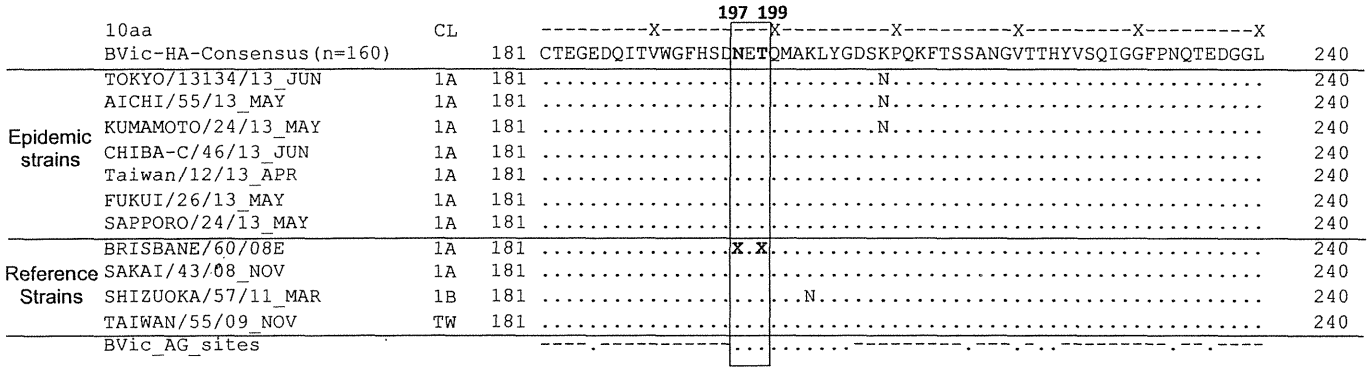
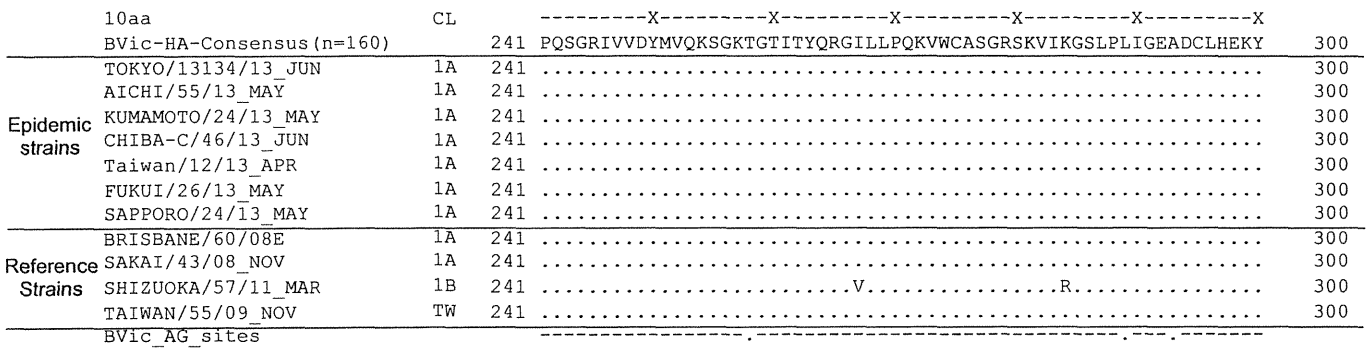
Influenza B (Victoria-lineage) HA1 amino acid comparison

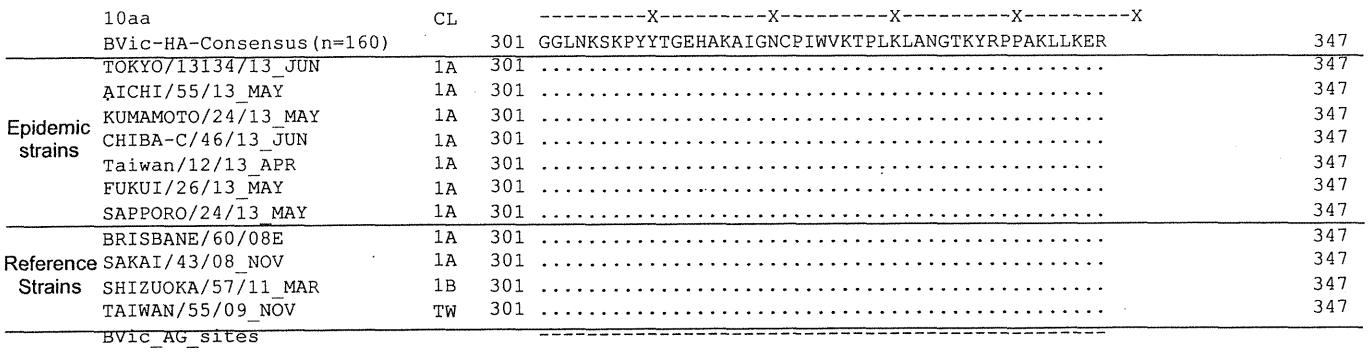
	10aa	CL		---------X---------X---------X---------X---------X---------X	
	BVic-HA-Consensus(n=160)		1	DRICTGITSSNSPHVVKTATQGEVNVTGVIPLTTTPTKSHFANLKGTETRGKLCPKCLNC	60
Epidemic strains	TOKYO/13134/13_JUN	1A	1	.....	60
	AICHI/55/13_MAY	1A	1	.....	60
	KUMAMOTO/24/13_MAY	1A	1	.....	60
	CHIBA-C/46/13_JUN	1A	1	.....	60
	Taiwan/12/13_APR	1A	1	.....	60
	FUKUI/26/13_MAY	1A	1	.....	60
	SAPPORO/24/13_MAY	1A	1	.....	60
Reference Strains	BRISBANE/60/08E	1A	1	.....	60
	SAKAI/43/08_NOV	1A	1	.....	60
	SHIZUOKA/57/11_MAR	1B	1	.....P..	60
	TAIWAN/55/09_NOV	TW	1	.....I.....P..	60
	BVic_AG_sites			----------	

	10aa	CL		---------X---------X---------X---------X---------X---------X	
	BVic-HA-Consensus(n=160)		61	TDLDVALGRPKCTGKIPSARVSILHEVRPVTSGCFPIMHDRTKIRQLPNLLRGYEHIRLS	120
Epidemic strains	TOKYO/13134/13_JUN	1A	61	.....	120
	AICHI/55/13_MAY	1A	61	.....	120
	KUMAMOTO/24/13_MAY	1A	61	.....	120
	CHIBA-C/46/13_JUN	1A	61	.....	120
	Taiwan/12/13_APR	1A	61	.....I.....	120
	FUKUI/26/13_MAY	1A	61	.....	120
	SAPPORO/24/13_MAY	1A	61	.....M.....	120
Reference Strains	BRISBANE/60/08E	1A	61	.....	120
	SAKAI/43/08_NOV	1A	61	.....	120
	SHIZUOKA/57/11_MAR	1B	61	.....	120
	TAIWAN/55/09_NOV	TW	61	.....N.....	120
	BVic_AG_sites			----------.---	

	10aa	CL		---------X---------X---------X---------X---------X---------X	
	BVic-HA-Consensus(n=160)		121	THNVINAENAPGGPYKIGTSGSCPNVTNGNGFFATMAWAVPKNDKNKTATNPLTIEVPYI	180
Epidemic strains	TOKYO/13134/13_JUN	1A	121	.....	180
	AICHI/55/13_MAY	1A	121	.....	180
	KUMAMOTO/24/13_MAY	1A	121	.....	180
	CHIBA-C/46/13_JUN	1A	121	.....	180
	Taiwan/12/13_APR	1A	121	.....E.....I...	180
	FUKUI/26/13_MAY	1A	121	.....	180
	SAPPORO/24/13_MAY	1A	121	.....T.....	180
Reference Strains	BRISBANE/60/08E	1A	121	.....I.....	180
	SAKAI/43/08_NOV	1A	121	.....T.....I.....	180
	SHIZUOKA/57/11_MAR	1B	121	.....	180
	TAIWAN/55/09_NOV	TW	121	.....N.....S.....	180
	BVic_AG_sites			----------.---------.---..-.....--------.....----------	


197 199
10aa
CL
BVic-HA-Consensus(n=160)
181 CTEGEDQITVWGFHSDNETQMAKLYGDSKPQKFTSSANGVTTHYVSQIGGFPNQTEDGGL 240
TOKYO/13134/13_JUN 1A 181 240
AICHI/55/13_MAY 1A 181 240
KUMAMOTO/24/13_MAY 1A 181 240
CHIBA-C/46/13_JUN 1A 181 240
Taiwan/12/13_APR 1A 181 240
FUKUI/26/13_MAY 1A 181 240
SAPPORO/24/13_MAY 1A 181 240
BRISBANE/60/08E 1A 181 240
SAKAI/43/08_NOV 1A 181 240
SHIZUOKA/57/11_MAR 1B 181 240
TAIWAN/55/09_NOV TW 181 240
BVic_AG_sites
Epidemic strains
Reference Strains


10aa
CL
BVic-HA-Consensus(n=160)
241 PQSGRIVVDYMVQKSGKTGTITYQRGILLPQKVWCASGRSKVIKGSLPLIGEADCLHEKY 300
TOKYO/13134/13_JUN 1A 241 300
AICHI/55/13_MAY 1A 241 300
KUMAMOTO/24/13_MAY 1A 241 300
CHIBA-C/46/13_JUN 1A 241 300
Taiwan/12/13_APR 1A 241 300
FUKUI/26/13_MAY 1A 241 300
SAPPORO/24/13_MAY 1A 241 300
BRISBANE/60/08E 1A 241 300
SAKAI/43/08_NOV 1A 241 300
SHIZUOKA/57/11_MAR 1B 241 300
TAIWAN/55/09_NOV TW 241 300
BVic_AG_sites
Epidemic strains
Reference Strains


10aa
CL
BVic-HA-Consensus(n=160)
301 GGLNKSKPYYTGEHAKAIGNCPIWVKTPLKLANGTKYRPPAKLLKER 347
TOKYO/13134/13_JUN 1A 301 347
AICHI/55/13_MAY 1A 301 347
KUMAMOTO/24/13_MAY 1A 301 347
CHIBA-C/46/13_JUN 1A 301 347
Taiwan/12/13_APR 1A 301 347
FUKUI/26/13_MAY 1A 301 347
SAPPORO/24/13_MAY 1A 301 347
BRISBANE/60/08E 1A 301 347
SAKAI/43/08_NOV 1A 301 347
SHIZUOKA/57/11_MAR 1B 301 347
TAIWAN/55/09_NOV TW 301 347
BVic_AG_sites
Epidemic strains
Reference Strains

Detection of antiviral resistant viruses in 2012/13 season:

- During February and August 2013, 117 A(H1N1)pdm09, 228 A(H3N2) and 372 B viruses isolated in Japan, Laos, Mongolia, Nepal, Taiwan and VietNam were tested for susceptibility to four neuraminidase (NA) inhibitors (oseltamivir, zanamivir, peramivir, and laninamivir). Those viruses were also subjected to real-time RT-PCR allelic determination (for A(H1N1)pdm09) and to NA gene sequencing for detection of mutations which correlate to the phenotype of antiviral resistance.
- Two H275Y A(H1N1)pdm09 mutant viruses were detected in Japan and they exhibited highly reduced susceptibility to oseltamivir and peramivir.
- Four and five viruses of B/Victoria-lineage showed reduced sensitivity to oseltamivir and peramivir, respectively, and they possessed both K343E and K107N substitutions in the NA protein.
- All viruses tested were sensitive to zanamivir and laninamivir.

Detection of NA inhibitor-resistant viruses from February to August 2013

Viruses	Oseltamivir				Peramivir				Zanamivir		Laninamivir	
	No. of viruses tested	Normal[a]	Reduced[a]	Highly reduced[a]	No. of viruses tested	Normal[a]	Reduced[a]	Highly reduced[a]	No. of viruses tested	Normal[a]	No. of viruses tested	Normal[a]
A(H1N1)pdm09	**117**	**115**	**0**	**2[b]**	**117**	**115**	**0**	**2[b]**	**117**	**117**	**117**	**117**
Japan	93	91	0	2	93	91	0	2	93	93	93	93
Laos	1	1	0	0	1	1	0	0	1	1	1	1
Mongolia	4	4	0	0	4	4	0	0	4	4	4	4
Nepal	15	15	0	0	15	15	0	0	15	15	15	15
Taiwan	2	2	0	0	2	2	0	0	2	2	2	2
Vietnam	2	2	0	0	2	2	0	0	2	2	2	2
A(H3N2)	**228**	**228**	**0**	**0**	**228**	**228**	**0**	**0**	**228**	**228**	**228**	**228**
Japan	208	208	0	0	208	208	0	0	208	208	208	208
Laos	3	3	0	0	3	3	0	0	3	3	3	3
Mongolia	4	4	0	0	4	4	0	0	4	4	4	4
Taiwan	11	11	0	0	11	11	0	0	11	11	11	11
Vietnam	2	2	0	0	2	2	0	0	2	2	2	2
B	**372**	**368**	**4[c]**	**0**	**372**	**367**	**5[c]**	**0**	**372**	**372**	**372**	**372**
Japan	330	326	4	0	330	325	5	0	330	330	330	330
Laos	27	27	0	0	27	27	0	0	27	27	27	27
Nepal	10	10	0	0	10	10	0	0	10	10	10	10
Taiwan	3	3	0	0	3	3	0	0	3	3	3	3
Vietnam	2	2	0	0	2	2	0	0	2	2	2	2

Viruses were examined by fluorescent-based NA-Fluor assay, chemiluminescent-based NA-XTD assay, real time RT-PCR allelic discrimination and/or NA sequencing.

[a] Fold difference in IC_{50} compared to the mean value of sensitive viruses. Influenza A viruses: Normal inhibition: <10-fold; Reduced inhibition: 10-100-fold; Highly reduced inhibition: >100-fold. Influenza B viruses: Normal inhibition: <5-fold; Reduced inhibition: 5-50-fold; Highly reduced inhibition: >50-fold.

[b] Viruses possessed an H275Y substitution in NA protein.

[C] Viruses possessed K107N and K343E substitutions in NA protein (B Victoria lineage).

Information for WHO Annual Consultation on the Composition of Influenza Vaccine in the Southern Hemisphere

September 23-25, 2013, Geneva, Switzerland

Serologic Response to Influenza Virus Vaccines

WHO Collaborating Center for Reference and Research on Influenza at Laboratory of Influenza Virus Surveillance, Center for Influenza Virus Research,

National Institute of Infectious Diseases, Tokyo, Japan

Serum panel for 12/13 Southern hemisphere human serology

Serum provided by	Population details (yrs)		No. of sera	Vaccine components
	Adults			
NIBSC, UK	Age range 21 - 55	Mean age 37.1	24	A/California/7/2009 (H1N1)pdm09 (X-179A)
(R. Newman)	Elderly			A/Texas/50/2012 (H3N2) (X-223A)
	Age range 61 - 80	Mean age 68.4	23	B/Massachusetts/02/2012

Antigen strains used for serology study by NIID

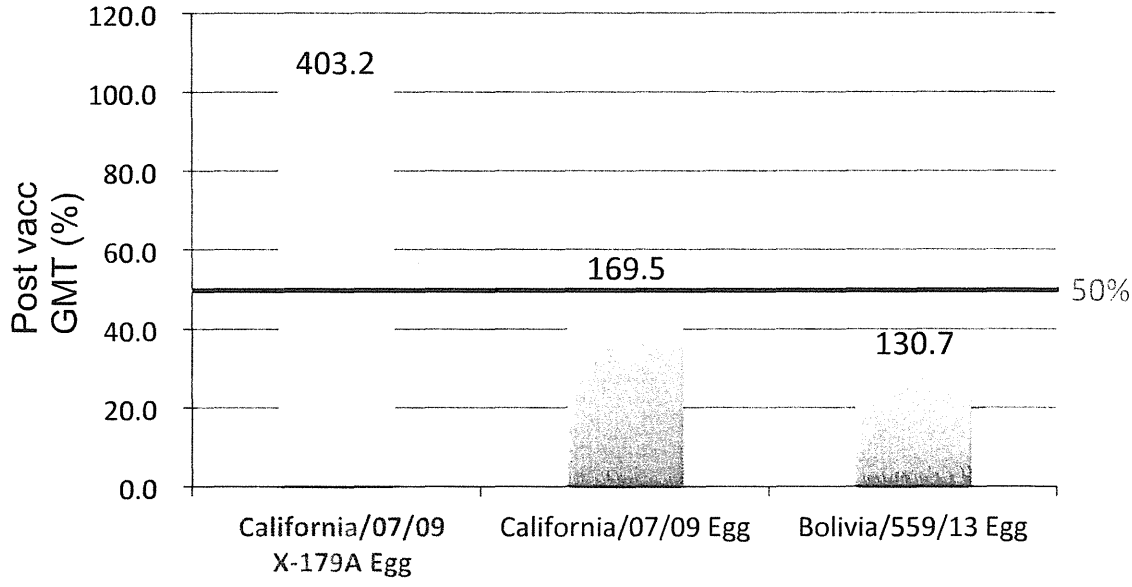
Type/Subtypes	Viruses	Passage history	Remarks
A(H1N1)pdm09	**A/California/7/2009 X-179A**	**Ex/E1+1**	**Vaccine virus**
	A/California/07/2009	E2 +3	Vaccine wild type (Egg grown)
	A/Bolivia/559/2013	E4+1	group6; K163Q, A256T
A(H3N2)	**A/Texas/50/2012 X-223**	**E4/E8+1**	**Vaccine virus**
	A/Texas/50/2012	E5+2	Vaccine wild type (Egg grown)
	A/Texas/50/2012	M 1/C 1 +1	Vaccine wild type (Cell grown)
	A/YOKOHAMA/153/2013	MDCK 3 +1	recent virus in subclade 3C.3 (N145S, R142G, T128A), cell-grown, A/Texas/50/2012-like
	A/OSAKA/32/2013	MDCK 2 +1	recent virus in subclade 3C.2b (N145S), cell-grown, A/Texas/50/2012-like
	A/New York/39/2012	E4+1	Subclade 3C.3 (N145S, R142G, T128A)
	A/New York/39/2012	C2+1	Subclade 3C.3 (N145S, R142G, T128A)
B-Yam	B/Massachusetts/2/2012 BX-51B	E3/E7+1	Vaccine virus (NIID)
	B/Massachusetts/02/2012	**E3/E7+1**	**Vaccine wild type (Egg grown), Vaccine virus (NIBSC)**
	B/Massachusetts/02/2012	M 1/C 2 +2	Vaccine wild type (Cell grown)
	B/FUKUI/24/2013	MDCK 1 +1	recent clade 2A, cell-grown B/Massachusetts/2/2012-like
	B/Hawaii/01/2013	C1+1	group2; T189A

HI antibody response to A(H1N1)pdm09 Influenza viruses

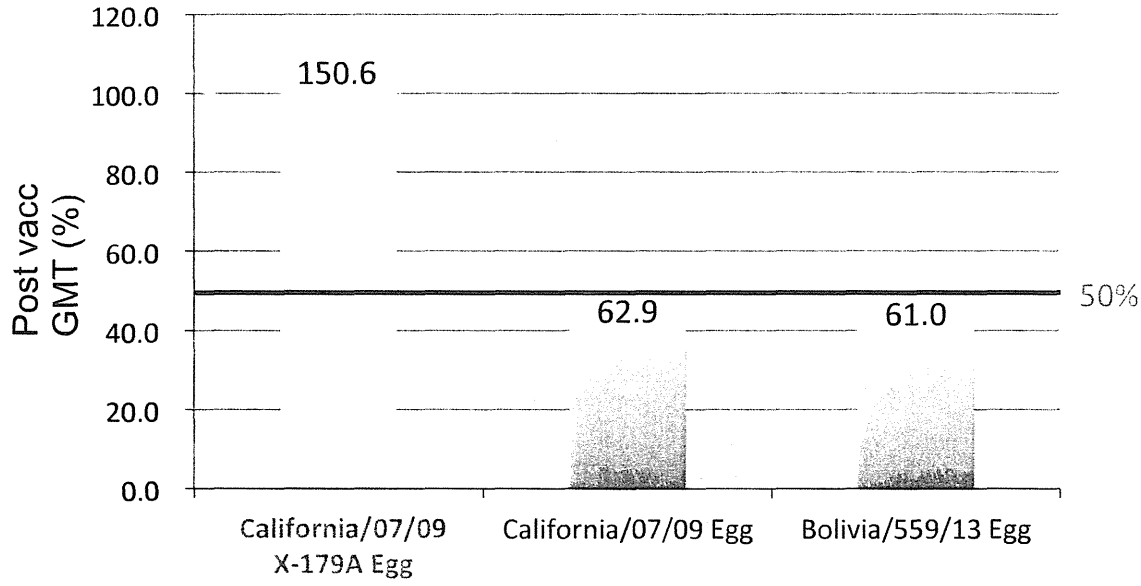
NIBSC Sample	Antigen	Passage History	(%) ≧40		% 4-Fold Rise	GMT		Post-Vaccine GMT Reduction (%) : X179A
			Pre	Post		Pre	Post	
Adult	**California/07/09 X-179A Egg**	**EX/E1+1**	**41.7**	**100.0**	**91.7**	**27.5**	**403.2**	
	California/07/09 Egg	E2 +3	25.0	95.8	83.3	14.6	169.5	58.0
	Bolivia/559/13 Egg	E4+1	25.0	95.8	83.3	13.0	130.7	67.6
Elderly	**California/07/09 X-179A Egg**	**EX/E1+1**	**30.4**	**95.7**	**65.2**	**23.3**	**150.6**	
	California/07/09 Egg	E2 +3	26.1	78.3	47.8	12.7	62.9	58.2
	Bolivia/559/13 Egg	E4+1	26.1	69.6	56.5	13.9	61.0	59.5

HI antibody response to A(H1N1)pdm09 viruses (NIBSC Sera) : X-179A

Adult



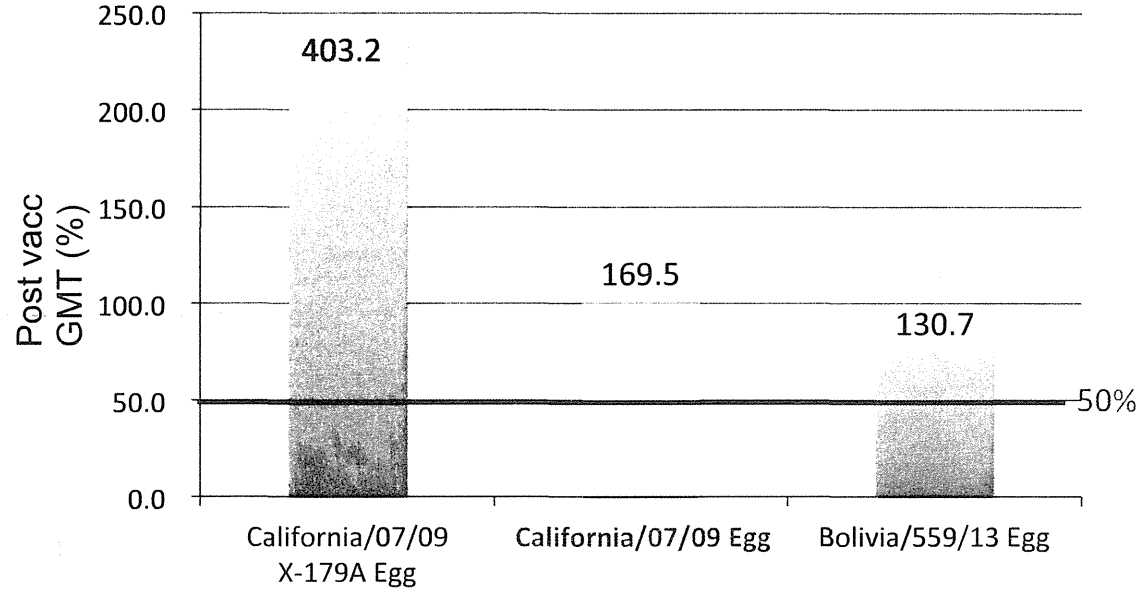
Elderly



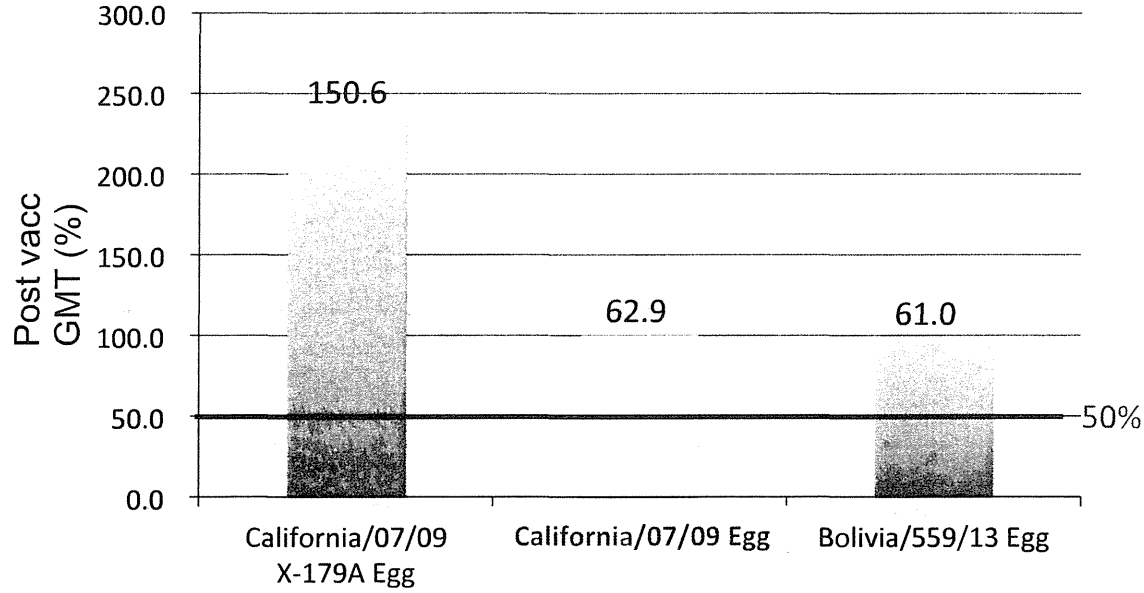
Numbers above the columns indicate the HI GMTs of viruses.

HI antibody response to A(H1N1)pdm09 viruses (NIBSC Sera) : Cal/7 Egg

Adult



Elderly



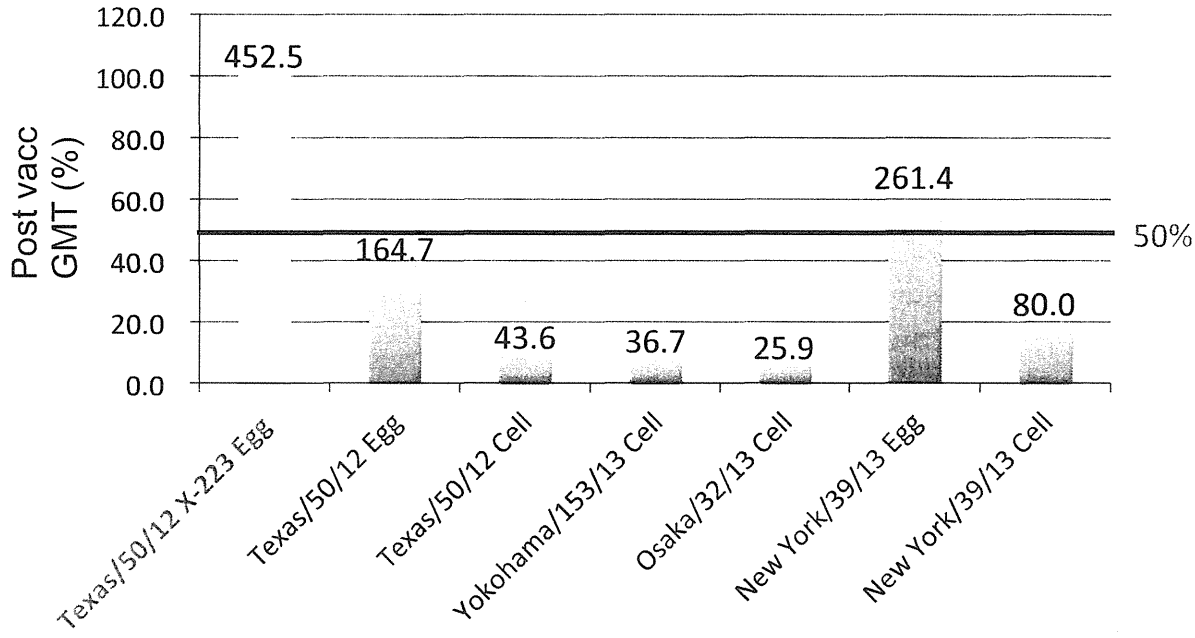
Numbers above the columns indicate the HI GMTs of viruses.

HI antibody response to A(H3N2) Influenza viruses

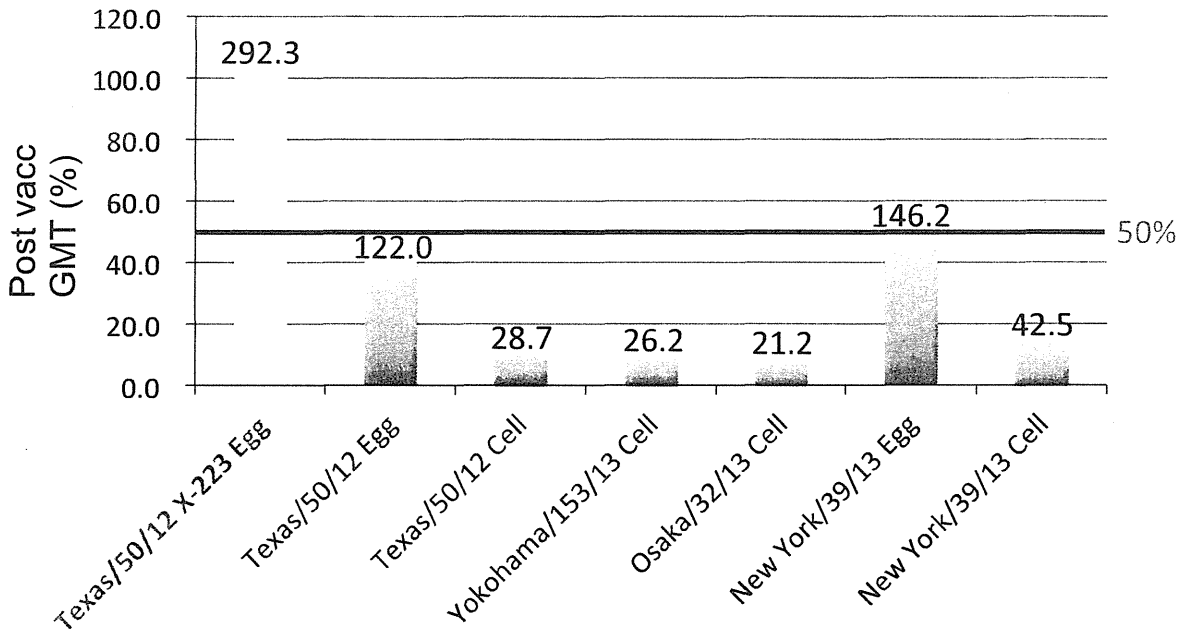
NIBSC Sample	Antigen	Passage History	(%) ≧40		% 4-Fold Rise	GMT		Post-Vaccine GMT Reduction (%) : X223	Post-Vaccine GMT Reduction (%) : Tex50 Egg
			Pre	Post		Pre	Post		
Adult	**Texas/50/12 X-223 Egg**	**E4/E8+1**	**41.7**	**100.0**	**91.7**	**26.7**	**452.5**		**-**
	Texas/50/12 Egg	E5+2	29.2	100.0	87.5	15.4	164.7	63.6	
	Texas/50/12 Cell	M 1+C 1+1	8.3	70.8	62.5	10.3	43.6	90.4	73.5
	Yokohama/153/13 Cell	MDCK 3+1	8.3	66.7	75.0	9.4	36.7	91.9	77.7
	Osaka/32/13 Cell	MDCK 2+1	8.3	45.8	62.5	8.2	25.9	94.3	84.3
	New York/39/13 Egg	E4+1	33.3	100.0	91.7	16.3	261.4	42.2	-
	New York/39/13 Cell	C 2+1	8.3	100.0	87.5	11.6	80.0	82.3	51.4
Elderly	**Texas/50/12 X-223 Egg**	**E4/E8+1**	**52.2**	**100.0**	**69.6**	**33.4**	**292.3**		**-**
	Texas/50/12 Egg	E5+2	34.8	78.3	60.9	19.4	122.0	58.3	
	Texas/50/12 Cell	M 1+C 1+1	17.4	34.8	21.7	13.9	28.7	90.2	76.5
	Yokohama/153/13 Cell	MDCK 3+1	17.4	34.8	39.1	10.9	26.2	91.0	78.5
	Osaka/32/13 Cell	MDCK 2+1	17.4	30.4	26.1	8.9	21.2	92.7	82.6
	New York/39/13 Egg	E4+1	30.4	87.0	69.6	22.6	146.2	50.0	-
	New York/39/13 Cell	C 2+1	21.7	60.9	47.8	14.4	42.5	85.5	65.2

HI antibody response to A(H3N2) viruses (NIBSC Sera) : X-223

Adult



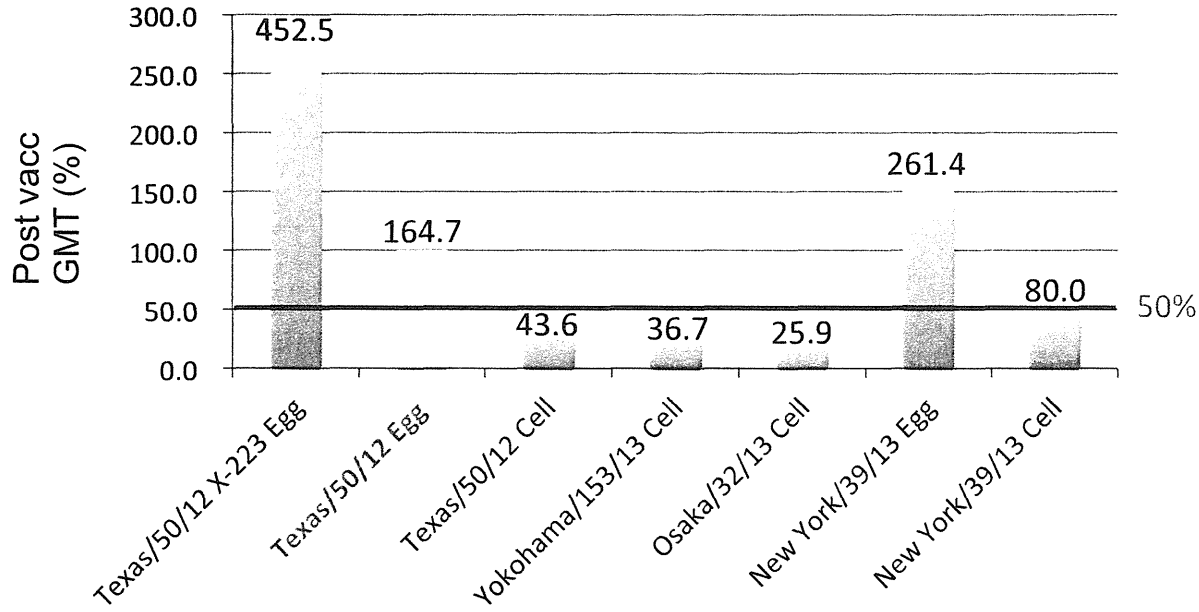
Elderly



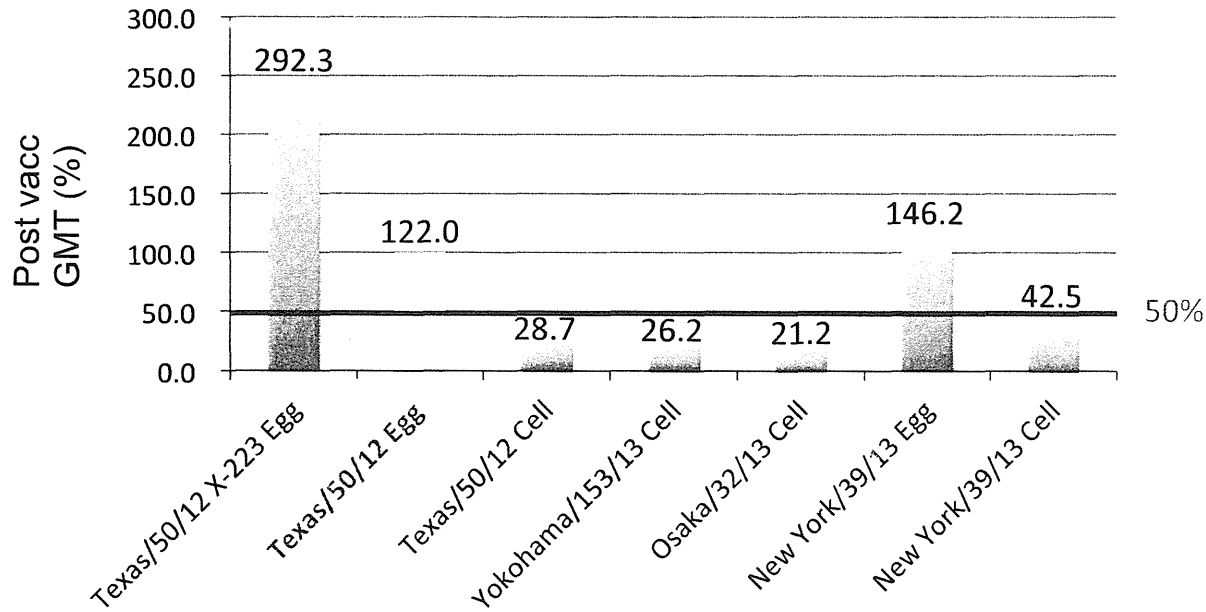
Numbers above the columns indicate the HI GMTs of viruses.

HI antibody response to A(H3N2) viruses (NIBSC Sera) : Texas50 Egg

Adult

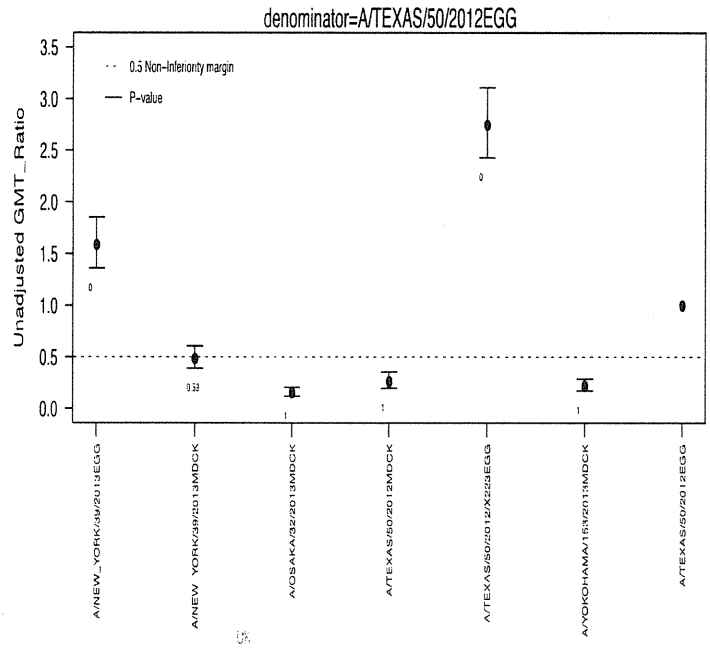


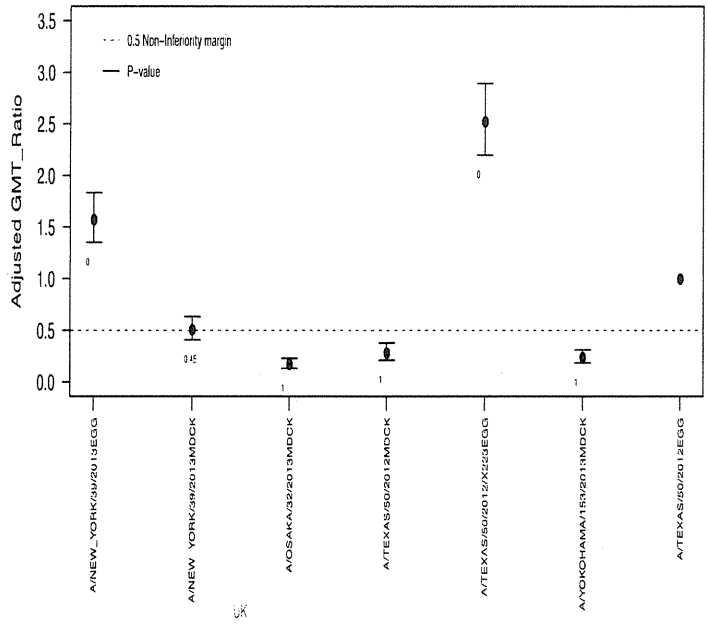
Elderly



Numbers above the columns indicate the HI GMTs of viruses.

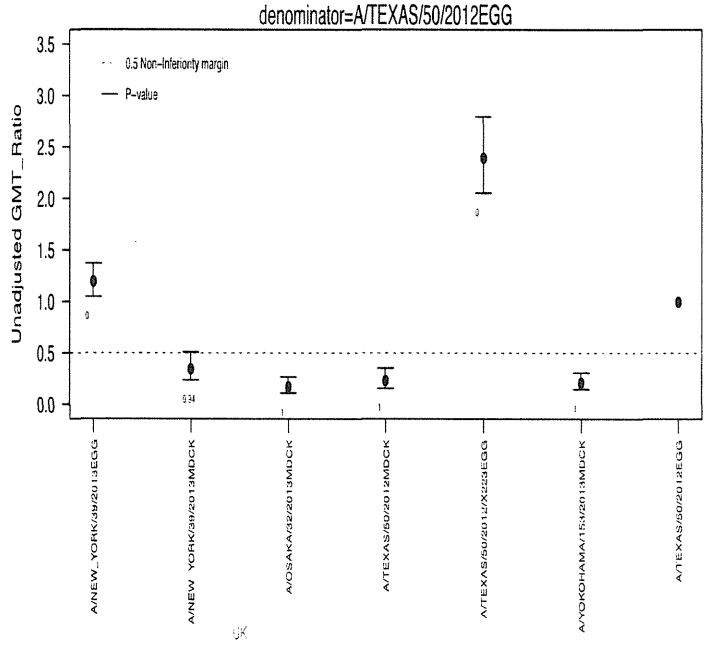
NIID Adult HI GMT-ratios

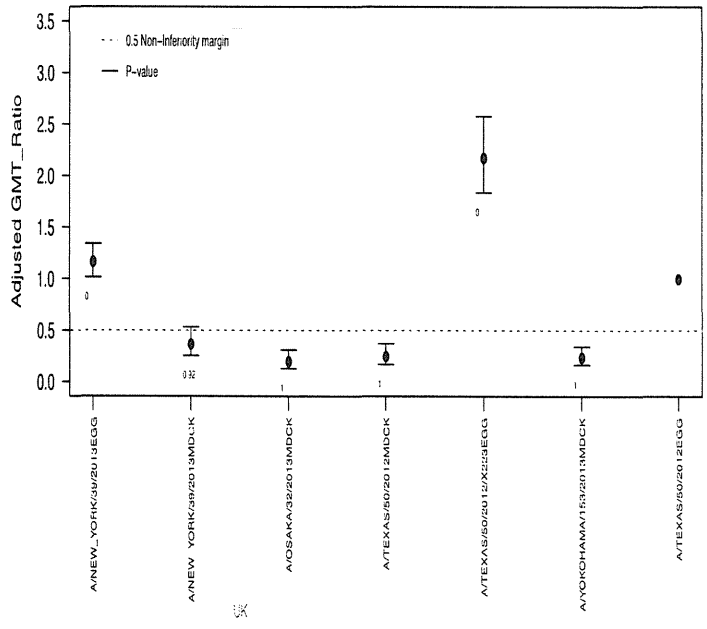




Analysis was done by US CDC.

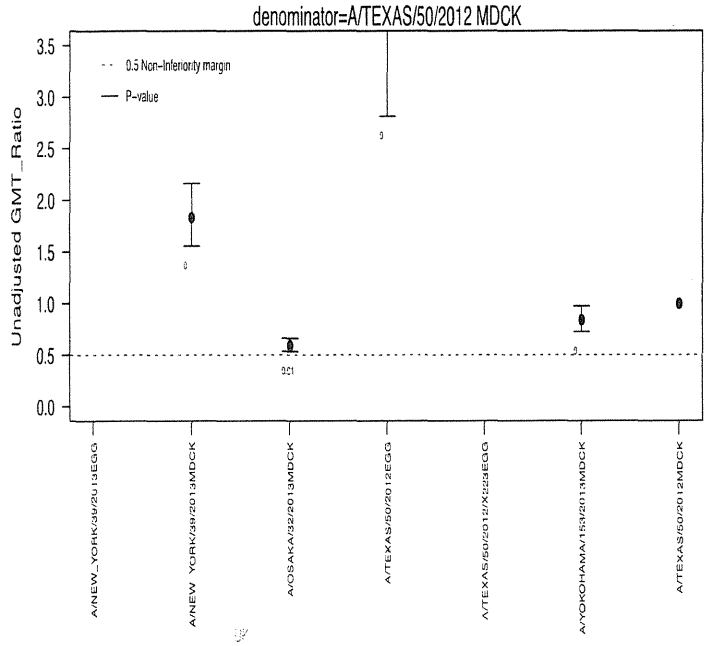
NIID Elderly HI GMT-ratios

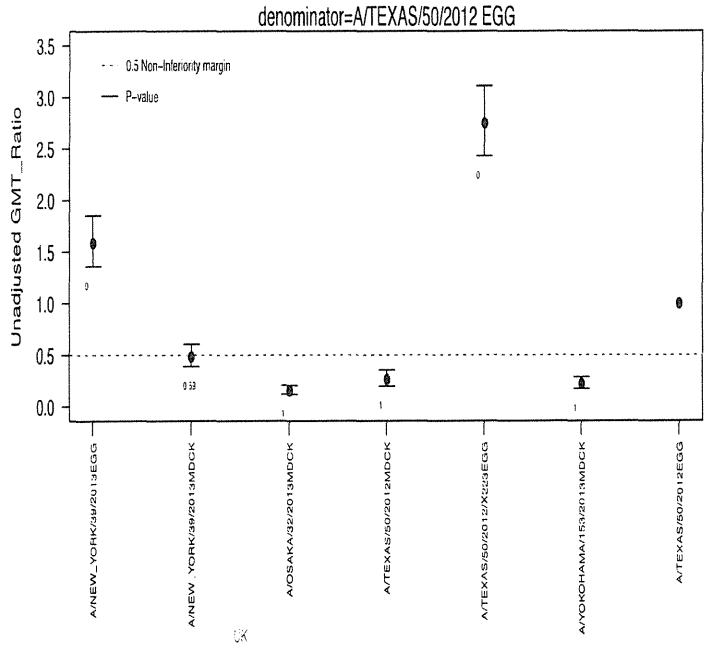




Analysis was done by US CDC.

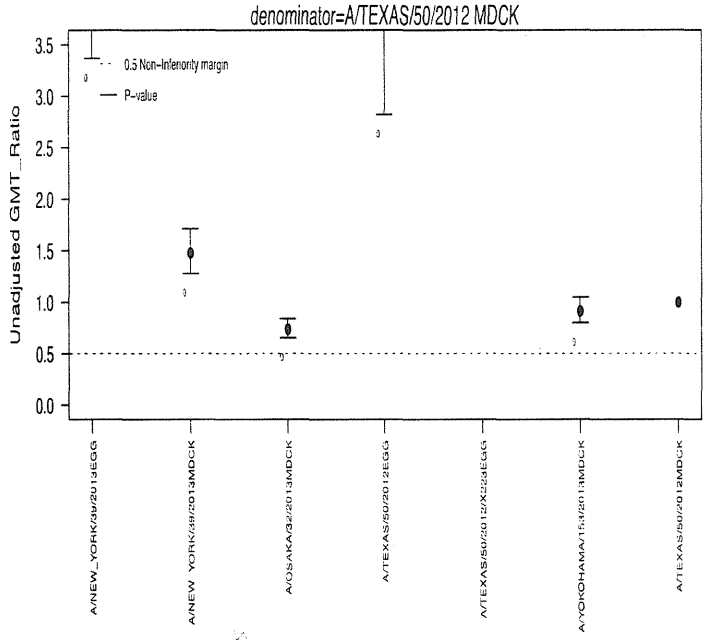
NIID Adult HI GMT-ratios

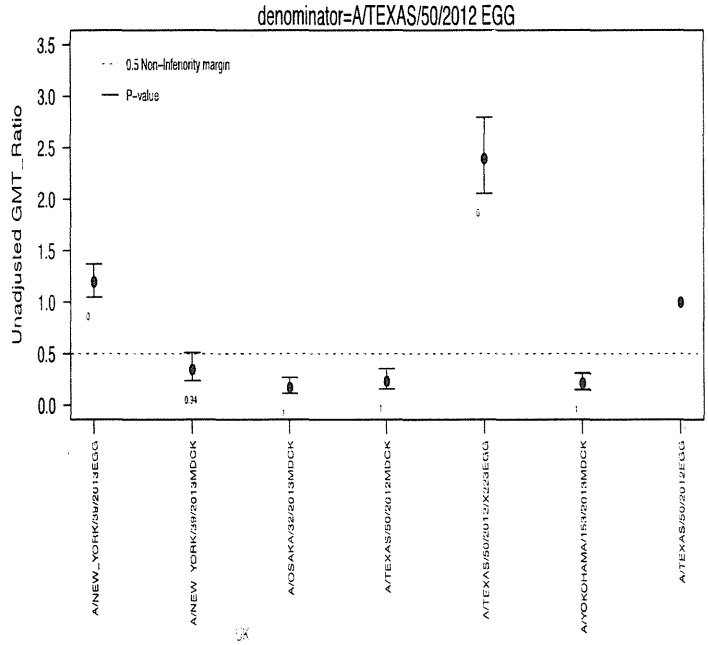




Analysis was done by US CDC.

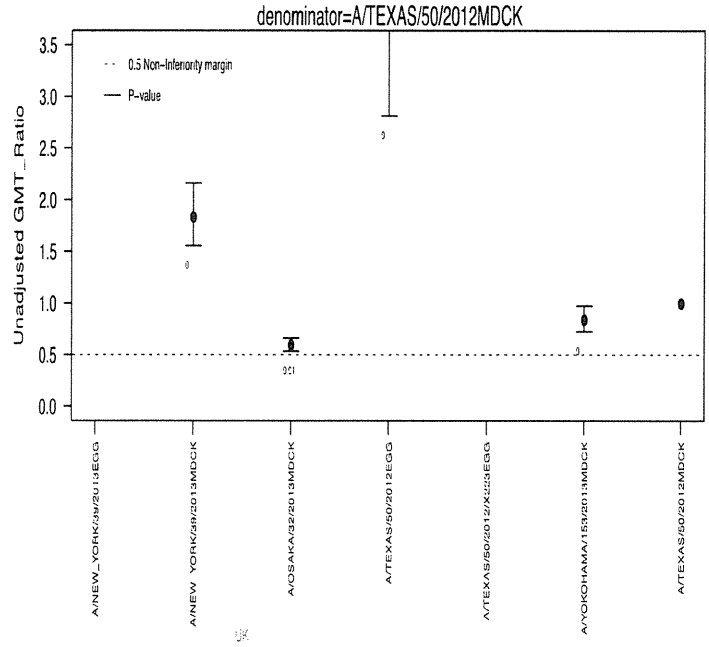
NIID Elderly HI GMT-ratios

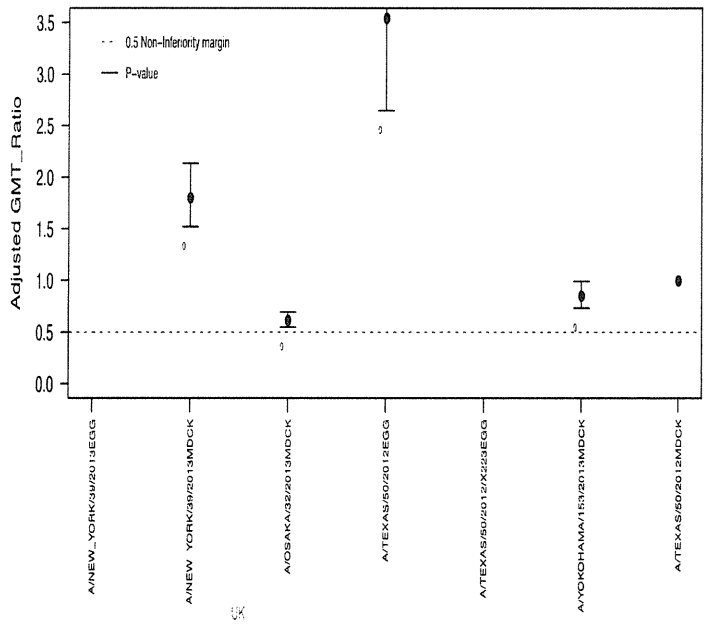




Analysis was done by US CDC.

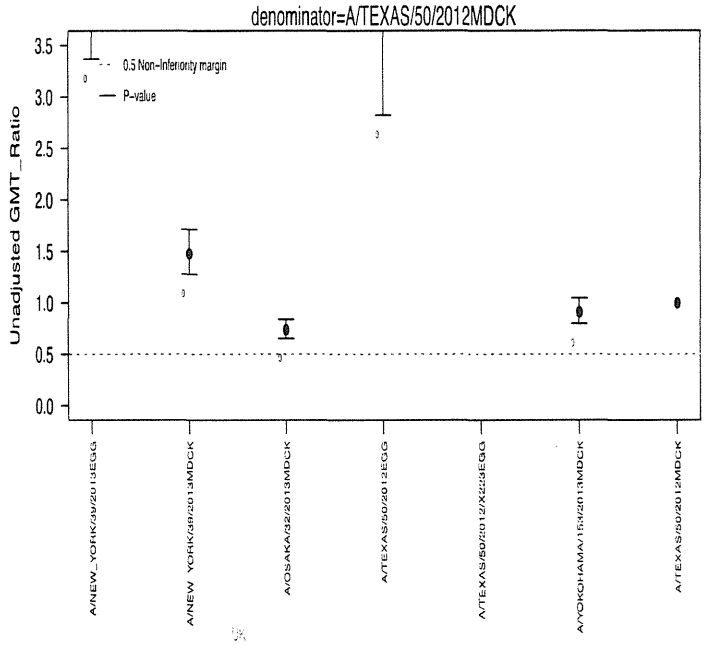
NIID Adult HI GMT-ratios

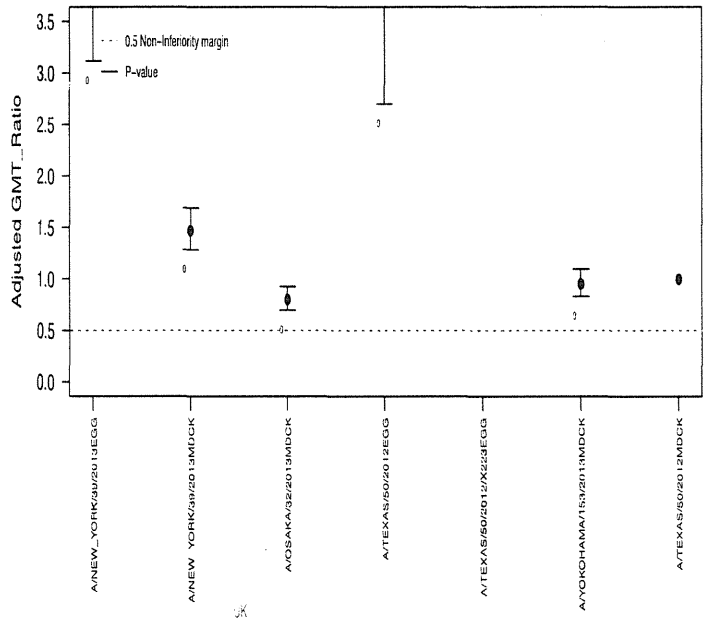




Analysis was done by US CDC.

NIID Elderly HI GMT-ratios





Analysis was done by US CDC.

HI antibody response to B (Yamagata-lineage) Influenza viruses

NIBSC Sample	Antigen	Passage History	(%) ≧40		% 4-Fold Rise	GMT		Post-Vaccine GMT Reduction (%) : BX-51B	Post-Vaccine GMT Reduction (%) : Mass2 Egg
			Pre	Post		Pre	Post		
Adult	Massachusetts/2/12 BX-51B Egg	E3/E7+1	16.7	95.8	87.5	13.3	106.8		-
	Massachusetts/2/12 Egg	**E3+2**	**8.3**	**87.5**	**75.0**	**11.9**	**84.8**	20.6	
	Massachusetts/2/12 Cell	M 1/C 2+2	37.5	95.8	70.8	18.3	119.9	-	-
	Fukui/24/13 Cell	MDCK 1+1	41.7	95.8	70.8	21.8	160.0	-	-
	Hawaii/01/13 Cell	C 1+1	54.2	95.8	70.8	25.9	213.6	-	-
Elderly	Massachusetts/2/12 BX-51B Egg	E3/E7+1	26.1	60.9	30.4	15.7	35.5		-
	Massachusetts/2/12 Egg	**E3+2**	**26.1**	**47.8**	**21.7**	**14.4**	**28.7**	19.2	
	Massachusetts/2/12 Cell	M 1/C 2+2	30.4	73.9	26.1	23.3	49.4	-	-
	Fukui/24/13 Cell	MDCK 1+1	34.8	78.3	34.8	29.6	66.8	-	-
	Hawaii/01/13 Cell	C 1+1	43.5	95.7	39.1	33.4	87.6	-	-