong/7/97</b>		h	ih n	ki	v_ngn			s_i		e_k
B/Sachsen/152/02		h	h n	ki	v_ngn			s_i		ea
<b>B/Tehran/80/02</b>		h	h n	ki	v_ngn			s_i		ei
B/Israel/67/02		h	h n	ki	v_ngn	v_		s_i		e
B/Egypt/245/02		h	h n	ki	v_ngn			s_i		ei
B/Lyon/328/02		h	h n	ki	v_ngn			s_i		es
B/Mauritius/219/02		h	h n	ki	v_ngn			s_i_g		en
<b>B/Hong Kong/330/01</b>		r	nh n	ki	v_ngn		e	s_i		se
B/Philippines/640/01		r	nh n	ki	v_ngn		e	s_i		ea
B/Genoa/20/02		r	nh n	ki	v_ngn		e	s_i		ea
B/Trieste/28/02		r	nh n	ki	v_ngn		e	s_i		e
B/Hong Kong/202/02		r	nh n e	ki	v_ngn		e	s_i		e
Consensus	RTKIRQLPNL	LRGYENIRLS	TQNVI-AEKA	PGGPYRLGTS	GSCPNATSKS	GFFATMAWAV	PKNDNNKTAT	NPLTVEVPYI	CTEGEDQITV	WGFHSDNKTQ

**Figure 10 (continued)**

	201									300
<b>B/Beijing/184/93</b>									v	
<b>B/Harbin/7/94</b>									v	
B/Hong Kong/547/00									v	n
<b>B/Hong Kong/557/00</b>									v	
B/Lyon/862/01									v	
B/Switzerland/6615/01									v	
B/St. Petersburg/150/02									v	~~~~~
B/Baden-Wuerttemberg/63/02									v	
B/Khabarovsk/155/02					p				v	~~~~~
B/Ulan Ude/4/02									v	
B/Finland/141/02									v	~~~~~
<b>B/Sichuan/379/99</b>										
B/Hong Kong/692/01										i
B/Lyon/1342/01										i
B/Israel/55/01										i
B/Lyon/246/02										i
B/Bratislava/60/02										i
B/Latvia/1116/02										i
B/Rome/2/02										i
B/Barcelona/1460/02										i
<b>B/Shandong/7/97</b>										
B/Sachsen/152/02										
<b>B/Tehran/80/02</b>										
B/Israel/67/02										
B/Egypt/245/02										
B/Lyon/328/02										
B/Mauritius/219/02										
<b>B/Hong Kong/330/01</b>										
B/Philippines/640/01										
B/Genoa/20/02										
B/Trieste/28/02										
B/Hong Kong/202/02										
Consensus	MKNLYGDSNP	QKFTSSANGV	TTHYVSQIGG	FPDQTEDGGL	PQSGRIVVDY	MVQKPGKTGT	IVYQRGILLP	QKVCASGRS	KVIKGSPLI	GEADCLHEKY





**Figure 12 (continued)**

	201									300
<b>B/Harbin/7/94</b>						k				e
<b>B/Hong Kong/557/01</b>										s
B/Madagascar/65186/02										k
B/St.Petersburg/15/02										k
B/Khabarovsk/55/02										k
B/Finland/141/02										k
<b>B/Sichuan/379/99</b>										n
B/Hong Kong/692/01										n
B/Lyon/246/02										n
B/Trento/3/02										n
B/Latvia/5008/02										n
B/Slovenia/94/02										n
<b>B/Tehran/80/02</b>										n
B/Lyon/328/02										e
B/Mauritius/219/02										n
<b>B/Shandong/7/97</b>										r
B/Hong Kong/9/01										i
<b>B/Hong Kong/330/01</b>										i
B/Philippines/640/01										i
B/Genoa/26/02										i
B/Trieste/19/02										i
Consensus	LLKIKYGEAY	TDTYHSYANN	ILRTQESACN	CIGGDCYLMI	TDGSASGISE	CRFLKIREGR	IIKEIFPTGR	VKHTTECTCG	FASNKTIECA	CRDNSYTAKR
	301									400
<b>B/Harbin/7/94</b>										
<b>B/Hong Kong/557/01</b>										e
B/Madagascar/65186/02						n				d
B/St.Petersburg/15/02										n
B/Khabarovsk/55/02										n
B/Finland/141/02										n
<b>B/Sichuan/379/99</b>										d
B/Hong Kong/692/01										r
B/Lyon/246/02										
B/Trento/3/02										
B/Latvia/5008/02										
B/Slovenia/94/02										
<b>B/Tehran/80/02</b>										a
B/Lyon/328/02										a
B/Mauritius/219/02										a
<b>B/Shandong/7/97</b>										n
B/Hong Kong/9/01										r
<b>B/Hong Kong/330/01</b>										e
B/Philippines/640/01										e
B/Genoa/26/02										e
B/Trieste/19/02										i
Consensus	PFVKLVNVEDT	TAEIRLMCTE	TYLDTPRPDD	GSITGPCESN	GDKGSGGIK	GFVHQRMASK	IGRWYSRTMS	KTKRMGMGLY	VKYDGDPTWD	SDALALSGVM

**Figure 12 (continued)**

	401					466	
<b>B/Harbin/7/94</b>				k			
<b>B/Hong Kong/557/01</b>					a		
B/Madagascar/65186/02							
B/St.Petersburg/15/02							
B/Khabarovsk/55/02							
<b>B/Finland/141/02</b>							
<b>B/Sichuan/379/99</b>				e			
B/Hong Kong/692/01				e			
B/Lyon/246/02				e			
B/Trento/3/02				e			
B/Latvia/5008/02				e			
<b>B/Slovenia/94/02</b>				e			
<b>B/Tehran/80/02</b>				e			
B/Lyon/328/02				e			
B/Mauritius/219/02				e			
<b>B/Shandong/7/97</b>	i			k			
B/Hong Kong/9/01	i						
<b>B/Hong Kong/330/01</b>	g_i					i	
B/Philippines/640/01	i						
B/Genoa/26/02	i						
B/Trieste/19/02	i						
Consensus	VSMEEPGWYS	FGFEIKDKKC	DVPCIGIEMV	HDGGKTTWHS	AATAIYCLMG	SGQLLWDTVT	GVDMAL