

FIG. 1

Pneumococcal serotype specific IgG Concentrations in individual donor sera drawn at different time points

Donor ID	Time Point	Sample ID	Serotype specific IgG concentration (µg/mL)											
			1	3	4	5	6B	7F	9V	14	18C	19A	19F	23F
Donor #34440	Pre	1010183980	2.14	0.13	0.19	0.57	0.15	0.81	0.04	0.65	0.57	0.25	1.10	1.29
	Week 4	1010187977	1086.8	2.12	28.50	3.24	4.56	12.82	10.27	0.56	10.12	23.76	166.82	56.74
	Week 8	1010191870	683.56	1.04	18.37	1.72	2.57	8.75	7.14	0.39	5.55	14.62	99.79	35.07
	Week 10	1010193841	894.33	2.85	27.24	2.74	2.80	12.26	8.92	0.66	7.88	18.69	118.51	51.77
	Week 12	1010195848	814.20	2.30	22.37	2.58	2.60	12.29	8.07	0.65	7.30	16.70	143.87	45.81
	Week 16	1010199412	632.08	1.90	19.35	2.32	2.21	10.83	6.47	0.81	6.71	15.16	103.09	39.97
Donor #7942	Pre	1010184203	0.52	0.32	<LOD	0.39	0.24	0.14	0.03	<LOD	<LOD	0.18	<LOD	0.36
	Week 4	1010187944	36.04	15.06	5.49	2.54	0.28	4.95	9.76	3.14	23.07	3.40	0.17	1.43
	Week 8	1010191587	33.01	10.17	3.92	2.35	0.27	2.85	8.91	3.23	19.45	2.11	0.24	1.63
	Week 10	1010193786	31.43	10.72	6.50	2.78	0.49	2.66	7.64	3.29	15.90	5.54	0.35	1.57
	Week 12	1010195777	26.03	8.66	5.42	2.82	0.48	2.22	6.99	3.18	14.71	6.26	0.30	1.62
	Week 16	1010200569	18.36	5.78	3.98	2.72	0.56	1.69	5.70	2.96	11.31	6.72	0.54	1.83
Donor #20003	Pre	1010184756	0.44	1.00	<LOD	13.52	3.90	1.26	0.68	2.38	1.17	6.54	17.69	2.85
	Week 4	1010188381	0.72	3.12	1.16	90.54	10.40	16.61	0.93	5.47	39.95	8.65	23.85	8.03
	Week 8	1010192000	0.76	2.48	1.06	84.87	8.83	9.42	0.78	4.34	27.09	9.24	23.12	7.03
	Week 10	1010193932	1.05	3.18	1.85	216.25	8.50	8.98	1.04	4.13	30.70	8.41	17.11	7.26
	Week 12	1010195963	1.08	2.49	1.49	251.97	6.82	5.63	0.99	3.37	20.26	6.96	14.72	5.80
	Week 16	1010200033	1.03	2.34	1.24	268.43	6.96	3.93	1.05	3.18	14.30	6.92	13.96	4.38
Donor #1892	Pre	1010184804	0.13	<LOD	<LOD	0.19	<LOD	0.04	<LOD	<LOD	<LOD	<LOD	0.06	<LOD
	Week 4	1010188291	22.30	1.98	0.59	0.52	0.37	41.00	1.25	0.49	18.30	3.92	1.50	1.98
	Week 8	1010192199	9.75	0.93	0.21	0.50	0.10	19.40	0.59	0.15	6.91	2.52	0.37	1.27

FIG. 1 (cont.)

	Week 10	1010194156	6.67	1.40	0.20	0.85	0.14	11.42	0.69	0.21	4.53	1.91	0.50	1.21
	Week 12	1010196213	6.77	1.29	0.17	1.08	0.12	10.79	0.67	0.17	4.05	2.15	0.34	1.25
	Week 16	1010200305	5.03	0.77	0.08	0.88	0.06	8.77	0.48	0.10	2.30	1.62	0.19	0.94
Donor #677	Pre	1010185343	0.15	1.12	0.17	0.34	1.87	1.18	1.38	0.70	6.70	4.00	1.28	0.60
	Week 4	1010189076	14.50	3.24	3.81	4.24	4.49	11.53	5.40	2.34	19.00	10.00	12.15	4.37
	Week 8	1010193275	12.50	2.62	2.92	3.40	4.21	9.45	5.67	2.71	20.30	9.89	11.66	3.53
	Week 10	1010195037	11.90	3.56	1.23	3.34	4.18	7.16	5.99	4.27	21.10	8.63	11.25	3.69
	Week 12	1010196826	10.70	3.27	2.63	3.99	3.98	6.28	5.40	4.48	19.27	12.47	9.80	3.48
	Week 16	1010200652	10.40	3.38	2.12	4.94	4.15	8.12	6.10	5.48	19.80	18.44	10.28	3.99
Donor #5462	Pre	1010184953	0.01	0.20	0.02	0.20	0.80	4.64	0.99	0.90	0.60	11.80	0.44	0.80
	Week 4	1010189023	0.13	3.05	2.36	0.76	116.68	59.50	36.45	10.10	28.60	18.91	12.17	70.93
	Week 8	1010192671	0.12	2.32	1.20	0.81	95.55	39.71	18.50	8.90	27.30	12.63	9.88	145.80
	Week 10	1010194625	0.22	3.70	1.05	1.02	81.89	38.20	27.86	9.40	36.70	16.53	13.60	150.66
	Week 12	1010196589	0.19	3.20	0.84	1.05	76.62	34.66	22.59	8.42	34.70	20.10	13.12	96.22
	Pre	1010185005	0.18	0.15	0.30	0.94	0.90	2.20	0.80	0.60	0.04	1.52	2.56	0.80
Donor #9722	Week 4	1010188743	2.28	1.24	8.43	8.69	34.41	12.66	5.40	2.43	0.48	4.42	15.60	35.23
	Week 8	1010192740	2.23	1.30	9.18	8.36	25.70	13.86	6.10	2.04	0.62	4.14	17.40	39.36
	Week 10	1010194693	3.50	1.80	8.98	5.00	21.38	12.24	5.10	2.47	0.91	2.62	17.90	40.74
	Week 12	1010196667	3.40	1.86	8.55	4.91	23.32	13.63	5.70	3.99	0.96	3.20	19.68	34.18
	Pre	1010185392	0.29	0.45	0.45	5.18	8.04	2.50	1.00	0.16	2.20	3.40	3.28	1.60
	Week 4	1010188487	8.85	1.13	2.10	69.74	13.50	32.50	5.33	1.80	19.10	8.52	10.21	41.06
Donor #6762	Week 8	1010192605	7.29	0.78	2.02	50.22	11.50	32.10	5.20	1.68	14.20	6.75	4.90	72.26
	Week 10	1010194533	5.67	0.72	2.45	72.33	9.36	23.80	4.40	2.34	14.30	7.10	5.15	61.24
	Week 12	1010197012	4.63	0.97	1.61	48.43	9.66	11.66	4.00	2.71	14.40	5.85	4.23	65.40
	Pre	1010188097	1.10	0.26	0.03	3.20	0.37	4.40	0.67	0.10	0.08	2.43	1.31	0.42
	Week 4	1010191949	12.80	1.21	1.51	13.04	3.77	79.70	2.50	0.33	0.18	5.50	21.87	2.56
	Week 8	1010195914	10.90	2.10	0.86	14.33	3.55	88.11	2.28	0.24	0.12	4.05	19.52	2.26

FIG. 1 (cont.)

	Week 10	1010197884	13.10	1.91	1.60	13.28	3.91	88.60	3.26	0.86	0.86	7.64	23.80	2.43
	Week 12	1010200542	12.80	1.86	1.91	11.66	3.13	92.10	2.40	1.90	0.67	5.91	18.55	2.21
	Pre	1010188158	1.10	5.53	0.05	0.68	0.02	0.20	0.40	0.09	0.04	1.00	1.77	0.50
	Week 4	1010191946	10.60	21.60	0.64	3.15	0.44	10.80	5.80	0.20	0.35	3.72	7.74	2.18
Donor #7689	Week 8		NOT COLLECTED											
	Week 10	1010197682	15.6	22.6	0.89	3.4	0.98	11.29	5.34	0.64	1	5.5	11.01	2.2
	Week 12	1010199903	9.7	1	0.71	2.43	0.71	9.61	3.6	0.45	0.72	4.8	10.07	2.1
Average Pre			0.61	0.89	0.12	2.52	1.44	1.74	0.60	0.55	1.2	2.77	2.95	0.92
Average Week 4			119.5	5.31	5.46	17.47	18.73	28.21	8.38	2.69	15.9	9.1	27.2	22.45
Average Week 8			84.46	4.74	4.42	18.51	16.92	24.85	6.13	2.96	13.5	7.33	20.76	34.25
Average Week 10			98.35	5.19	5.2	32.1	13.36	21.66	7.0	2.83	13.39	8.26	21.92	32.28
Average Week 12			89	2.69	4.57	33.1	12.82	19.89	6.04	2.93	11.7	8.44	23.47	25.81
Pooled Pre			3	0.99	0.2	3.5	1.9	6.3	0.7	1	1.4	4	4.2	1
Pooled Week 12			91	2.6	4.5	32.1	12.8	24.2	5.8	3.2	11	9	23.1	24.5
Fold Increase			30	2.6	22	9	6.7	3.8	8.3	3.2	7.9	2.2	5.5	24.5

FIG. 2 (cont.)

FIG. 2

OPK titers in individual donor sera drawn at different time points

Donor ID	Time Point	Sample ID	OPK Titer											
			1	3	4	5	6B	7F	9V	14	18C	19A	19F	23F
Donor #34440	Pre	1010183980	256	32	64	64	16	64	4	64	16	32	16	8
	Week 4	1010187977	161072	128	1024	128	256	1024	512	64	128	8192	128	128
	Week 8	1010191870	65536	256	2048	256	128	1024	1024	128	512	8192	128	256
	Week 10	1010193841	131072	256	4096	256	128	1024	512	128	256	8192	64	128
	Week 12	1010195848	131072	256	2048	256	128	1024	512	128	256	8192	32	128
	Week 16	1010199412	32768	128	2048	256	128	1024	512	128	256	8192	32	128
Donor #7942	Pre	1010184203	64	32	4	16	64	16	4	4	32	32	4	8
	Week 4	1010187944	1024	256	128	128	64	128	256	128	128	256	32	128
	Week 8	1010191587	2048	128	64	64	64	64	512	128	128	256	32	128
	Week 10	1010193786	2048	256	256	128	128	64	256	128	512	512	64	128
	Week 12	1010195777	2048	256	256	128	256	64	256	128	128	256	64	128
	Week 16	1010200569	1024	128	256	256	128	256	64	256	128	256	64	128
Donor #20003	Pre	1010184756	32	64	4	512	256	256	64	128	16	256	8	16
	Week 4	1010188381	64	128	64	4096	1024	2048	128	256	64	512	32	32
	Week 8	1010192000	32	256	64	4096	2048	1024	128	512	128	1024	32	128
	Week 10	1010193932	128	256	128	16384	2048	1024	64	512	256	512	32	512
	Week 12	1010195963	128	256	128	16384	1024	1024	64	512	128	512	32	512
	Week 16	1010200033	128	256	128	32768	1024	1024	64	512	256	512	32	512
Donor #1892	Pre	1010184804	32	4	4	16	4	4	4	4	16	4	32	4
	Week 4	1010188291	512	256	256	64	64	4096	64	64	32	256	128	256
	Week 8	1010192199	256	128	128	64	32	4096	64	32	32	256	128	128

FIG. 2 (cont.)

	Week 10	1010194156	256	256	128	128	32	2048	64	32	128	256	128	128
	Week 12	1010196213	256	256	128	128	32	2048	64	32	256	256	128	128
	Week 16	1010200305	512	256	128	128	16	2048	64	32	256	256	64	64
Donor #677	Pre	1010185343	32	64	32	64	128	256	64	64	32	128	32	64
	Week 4	1010189076	512	256	128	256	512	1024	512	128	128	1024	256	512
	Week 8	1010193275	1024	128	128	256	512	1024	512	128	128	1024	256	256
	Week 10	1010195037	512	256	128	256	512	1024	1024	256	64	1024	256	256
	Week 12	1010196826	512	256	256	256	256	1024	1024	256	64	1024	256	512
	Week 16	1010200652	1024	256	256	256	512	1024	1024	256	64	1024	512	512
	Pre	1010184953	4	16	4	16	64	256	128	8	64	1024	64	128
	Week 4	1010189023	32	128	128	128	16384	8192	8192	128	4096	4096	512	16384
Donor #5462	Week 8	1010192671	64	256	64	128	8192	8192	16384	128	8192	2048	1024	32768
	Week 10	1010194625	128	256	64	128	32758	8192	16384	128	8192	2048	1024	32768
	Week 12	1010196589	128	256	64	128	16384	8192	16384	256	16384	2048	1024	16384
	Pre	1010185005	64	32	32	64	128	128	64	32	4	128	256	128
Donor #9722	Week 4	1010188743	256	128	1024	512	1024	1024	1024	64	64	256	8192	4096
	Week 8	1010192740	256	128	1024	512	2048	2048	512	128	64	512	8192	8192
	Week 10	1010194693	512	128	1024	1024	2048	2048	1024	128	64	256	16384	8192
	Week 12	1010196667	512	128	1024	1024	2048	2048	512	128	128	512	8192	8192
Donor #6762	Pre	1010185392	64	64	32	1024	1024	128	64	16	128	128	256	128
	Week 4	1010188487	512	128	256	4096	2048	2048	512	128	2048	1024	1024	4096
	Week 8	1010192605	512	128	256	8192	2048	4096	1024	64	4096	1024	256	8192
	Week 10	1010194533	1024	128	256	8192	2048	2048	1024	64	4096	512	256	8192
Donor #17767	Week 12	1010197012	512	128	128	8192	2048	4096	512	64	4096	1024	256	8192
	Pre	1010188097	128	64	4	128	128	128	32	16	4	128	64	64
	Week 4	1010191949	2048	128	128	2048	512	16384	512	64	64	512	4096	512
	Week 8	1010195914	1024	256	64	2048	512	16384	512	64	64	512	8192	512

FIG. 2 (cont.)

	Week 10	1010197884	2048	128	128	4096	512	16381	128	64	128	512	8192	512
	Week 12	1010200542	2048	128	128	2048	1024	16384	512	64	128	512	8192	512
	Pre	1010188158	64	256	4	64	4	32	64	8	4	64	128	64
	Week 4	1010191946	512	4096	64	128	64	512	512	16	64	256	1024	256
Donor #7689	Week 8													
	Week 10	1010197682	1024	4096	128	256	128	512	512	16	64	256	4096	256
	Week 12	1010199903	1024	4096	128	128	128	1024	512	64	64	256	2048	256
	Average Pre		74	62.8	18.4	196.8	196.8	126.8	49.2	22	31	192.4	86	61
	Average Week 4		16654	563.2	320	1158	2195	3852	1222	110	681	1638	1542	2649
	Average Week 8		7804	1436	427	1735	1732	4217	2296	145	1482	1649	2027	5617
	Average Week 10		13875	601	1030	3084	4034	2150	2099	146	1376	1408	3049	5107
	Average Week 12		7899	601	428	2867	2333	3693	2035	163	2163	1459	2022	3494
	Pooled Pre		256	64	32	256	256	2048	64	64	32	256	128	64
	Pooled Week 12		16384	1024	512	4096	2048	8192	2048	16384	2048	2048	2048	4096
	Fold Increase OPK Titer		64	16	16	16	8	4	32	256	64	8	16	64

FIG. 3

Pneumococcal serotype specific IgG Concentrations in pooled donor sera drawn at different time points after immunization

Time Point	Serotype specific antibody concentration (µg/mL)											
	1	3	4	5	6B	7F	9V	14	18C	19A	19F	23F
Pre	1.38	1.15	0.13	2.08	0.99	4.79	0.21	2.20	1.82	1.58	0.55	0.57
Week 8	42.25	9.17	5.85	47.24	7.74	31.43	6.88	17.64	24.85	14.97	11.57	36.73
Week 10	42.76	7.80	4.55	39.87	7.46	25.66	6.46	13.89	20.59	16.46	10.88	27.40
Week 12	39.03	7.09	4.58	32.71	6.81	26.14	8.11	12.62	18.35	16.03	12.60	26.82
Week 16	34.36	6.83	3.97	29.73	5.37	17.27	4.82	8.90	11.43	11.73	7.61	17.21
Month 5	29.58	5.52	3.05	24.38	4.95	19.50	3.71	10.31	13.22	12.13	6.03	6.40
Average--Post Only	37.59	7.28	4.40	34.79	6.46	24.00	6.00	12.67	17.69	14.26	9.74	22.91

FIG. 4

Fold increase in pneumococcal serotype specific IgG Concentrations in pooled donor sera drawn at different time points after immunization

Time Point	Fold Increase											
	1	3	4	5	6B	7F	9V	14	18C	19A	19F	23F
Pre*	1.38	1.15	0.13	2.08	0.99	4.79	0.21	2.20	1.82	1.58	0.55	0.57
Week 8	30.62	7.98	44.12	22.69	7.78	6.57	32.54	8.02	13.67	9.44	21.23	64.22
Week 10	30.99	6.78	34.35	19.15	7.50	5.36	30.55	6.31	11.33	10.39	19.96	47.90
Week 12	28.29	6.17	34.53	15.71	6.85	5.46	38.33	5.74	10.09	10.11	23.12	46.88
Week 16	24.90	5.95	29.99	14.28	5.40	3.61	22.79	4.05	6.29	7.40	13.96	30.08
Month 5	21.44	4.81	23.05	11.71	4.97	4.07	17.55	4.69	7.27	7.66	11.07	11.19
Average--Post/Pre	27.25	6.34	33.21	16.71	6.50	5.01	28.35	5.76	9.73	9.00	17.87	40.06

* = baseline

FIG. 5

Pneumococcal serotype specific OPK titers in pooled donor sera drawn at different time points after immunization

Time Point	OPK titer											
	1	3	4	5	6B	7F	9V	14	18C	19A	19F	23F
Pre	32.00	16.00	8.00	64.00	16.00	128.00	8.00	32.00	32.00	32.00	16.00	16.00
Week 8	32768.00	256.00	128.00	1024.00	1024.00	2048.00	256.00	1024.00	2048.00	1024.00	512.00	2048.00
Week 10	65536.00	256.00	64.00	1024.00	1024.00	1024.00	256.00	2048.00	2048.00	1024.00	512.00	2048.00
Week 12	32768.00	128.00	64.00	512.00	2048.00	2048.00	128.00	2048.00	1024.00	1024.00	256.00	2048.00
Week 16	32768.00	256.00	128.00	1024.00	512.00	2048.00	128.00	1024.00	1024.00	512.00	256.00	1024.00
Month 5	16384.00	128.00	64.00	1024.00	512.00	1024.00	64.00	1024.00	1024.00	512.00	256.00	1024.00
Average--Post Only	36044.80	204.80	89.60	921.60	1024.00	1638.40	166.40	1433.60	1433.60	819.20	358.40	1638.40

FIG.6

Pneumococcal serotype specific IgG Concentrations in purified IgG made from pooled donor plasma which was drawn at different time points after immunization

Time Point	Serotype specific antibody concentration (µg/mL)											
	1	3	4	5	6B	7F	9V	14	18C	19A	19F	23F
Pre	0.81	1.0	0.09	2.05	0.72	3.31	0.15	1.91	1.11	1.04	0.61	0.44
Week 12	33.2	7.37	4.28	34.23	3.96	13.58	6.91	10.19	8.43	7.77	11.5	18.54
Week 16	19.36	4.22	2.67	23.15	3.63	11.96	5.22	10.33	6.81	6.21	8.3	15.5
Month 5	17.28	3.87	2.54	19.23	3.01	11.29	3.61	10.86	7.47	6.07	6.71	12.42
Average Post only	23.3	5.2	3.2	25.5	3.5	12.3	5.2	10.5	7.6	6.7	8.8	15.5

FIG. 7

Pneumococcal serotype specific OPK titers in purified IgG made from pooled donor plasma which was drawn at different time points after immunization

Time Point	OPK titer											
	1	3	4	5	6B	7F	9V	14	18C	19A	19F	23F
Pre	32	128	4	64	64	256	16	128	64	32	32	16
Week 12	4096	1024	64	4096	256	8192	1024	2048	1024	256	256	4096
Week 16	2048	1024	128	4096	512	8192	512	4096	1024	256	256	8192
Month 5	2048	512	128	4096	512	1096	256	2048	512	128	128	2048
Average Post only	2730.7	853.3	106.7	4096.0	426.7	5826.7	597.3	2730.7	853.3	213.3	1109.3	4778.7

FIG. 8

Comparison of Pneumococcal serotype specific OPK titers in 9 different lots of commercial immunoglobulin as compared to a hyperimmune globulin preparation purified from a pool of plasma donors 12 weeks post immunization

OPK Serotype Titer												
Sample ID	1	3	4	5	6B	7F	9V	14	18C	19A	19F	23F
A160314-A	128	4	32	16	1024	2048	64	64	64	32	8	64
A160314-B	128	4	64	256	256	1024	64	128	256	32	32	128
A160314-C	64	4	32	32	256	2048	32	128	16	32	16	64
A160314-D	16	4	32	16	64	2048	32	4	16	32	16	64
A160314-E	32	4	16	64	32	1024	16	4	4	256	32	256
A160314-F	16	4	32	16	16	64	32	128	4	64	16	512
A160314-G	16	4	16	32	16	64	16	4	4	8	8	1024
A160314-H	32	4	16	32	8	512	16	16	16	8	32	16
A160314-I	32	4	64	16	16	256	16	16	16	8	16	16
IVIG Average	52	4	34	53	188	1010	32	55	44	52	20	238
Pre	16	128	8	128	32	512	32	128	128	64	64	32
Hyper Immune IVIG	2048	1024	256	4096	512	8192	1024	2048	1024	256	1024	8192
Fold Increase over commercial IVIG	40	256	8	77	3	16	32	37	23	5.00	52	34

FIG. 9A

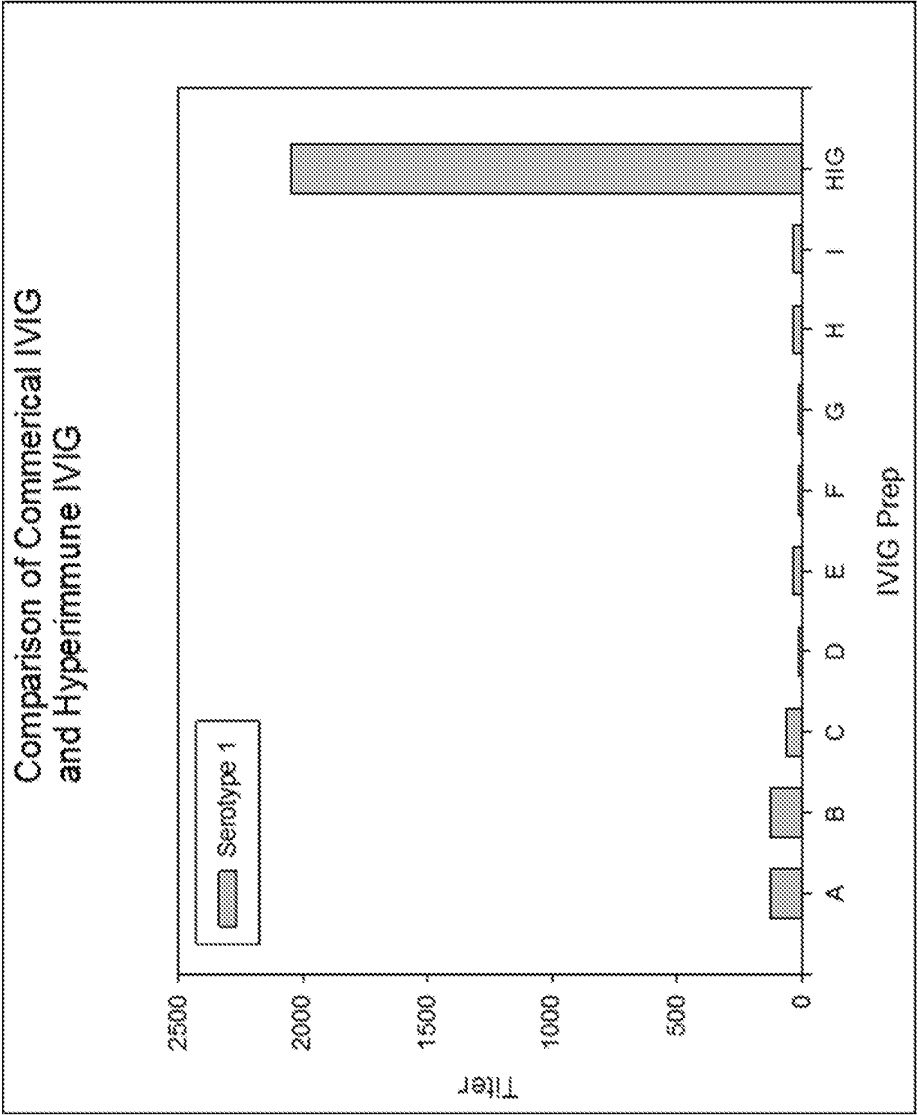


FIG. 9B

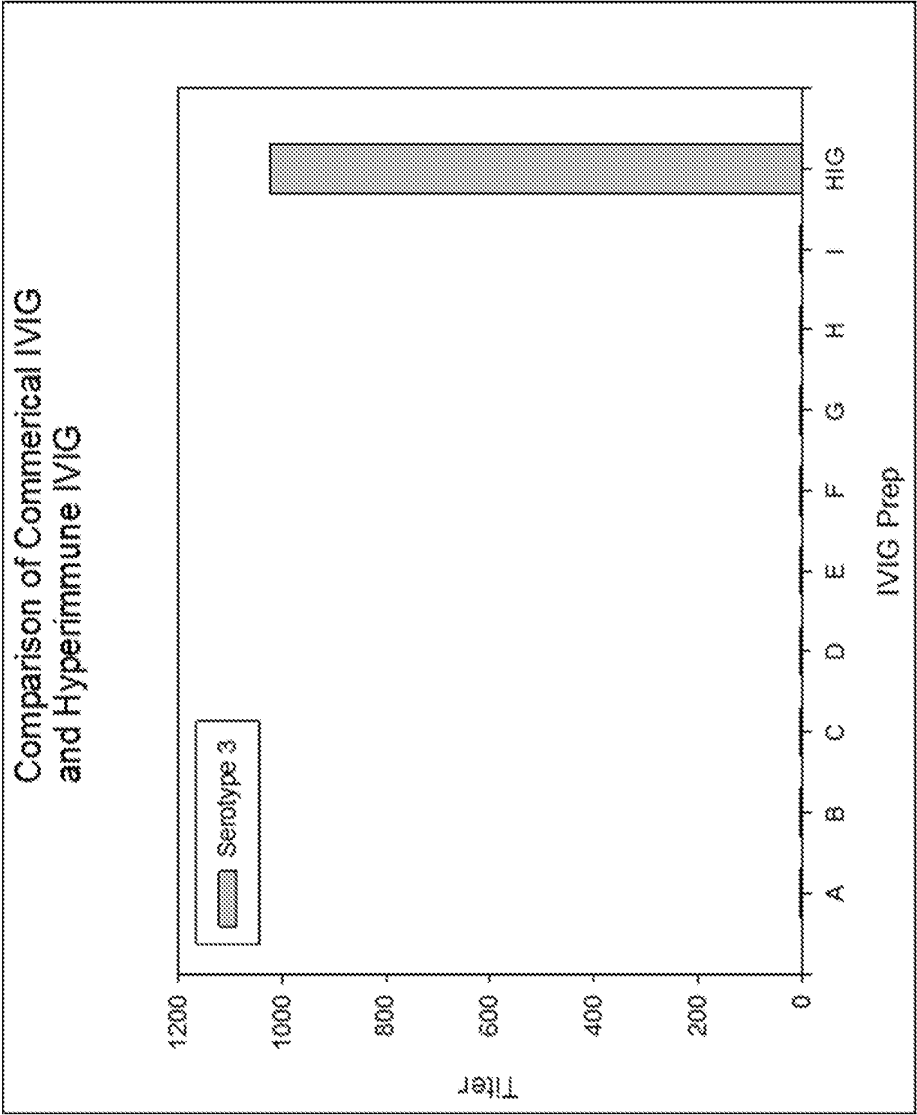


FIG. 9C

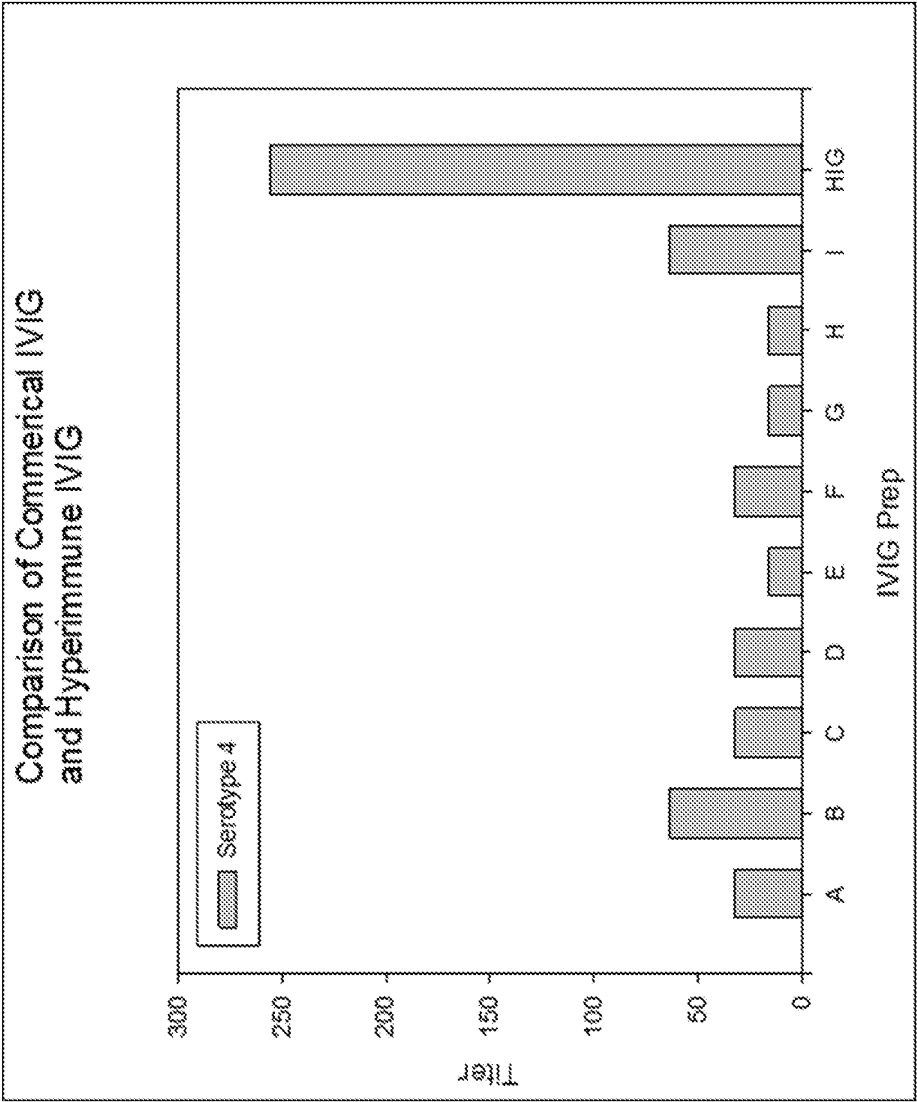


FIG. 9D

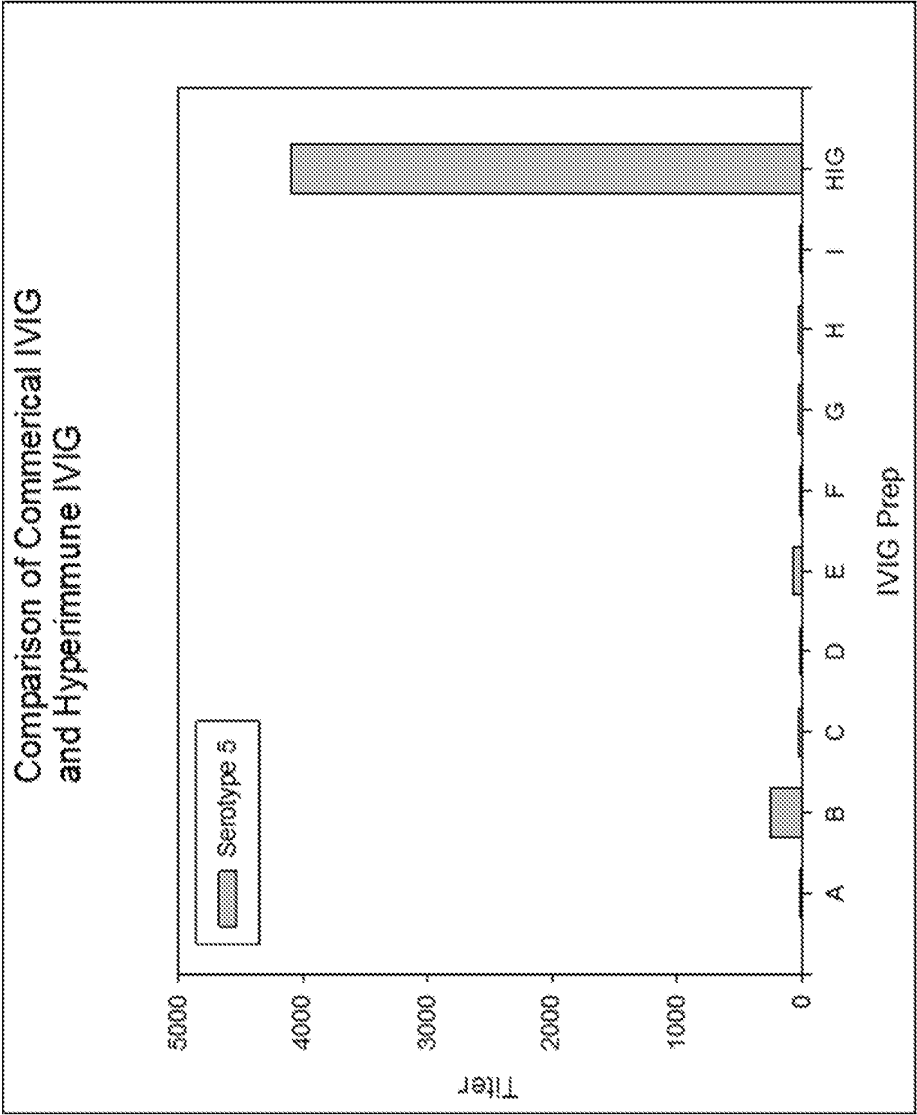


FIG. 9E

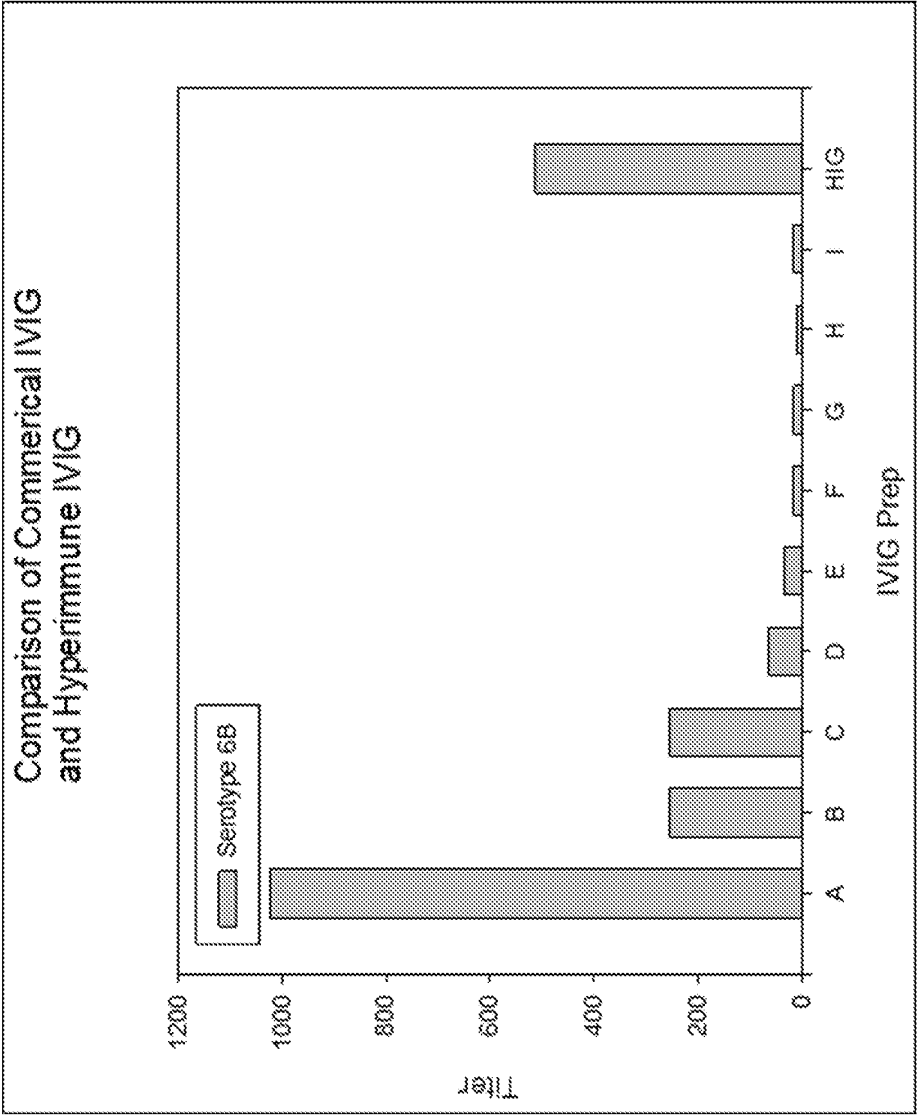


FIG. 9F

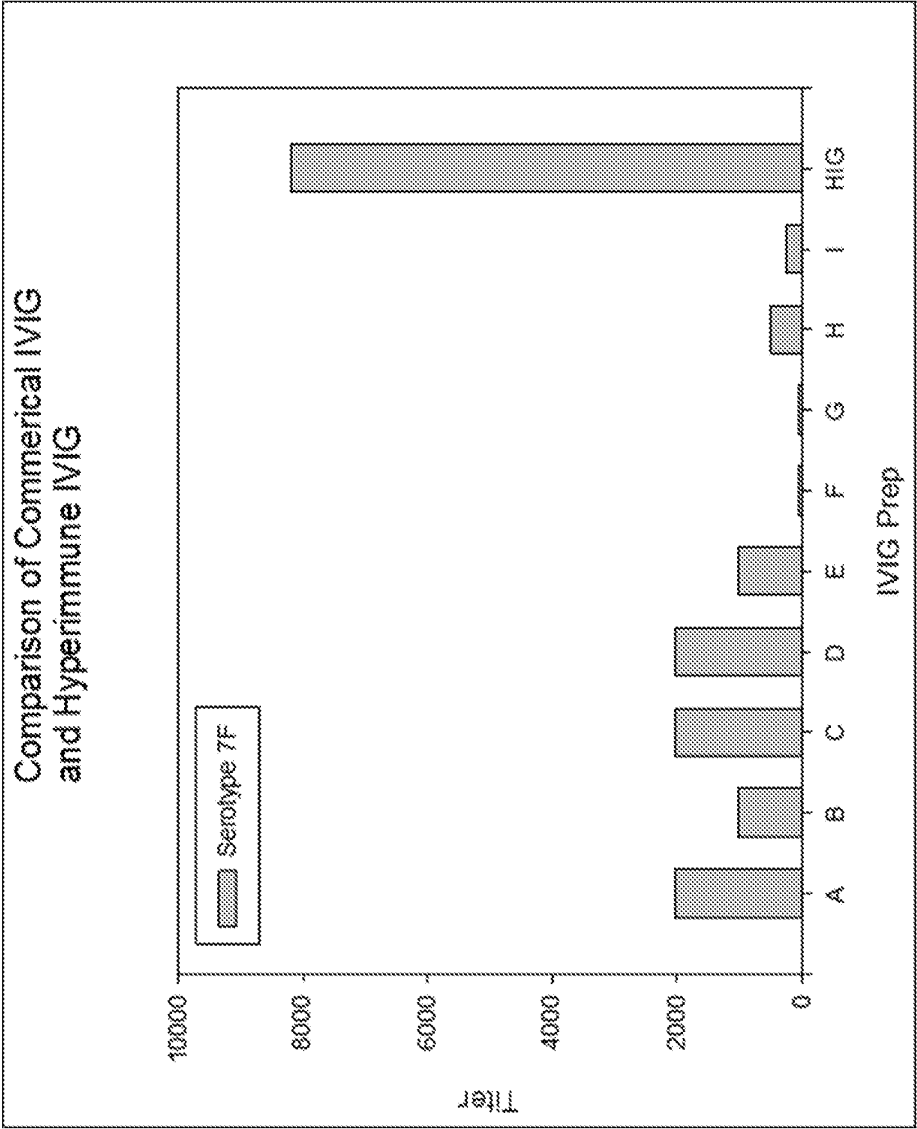


FIG. 9G

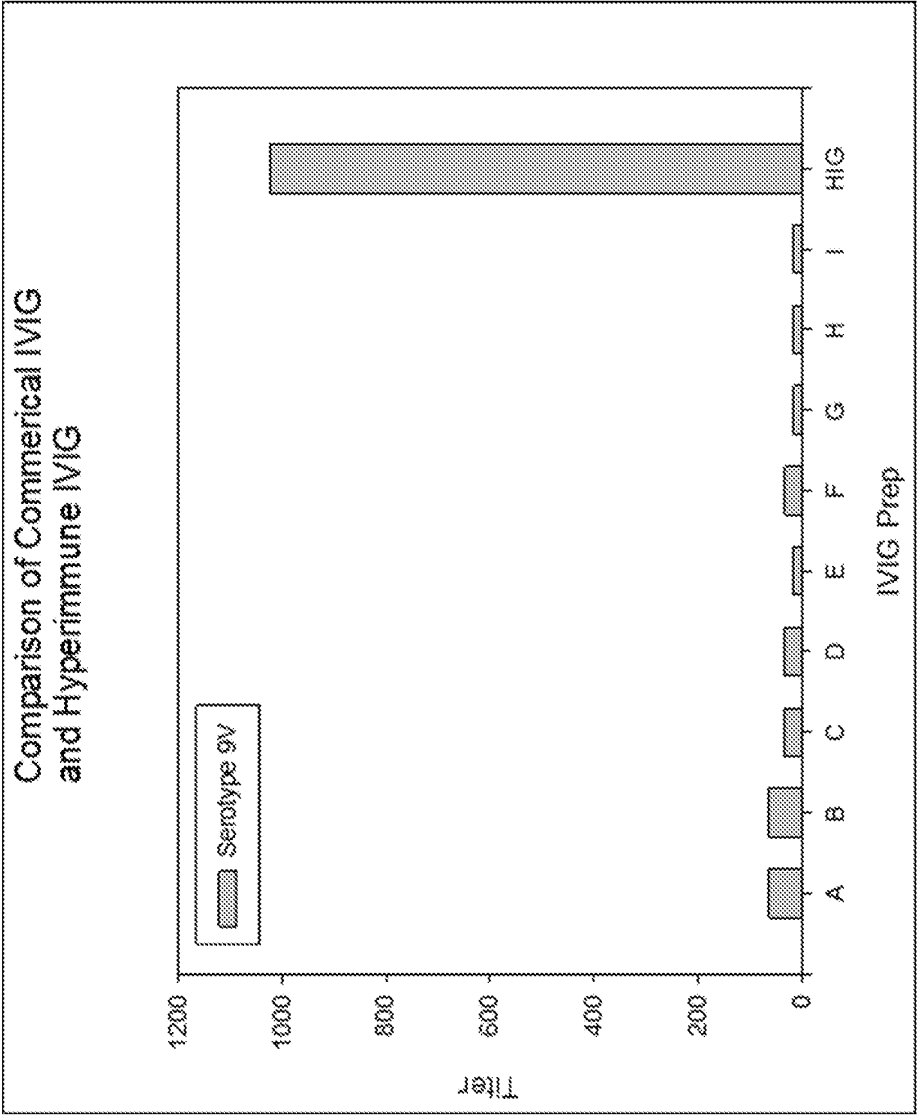


FIG. 9H

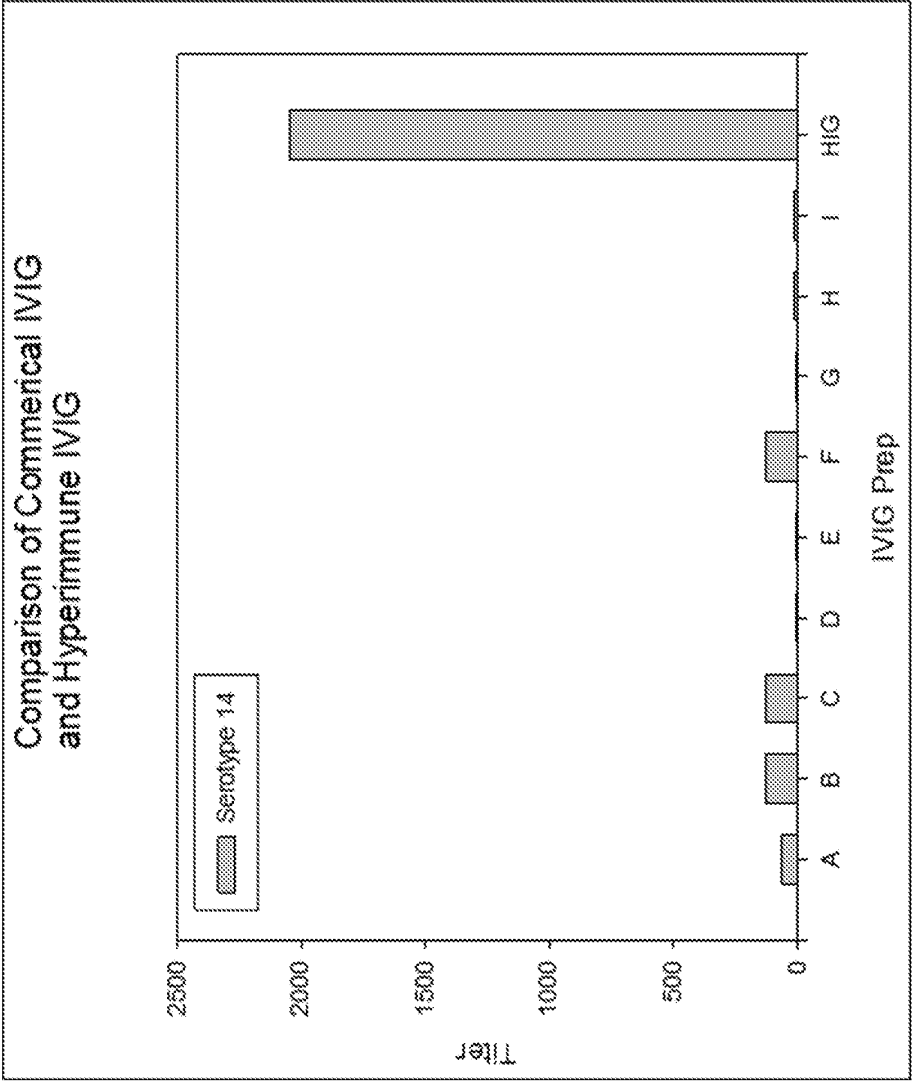


FIG. 9I

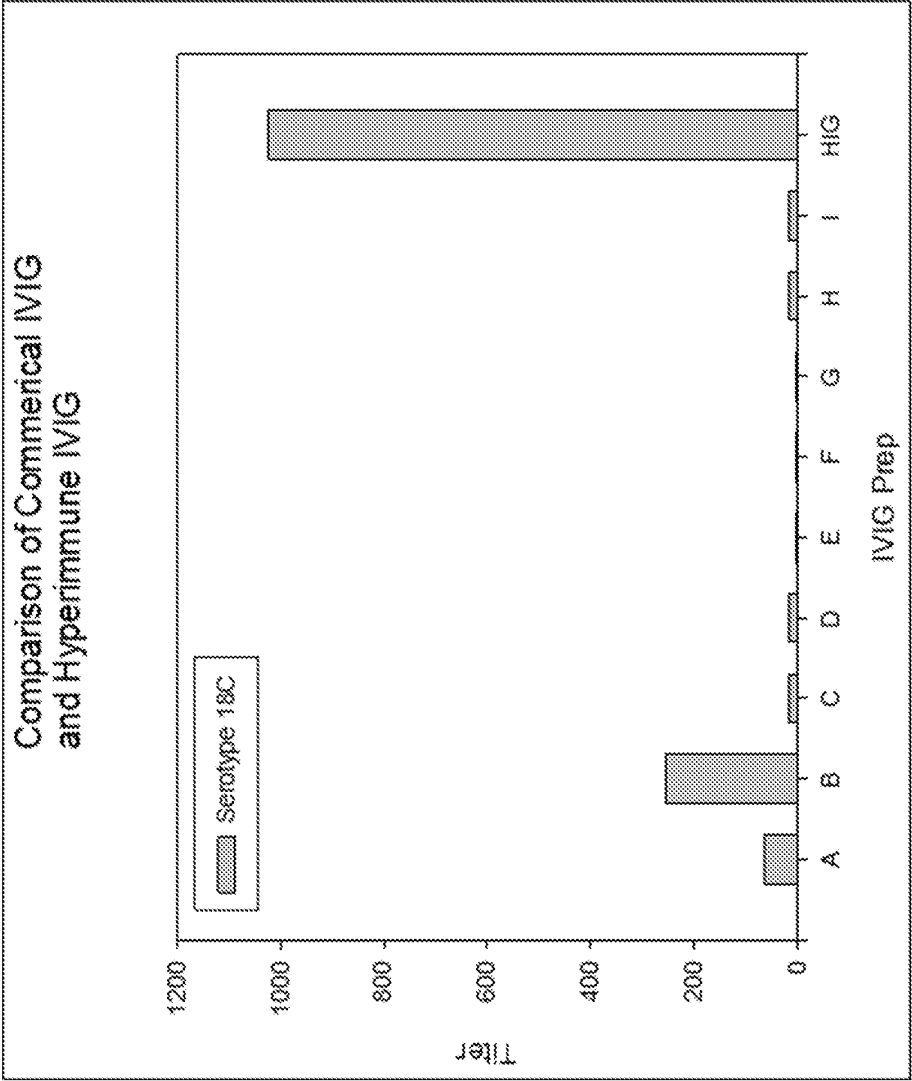


FIG. 9J

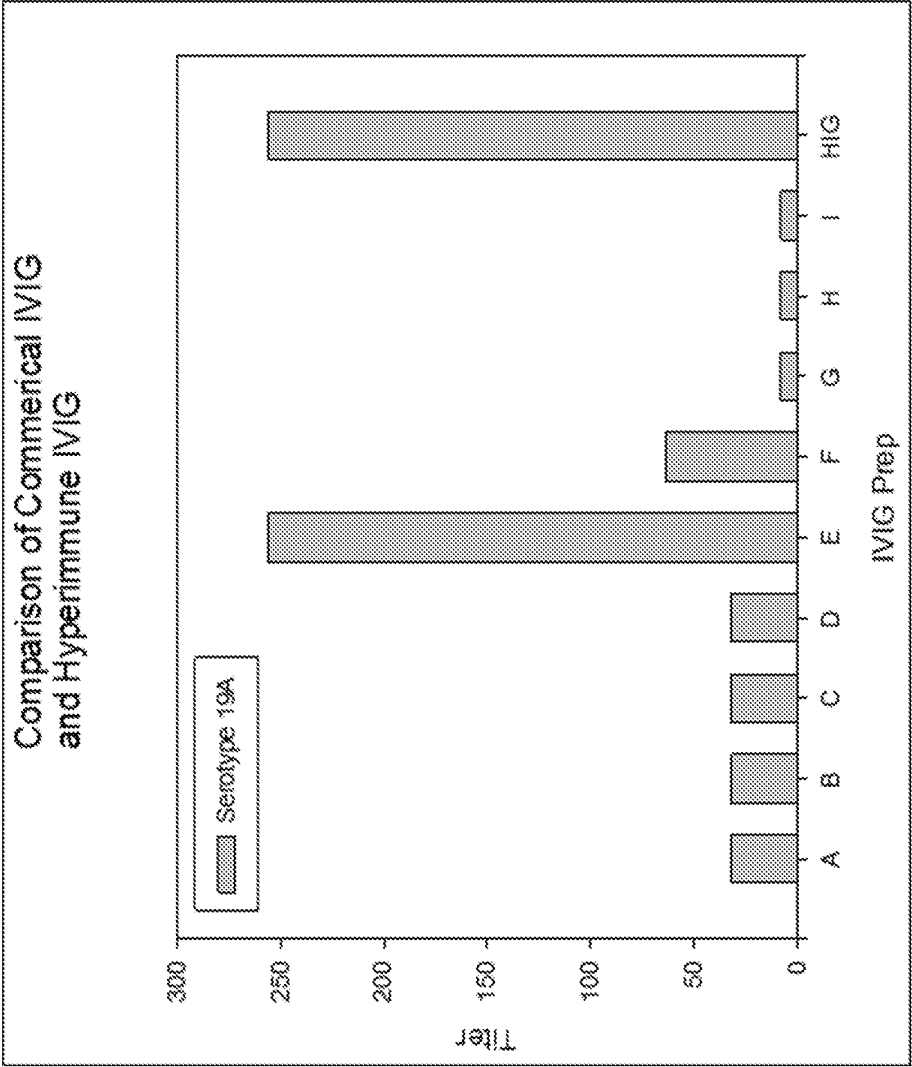


FIG. 9K

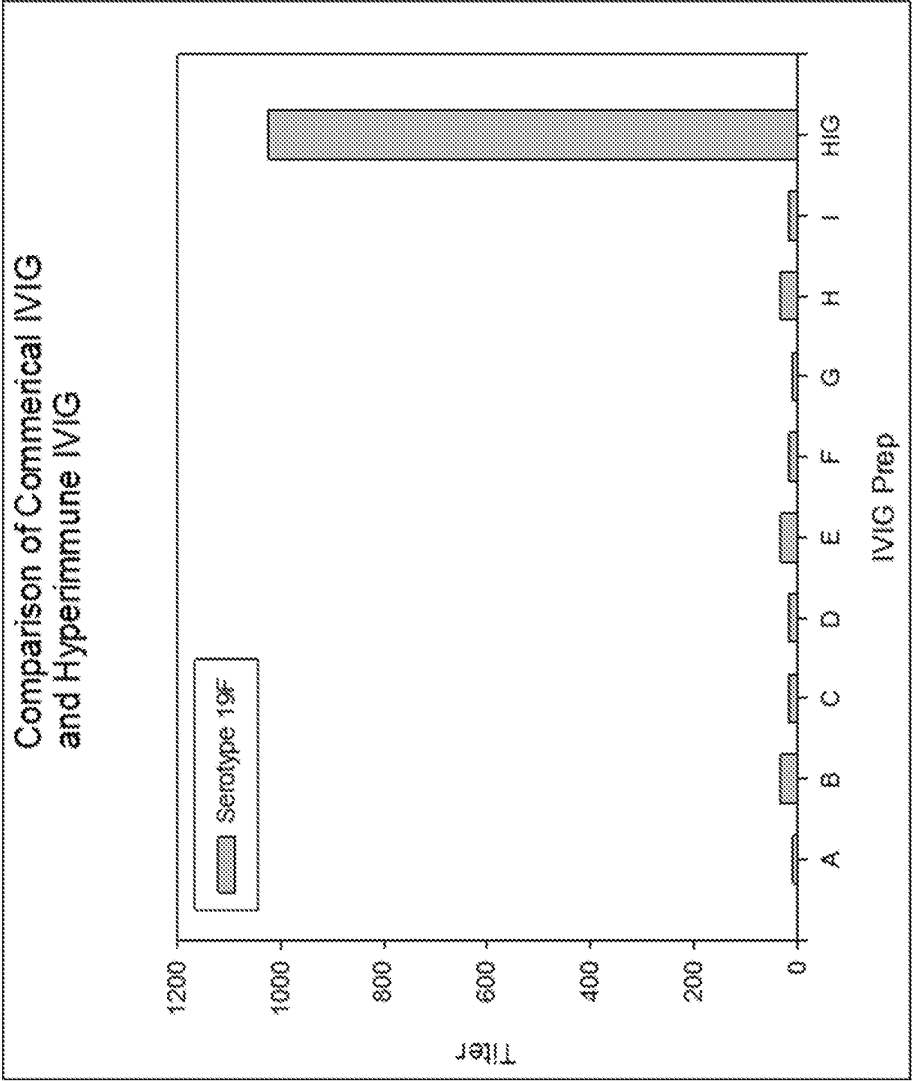


FIG. 9L

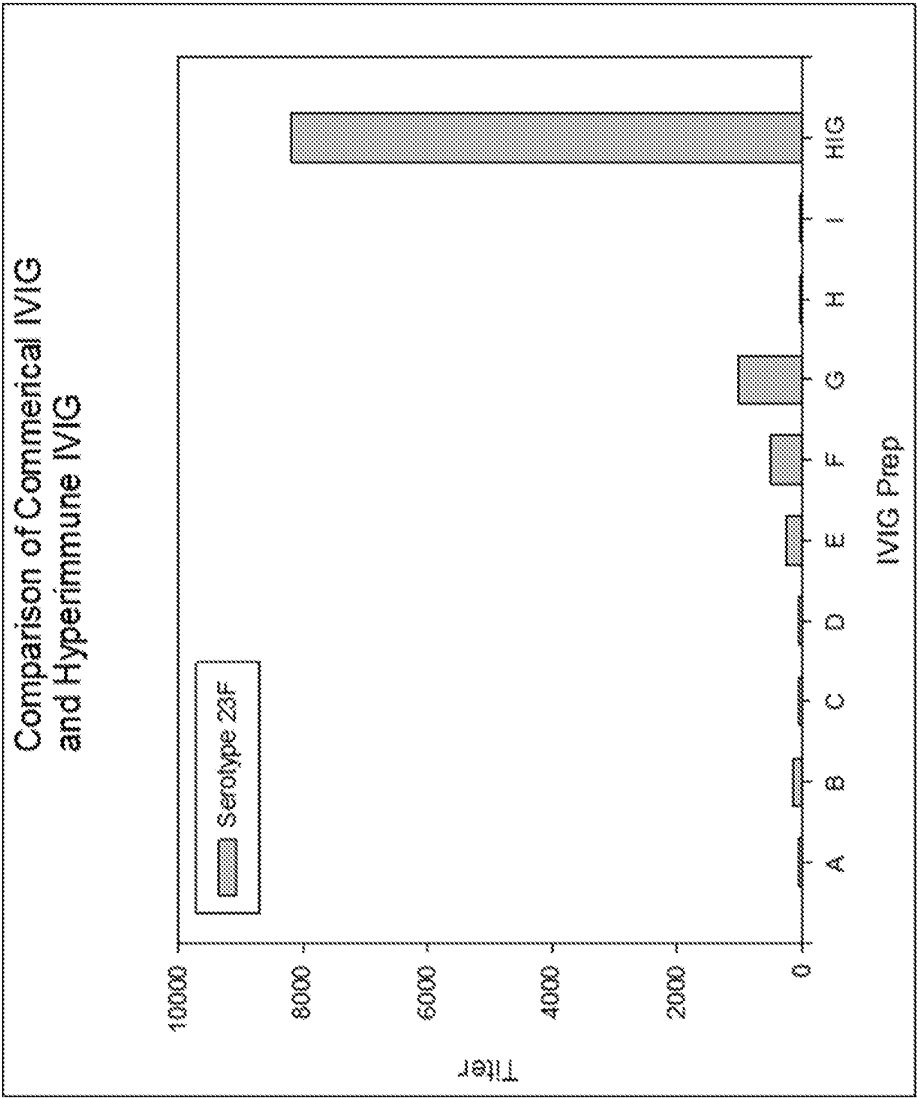


FIG. 10

Percentage of subjects with primary immune deficiency disease that fall below protective levels (1.2 µg/ml) of anti-*S pneumonia* binding antibodies at trough after infusion of conventional IVIG

Serotype 1	47.5
Serotype 3	49.2
Serotype 4	94.9
Serotype 5	none
Serotype 6B	52.5
Serotype 7F	31.0
Serotype 9V	39.0
Serotype 14	none
Serotype 18C	none
Serotype 19A	none
Serotype 19F	none
Serotype 23F	61.0