Figure 1

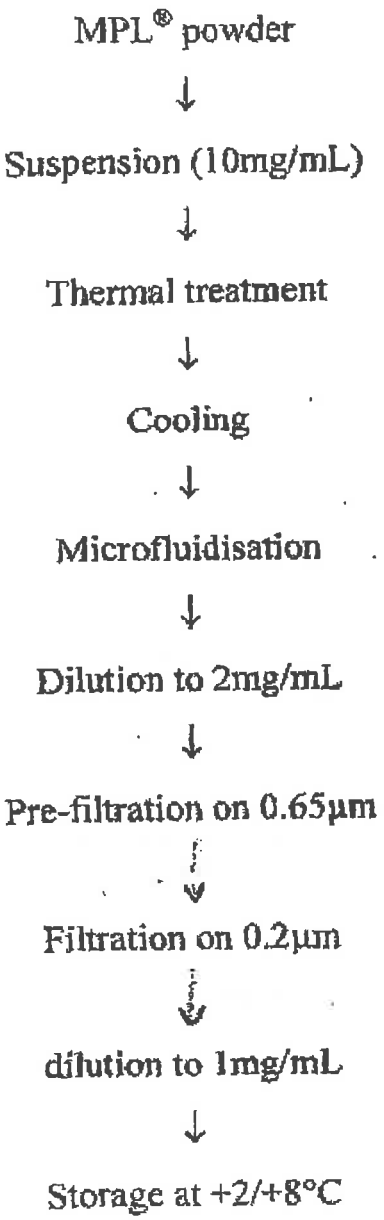
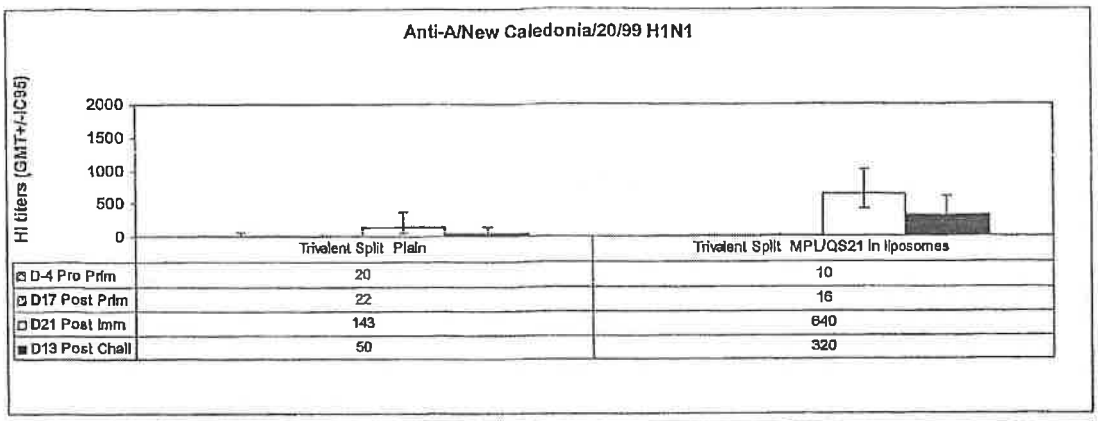
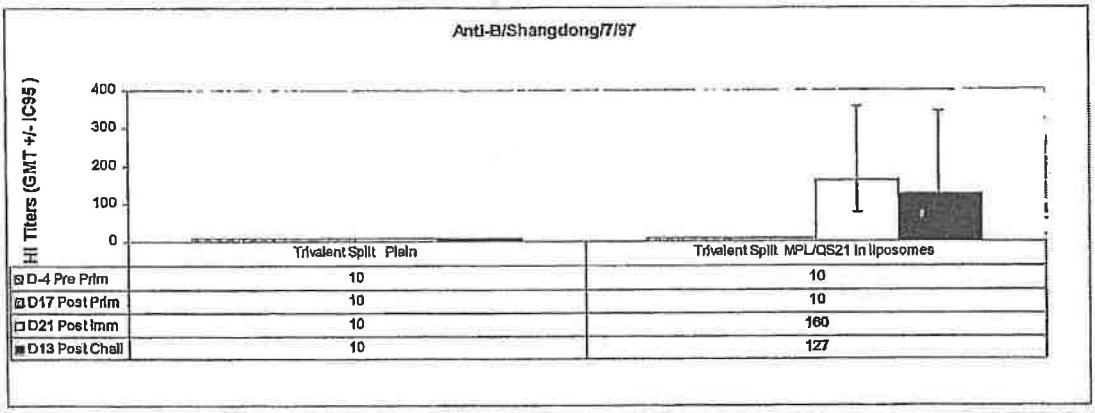
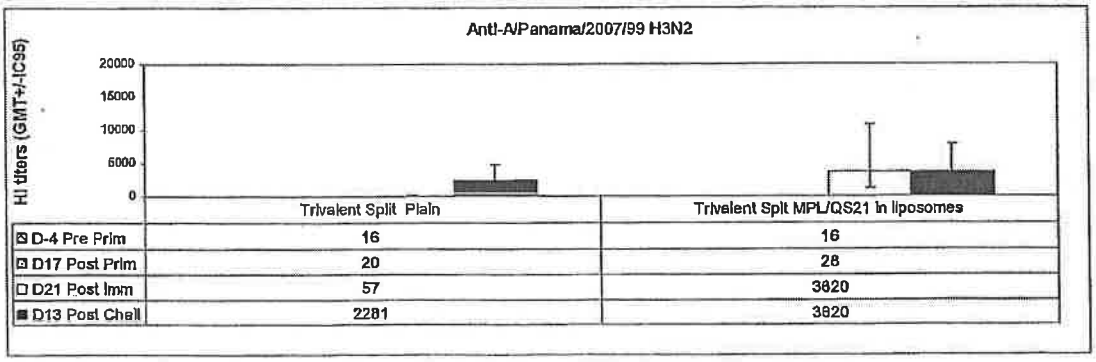
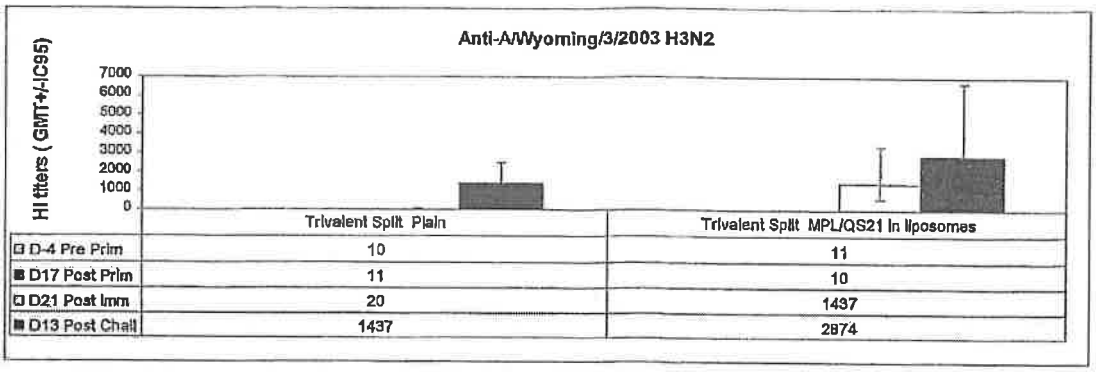

MPL® powder
Suspension (10mg/mL)
Thermal treatment
Cooling
Microfluidisation
Dilution to 2mg/mL
Pre-filtration on 0.65µm
Filtration on 0.2µm
dilution to 1mg/mL
Storage at +2/+8°C

Figure 2


Anti-A/New Caledonia/20/99 H1N1
HI titers (GMT+/-IC95)
2000
1500
1000
500
0
Trivalent Split Plain
Trivalent Split MPL/QS21 in liposomes
D-4 Pre Prim 20 10
D17 Post Prim 22 16
D21 Post Imm 143 640
D13 Post Chall 50 320

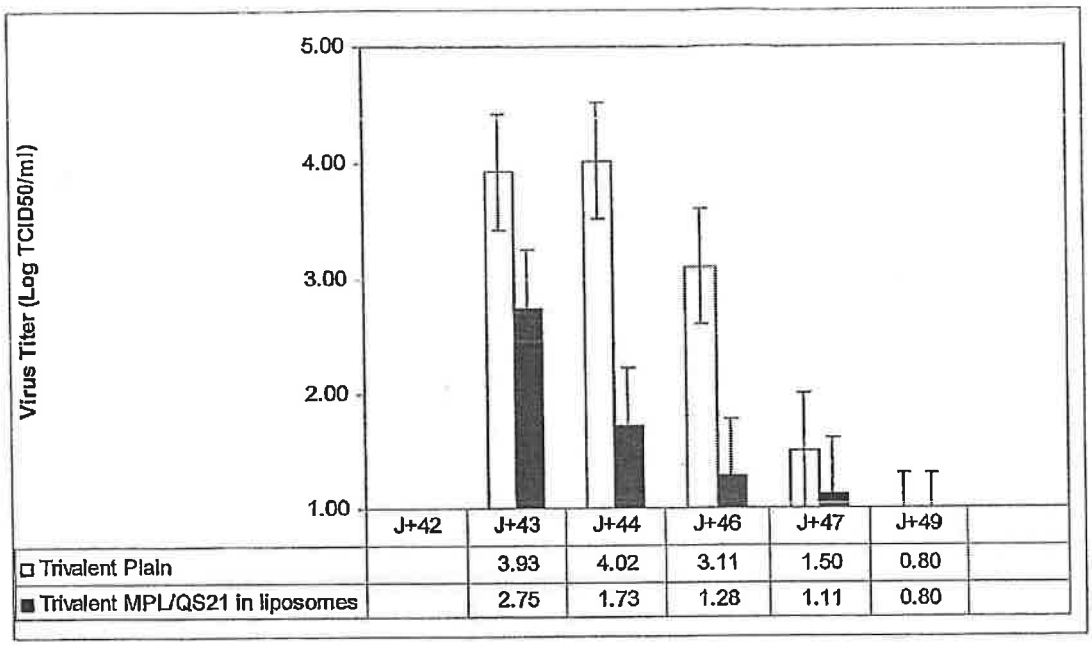

Anti-B/Shangdong/7/97
HI Titers (GMT +/- IC95)
400
300
200
100
0
Trivalent Split Plain
Trivalent Split MPL/QS21 in liposomes
D-4 Pre Prim 10 10
D17 Post Prim 10 10
D21 Post Imm 10 160
D13 Post Chall 10 127


Anti-A/Panama/2007/99 H3N2
HI titers (GMT+/-IC95)
20000
15000
10000
5000
0
Trivalent Split Plain
Trivalent Split MPL/QS21 in liposomes
D-4 Pre Prim 16 16
D17 Post Prim 20 28
D21 Post Imm 57 3820
D13 Post Chall 2281 3820



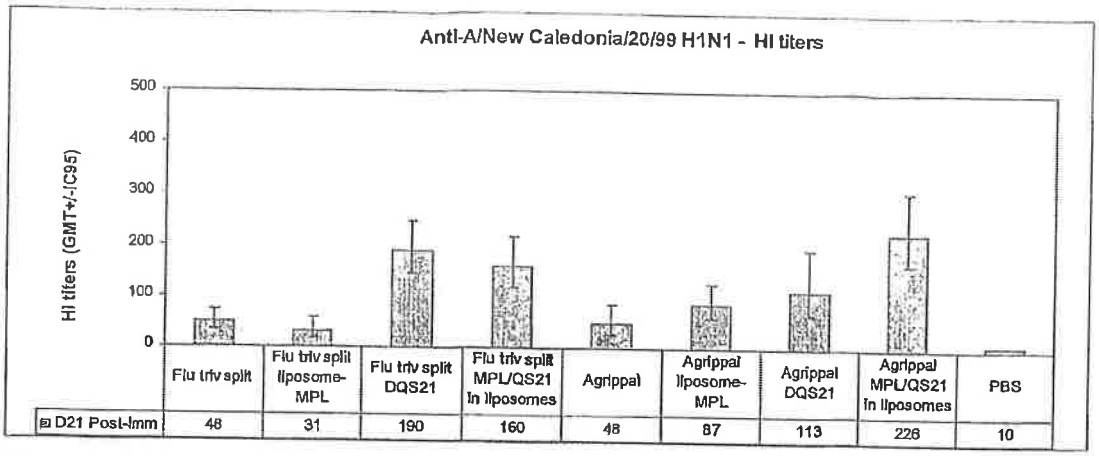
	Trivalent Split Plain	Trivalent Split MPL/QS21 in liposomes
D-4 Pre Prim	10	11
D17 Post Prim	11	10
D21 Post Imm	20	1437
D13 Post Chall	1437	2874

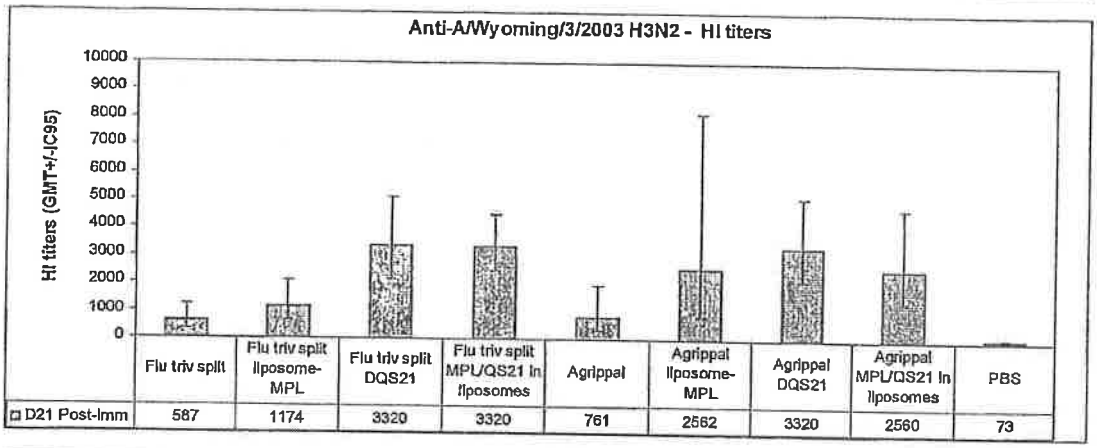
Figure 3



	J+42	J+43	J+44	J+46	J+47	J+49	
□ Trivalent Plain		3.93	4.02	3.11	1.50	0.80	
■ Trivalent MPL/QS21 in liposomes		2.75	1.73	1.28	1.11	0.80	

Figure 4


Anti-A/New Caledonia/20/99 H1N1 - HI titers
HI titers (GMT+/-IC95)
500
400
300
200
100
0
Flu triv split
Flu triv split liposome-MPL
Flu triv split DQS21
Flu triv split MPL/QS21 in liposomes
Agrippal
Agrippal liposome-MPL
Agrippal DQS21
Agrippal MPL/QS21 in liposomes
PBS
D21 Post-Imm
48
31
190
160
48
87
113
226
10


Anti-A/Wyoming/3/2003 H3N2 - HI titers
HI titers (GMT+/-IC95)
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Flu triv split
Flu triv split liposome-MPL
Flu triv split DQS21
Flu triv split MPL/QS21 in liposomes
Agrippal
Agrippal liposome-MPL
Agrippal DQS21
Agrippal MPL/QS21 in liposomes
PBS
D21 Post-Imm
587
1174
3320
3320
761
2562
3320
2560
73

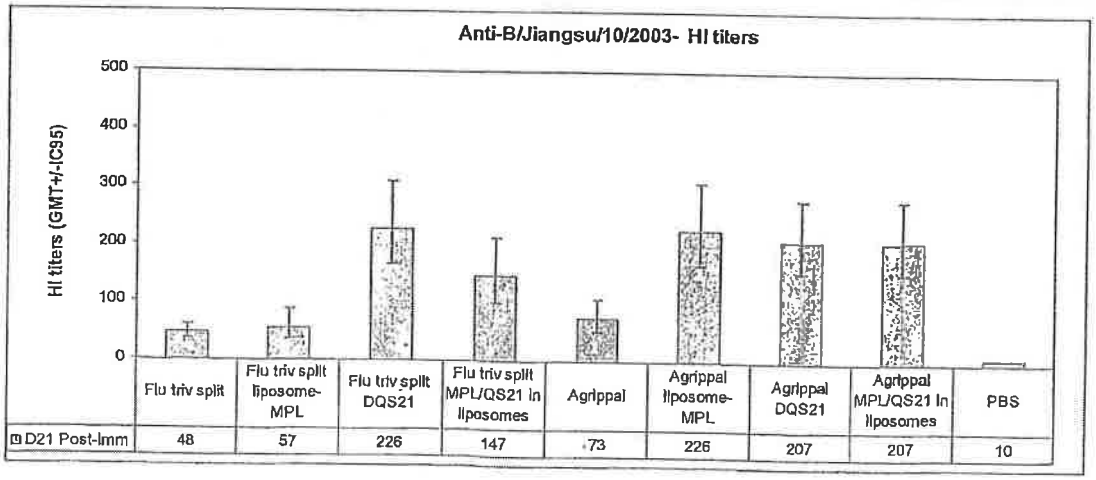
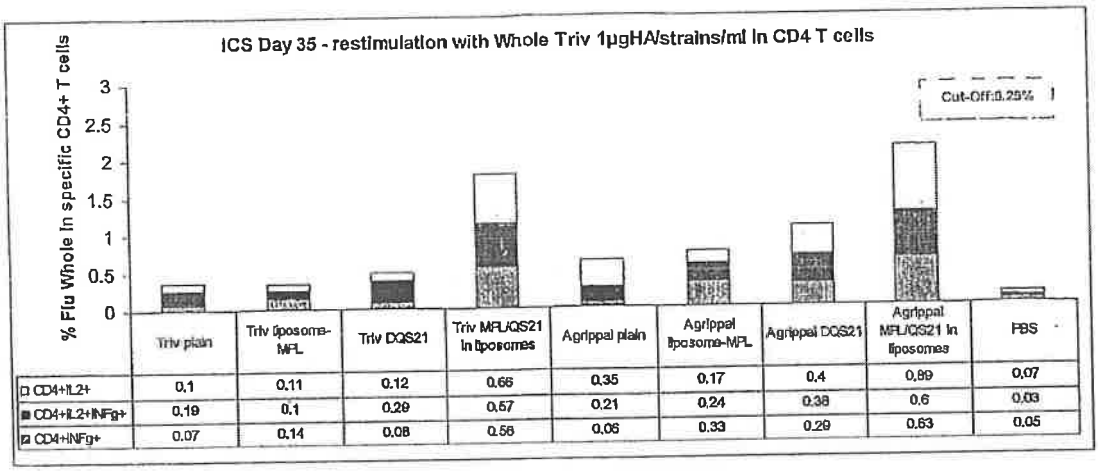

Anti-B/Jiangsu/10/2003- HI titers
HI titers (GMT+/-IC95)
500
400
300
200
100
0
Flu triv split
Flu triv split liposome-MPL
Flu triv split DQS21
Flu triv split MPL/QS21 in liposomes
Agrippal
Agrippal liposome-MPL
Agrippal DQS21
Agrippal MPL/QS21 in liposomes
PBS
D21 Post-Imm
48
57
226
147
73
226
207
207
10

Figure 5


ICS Day 35 - restimulation with Whole Triv 1µgHA/strains/ml in CD4 T cells
% Flu Whole in specific CD4+ T cells
Cut-Off:0.29%
Triv plain
Triv liposome-MPL
Triv DQS21
Triv MPL/QS21 in liposomes
Agrippal plain
Agrippal liposome-MPL
Agrippal DQS21
Agrippal MPL/QS21 in liposomes
PBS
CD4+IL2+ 0.1 0.11 0.12 0.66 0.35 0.17 0.4 0.89 0.07
CD4+IL2+INFg+ 0.19 0.1 0.29 0.67 0.21 0.24 0.38 0.6 0.09
CD4+INFg+ 0.07 0.14 0.08 0.56 0.06 0.33 0.29 0.63 0.05

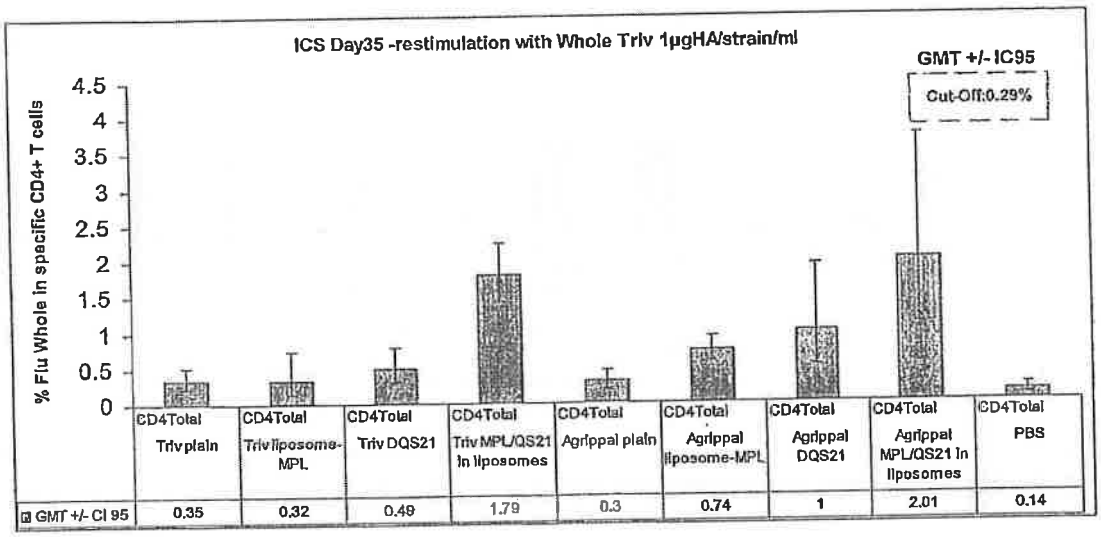

ICS Day35 -restimulation with Whole Triv 1µgHA/strain/ml
GMT +/- IC95
Cut-Off:0.29%
% Flu Whole in specific CD4+ T cells
CD4Total Triv plain
CD4Total Triv liposome-MPL
CD4Total Triv DQS21
CD4Total Triv MPL/QS21 in liposomes
CD4Total Agrippal plain
CD4Total Agrippal liposome-MPL
CD4Total Agrippal DQS21
CD4Total Agrippal MPL/QS21 in liposomes
CD4Total PBS
GMT +/- CI 95 0.35 0.32 0.49 1.79 0.3 0.74 1 2.01 0.14

Figure 6

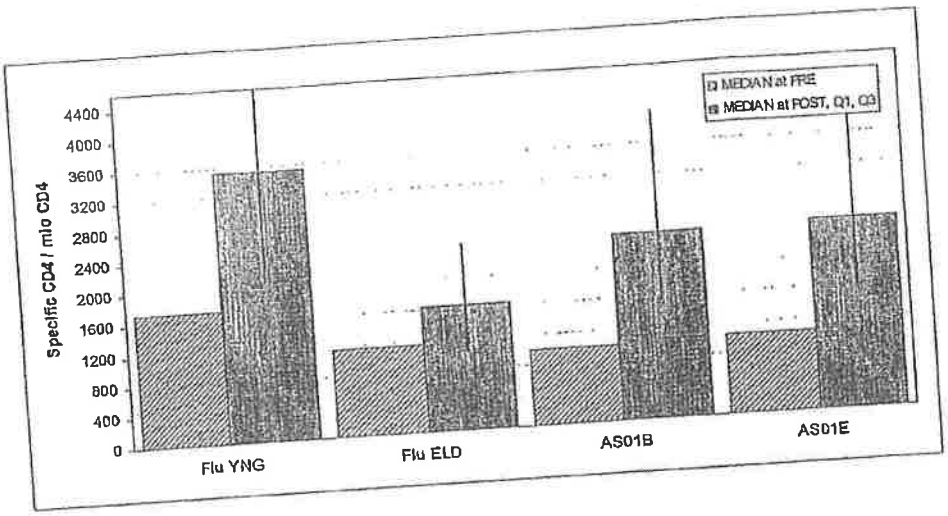


Figure 7

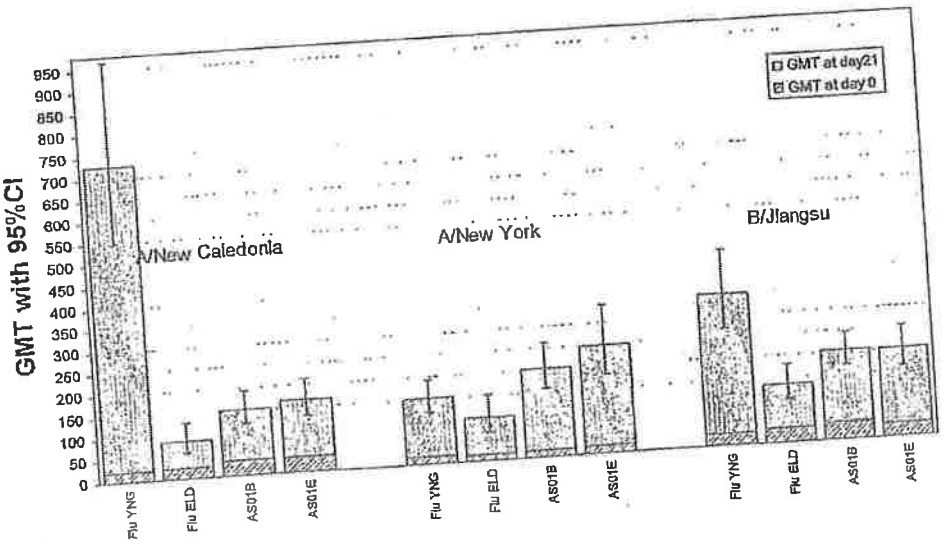


Figure 8

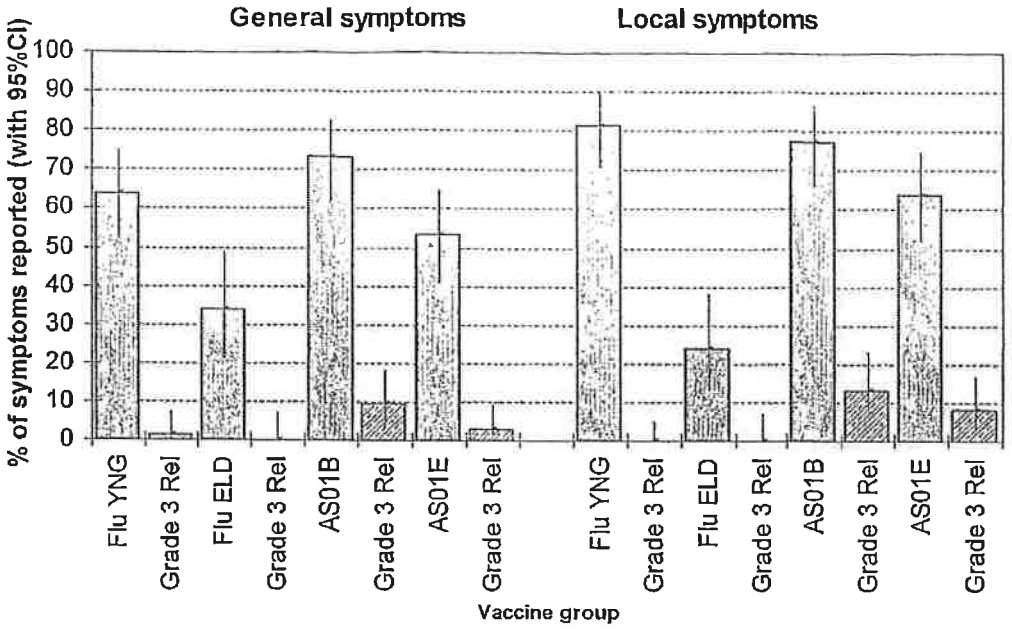
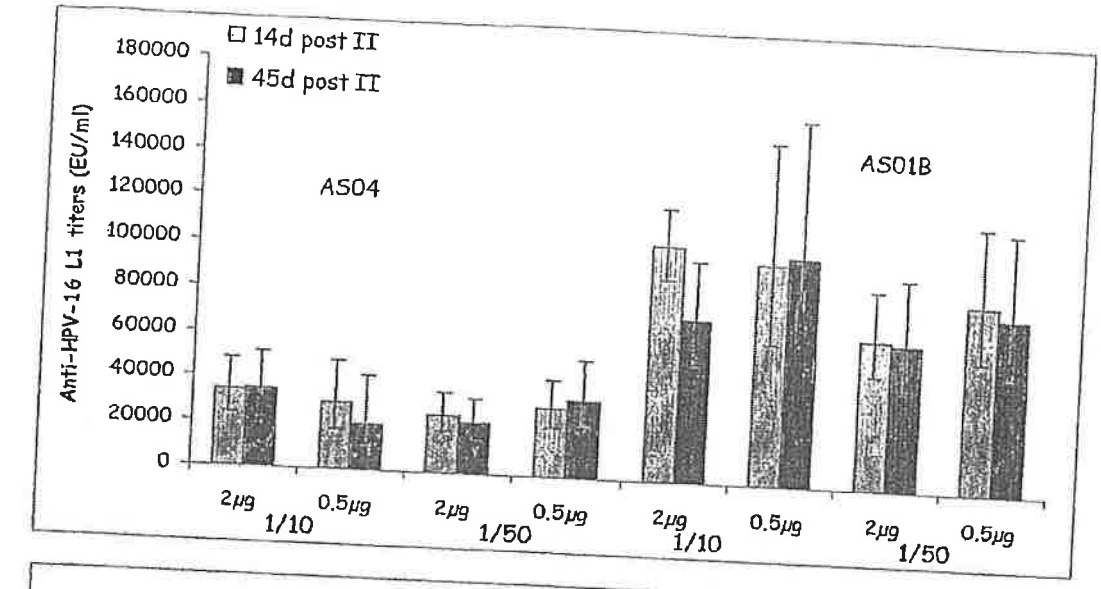

General symptoms
Local symptoms
% of symptoms reported (with 95%CI)
100
90
80
70
60
50
40
30
20
10
0
Flu YNG
Grade 3 Rel
Flu ELD
Grade 3 Rel
AS01B
Grade 3 Rel
AS01E
Grade 3 Rel
Flu YNG
Grade 3 Rel
Flu ELD
Grade 3 Rel
AS01B
Grade 3 Rel
AS01E
Grade 3 Rel
Vaccine group

Figure 9:


14d post II
45d post II
Anti-HPV-16 L1 titers (EU/ml)
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
AS04
AS01B
2µg
0.5µg
1/10
1/50

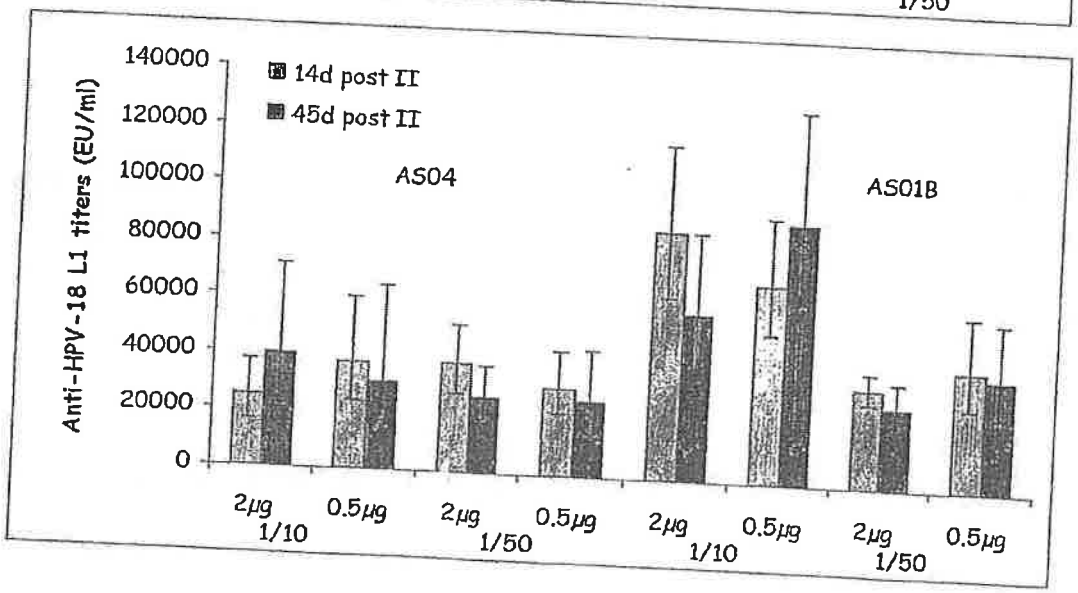
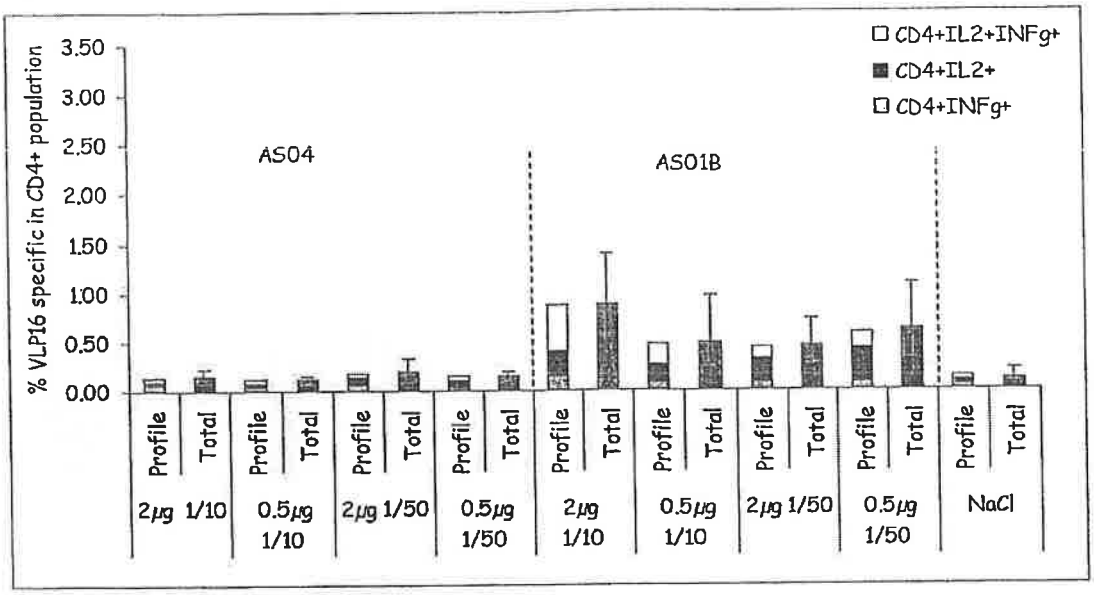

14d post II
45d post II
Anti-HPV-18 L1 titers (EU/ml)
140000
120000
100000
80000
60000
40000
20000
0
AS04
AS01B
2µg
0.5µg
1/10
1/50

Figure 10:


% VLP16 specific in CD4+ population
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
CD4+IL2+INFg+
CD4+IL2+
CD4+INFg+
AS04
AS01B
Profile
Total
2µg 1/10
0.5µg 1/10
2µg 1/50
0.5µg 1/50
2µg 1/10
0.5µg 1/10
2µg 1/50
0.5µg 1/50
NaCl

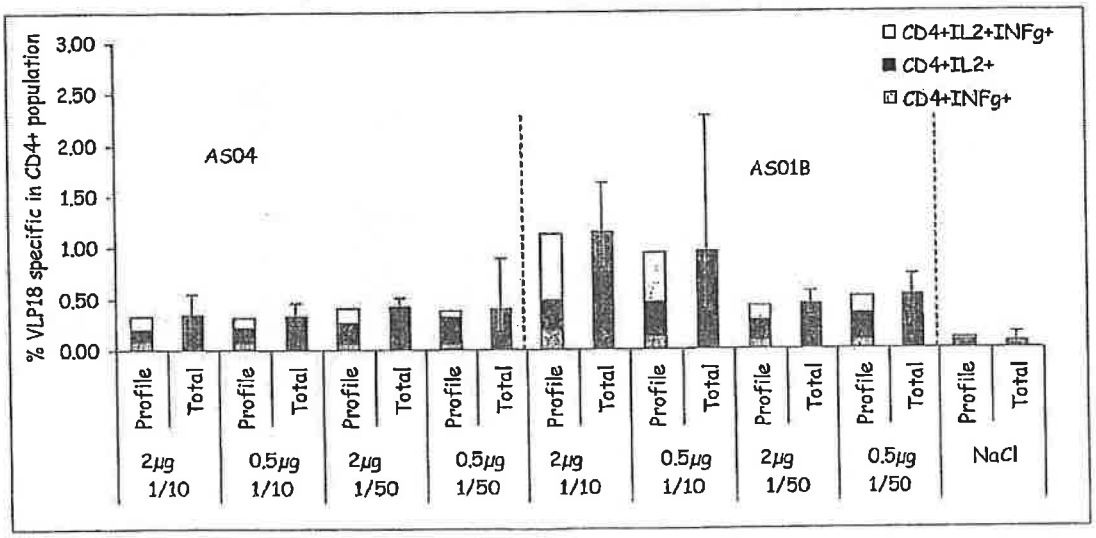
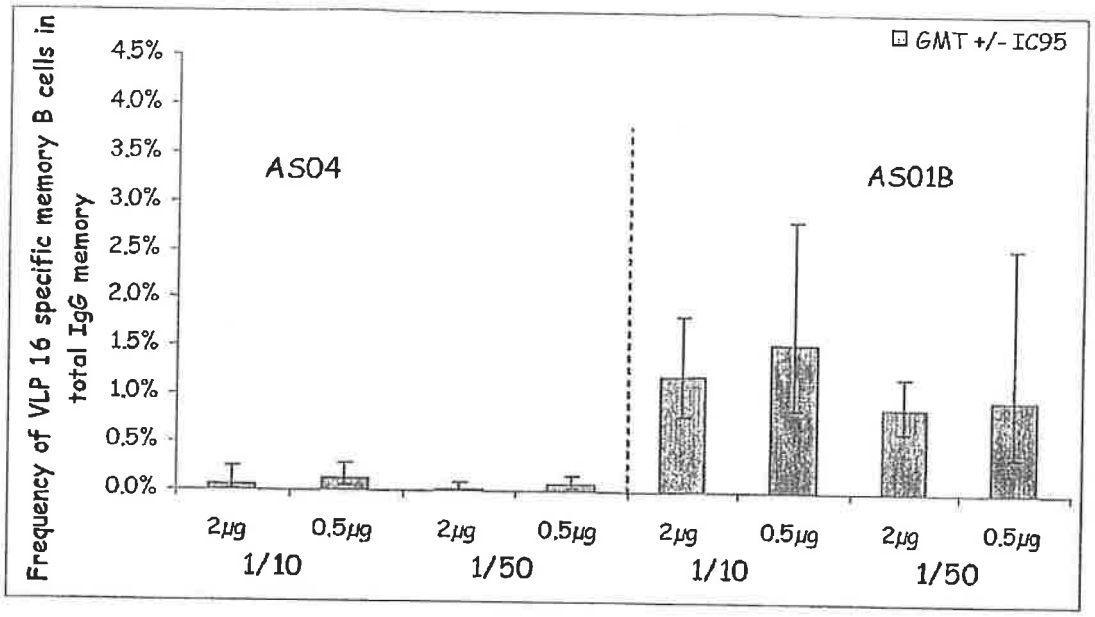

% VLP18 specific in CD4+ population
3.00
2.50
2.00
1.50
1.00
0.50
0.00
CD4+IL2+INFg+
CD4+IL2+
CD4+INFg+
AS04
AS01B
Profile
Total
2µg 1/10
0.5µg 1/10
2µg 1/50
0.5µg 1/50
2µg 1/10
0.5µg 1/10
2µg 1/50
0.5µg 1/50
NaCl

Figure 11:


Frequency of VLP 16 specific memory B cells in total IgG memory
GMT +/- IC95
4.5%
4.0%
3.5%
3.0%
2.5%
2.0%
1.5%
1.0%
0.5%
0.0%
AS04
AS01B
2µg
0.5µg
2µg
0.5µg
2µg
0.5µg
2µg
0.5µg
1/10
1/50
1/10
1/50

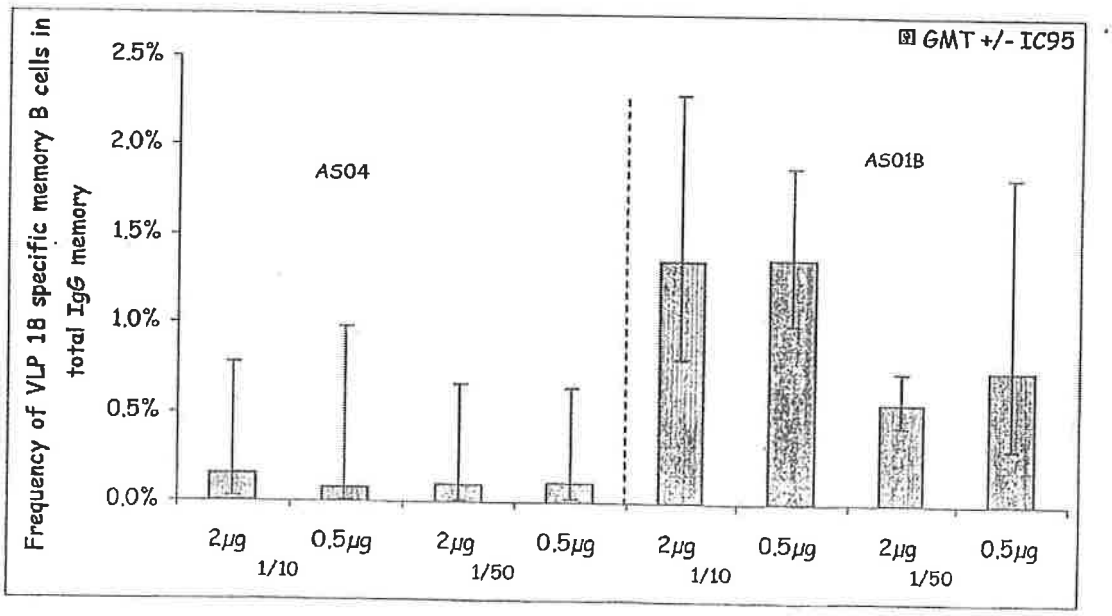

Frequency of VLP 18 specific memory B cells in total IgG memory
GMT +/- IC95
2.5%
2.0%
1.5%
1.0%
0.5%
0.0%
AS04
AS01B
2µg
0.5µg
2µg
0.5µg
2µg
0.5µg
2µg
0.5µg
1/10
1/50
1/10
1/50

Figure12 :

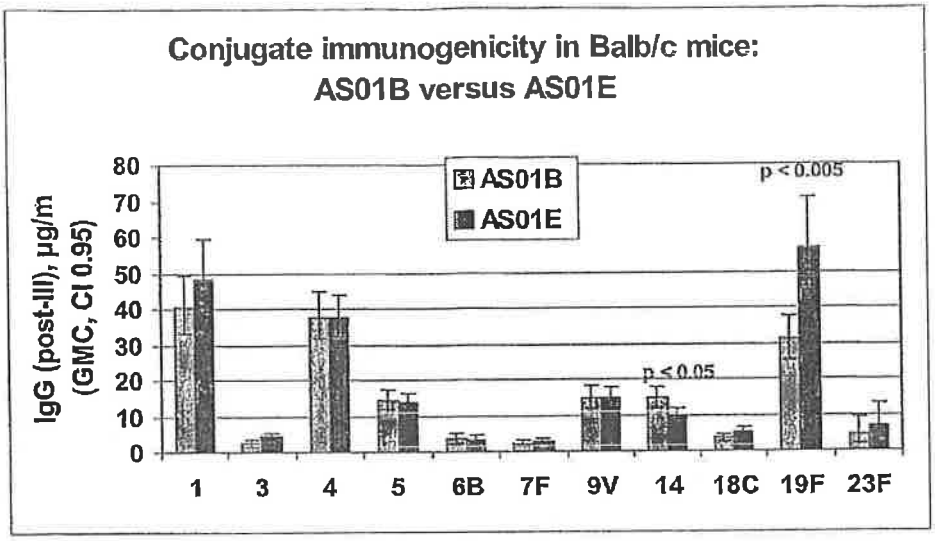

Conjugate immunogenicity in Balb/c mice:
AS01B versus AS01E
IgG (post-III), µg/m
(GMC, CI 0.95)
AS01B
AS01E
p < 0.005
p ≤ 0.05
80
70
60
50
40
30
20
10
0
1
3
4
5
6B
7F
9V
14
18C
19F
23F

Figure 13:

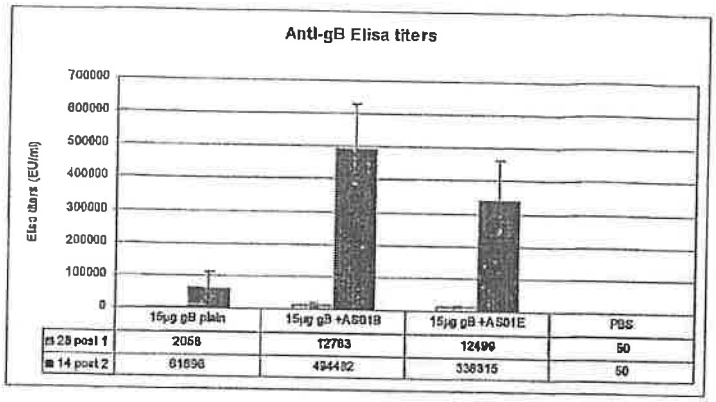


Figure 14:

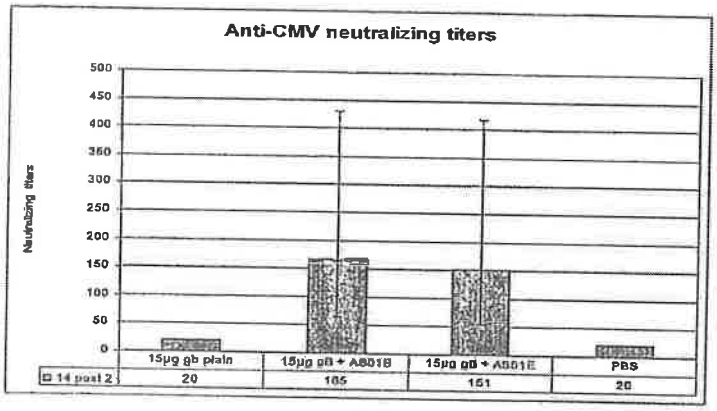


Figure 15:

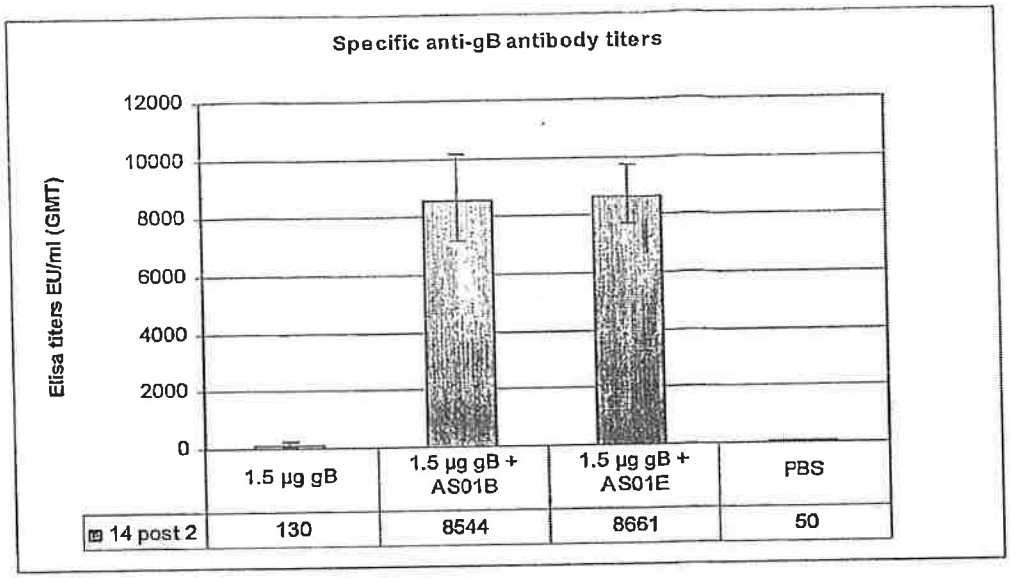


Figure 16:

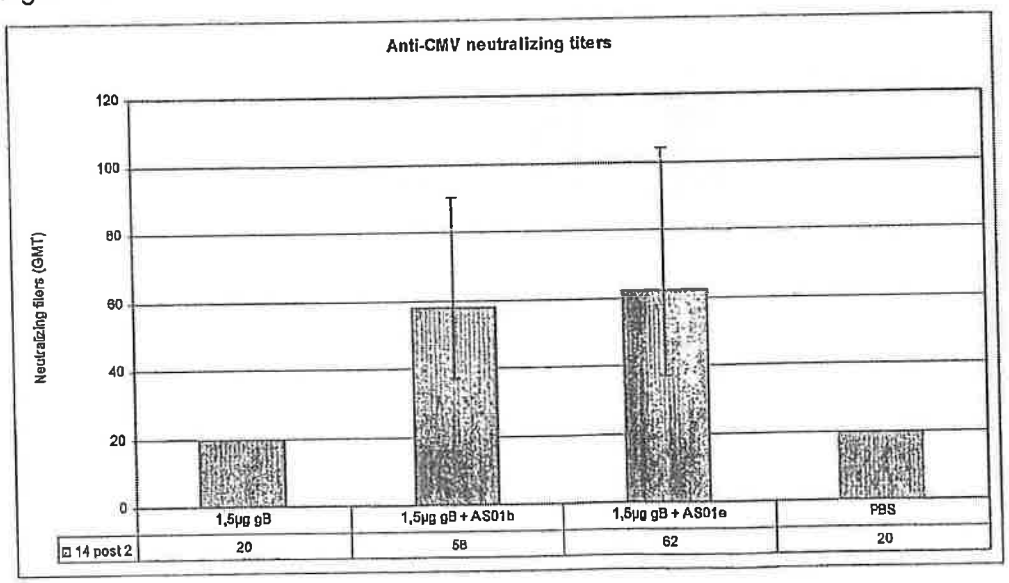
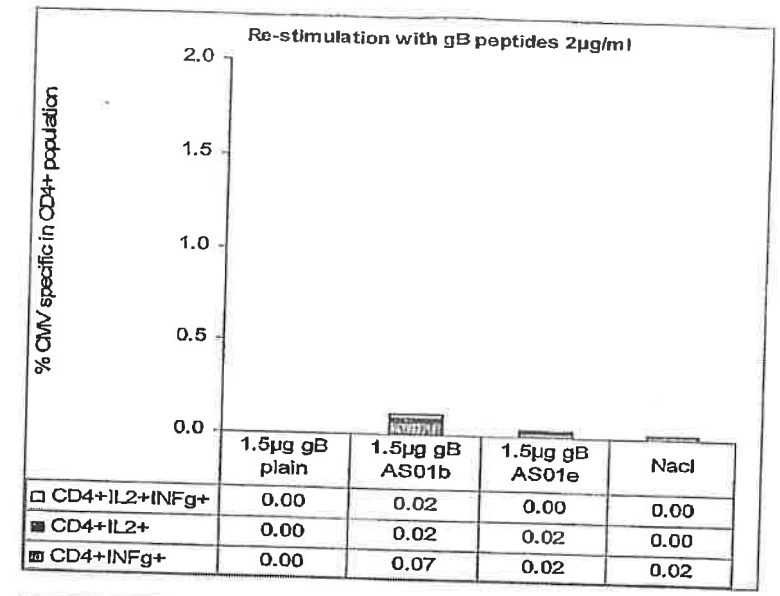
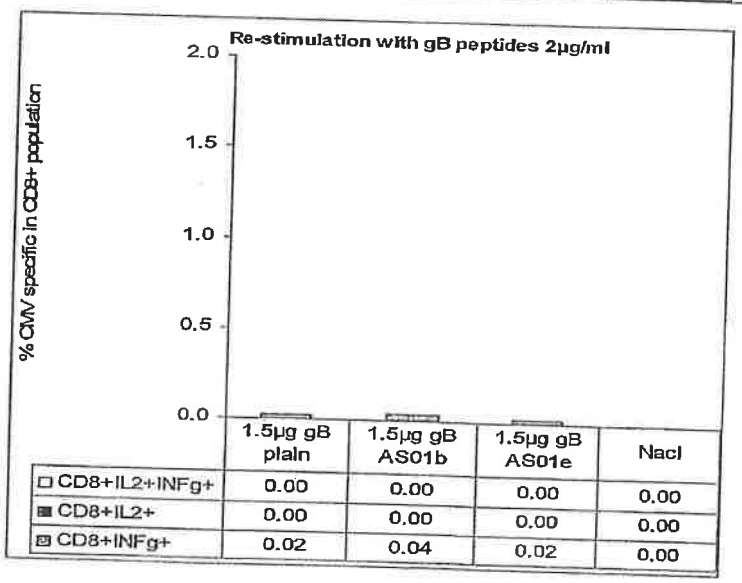


Figure 17:

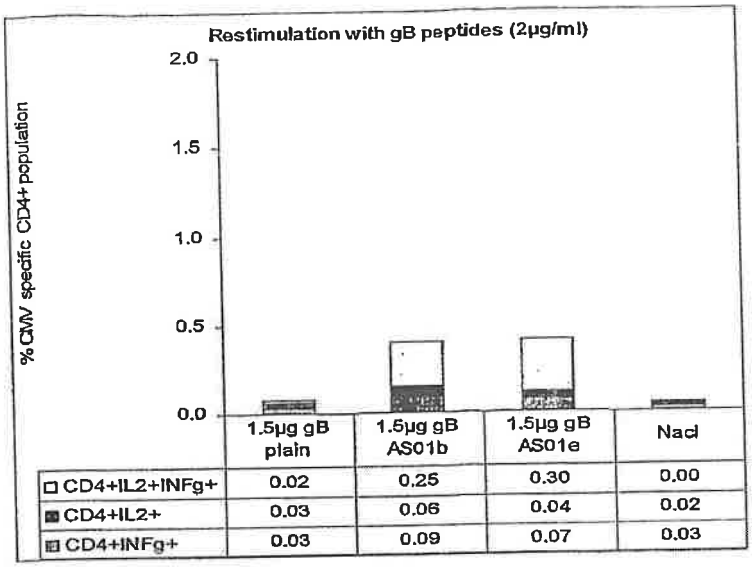


	1.5µg gB plain	1.5µg gB AS01b	1.5µg gB AS01e	Nacl
CD4+IL2+INFg+	0.00	0.02	0.00	0.00
CD4+IL2+	0.00	0.02	0.02	0.00
CD4+INFg+	0.00	0.07	0.02	0.02

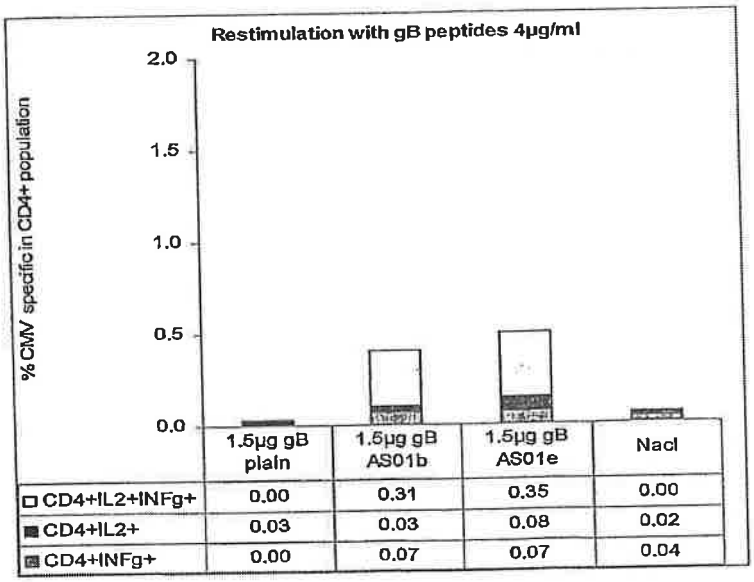


	1.5µg gB plain	1.5µg gB AS01b	1.5µg gB AS01e	Nacl
CD8+IL2+INFg+	0.00	0.00	0.00	0.00
CD8+IL2+	0.00	0.00	0.00	0.00
CD8+INFg+	0.02	0.04	0.02	0.00

Figure 18:

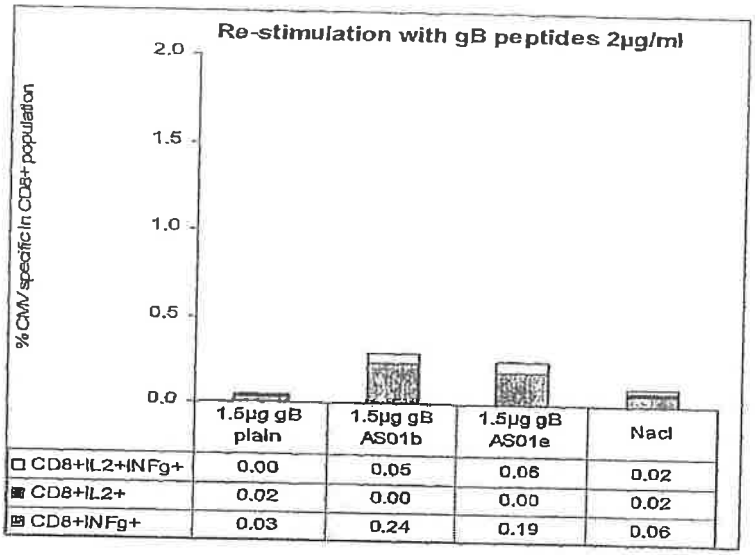


	1.5µg gB plain	1.5µg gB AS01b	1.5µg gB AS01e	Nacl
CD4+IL2+INFg+	0.02	0.25	0.30	0.00
CD4+IL2+	0.03	0.06	0.04	0.02
CD4+INFg+	0.03	0.09	0.07	0.03

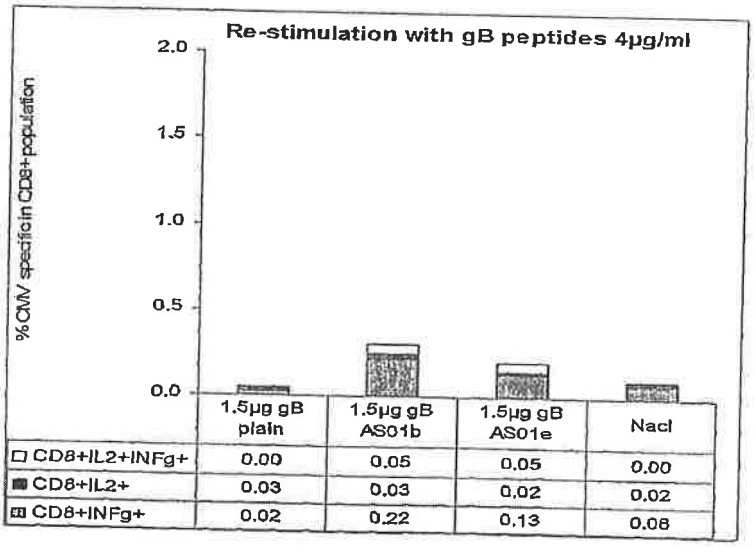


	1.5µg gB plain	1.5µg gB AS01b	1.5µg gB AS01e	Nacl
CD4+IL2+INFg+	0.00	0.31	0.35	0.00
CD4+IL2+	0.03	0.03	0.08	0.02
CD4+INFg+	0.00	0.07	0.07	0.04

Figure 19:



	1.5µg gB plain	1.5µg gB AS01b	1.5µg gB AS01e	Nacl
CD8+IL2+INFg+	0.00	0.05	0.06	0.02
CD8+IL2+	0.02	0.00	0.00	0.02
CD8+INFg+	0.03	0.24	0.19	0.06



	1.5µg gB plain	1.5µg gB AS01b	1.5µg gB AS01e	Nacl
CD8+IL2+INFg+	0.00	0.05	0.05	0.00
CD8+IL2+	0.03	0.03	0.02	0.02
CD8+INFg+	0.02	0.22	0.13	0.08

Figure 20:

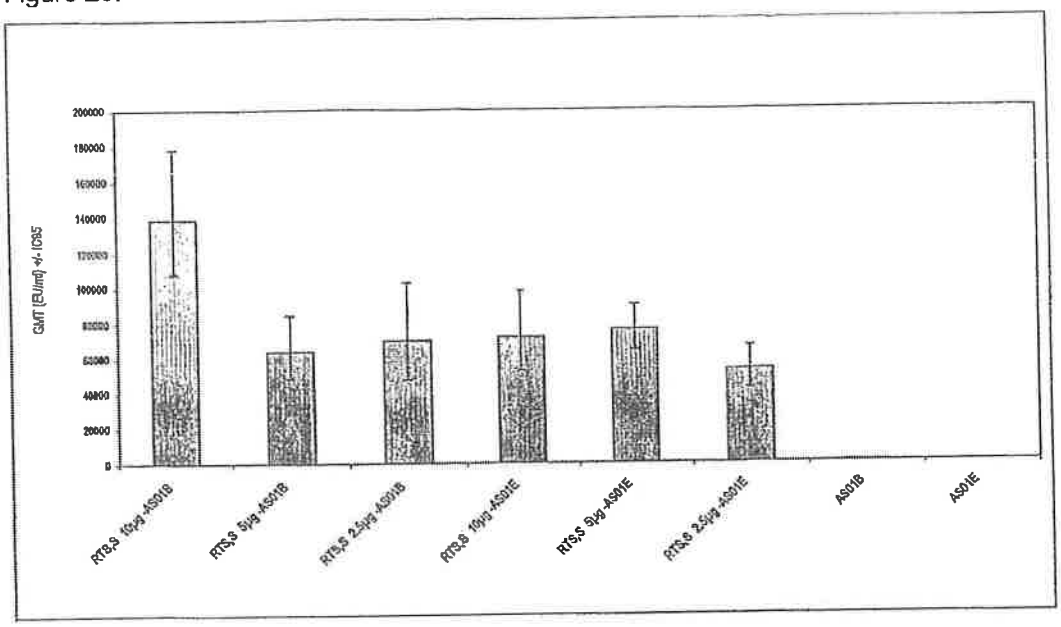


Figure 21:

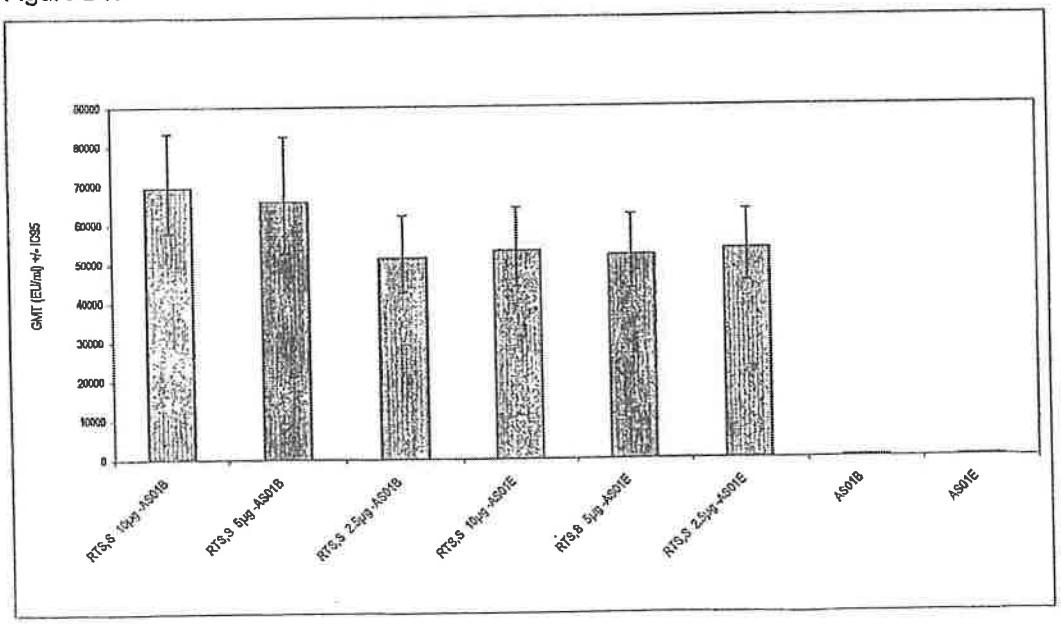
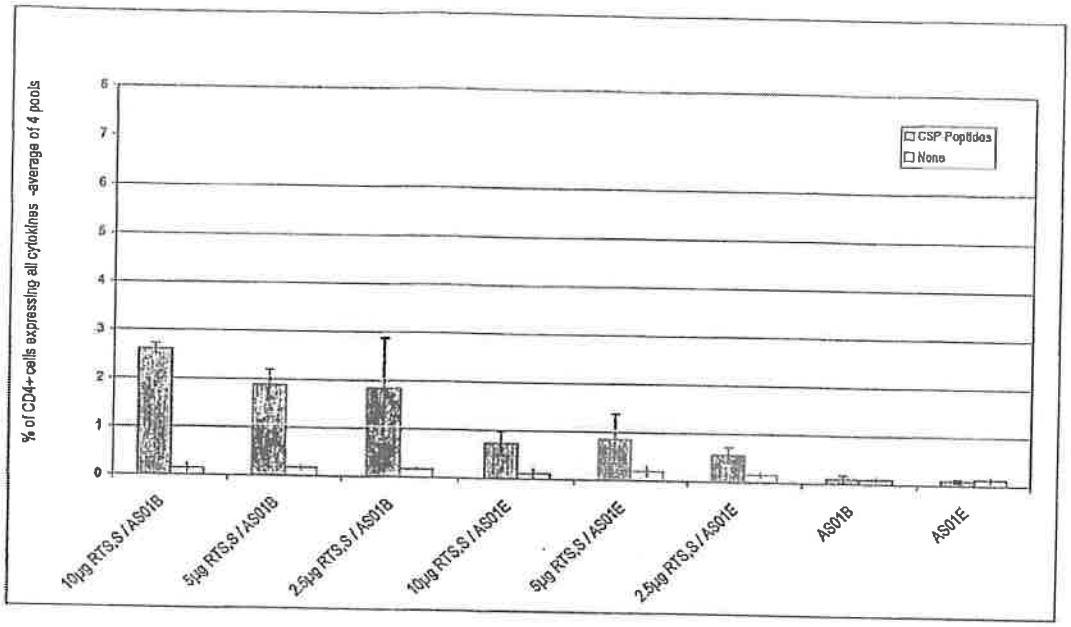


Figure 22:


% of CD4+ cells expressing all cytokines -average of 4 pools
CSP Peptides
None
10µg RTS,S / AS01B
5µg RTS,S / AS01B
2.5µg RTS,S / AS01B
10µg RTS,S / AS01E
5µg RTS,S / AS01E
2.5µg RTS,S / AS01E
AS01B
AS01E

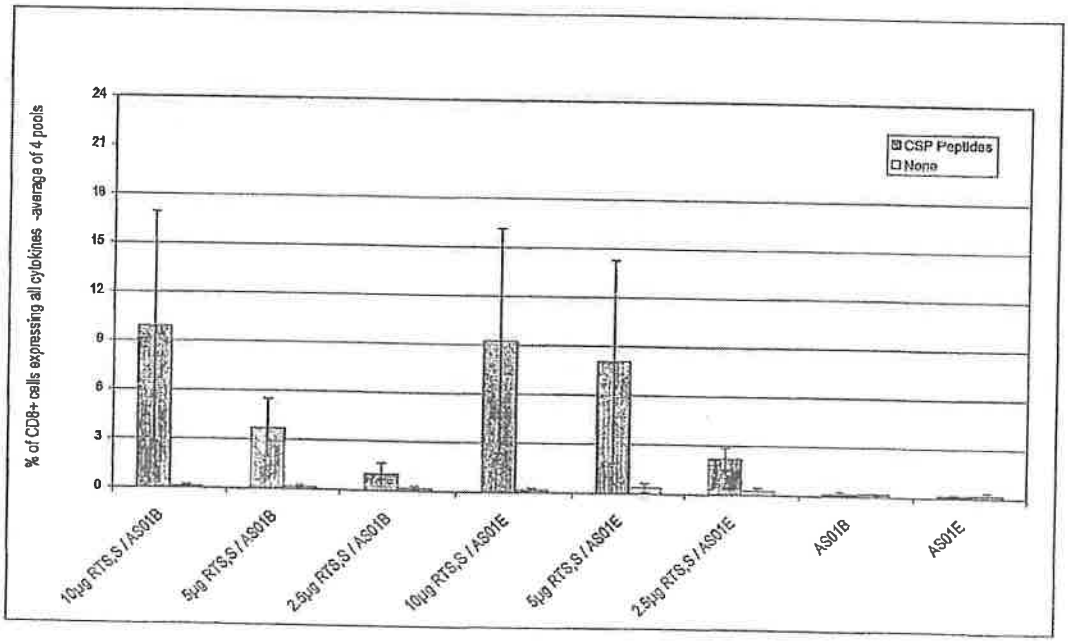
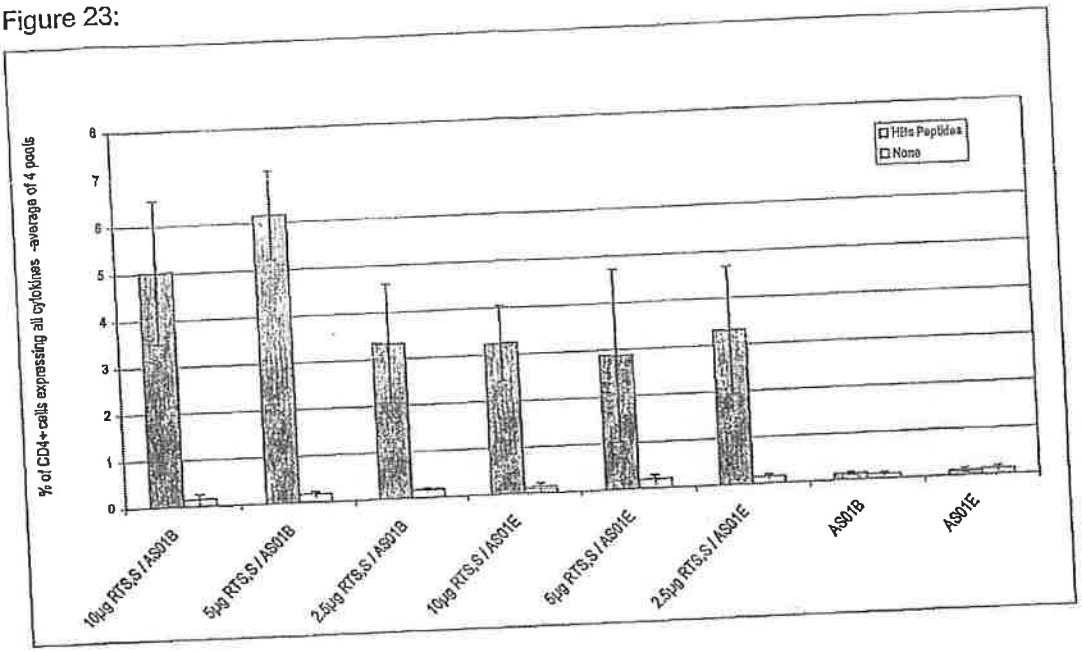

% of CD8+ cells expressing all cytokines -average of 4 pools
CSP Peptides
None
10µg RTS,S / AS01B
5µg RTS,S / AS01B
2.5µg RTS,S / AS01B
10µg RTS,S / AS01E
5µg RTS,S / AS01E
2.5µg RTS,S / AS01E
AS01B
AS01E

Figure 23:


% of CD4+ cells expressing all cytokines -average of 4 pools
HBs Peptides
None
0
1
2
3
4
5
6
7
8
10µg RTS,S / AS01B
5µg RTS,S / AS01B
2.5µg RTS,S / AS01B
10µg RTS,S / AS01E
5µg RTS,S / AS01E
2.5µg RTS,S / AS01E
AS01B
AS01E

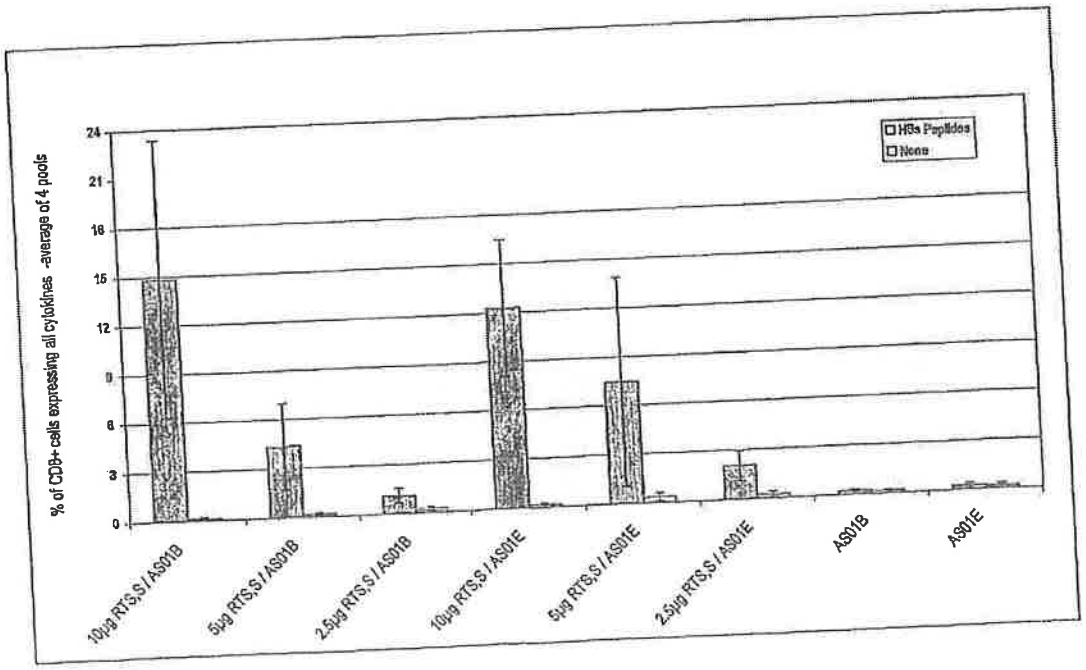
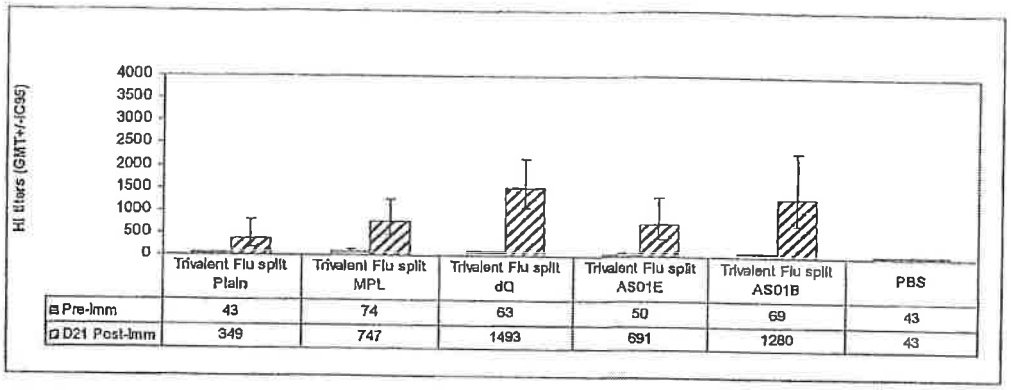
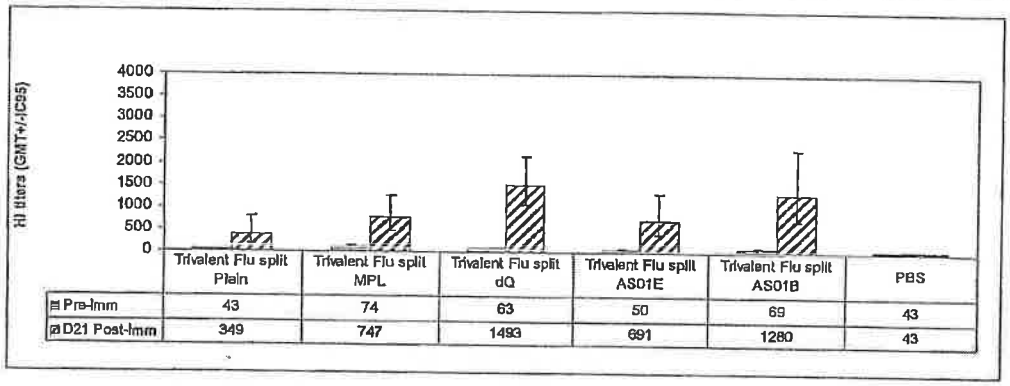

% of CD8+ cells expressing all cytokines -average of 4 pools
HBs Peptides
None
0
3
6
9
12
15
18
21
24
10µg RTS,S / AS01B
5µg RTS,S / AS01B
2.5µg RTS,S / AS01B
10µg RTS,S / AS01E
5µg RTS,S / AS01E
2.5µg RTS,S / AS01E
AS01B
AS01E

Figure 24:


HI titers (GMT+/-IC95)
4000
3500
3000
2500
2000
1500
1000
500
0
Trivalent Flu split Plain
Trivalent Flu split MPL
Trivalent Flu split dQ
Trivalent Flu split AS01E
Trivalent Flu split AS01B
PBS
Pre-Imm 43 74 63 50 69 43
D21 Post-Imm 349 747 1493 691 1280 43


HI titers (GMT+/-IC95)
4000
3500
3000
2500
2000
1500
1000
500
0
Trivalent Flu split Plain
Trivalent Flu split MPL
Trivalent Flu split dQ
Trivalent Flu split AS01E
Trivalent Flu split AS01B
PBS
Pre-Imm 43 74 63 50 69 43
D21 Post-Imm 349 747 1493 691 1280 43

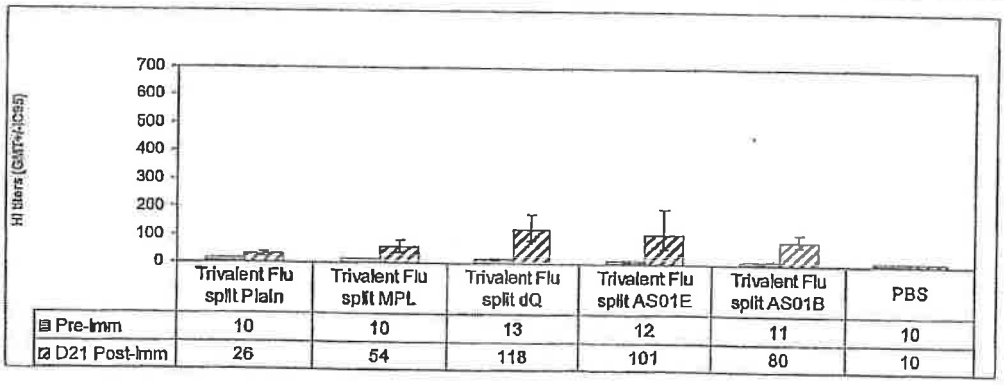
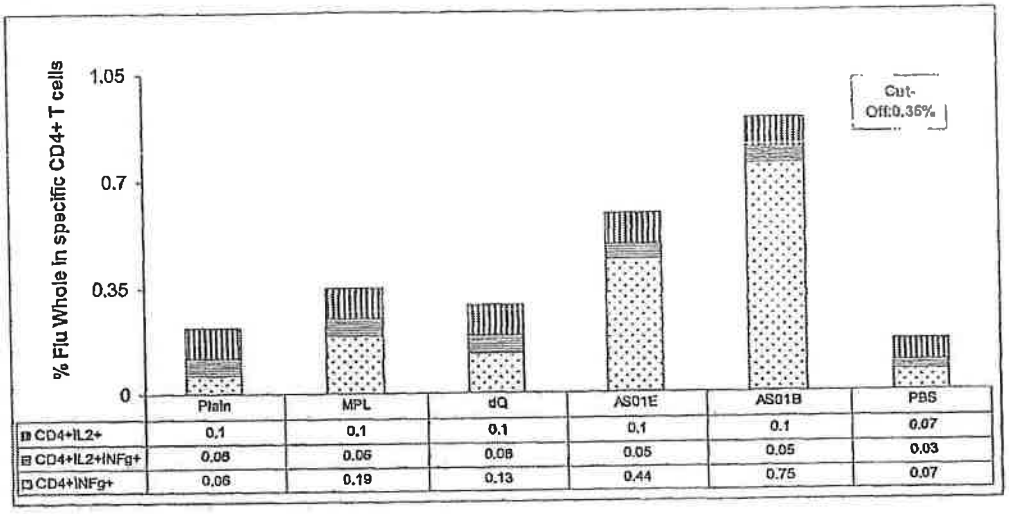
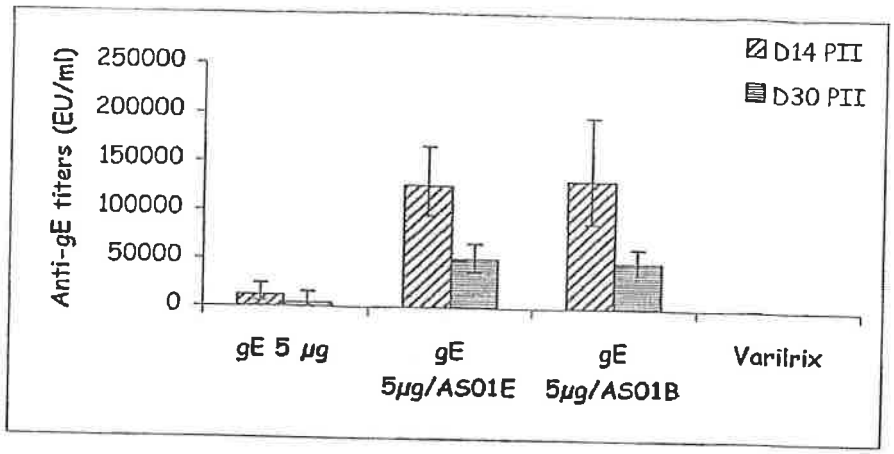

HI titers (GMT+/-IC95)
700
600
500
400
300
200
100
0
Trivalent Flu split Plain
Trivalent Flu split MPL
Trivalent Flu split dQ
Trivalent Flu split AS01E
Trivalent Flu split AS01B
PBS
Pre-Imm 10 10 13 12 11 10
D21 Post-Imm 26 54 118 101 80 10

Figure 25:



	Plain	MPL	dQ	AS01E	AS01B	PBS
CD4+IL2+	0.1	0.1	0.1	0.1	0.1	0.07
CD4+IL2+INFg+	0.08	0.06	0.08	0.05	0.05	0.03
CD4+INFg+	0.06	0.19	0.13	0.44	0.75	0.07

Figure 26:


Anti-gE titers (EU/ml)
250000
200000
150000
100000
50000
0
D14 PII
D30 PII
gE 5 µg
gE 5µg/AS01E
gE 5µg/AS01B
Varilrix

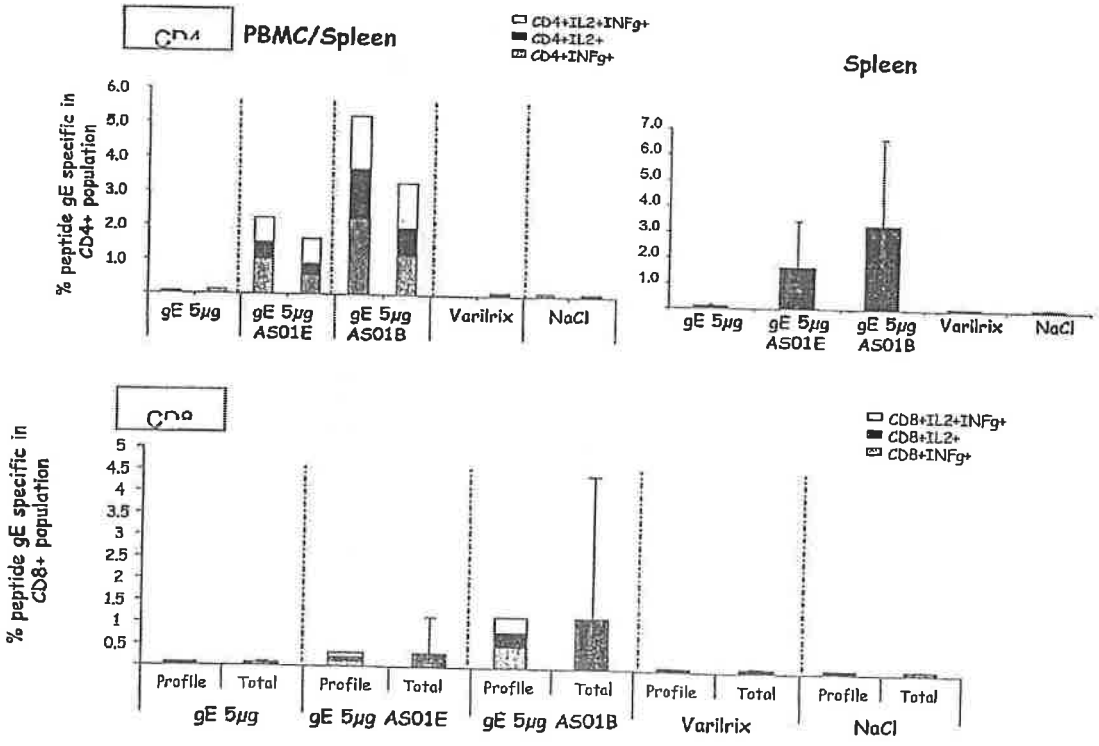

CD4
PBMC/Spleen
CD4+IL2+INFg+
CD4+IL2+
CD4+INFg+
% peptide gE specific in CD4+ population
gE 5µg
gE 5µg AS01E
gE 5µg AS01B
Varilrix
NaCl
Spleen
CD8
CD8+IL2+INFg+
CD8+IL2+
CD8+INFg+
% peptide gE specific in CD8+ population
Profile
Total
gE 5µg
gE 5µg AS01E
gE 5µg AS01B
Varilrix
NaCl

Figure 27

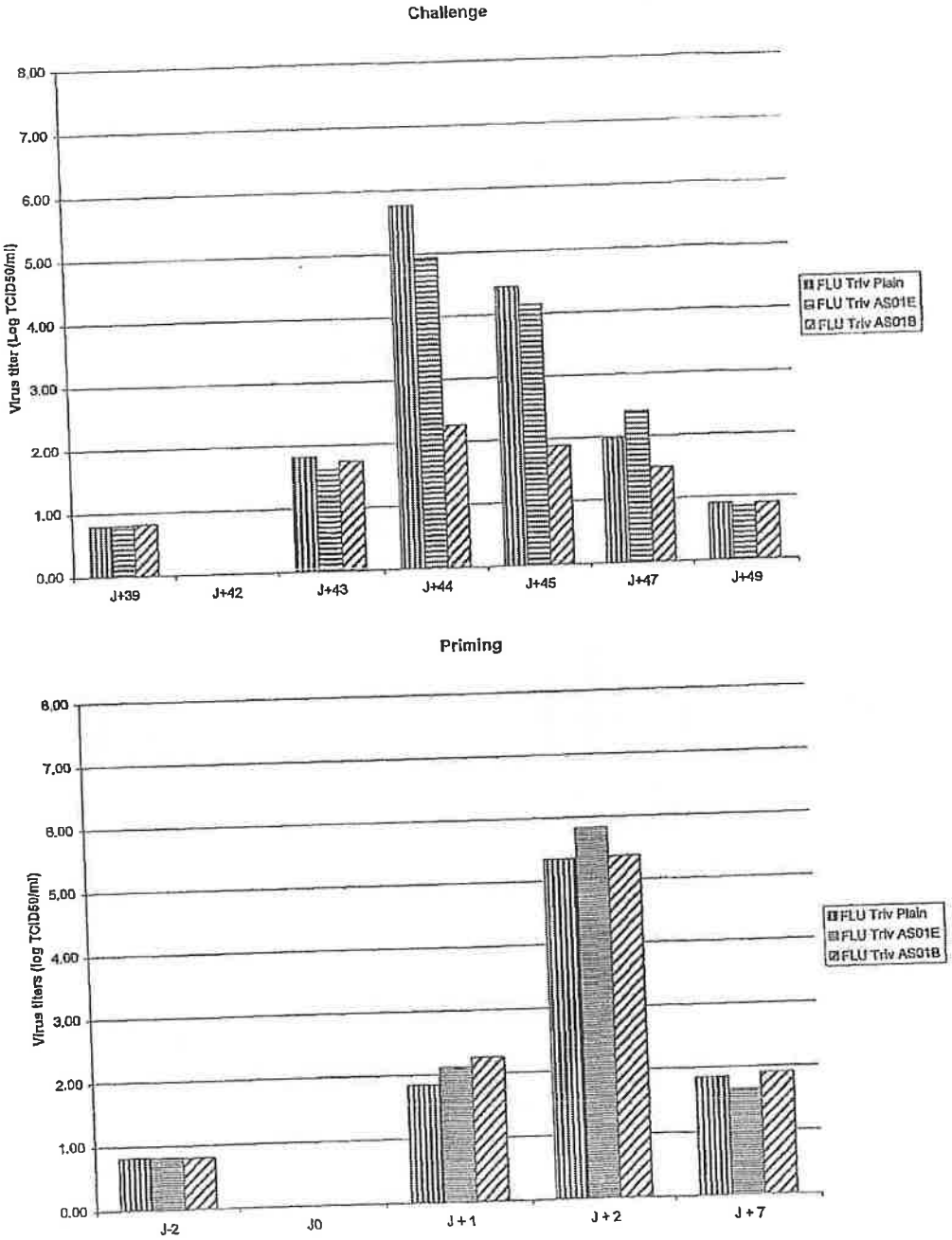
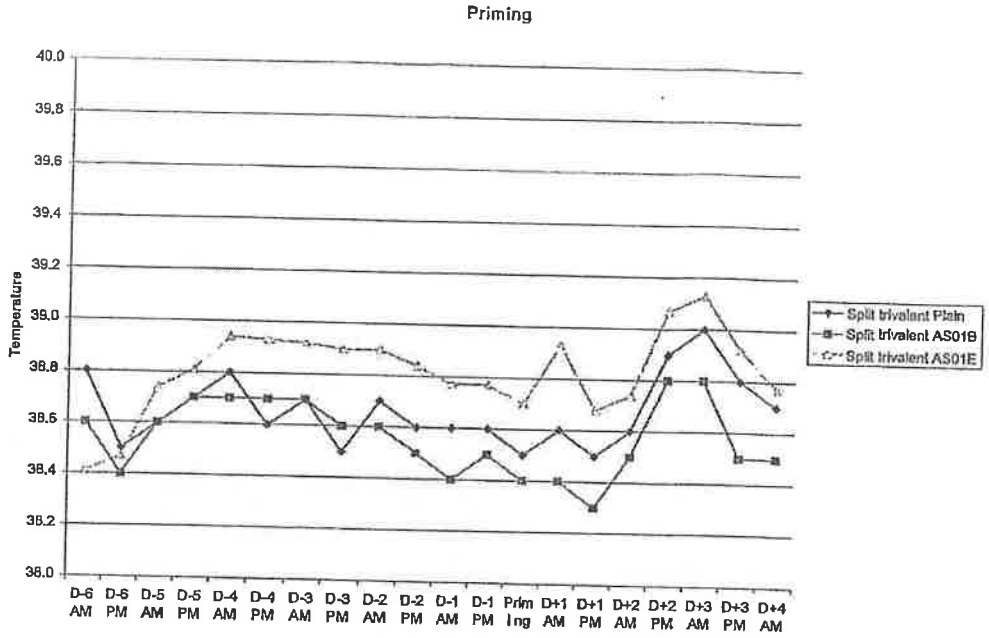

Challenge
Virus titer (Log TCID50/ml)
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
J+39
J+42
J+43
J+44
J+45
J+47
J+49
FLU Triv Plain
FLU Triv AS01E
FLU Triv AS01B
Priming
Virus titers (log TCID50/ml)
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
J-2
J0
J+1
J+2
J+7
FLU Triv Plain
FLU Triv AS01E
FLU Triv AS01B

Figure 28:


Priming
Temperature
40.0
39.8
39.6
39.4
39.2
39.0
38.8
38.6
38.4
38.2
38.0
D-6 AM
D-6 PM
D-5 AM
D-5 PM
D-4 AM
D-4 PM
D-3 AM
D-3 PM
D-2 AM
D-2 PM
D-1 AM
D-1 PM
Prim ing
D+1 AM
D+1 PM
D+2 AM
D+2 PM
D+3 AM
D+3 PM
D+4 AM
Split trivalent Plain
Split trivalent AS01B
Split trivalent AS01E

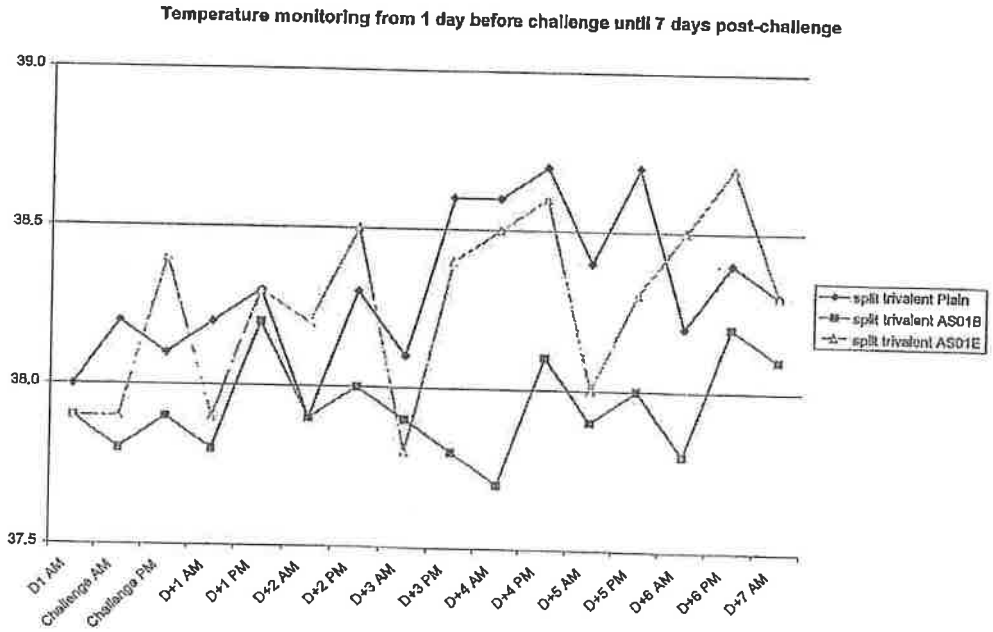
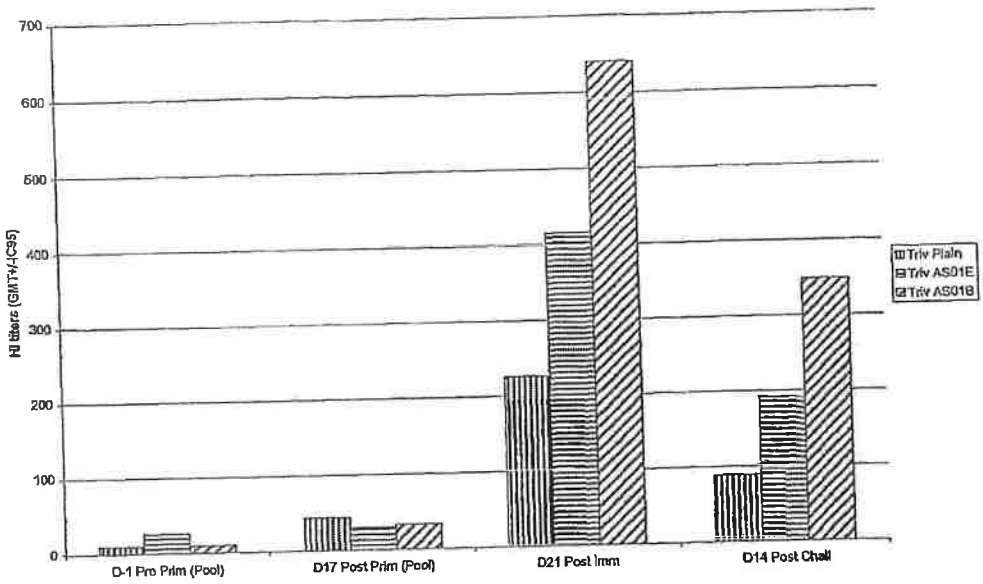

Temperature monitoring from 1 day before challenge until 7 days post-challenge
39.0
38.5
38.0
37.5
D1 AM
Challenge AM
Challenge PM
D+1 AM
D+1 PM
D+2 AM
D+2 PM
D+3 AM
D+3 PM
D+4 AM
D+4 PM
D+5 AM
D+5 PM
D+6 AM
D+6 PM
D+7 AM
split trivalent Plain
split trivalent AS01B
split trivalent AS01E

Figure 29:

Anti-A/New Caledonia/20/99 H1N1 - H1 titers



Anti-A/Wyoming/3/2003 H3N2 - H1 titers

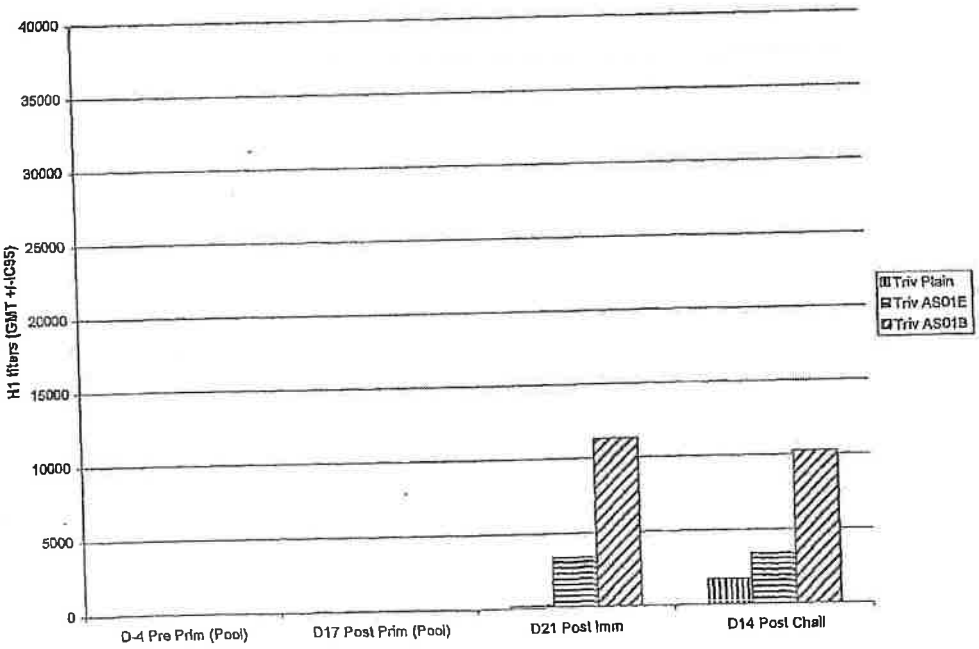
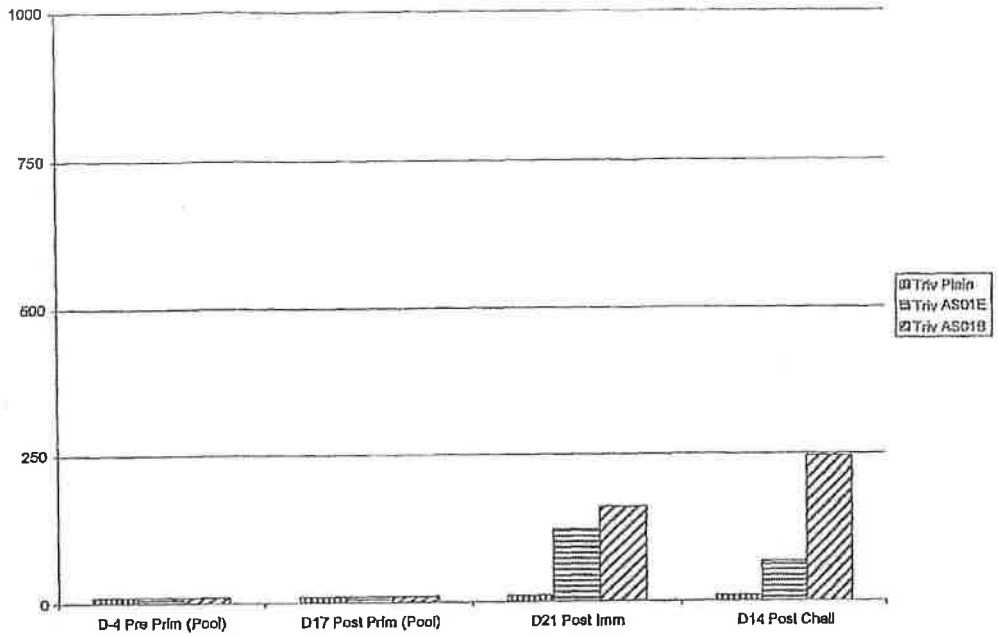


Figure 30:

Anti-B/Jiangsu/10/2003 - H1 titers



Anti-A/New York/55/2004 H3N2 H titers

