ATGAATCCAAATCAAAAGATAATAGCACTTGGCTCTGTTTCTATAACTATTGCGACAATATG
TTTACTCATGCAGATTGCCATCTTAGCAACGACTATGACACTACATTTCAATGAATGTACCA
ACCCATCGAACAATCAAGCAGTGCCATGTGAACCAATCATAATAGAAAGGAACATAACAGAG
ATAGTGCATTTGAATAATACTACCATAGAGAAGGAAAGTTGTCCTAAAGTAGCAGAATACAA
GAATTGGTCAAAACCGCAATGTCAAATTACAGGGTTCGCCCCTTTCTCCAAGGACAACTCAA
TTAGGCTTTCTGCAGGCGGGGATATTTGGGTGACAAGAGAACCTTATGTATCGTGCGGTCTT
GGTAAATGTTACCAATTTGCACTTGGGCAGGGAACCACTTTGAACAACAAACACTCAAATGG
CACAATACATGATAGGAGTCCCCATAGAACCCTTTTAATGAACGAGTTGGGTGTTCCATTTC
ATTTGGGAACCAAACAAGTGTGCATAGCATGGTCCAGCTCAAGCTGCCATGATGGGAAGGCA
TGGTTACATGTTTGTGTCACTGGGGATGATAGAAATGCGACTGCTAGCATCATTTATGATGG
GATGCTTACCGACAGTATTGGTTCATGGTCTAAGAACATCCTCAGAACTCAGGAGTCAGAAT
GCGTTTGCATCAATGGAACTTGTACAGTAGTAATGACTGATGGAAGTGCATCAGGAAGGGCT
GATACTAAAATACTATTCATTAGAGAAGGGAAAATTGTCCACATTGGTCCACTGTCAGGAAG
TGCTCAGCATGTGGAGGAATGCTCCTGTTACCCCCGGTATCCAGAAGTTAGATGTGTTTGCA
GAGACAATTGGAAGGGCTCCAATAGACCCGTGCTATATATAAATGTGGCAGATTATAGTGTT
GATTCTAGTTATGTGTGCTCAGGACTTGTTGGCGACACACCAAGAAATGACGATAGCTCCAG
CAGCAGTAACTGCAGGGATCCTAATAACGAGAGAGGGGGCCCAGGAGTGAAAGGGTGGGCCT
TTGACAATGGAAATGATGTTTGGATGGGACGAACAATCAAGAAAGATTCGCGCTCTGGTTAT
GAGACTTTCAGGGTCGTTGGTGGTTGGACTACGGCTAATTCCAAGTCACAAATAAATAGGCA
AGTCATAGTTGACAGTGATAACTGGTCTGGGTATTCTGGTATATTCTCTGTTGAAGGAAAAA
CCTGCATCAACAGGTGTTTTTATGTGGAGTTGATAAGAGGGAGACCACAGGAGACCAGAGTA
TGGTGGACTTCAAATAGCATCATTGTATTTTGTGGAACTTCAGGTACCTATGGAACAGGCTC
ATGGCCCGATGGAGCGAATATCAATTTCATGTCTATA**TAA**

FIGURE 1

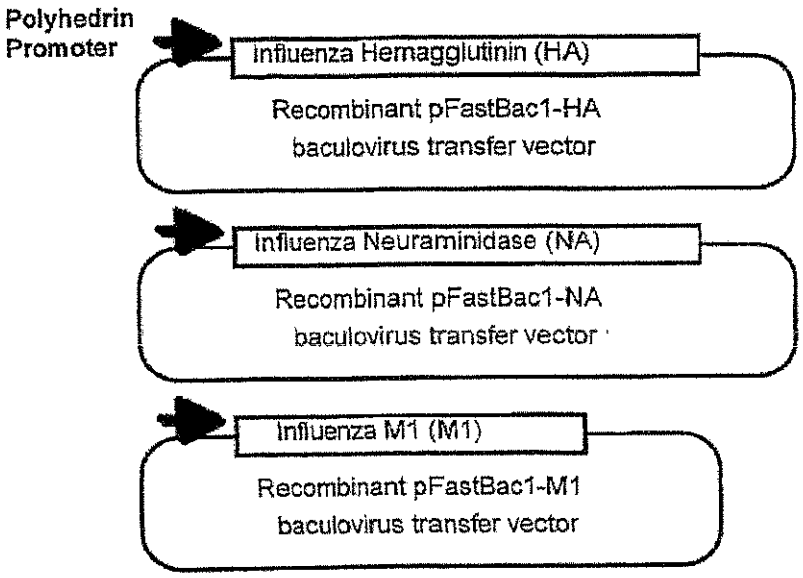
ATGGAAACAATATCACTAATAACTATACTACTAGTAGTAACAGCAAGCAATGCAGATAAAAT
CTGCATCGGCCACCAGTCAACAAACTCCACAGAAACTGTGGACACGCTAACAGAAACCAATG
TTCCTGTGACACATGCCAAAGAATTGCTCCACACAGAGCATAATGGAATGCTGTGTGCAACA
AGCCTGGGACATCCCCTCATTCTAGACACATGCACTATTGAAGGACTAGTCTATGGCAACCC
TTCTTGTGACCTGCTGTTGGGAGGAAGAGAATGGTCCTACATCGTCGAAAGATCATCAGCTG
TAAATGGAACGTGTTACCCTGGGAATGTAGAAAACCTAGAGGAACTCAGGACACTTTTTAGT
TCCGCTAGTTCCTACCAAAGAATCCAAATCTTCCCAGACACAACCTGGAATGTGACTTACAC
TGGAACAAGCAGAGCATGTTCAGGTTCATTCTACAGGAGTATGAGATGGCTGACTCAAAAGA
GCGGTTTTTACCCTGTTCAAGACGCCCAATACACAAATAACAGGGGAAAGAGCATTCTTTTC
GTGTGGGGCATACATCACCCACCCACCTATACCGAGCAAACAAATTTGTACATAAGAAACGA
CACAACAACAAGCGTGACAACAGAAGATTTGAATAGGACCTTCAAACCAGTGATAGGGCCAA
GGCCCCTTGTCAATGGTCTGCAGGGAAGAATTGATTATTATTGGTCGGTACTAAAACCAGGC
CAAACATTGCGAGTACGATCCAATGGGAATCTAATTGCTCCATGGTATGGACACGTTCTTTC
AGGAGGGAGCCATGGAAGAATCCTGAAGACTGATTTAAAAGGTGGTAATTGTGTAGTGCAAT
GTCAGACTGAAAAAGGTGGCTTAAACAGTACATTGCCATTCCACAATATCAGTAAATATGCA
TTTGGAACCTGCCCCAAATATGTAAGAGTTAATAGTCTCAAACTGGCAGTCGGTCTGAGGAA
CGTGCCTGCTAGATCAAGTAGAGGACTATTTGGAGCCATAGCTGGATTCATAGAAGGAGGTT
GGCCAGGACTAGTCGCTGGCTGGTATGGTTTCCAGCATTCAAATGATCAAGGGGTTGGTATG
GCTGCAGATAGGGATTCAACTCAAAAGGCAATTGATAAAATAACATCCAAGGTGAATAATAT
AGTCGACAAGATGAACAAGCAATATGAAATAATTGATCATGAATTCAGTGAGGTTGAAACTA
GACTCAATATGATCAATAATAAGATTGATGACCAAATACAAGACGTATGGGCATATAATGCA
GAATTGCTAGTACTACTTGAAAATCAAAAAACACTCGATGAGCATGATGCGAACGTGAACAA
TCTATATAACAAGGTGAAGAGGGCACTGGGCTCCAATGCTATGGAAGATGGGAAAGGCTGTT
TCGAGCTATACCATAAATGTGATGATCAGTGCATGGAAACAATTCGGAACGGGACCTATAAT
AGGAGAAAGTATAGAGAGGAATCAAGACTAGAAAGGCAGAAAATAGAGGGGGTTAAGCTGGA
ATCTGAGGGAACTTACAAAATCCTCACCATTTATTCGACTGTCGCCTCATCTCTTGTGCTTG
CAATGGGGTTTGCTGCCTTCCTGTTCTGGGCCATGTCCAATGGATCTTGCAGATGCAACATT
TGTATA**TAA**

FIGURE 2

ATGAGTCTTCTAACCGAGGTCGAAACGTACGTTCTCTCTATCATCCCATCAGGCCCCCTCAA
AGCCGAGATCGCGCAGAGACTTGAGGATGTTTTTGCAGGGAAGAACACAGATCTTGAGGCTC
TCATGGAATGGCTAAAGACAAGACCAATCCTGTCACCTCTGACTAAGGGGATTTTAGGGTTT
GTGTTCACGCTCACCGTGCCCAGTGAGCGAGGACTGCAGCGTAGACGATTTGTCCAAAATGC
CCTAAATGGGAATGGAGACCCAAACAACATGGACAGGGCAGTTAAACTATACAAGAAGCTGA
AGAGGGAAATGACATTCCATGGAGCAAAGGAAGTTGCACTCAGTTACTCAACTGGTGCGCTT
GCCAGTTGCATGGGTCTCATATACAACCGGATGGGAACAGTGACCACAGAAGTGGCTCTTGG
CCTAGTATGTGCCACTTGTGAACAGATTGCTGATGCCCAACATCGGTCCCACAGGCAGATGG
CGACTACCACCAACCCACTAATCAGGCATGAGAACAGAATGGTACTAGCCAGCACTACGGCT
AAGGCCATGGAGCAGATGGCTGGATCAAGTGAGCAGGCAGCAGAAGCCATGGAAGTCGCAAG
TCAGGCTAGGCAAATGGTGCAGGCTATGAGGACAATTGGGACTCACCCTAGTTCCAGTGCAG
GTCTAAAAGATGATCTTATTGAAAATTTGCAGGCTTACCAGAAACGGATGGGAGTGCAAATG
CAGAGATTCAAG**TGA**

FIGURE 3

(A)


Polyhedrin
Promoter
Influenza Hemagglutinin (HA)
Recombinant pFastBac1-HA
baculovirus transfer vector
Influenza Neuraminidase (NA)
Recombinant pFastBac1-NA
baculovirus transfer vector
Influenza M1 (M1)
Recombinant pFastBac1-M1
baculovirus transfer vector

(B)

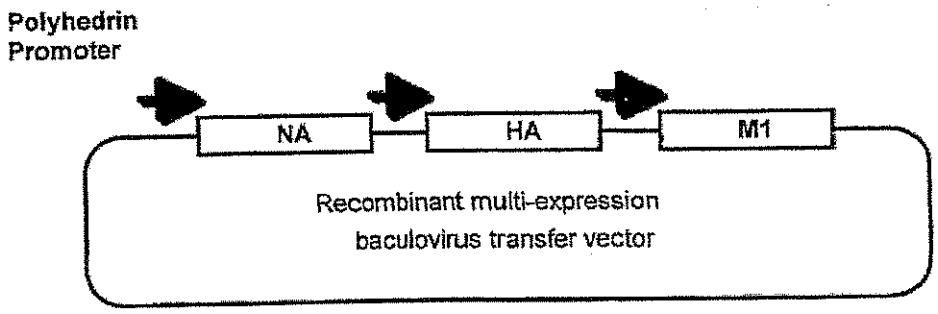

Polyhedrin
Promoter
NA
HA
M1
Recombinant multi-expression
baculovirus transfer vector

FIGURE 4

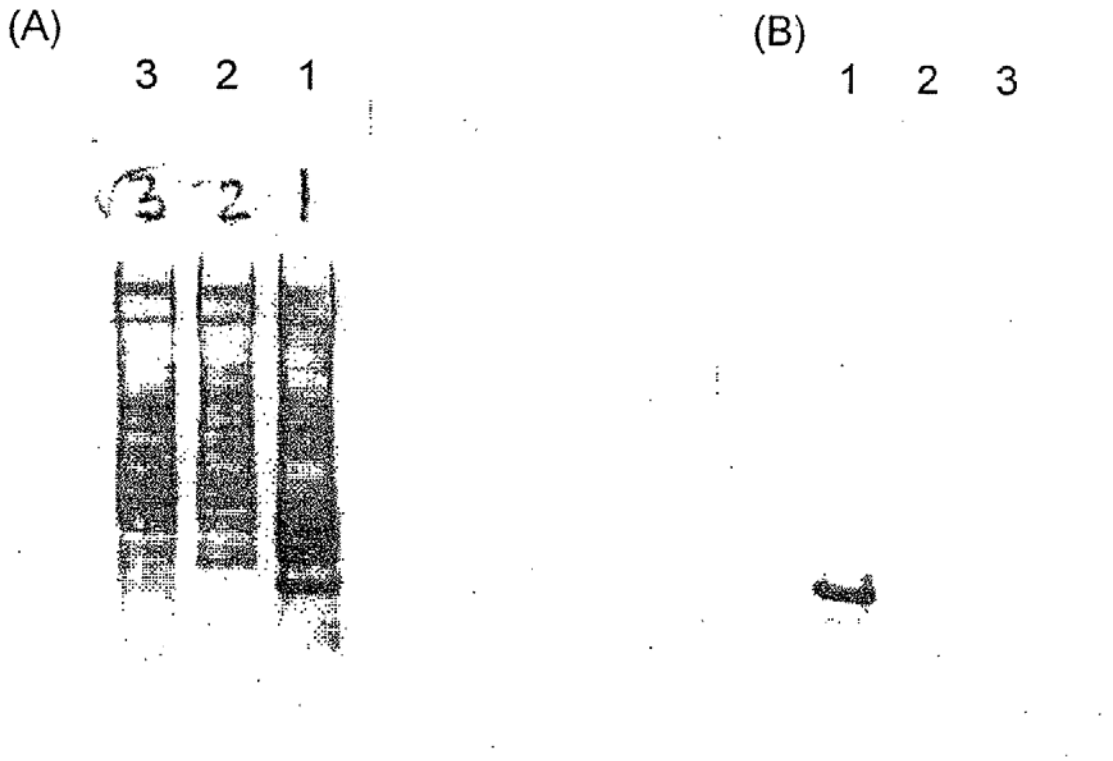


FIGURE 5

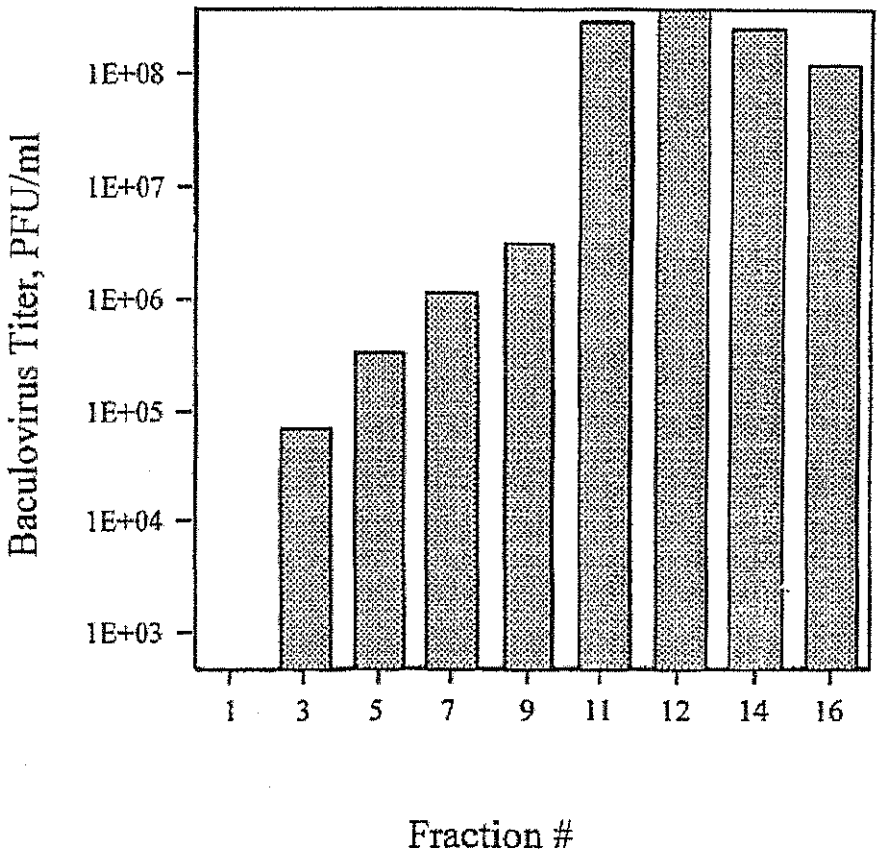

Baculovirus Titer, PFU/ml
1E+08
1E+07
1E+06
1E+05
1E+04
1E+03
1
3
5
7
9
11
12
14
16
Fraction #

FIGURE 6

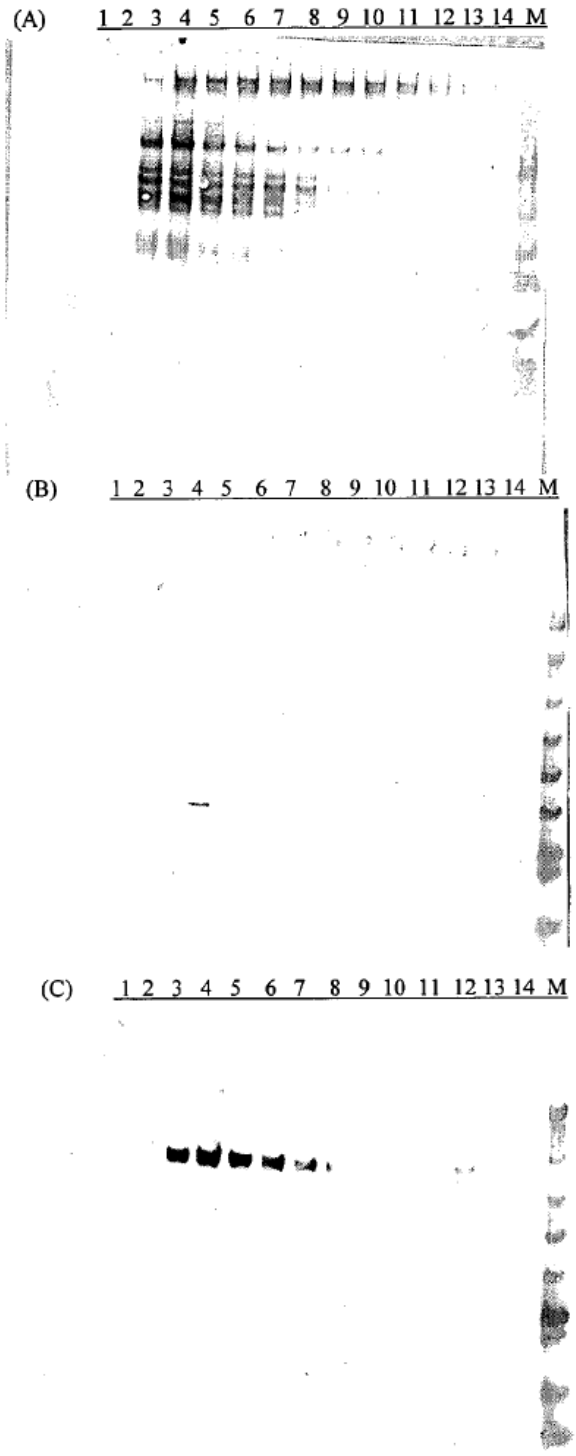

(A) 1 2 3 4 5 6 7 8 9 10 11 12 13 14 M
(B) 1 2 3 4 5 6 7 8 9 10 11 12 13 14 M
(C) 1 2 3 4 5 6 7 8 9 10 11 12 13 14 M

FIGURE 7

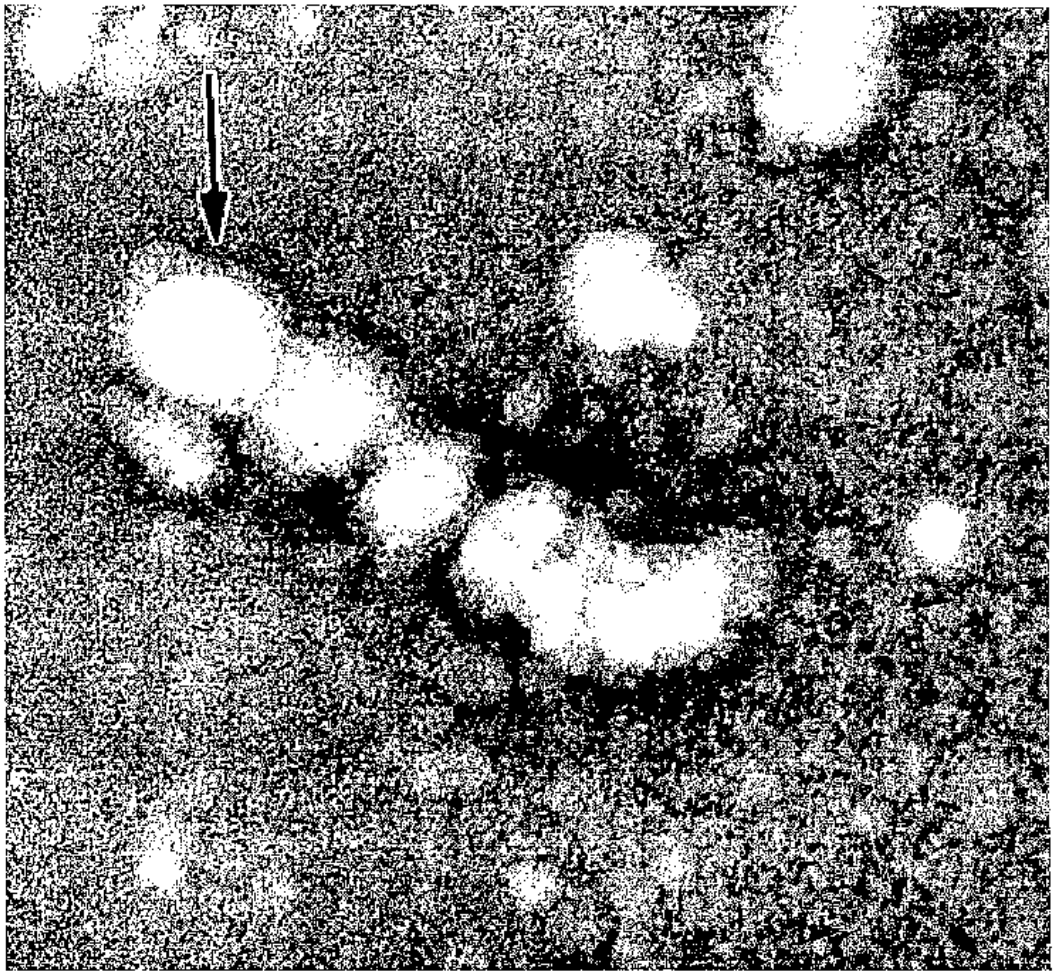


FIGURE 8

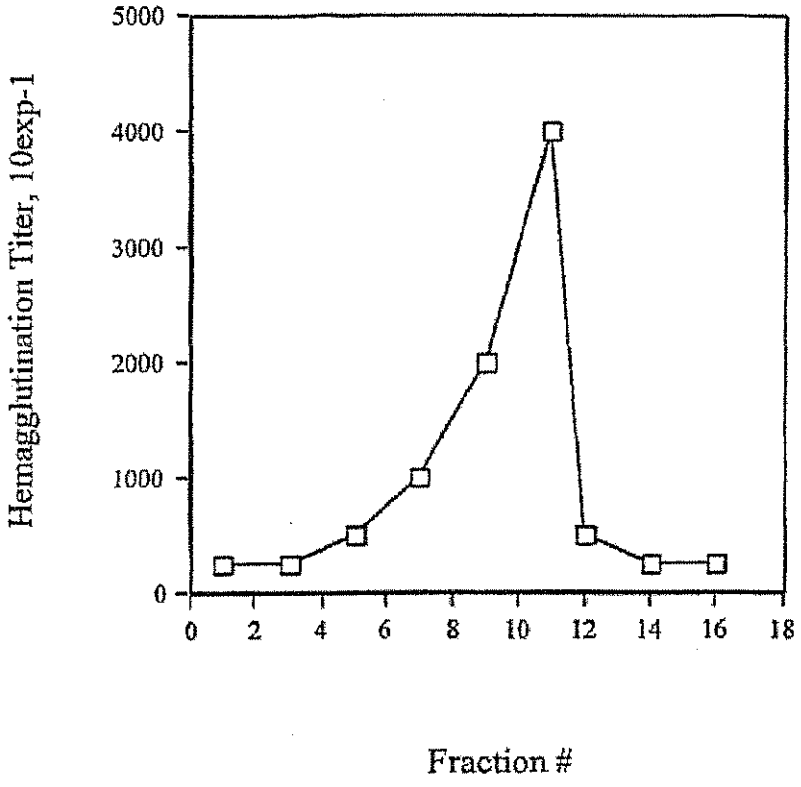

Hemagglutination Titer, 10exp-1
5000
4000
3000
2000
1000
0
0
2
4
6
8
10
12
14
16
18
Fraction #

FIGURE 9

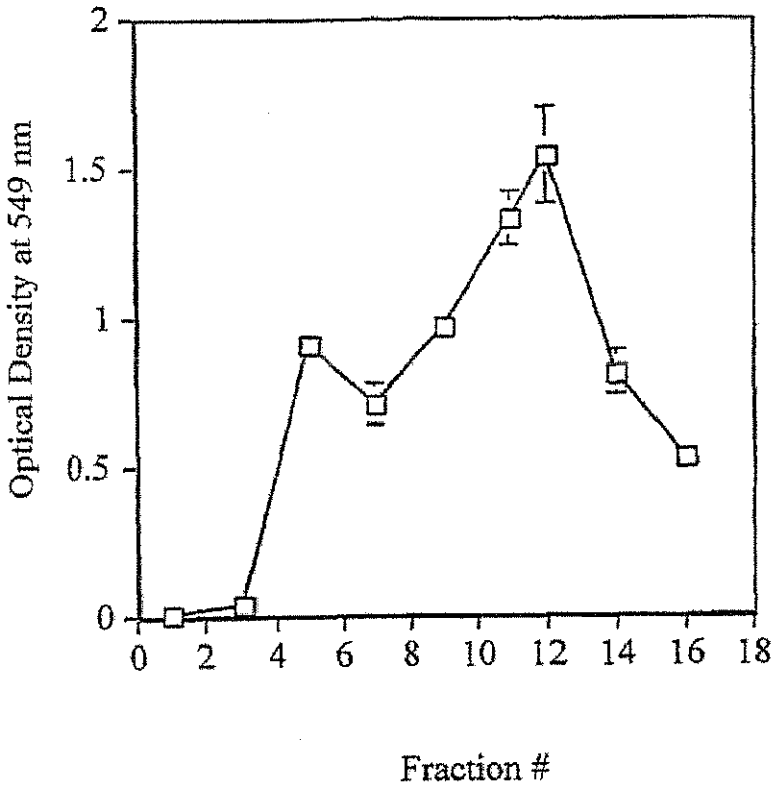

Optical Density at 549 nm
2
1.5
1
0.5
0
0
2
4
6
8
10
12
14
16
18
Fraction #

FIGURE 10

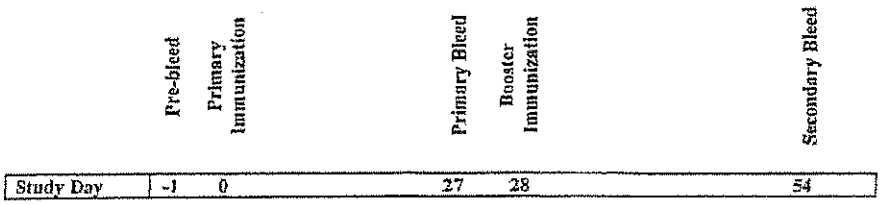

Pre-bleed
Primary Immunization
Primary Bleed
Booster Immunization
Secondary Bleed
Study Day
-1
0
27
28
54

FIGURE 11

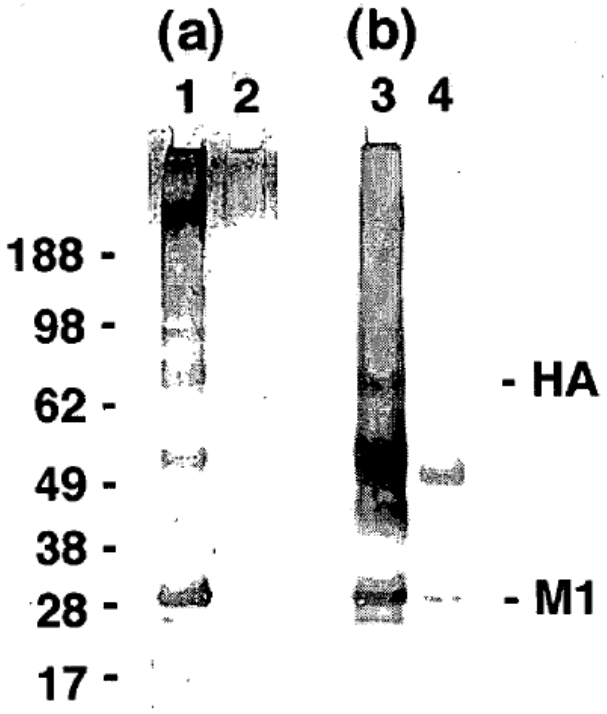


FIGURE 12

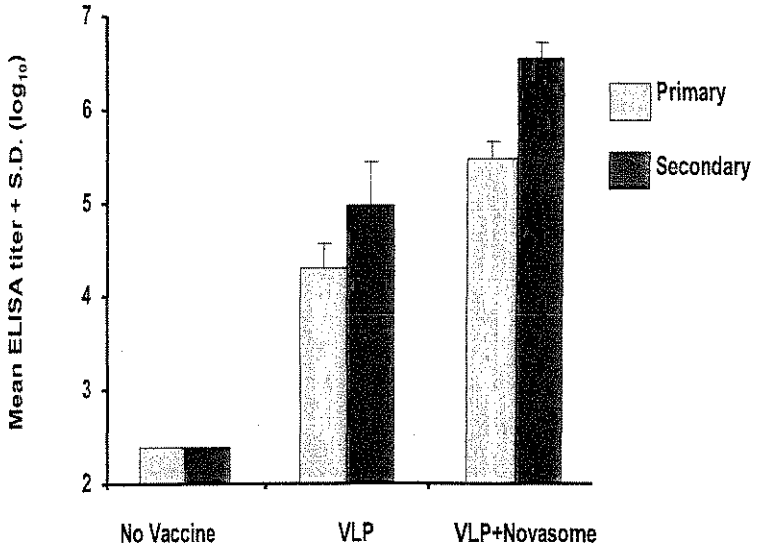

Mean ELISA titer + S.D. (log_{10})
7
6
5
4
3
2
Primary
Secondary
No Vaccine
VLP
VLP+Novasome

FIGURE 13

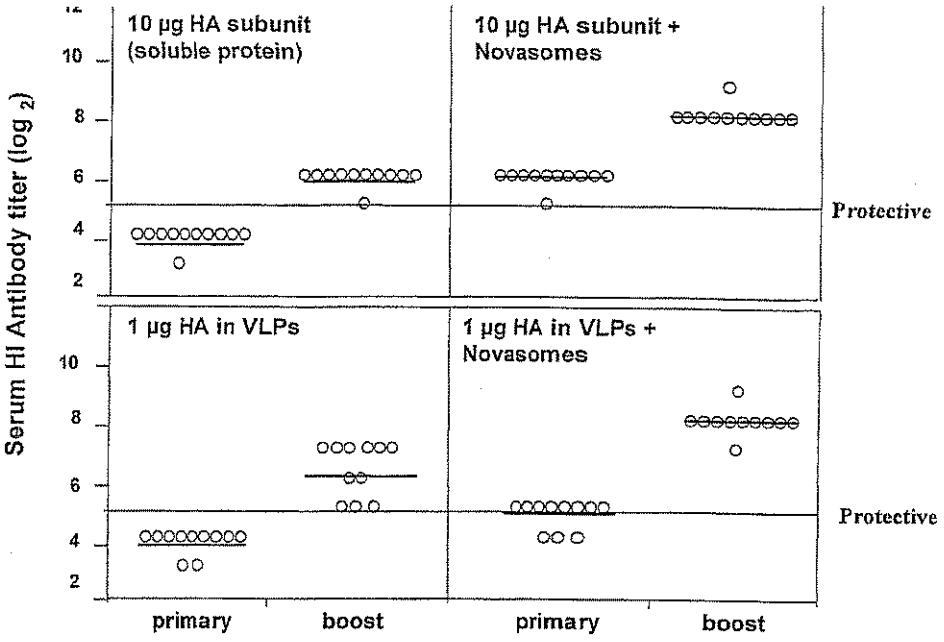

10 µg HA subunit
(soluble protein)
10 µg HA subunit +
Novasomes
1 µg HA in VLPs
1 µg HA in VLPs +
Novasomes
Serum HI Antibody titer (log 2)
10
8
6
4
2
Protective
Protective
primary
boost
primary
boost

FIGURE 14

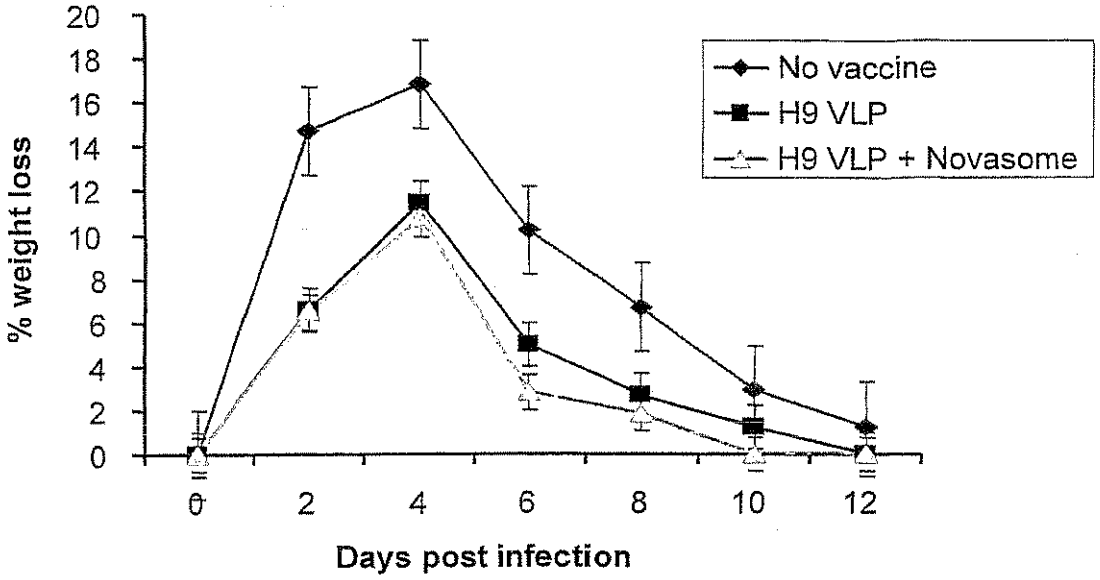

20
18
16
14
12
10
8
6
4
2
0
% weight loss
0
2
4
6
8
10
12
Days post infection
No vaccine
H9 VLP
H9 VLP + Novasome

FIGURE 15

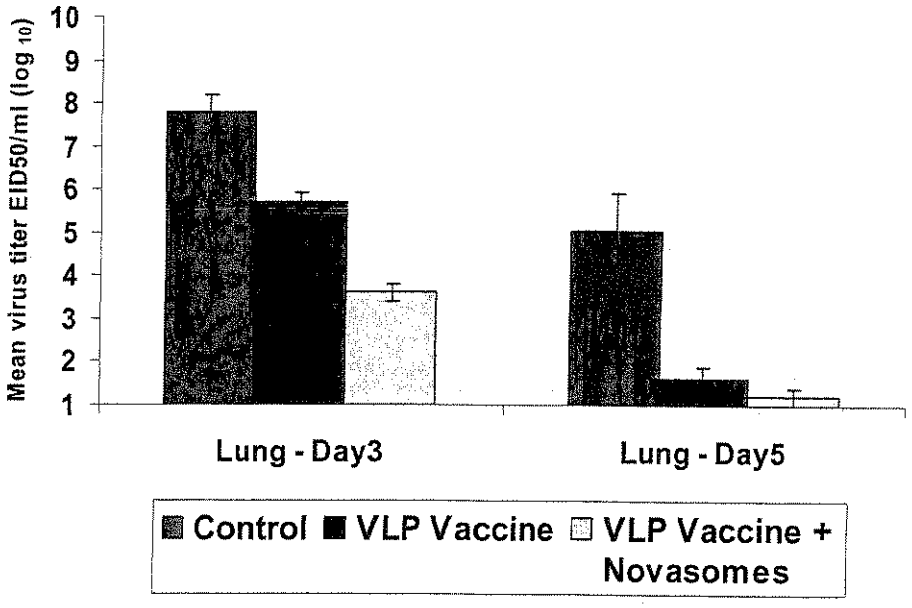

Mean virus titer EID50/ml (log 10)
10
9
8
7
6
5
4
3
2
1
Lung - Day3
Lung - Day5
Control
VLP Vaccine
VLP Vaccine + Novasomes

FIGURE 16

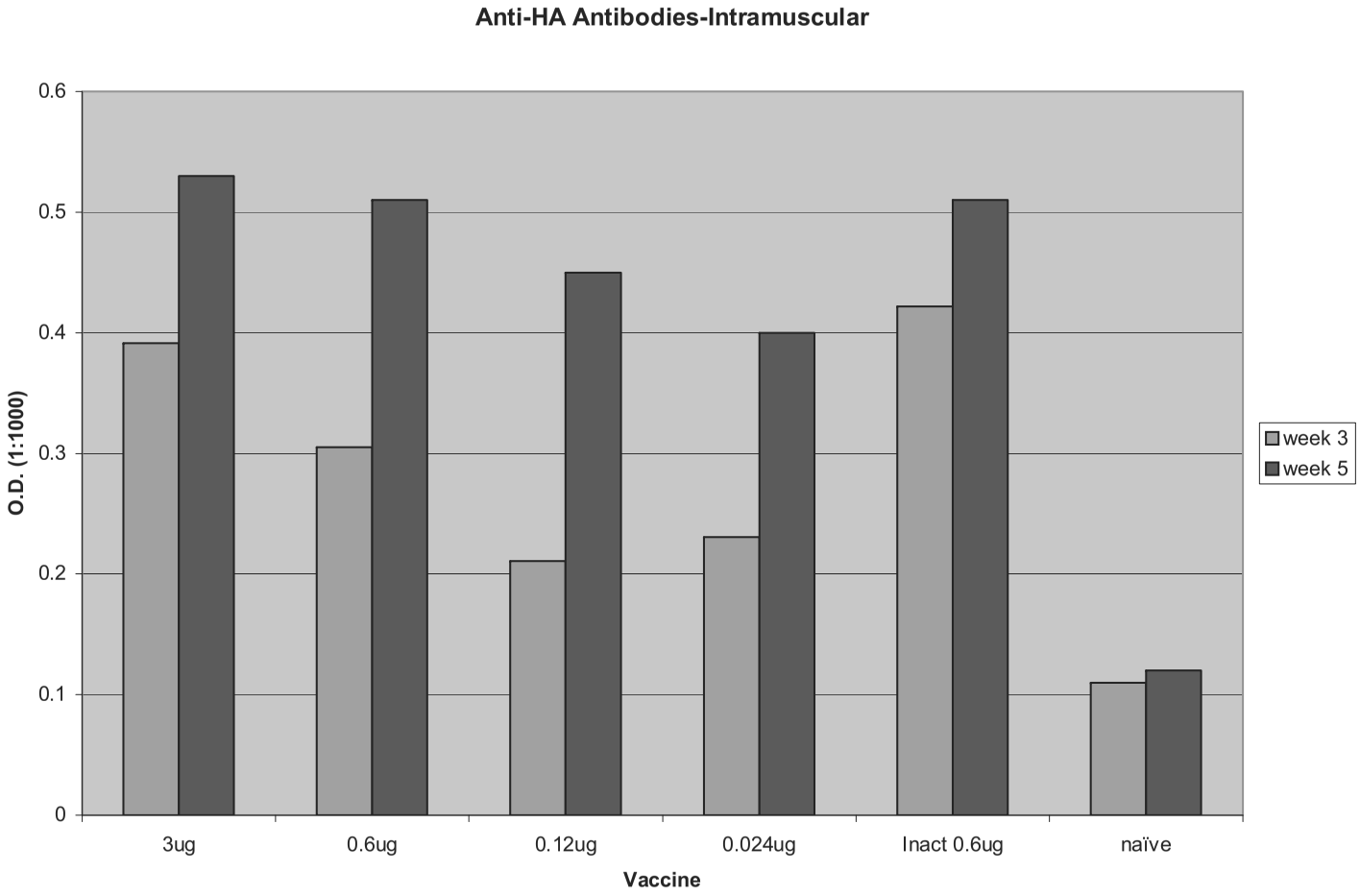

Anti-HA Antibodies-Intramuscular
O.D. (1:1000)
0.6
0.5
0.4
0.3
0.2
0.1
0
3ug
0.6ug
0.12ug
0.024ug
Inact 0.6ug
naïve
Vaccine
week 3
week 5

FIGURE 17 A

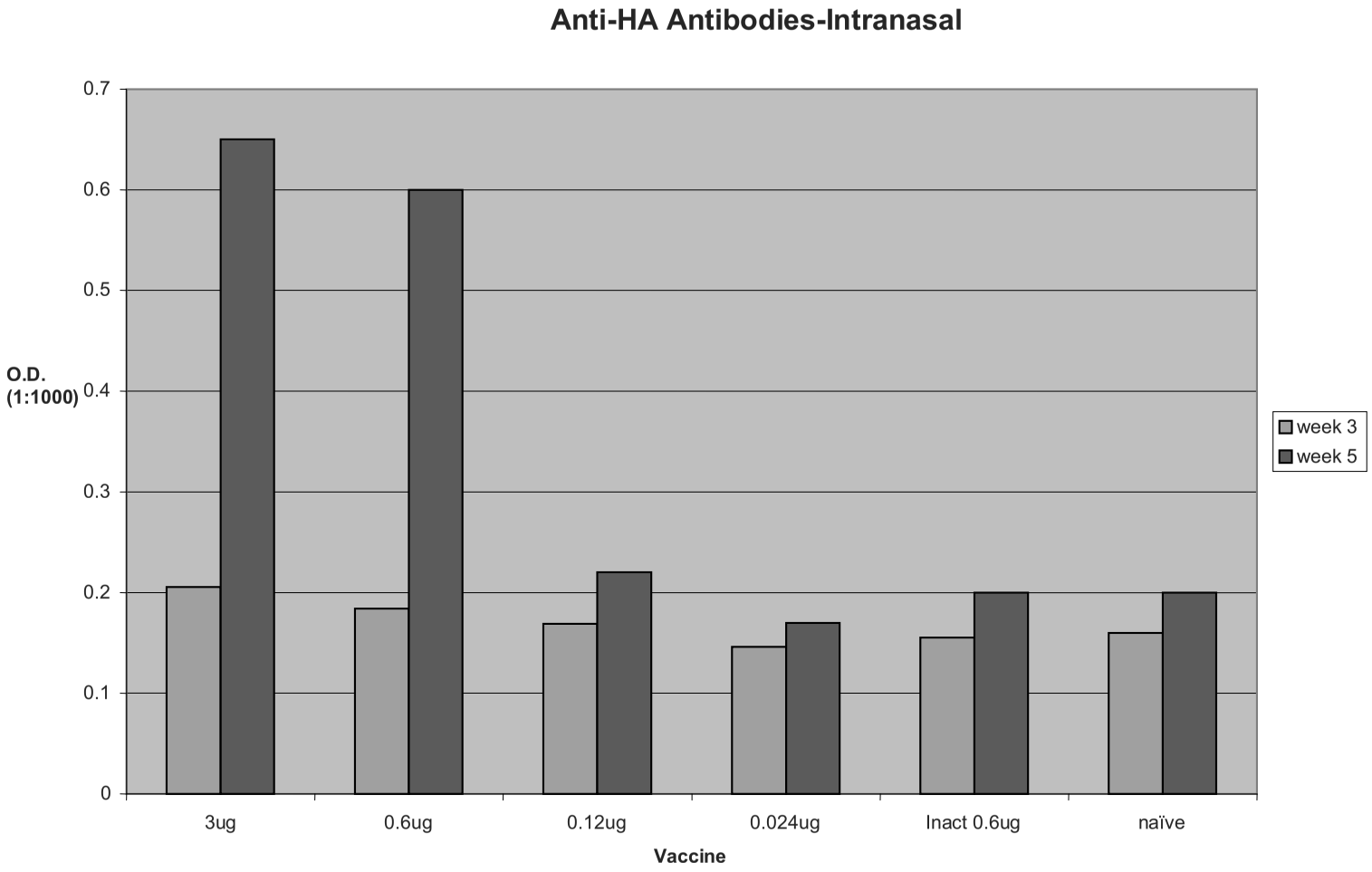

Anti-HA Antibodies-Intranasal
O.D. (1:1000)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
3ug
0.6ug
0.12ug
0.024ug
Inact 0.6ug
naïve
Vaccine
week 3
week 5

FIGURE 17 B

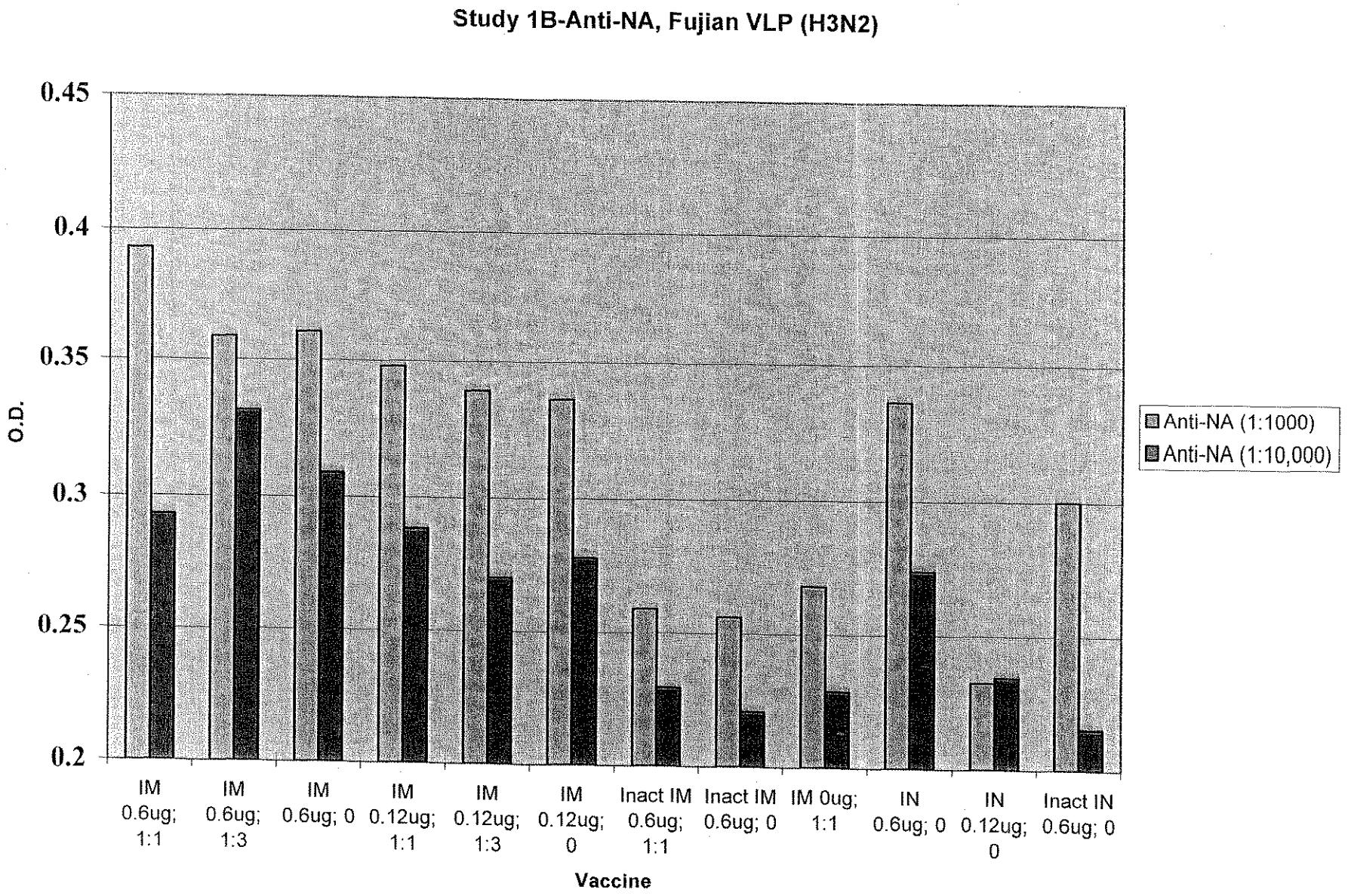

Study 1B-Anti-NA, Fujian VLP (H3N2)
0.45
0.4
0.35
0.3
0.25
0.2
O.D.
Anti-NA (1:1000)
Anti-NA (1:10,000)
IM 0.6ug; 1:1
IM 0.6ug; 1:3
IM 0.6ug; 0
IM 0.12ug; 1:1
IM 0.12ug; 1:3
IM 0.12ug; 0
Inact IM 0.6ug; 1:1
Inact IM 0.6ug; 0
IM 0ug; 1:1
IN 0.6ug; 0
IN 0.12ug; 0
Inact IN 0.6ug; 0
Vaccine

FIGURE 17 C

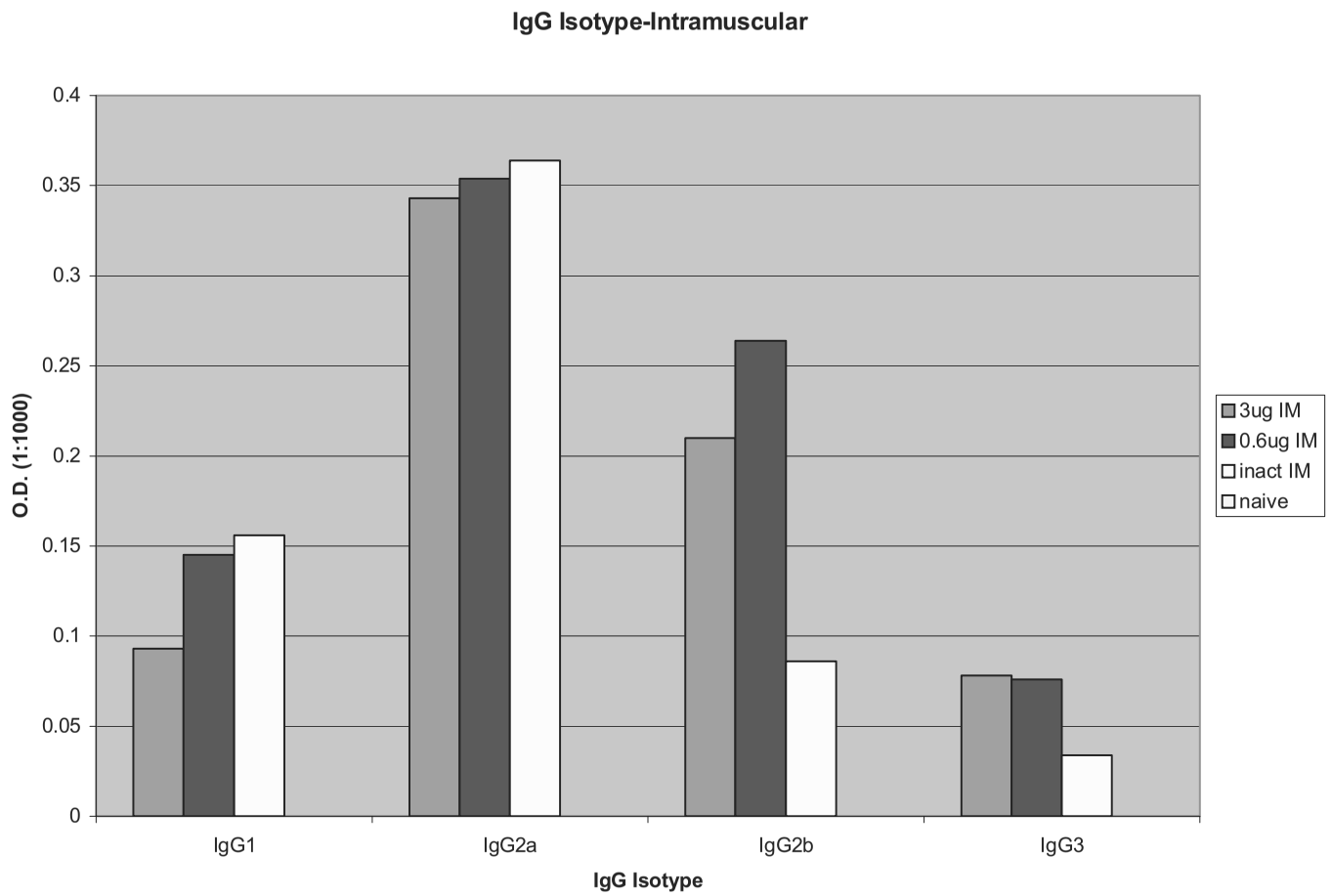

IgG Isotype-Intramuscular
O.D. (1:1000)
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
IgG1
IgG2a
IgG2b
IgG3
IgG Isotype
3ug IM
0.6ug IM
inact IM
naive

FIGURE 18 A

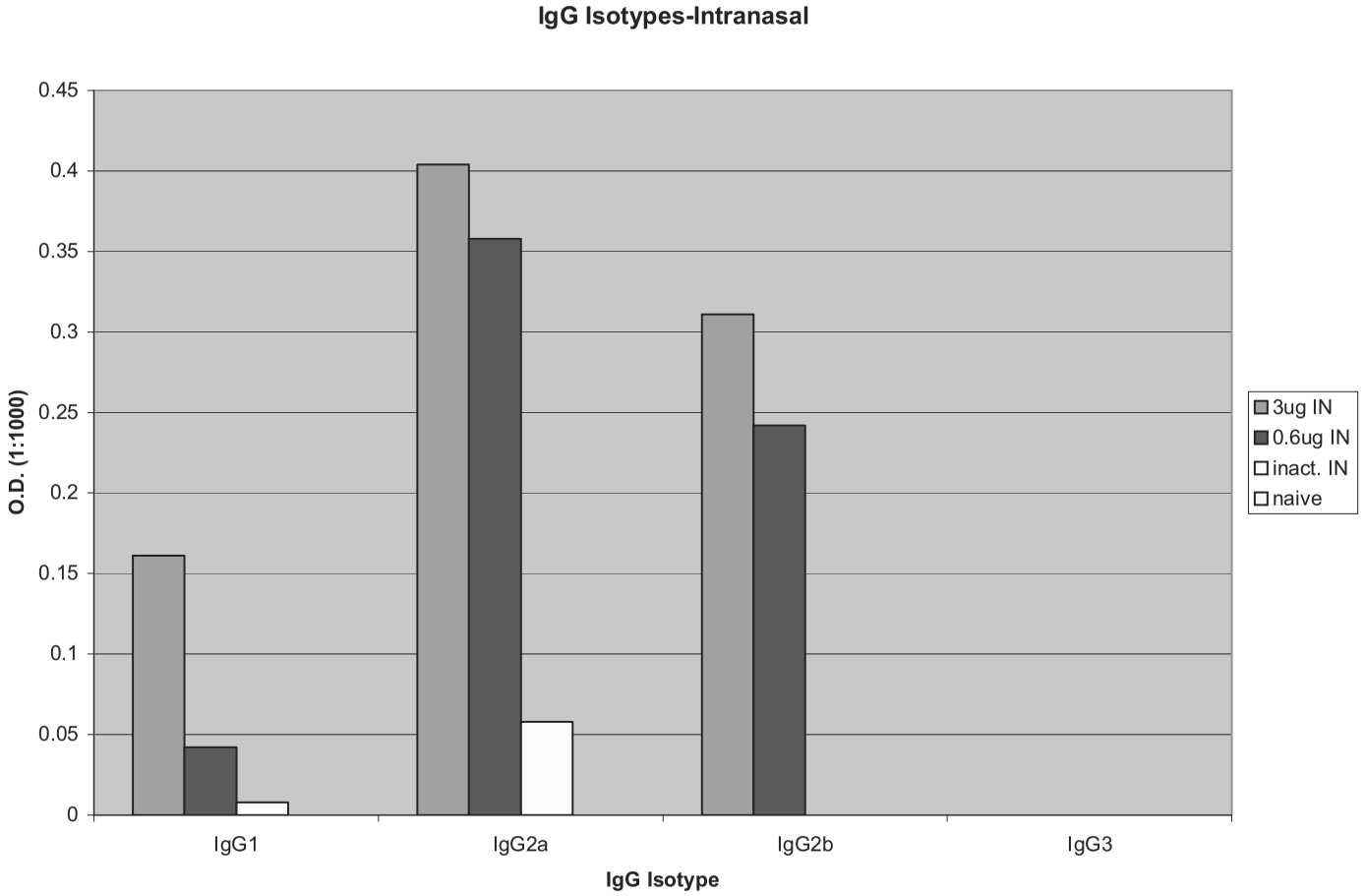

IgG Isotypes-Intranasal
O.D. (1:1000)
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
IgG1
IgG2a
IgG2b
IgG3
IgG Isotype
3ug IN
0.6ug IN
inact. IN
naive

FIGURE 18 B

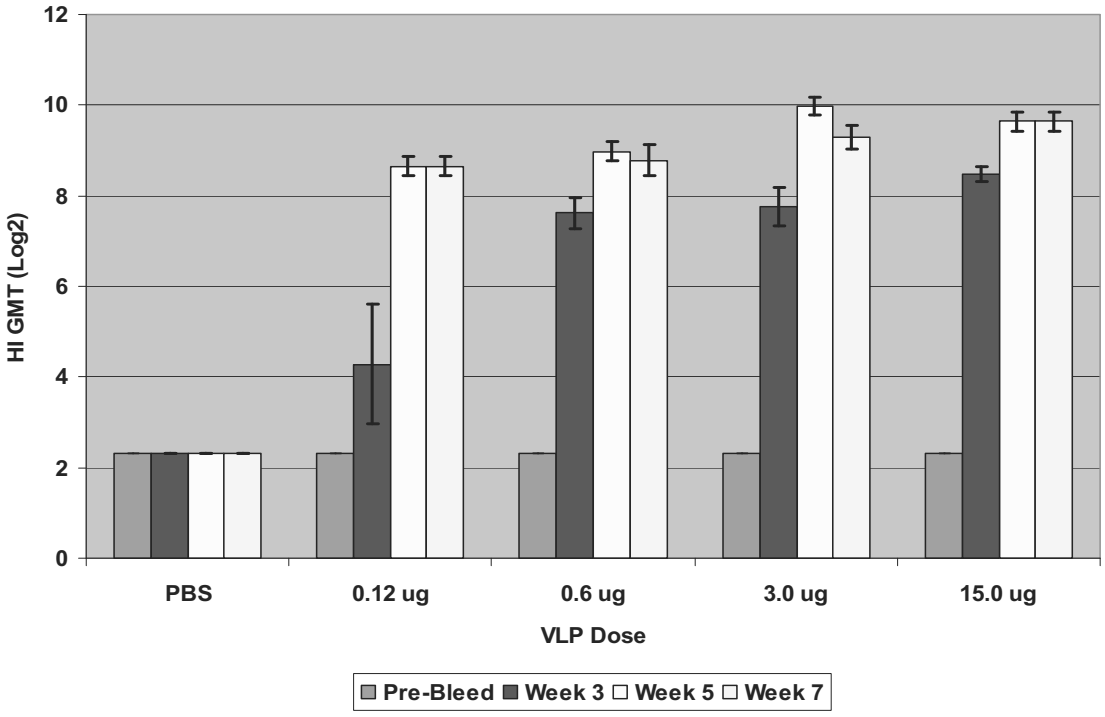

12
10
8
6
4
2
0
HI GMT (Log2)
PBS
0.12 ug
0.6 ug
3.0 ug
15.0 ug
VLP Dose
Pre-Bleed
Week 3
Week 5
Week 7

FIGURE 19

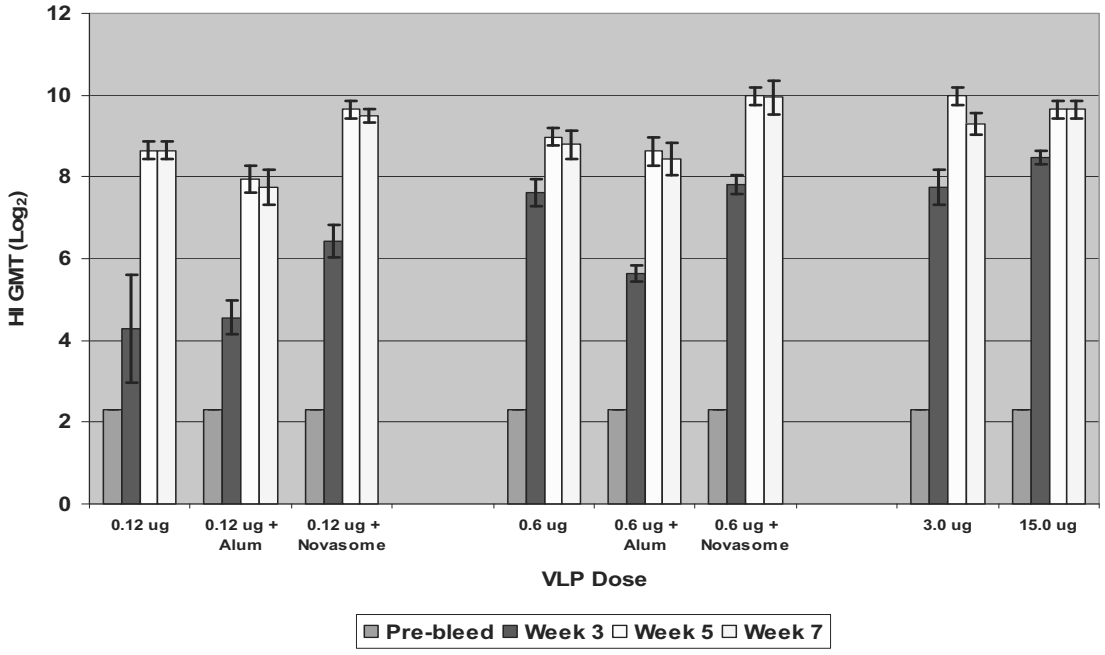

12
10
8
6
4
2
0
HI GMT (Log2)
0.12 ug
0.12 ug + Alum
0.12 ug + Novasome
0.6 ug
0.6 ug + Alum
0.6 ug + Novasome
3.0 ug
15.0 ug
VLP Dose
Pre-bleed
Week 3
Week 5
Week 7

FIGURE 20 A

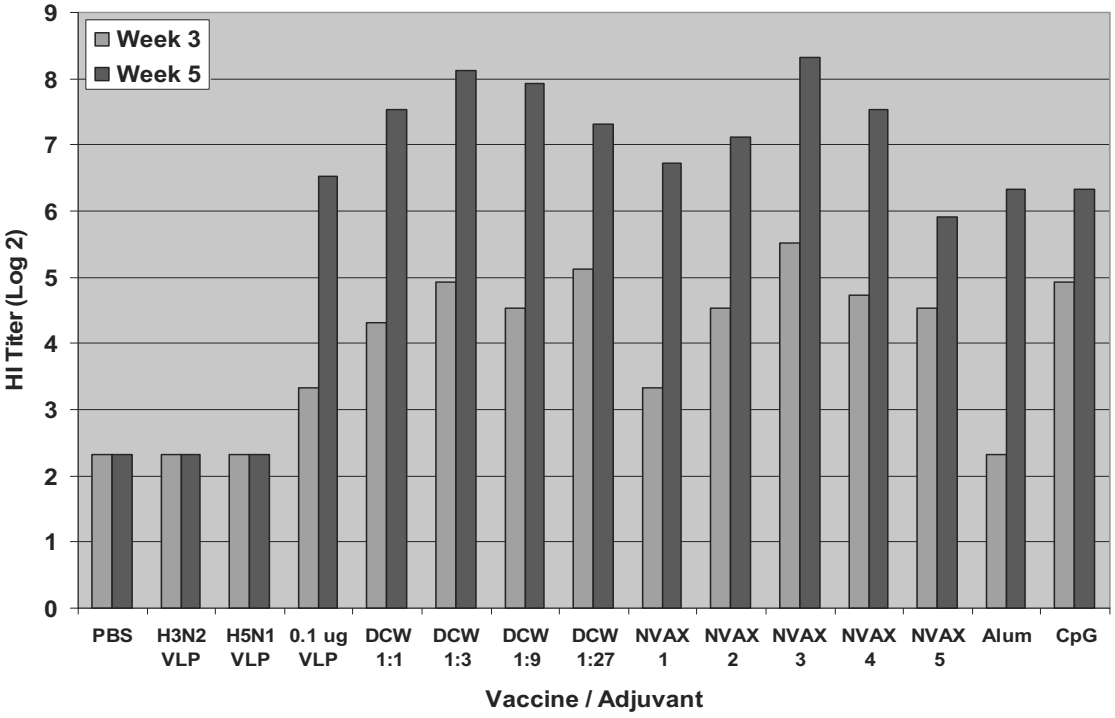

Week 3
Week 5
HI Titer (Log 2)
0
1
2
3
4
5
6
7
8
9
PBS
H3N2 VLP
H5N1 VLP
0.1 ug VLP
DCW 1:1
DCW 1:3
DCW 1:9
DCW 1:27
NVAX 1
NVAX 2
NVAX 3
NVAX 4
NVAX 5
Alum
CpG
Vaccine / Adjuvant

Figure 20 B

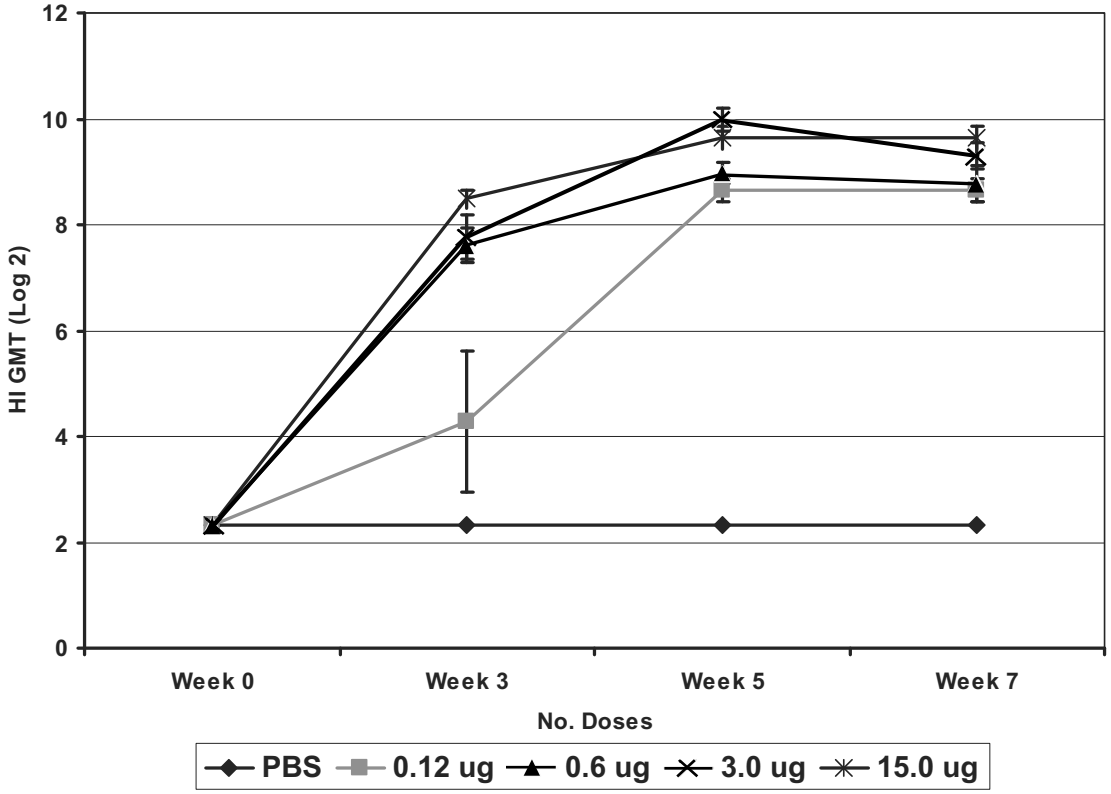

12
10
8
6
4
2
0
HI GMT (Log 2)
Week 0
Week 3
Week 5
Week 7
No. Doses
PBS
0.12 ug
0.6 ug
3.0 ug
15.0 ug

FIGURE 21

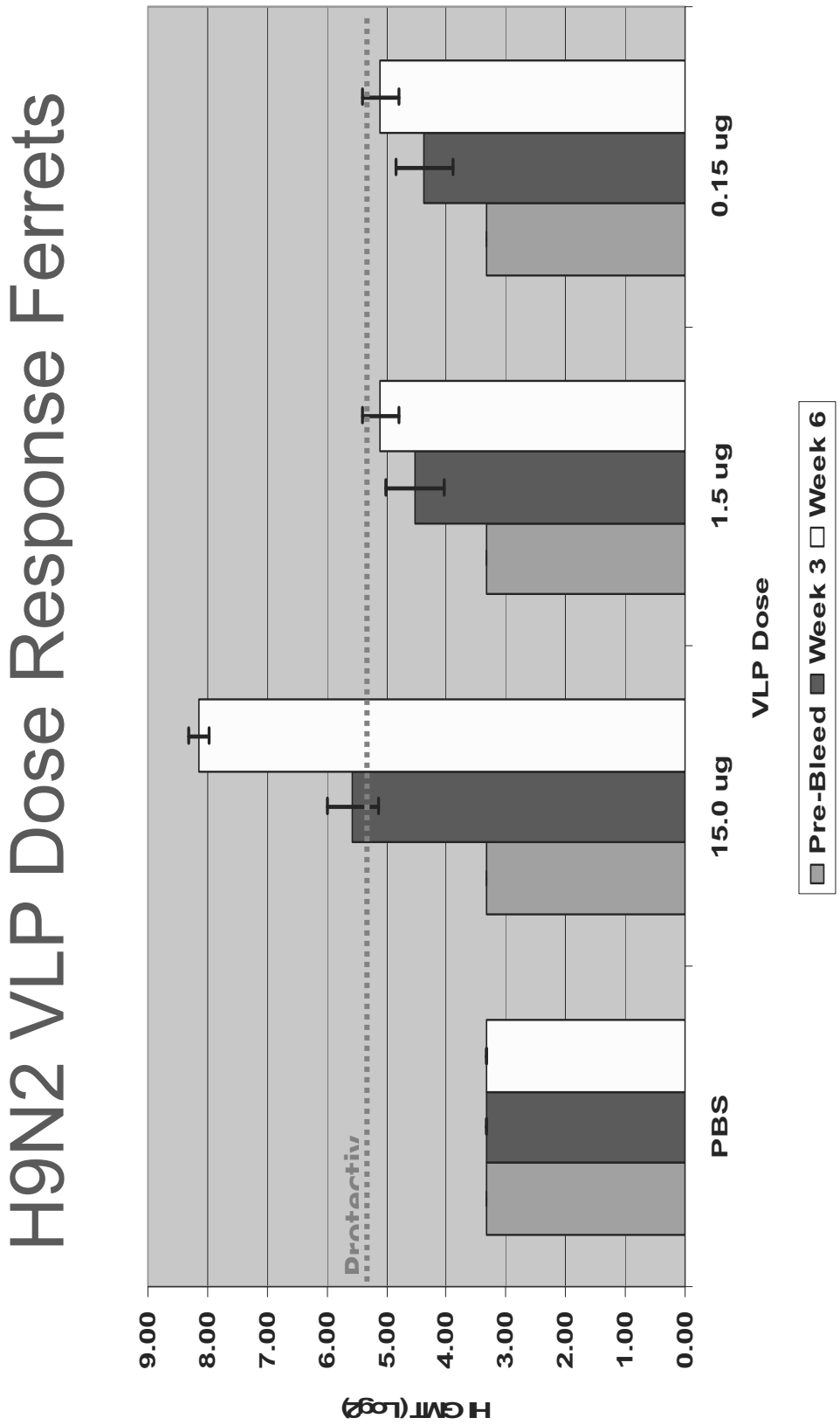

H9N2 VLP Dose Response Ferrets
H GMT (Log2)
9.00
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
Protectiv
PBS
15.0 ug
1.5 ug
0.15 ug
VLP Dose
Pre-Bleed
Week 3
Week 6

FIGURE 22

Table X. Hemagglutinin-Inhibition Titers-Ferrets

	H3N2				H1N1
Vaccine	CA/04	Fuj/02	Well/01	Pan/99	NC/99
Intramuscular					
VLP (15 ug)	640	905	508	40	10
VLP (3 ug)	160	640	226	57	10
VLP (0.6 ug)	50	320	143	67	10
VLP (0.12 ug)	10	184	70	50	10
rHA (15 ug)	80	254	143	56	10
Mock	10	10	10	10	10

FIGURE 23

Extreme Dose Sparing
Intramuscular-H5N1 Vietnam/1203/2003 VLP

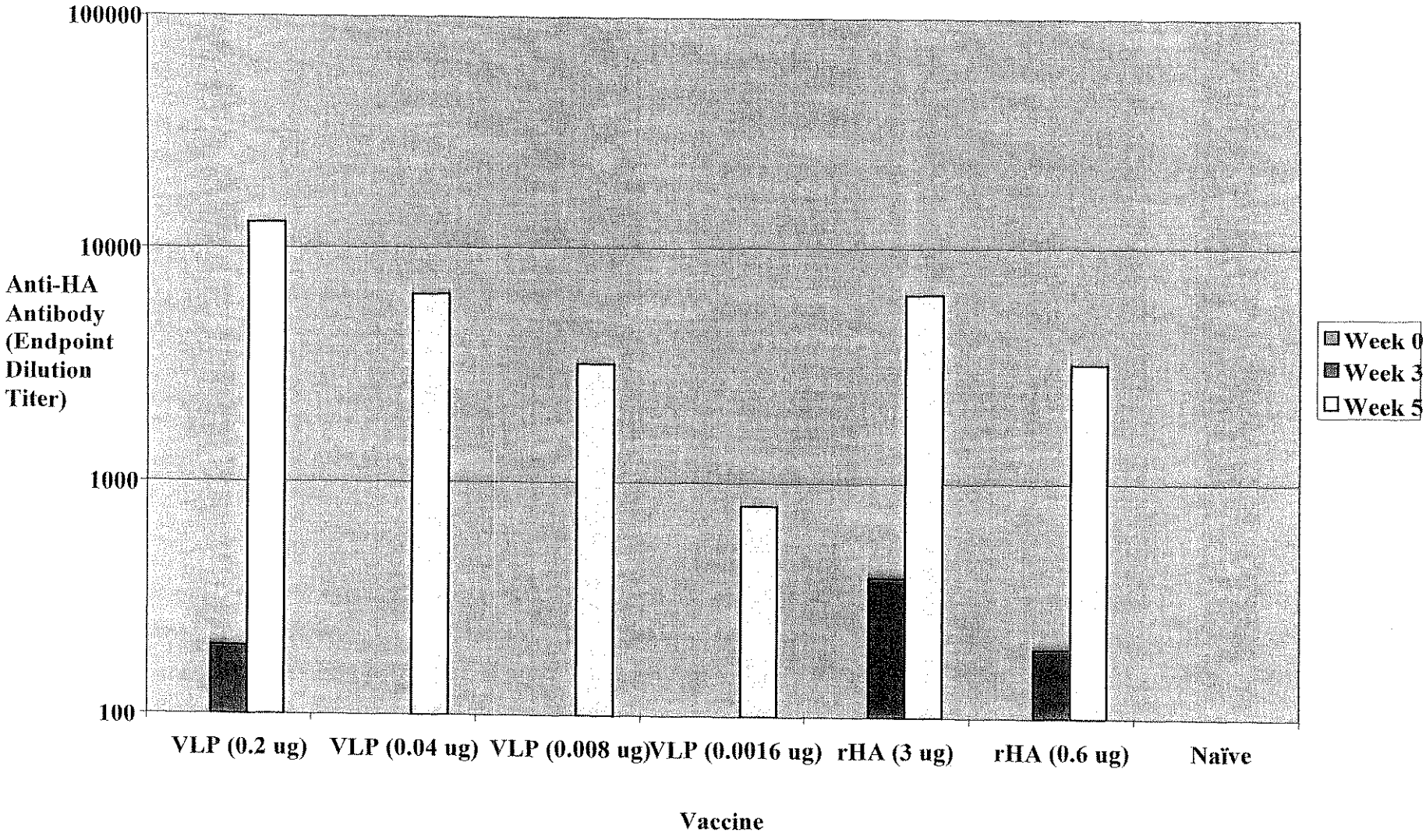


FIGURE 24

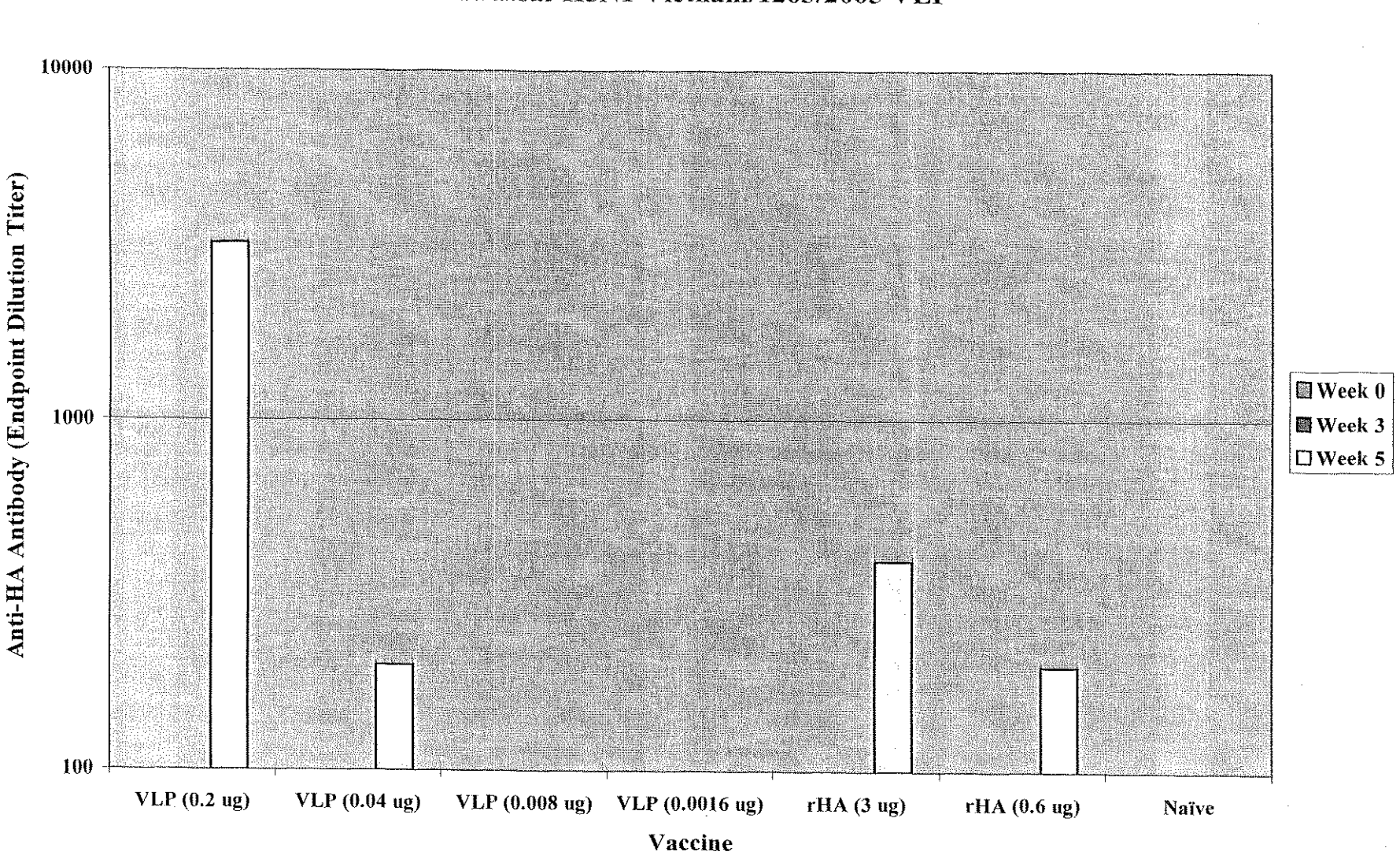
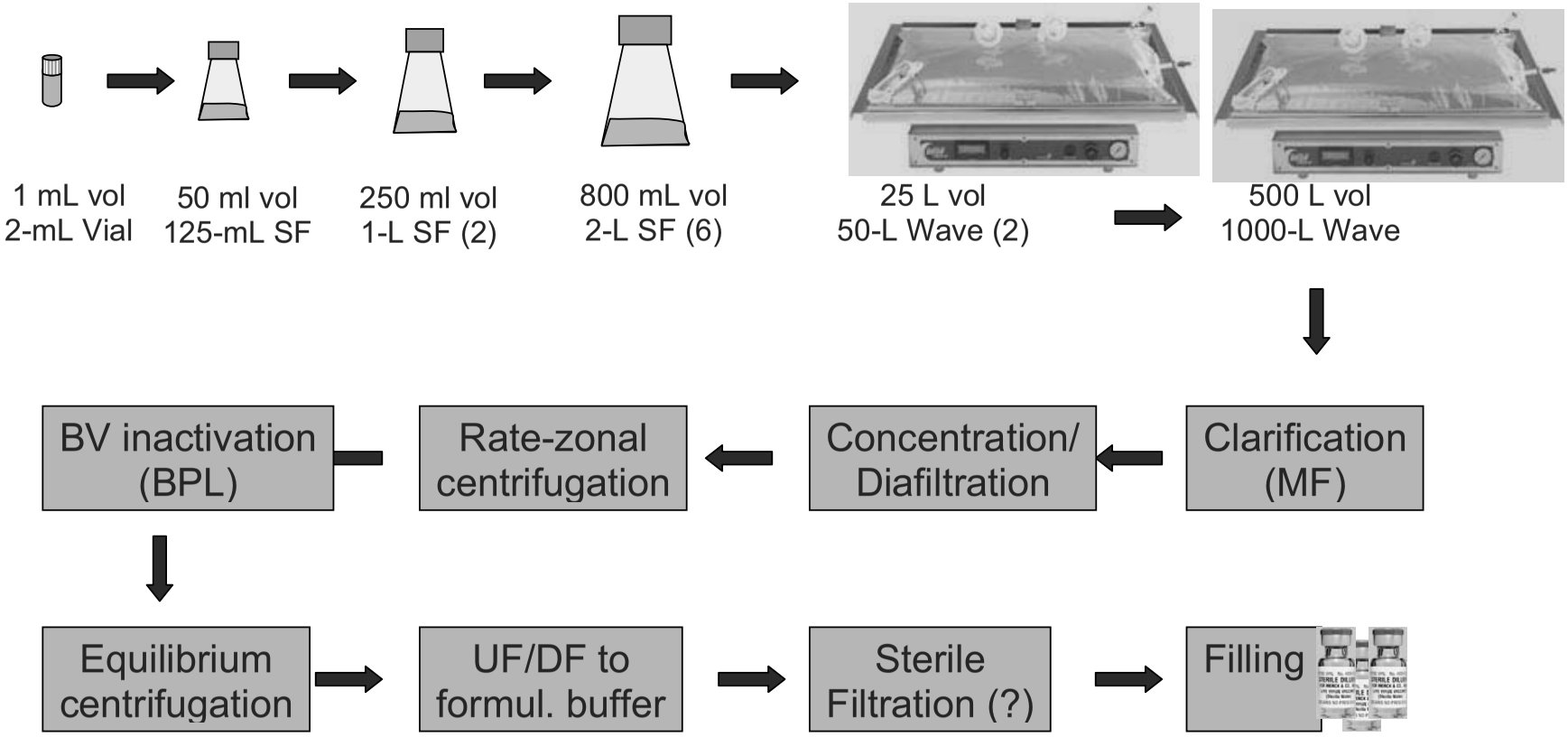

Study 2A-Extreme Dose Sparing
Intranasal-H5N1 Vietnam/1203/2005 VLP
Anti-HA Antibody (Endpoint Dilution Titer)
10000
1000
100
Week 0
Week 3
Week 5
VLP (0.2 ug)
VLP (0.04 ug)
VLP (0.008 ug)
VLP (0.0016 ug)
rHA (3 ug)
rHA (0.6 ug)
Naïve
Vaccine

FIGURE 25

Portable and Disposable Production Process for Influenza VLP Vaccine Production



Entire upstream cell culture process and downstream unit operations are targeted to be portable, disposable, and scalable, with surge capacity.

FIGURE 26

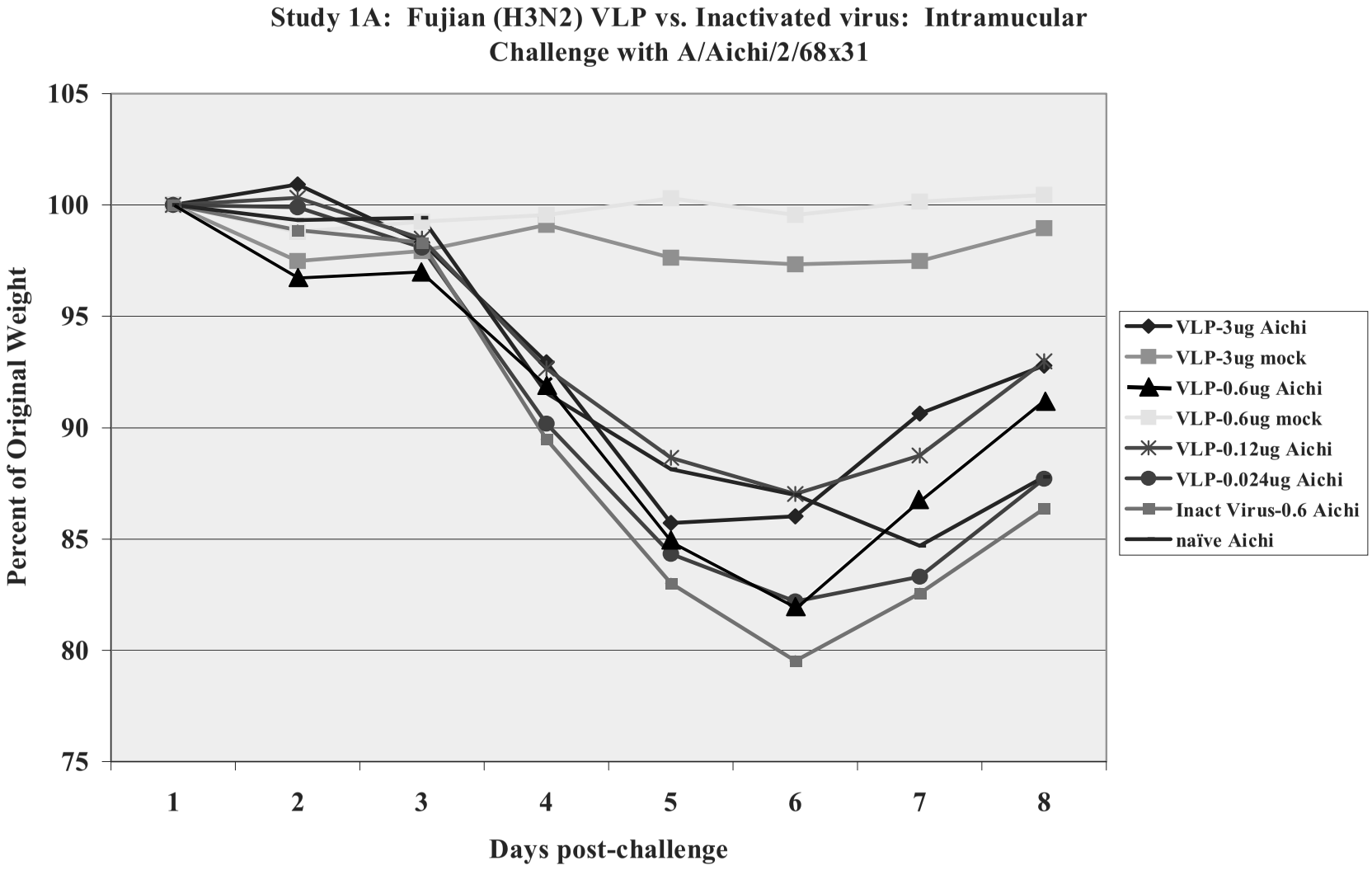

Study 1A: Fujian (H3N2) VLP vs. Inactivated virus: Intramucular Challenge with A/Aichi/2/68x31
Percent of Original Weight
105
100
95
90
85
80
75
1
2
3
4
5
6
7
8
Days post-challenge
VLP-3ug Aichi
VLP-3ug mock
VLP-0.6ug Aichi
VLP-0.6ug mock
VLP-0.12ug Aichi
VLP-0.024ug Aichi
Inact Virus-0.6 Aichi
naïve Aichi

FIGURE 27

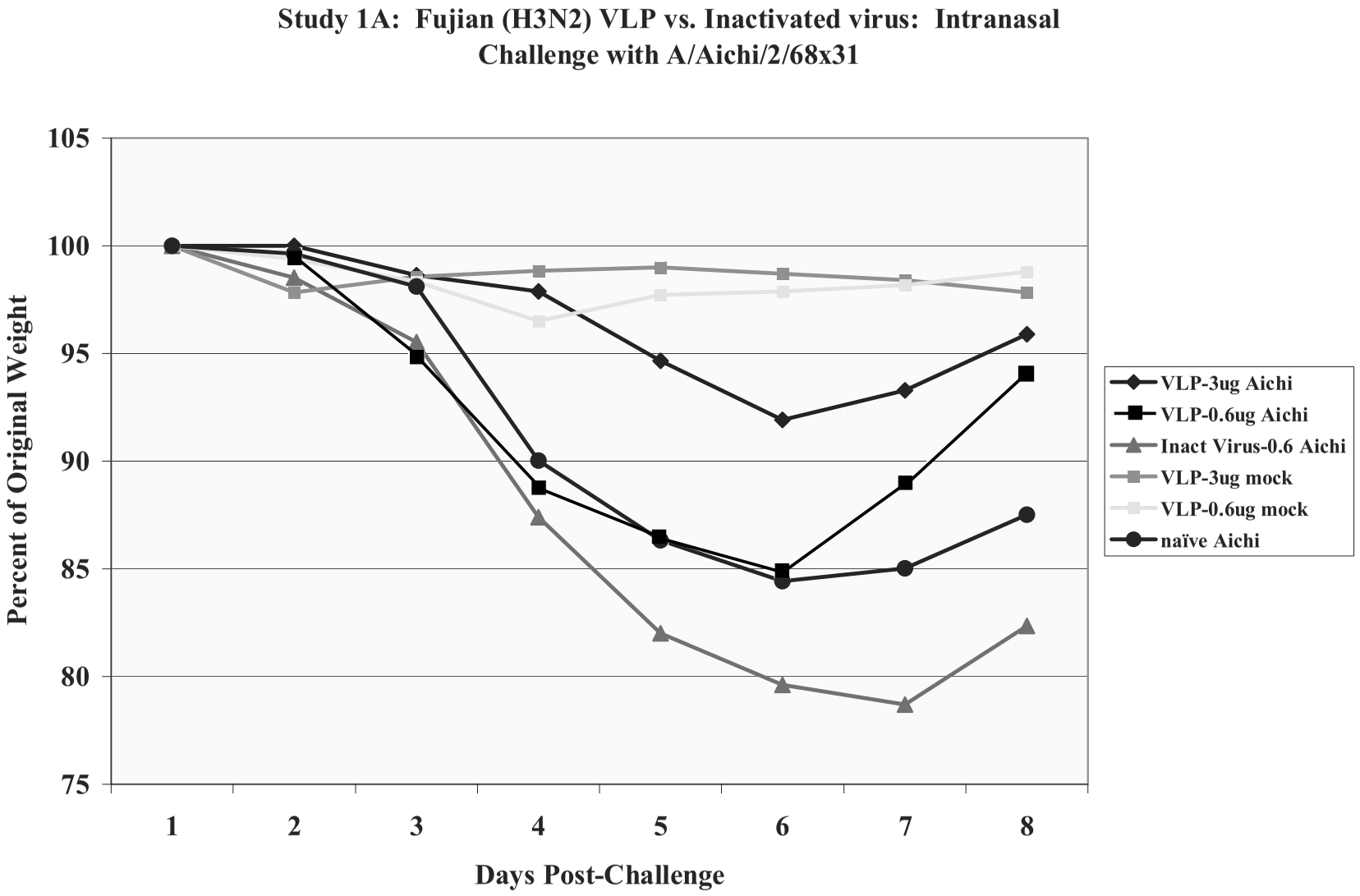

Study 1A: Fujian (H3N2) VLP vs. Inactivated virus: Intranasal Challenge with A/Aichi/2/68x31
Percent of Original Weight
105
100
95
90
85
80
75
1
2
3
4
5
6
7
8
Days Post-Challenge
VLP-3ug Aichi
VLP-0.6ug Aichi
Inact Virus-0.6 Aichi
VLP-3ug mock
VLP-0.6ug mock
naïve Aichi

FIGURE 28

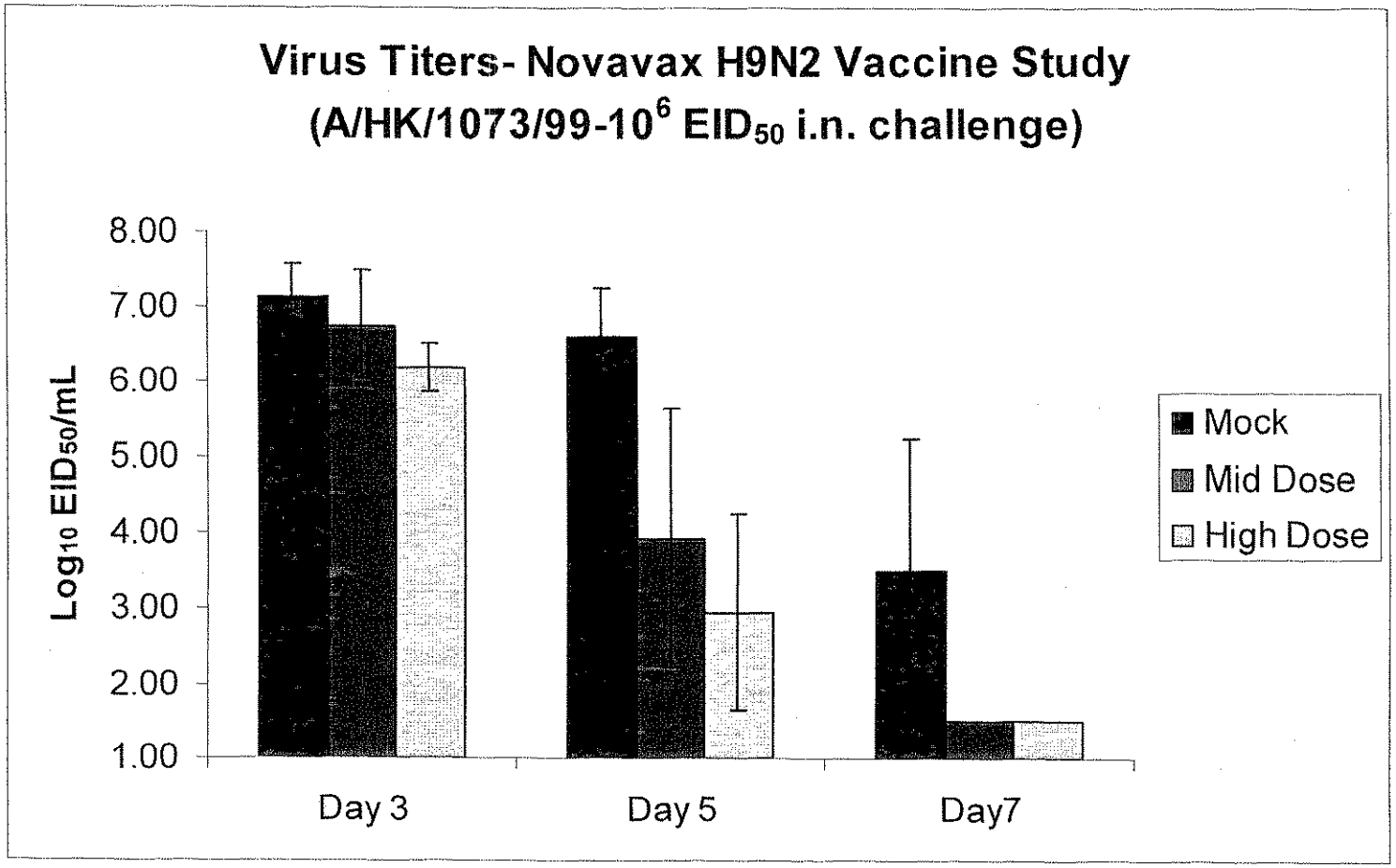

Virus Titers- Novavax H9N2 Vaccine Study
(A/HK/1073/99-10^6 EID50 i.n. challenge)
Log10 EID50/mL
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
Day 3
Day 5
Day7
Mock
Mid Dose
High Dose

FIGURE 29

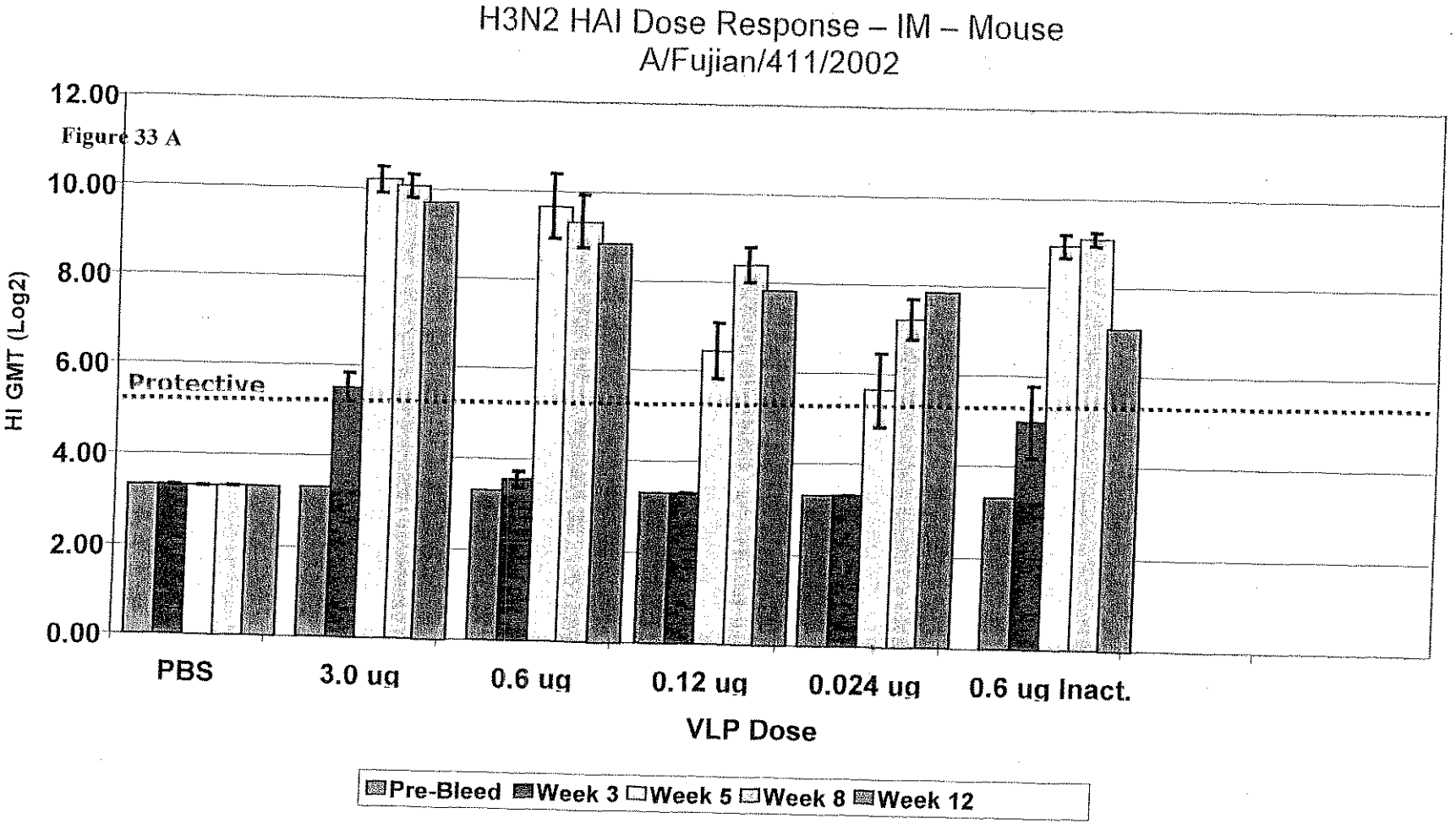

H3N2 HAI Dose Response – IM – Mouse
A/Fujian/411/2002
Figure 33 A
12.00
10.00
8.00
6.00
4.00
2.00
0.00
HI GMT (Log2)
Protective
PBS
3.0 ug
0.6 ug
0.12 ug
0.024 ug
0.6 ug Inact.
VLP Dose
Pre-Bleed
Week 3
Week 5
Week 8
Week 12

FIGURE 30 A

HI titer to A/Fujian/411/2002 (H3N2) after intranasal inoculation with H3H2 VLPs

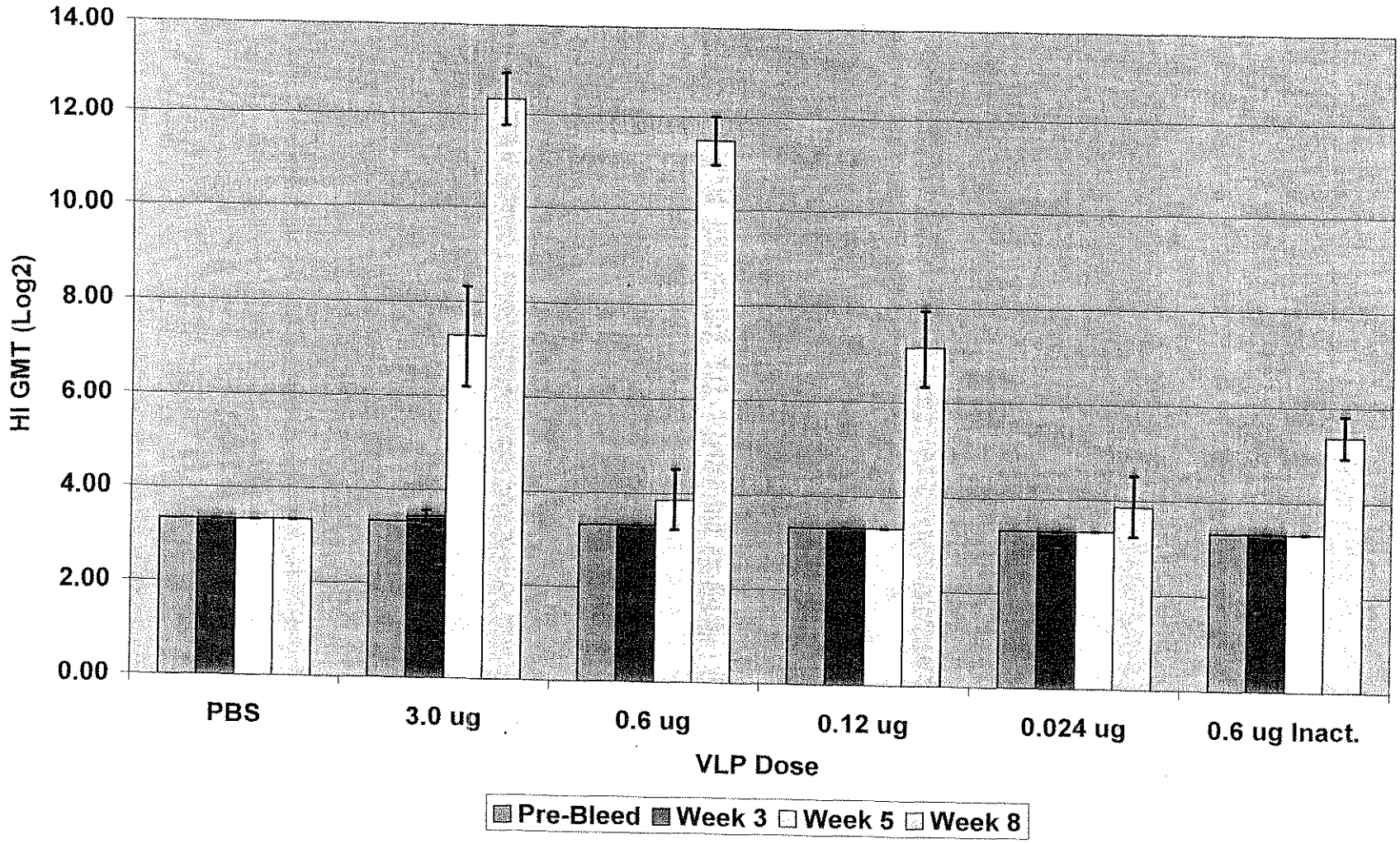


FIGURE 30 B

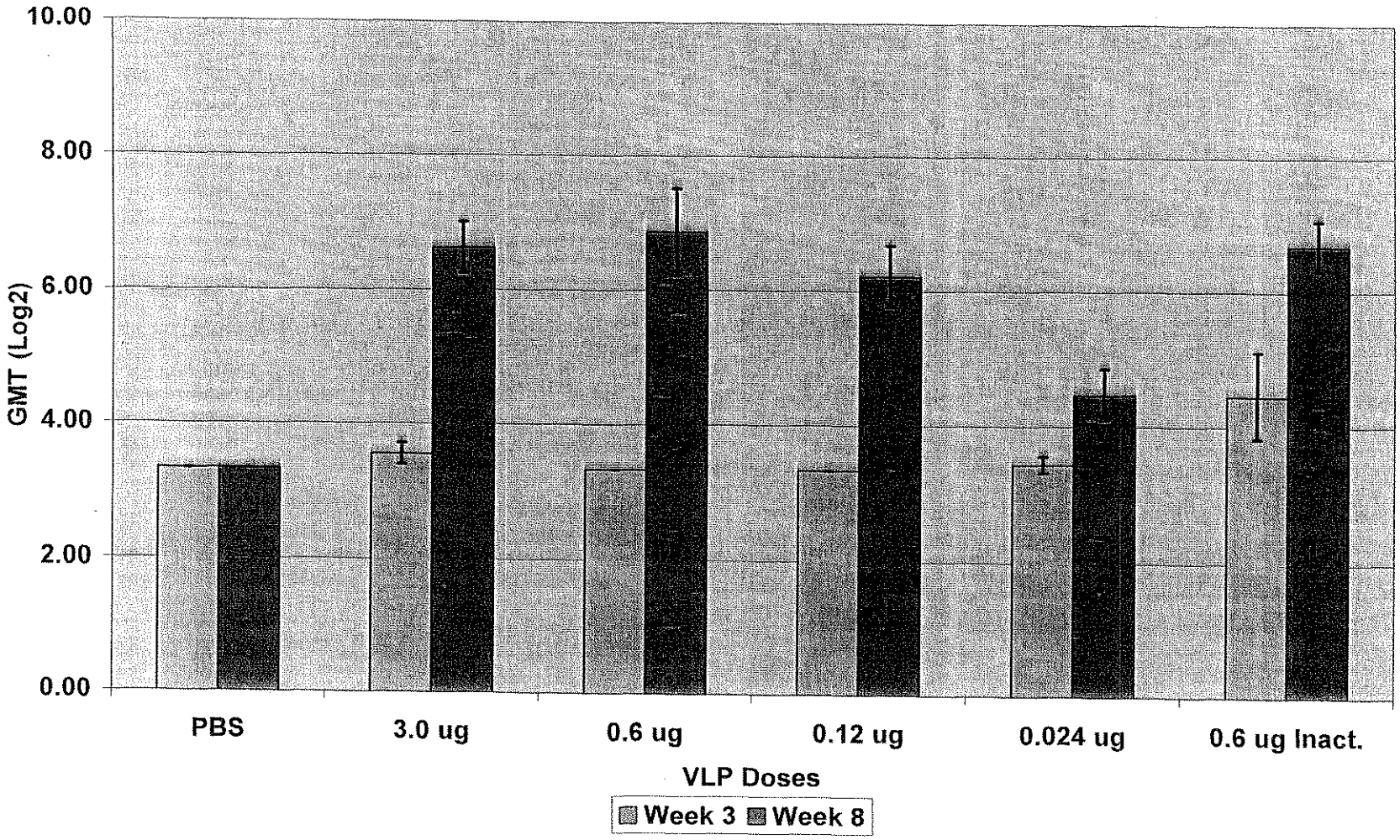

HI titer to A/Panama/2007/99 (H3N2) after intramuscular inoculation with H3H2 VLPs
10.00
8.00
6.00
4.00
2.00
0.00
GMT (Log2)
PBS
3.0 ug
0.6 ug
0.12 ug
0.024 ug
0.6 ug Inact.
VLP Doses
Week 3
Week 8

FIGURE 30 C

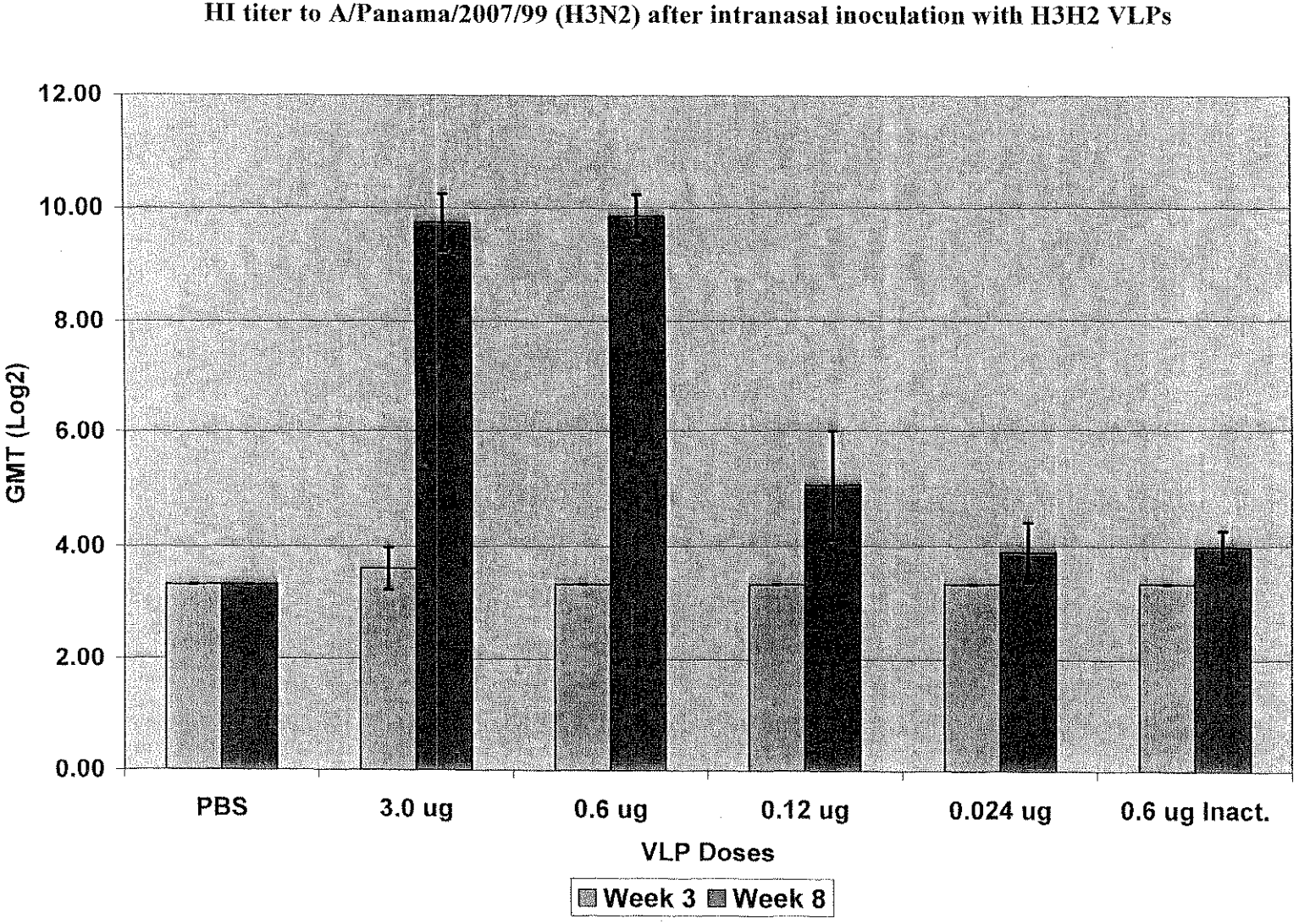

HI titer to A/Panama/2007/99 (H3N2) after intranasal inoculation with H3H2 VLPs
12.00
10.00
8.00
6.00
4.00
2.00
0.00
GMT (Log2)
PBS
3.0 ug
0.6 ug
0.12 ug
0.024 ug
0.6 ug Inact.
VLP Doses
Week 3
Week 8

FIGURE 30 D

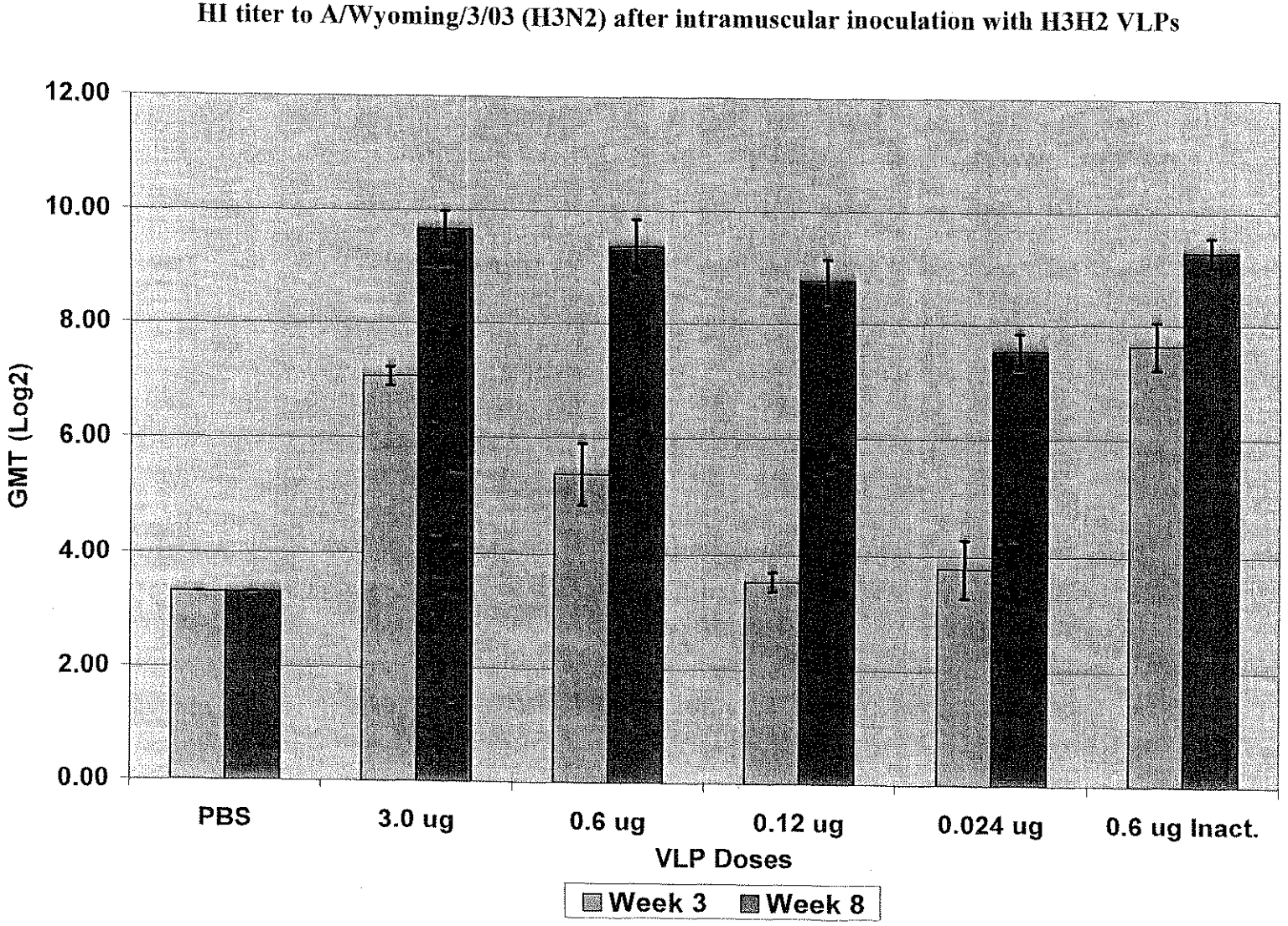

HI titer to A/Wyoming/3/03 (H3N2) after intramuscular inoculation with H3H2 VLPs
12.00
10.00
8.00
6.00
4.00
2.00
0.00
GMT (Log2)
PBS
3.0 ug
0.6 ug
0.12 ug
0.024 ug
0.6 ug Inact.
VLP Doses
Week 3
Week 8

FIGURE 30 E

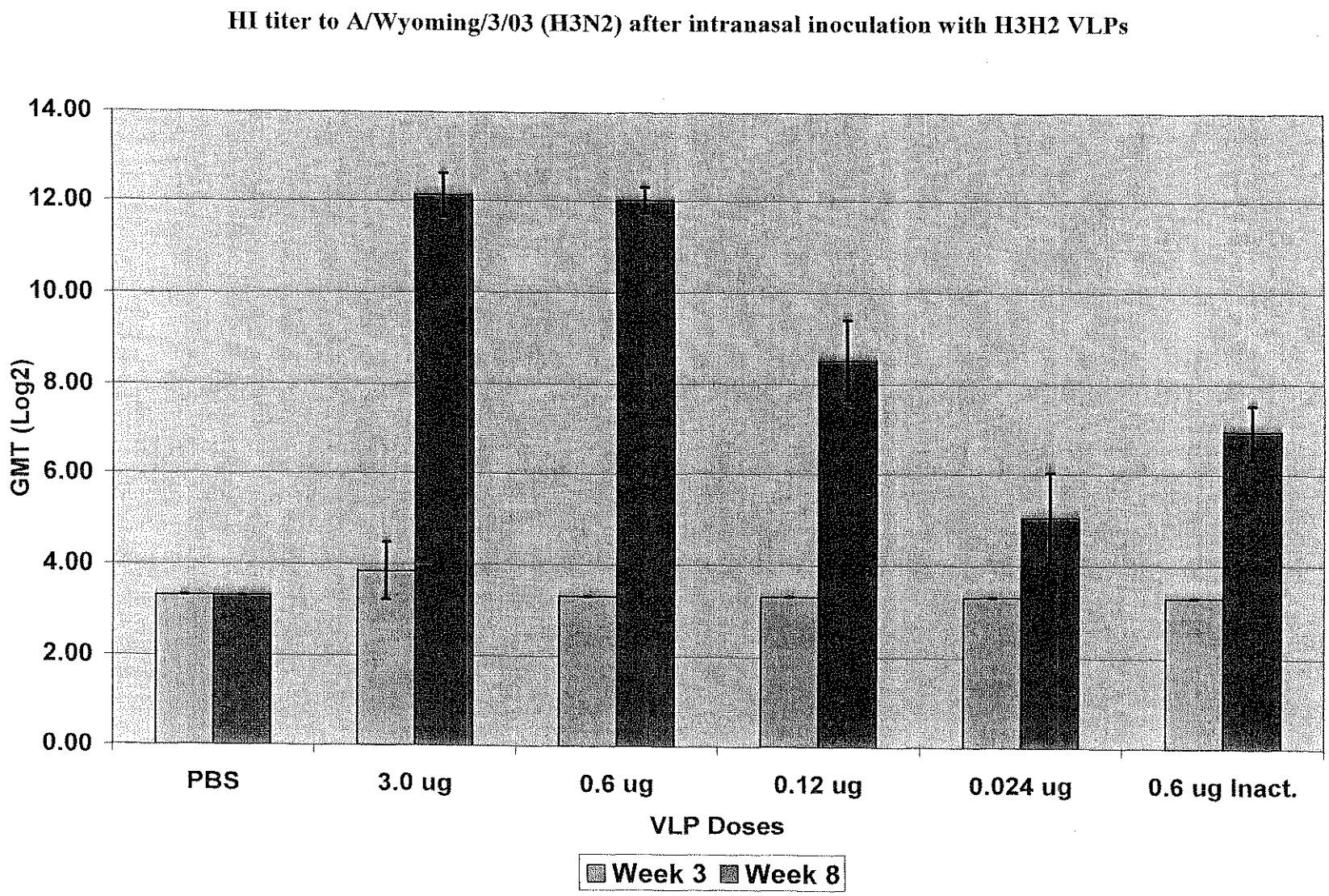

HI titer to A/Wyoming/3/03 (H3N2) after intranasal inoculation with H3H2 VLPs
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
GMT (Log2)
PBS
3.0 ug
0.6 ug
0.12 ug
0.024 ug
0.6 ug Inact.
VLP Doses
Week 3
Week 8

FIGURE 30 F

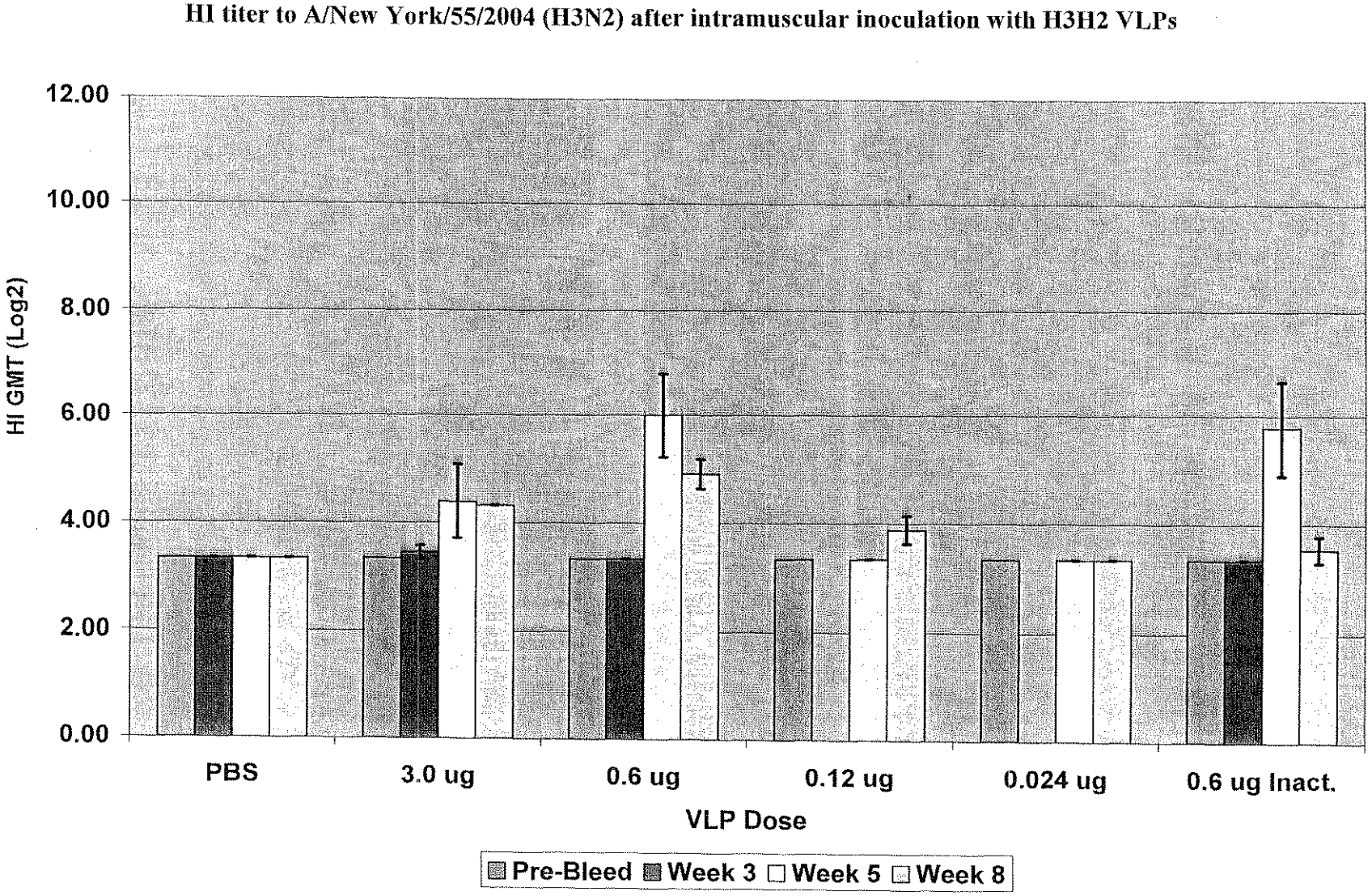

HI titer to A/New York/55/2004 (H3N2) after intramuscular inoculation with H3H2 VLPs
HI GMT (Log2)
12.00
10.00
8.00
6.00
4.00
2.00
0.00
PBS
3.0 ug
0.6 ug
0.12 ug
0.024 ug
0.6 ug Inact.
VLP Dose
Pre-Bleed
Week 3
Week 5
Week 8

FIGURE 30 G

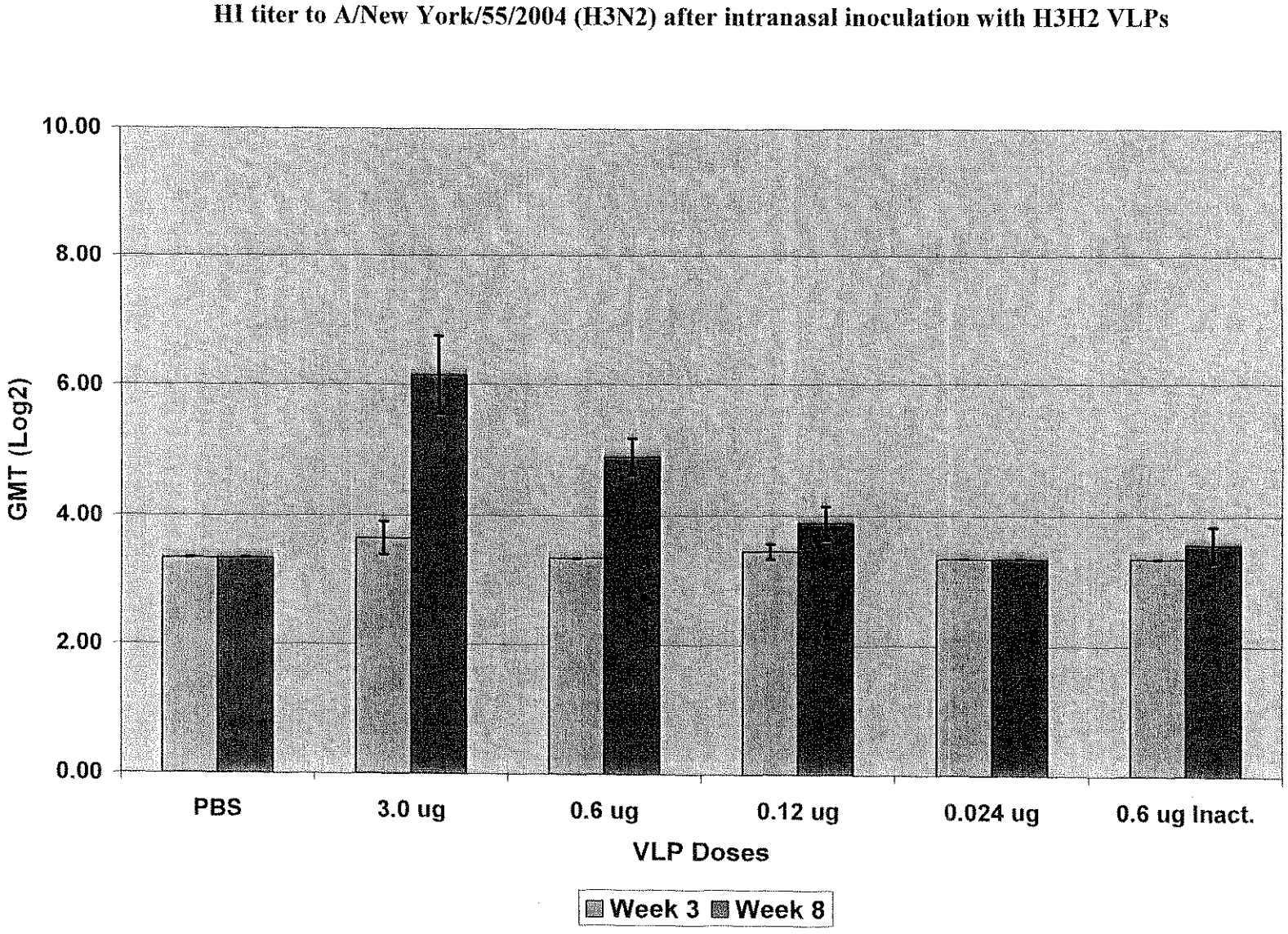

HI titer to A/New York/55/2004 (H3N2) after intranasal inoculation with H3H2 VLPs
10.00
8.00
6.00
4.00
2.00
0.00
GMT (Log2)
PBS
3.0 ug
0.6 ug
0.12 ug
0.024 ug
0.6 ug Inact.
VLP Doses
Week 3
Week 8

FIGURE 30 H