## **Supplementary Table 7**

PB2	substitution	season	support
	R251K	2013S	0.971
	R54K	2013N	0.95
	M66I	2013N	0.95
	D195N	2013N	0.939
	A184T	2015N	0.849
	V344M	2011N	0.749
	<i>I354L</i>	2011N	0.424
	R293K	2013N	0.375
	V731I	2013N	0.088
PB1	substitution	season	support
	K52R	2013S	0.977
	I435T	2013N	0.948
	R211K	2015N	0.859
	I397M	2012N	0.84
	G154D	2013N	0.8
	<i>I435T</i>	2012N	0.199
PA	substitution	season	support
	R362K	2013S	0.983
	K361R	2013S	0.983
	P560H	2013S	0.953
	I387V	2014S	0.911
	S522G	2014S	0.906
	N321K	2011N	0.893
	V100I	2013S	0.872
	I330V	2013S	0.863
	A343T	2012N	0.819
	L581M	2009S	0.405
HA	substitution	season	support
	K283E	2013N	0.926
	A197T	2013N	0.897
	S185T	2012IN 2011N	0.896
	N260D	2012N	0.879
	K163Q	2012K	0.87
	S69T	2013B	0.84
	K283E	2013S	0.837
	A256T	2013S	0.835
	D97N	2013N	0.816
	V234I	2013N	0.788
	S203T	2009S	0.766
	S143G	2003S 2012N	0.191
	51750	201211	0.171

NP	substitution	season	cupport
111	N377S	2013S	support 0.98
	E454D	2013S	0.98
	M105T	2014S	0.909
	A22T	2014S	0.909
	V425I	2015N	0.878
	V444I	2015N	0.845
	V100I	2009S	0.834
	S498N	2013N	0.787
	I373T	2009S	0.781
<b>3.7.</b> 4			
NA	substitution	season	support
	N386K	2015N	0.908
	V241I	2013N	0.905
	N248D	2013N	0.905
	N369K	2011N	0.896
	G41R	2012N	0.892
	V241I	2011N	0.866
	I34V	2014N	0.846
	I117M	2015N	0.828
	N44S	2013N	0.801
	V106I	2009S	0.8
	I321V	2013S	0.798
	N44S	2012N	0.797
	N200S	2013N	0.787
	I106V	2013N	0.744
	N248D	2009S	0.733
	K432E	2014N	0.715
	L40I	2015N	0.515
<b>M1</b>	substitution	season	support
	V80I	2014S	1
	K230R	2013N	0.92
	V80I	2013N	0.913
	M192V	2013N	0.844
	V80I	2011N	0.73
	M192V	2014S	0.428
	1111/21	20145	0.720
<b>M2</b>	substitution	season	support
	V21G	2013N	support 1
	D21G	2013N 2013S	1
	G21V	2015S 2015N	0.912
	S13N	2013N 2012N	0.912
	31311	2012I <b>N</b>	0.041
NIC 4			
NS1	substitution	season	support
	I123V	2009S	1

	K131E	2014N	0.935
	T80A	2013S	0.892
	E55K	2014N	0.875
	L90I	2012N	0.843
	N205S	2013N	0.026
	112035	201311	0.020
NS2			
1152	substitution	season	support
	T48A	2013N	1
	N29S	2013S	0.641
<b>HA (H3N2)</b>	substitution	season	support
	K145N	2004S	1
	W222R	2003N	0.999
	V202I	2003N	0.999
	E83K	2003N	0.999
	L25I	2003N	0.998
	H75Q	2003N	0.998
	H155T	2003N	0.998
	A106V	2002N	0.996
	S247C	2000S	0.995
	S199P	2000S	0.995
	R50G	2000S	0.995
	K140I	2007N	0.99
	Q311H	2014S	0.972
	N144S	2015N	0.972
	L3I	2015N	0.972
	K160T	2015N	0.972
	Q33H	2000N	0.952
	K92T	2000N	0.952
	G5V	2000N	0.952
	T128A	2013S	0.951
	R142G	2013S	0.951
	S193F	2005S	0.951
	D225N	2005S	0.951
	D53N	2011N	0.944
	E280A	2011N	0.943
	S45N	2013N	0.94
	N189K	2010S	0.936
	K158N	2010S	0.936
	R50G	2003N	0.926
	G225D	2003N	0.926
	N45S	2010S	0.924
	K173Q	2008N	0.923
	Y159F	2004S	0.921
	Q156H	2003N	0.918
	N126D	2003S	0.918
	S157L	2013N	0.908
	P273S	2000S	0.907
	F159Y	2015N	0.904
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Y105H	2003S	0.903
N145S	2013N	0.892
V226I	2004S	0.881
N144K	2009S	0.88
V223I	2011S	0.876
N145S	2011S	0.876
N53D	2013N	0.869
P194L	2009S	0.867
N144D	2002N	0.845
A131T	2003N	0.833
S227P	2004S	0.829
D271N	2000N	0.816
G50E	2006S	0.816
N225D	2014S	0.803
I230V	2011S	0.801
S189N	2004S	0.799
N312S	2011S	0.795
S186G	2003N	0.793
Q261R	2007N	0.785
N278K	2013N	0.784
A198S	2011S	0.723
N189K	2009S	0.592
Y94H	2011N	0.505
T212A	2010S	0.468
T48I	2013N	0.442
Q33R	2013N	0.442
V213A	2009S	0.411
S186G	2002N	0.398
K158N	2009S	0.378
E62K	2009S	0.378
G50E	2007N	0