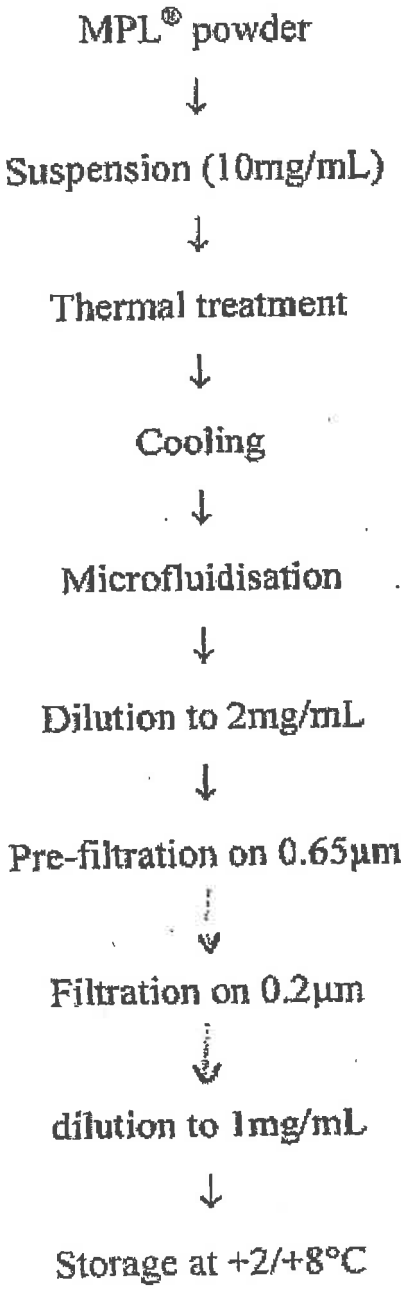
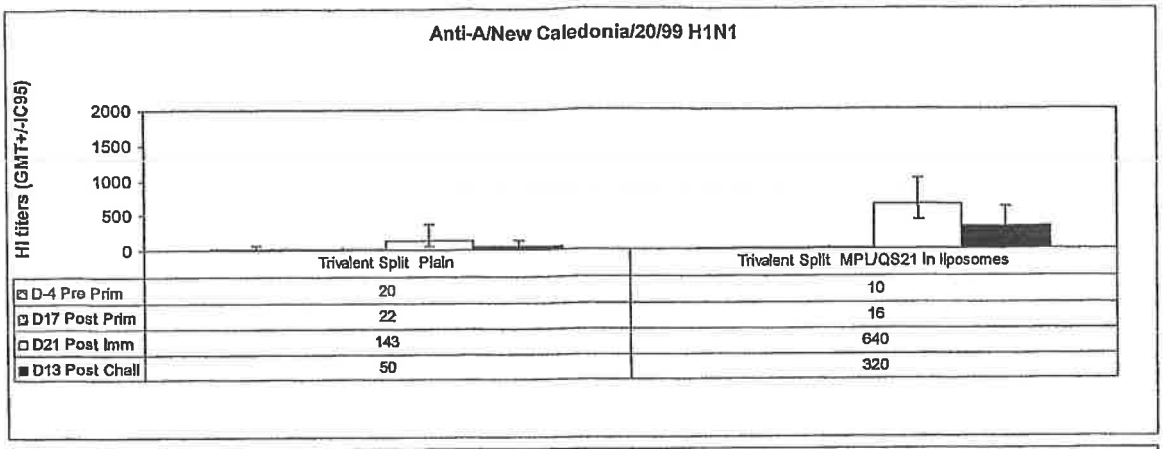
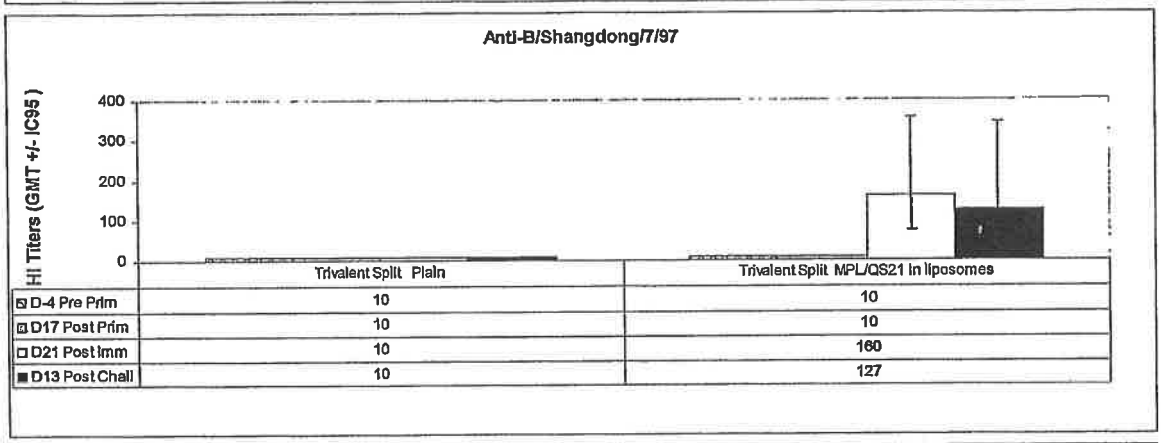
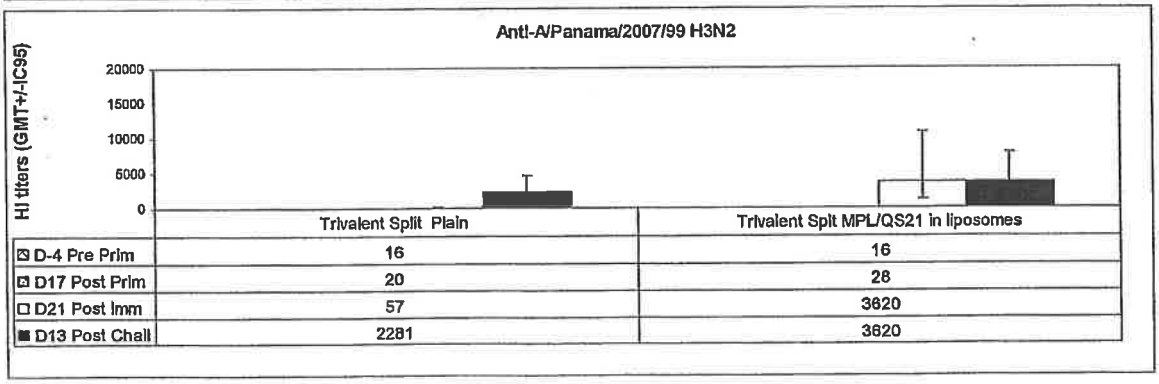
Figure 1

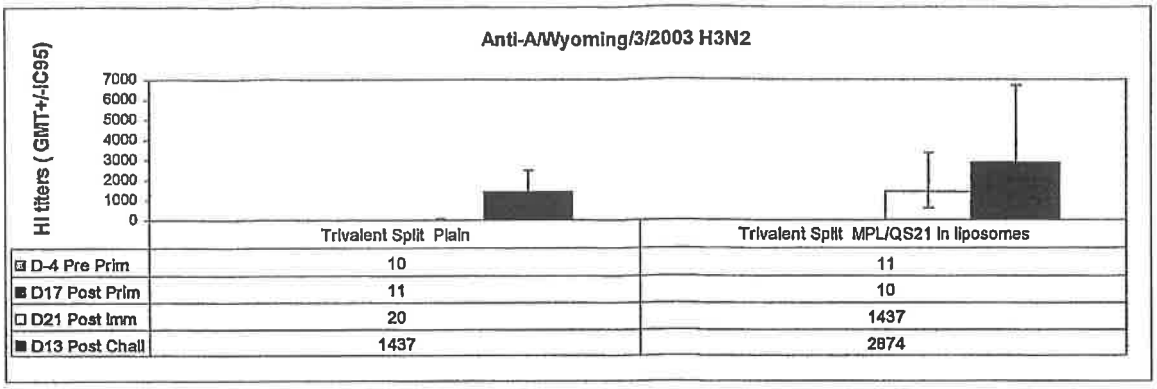

MPL® powder
Suspension (10mg/mL)
Thermal treatment
Cooling
Microfluidisation
Dilution to 2mg/mL
Pre-filtration on 0.65µm
Filtration on 0.2µm
dilution to 1mg/mL
Storage at +2/+8°C

## 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

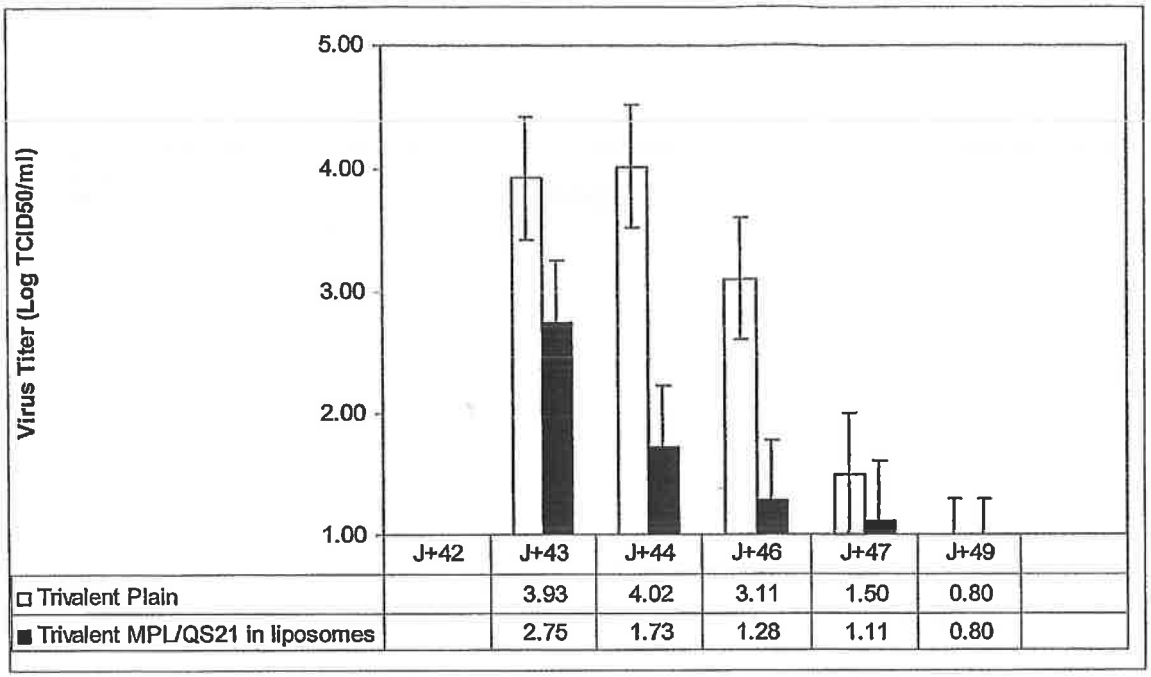

Anti-B/Shangdong/7/97
HI Titers (GMT +/- IC95 )
400
300
200
100
0
Trivalent Split Plain
Trivalent Split MPL/QS21 in liposomes
D-4 Pre Prim 10 10
D17 Post Prim 10 10
D21 Post Imm 10 160
D13 Post Chall 10 127


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 3620
D13 Post Chall 2281 3620



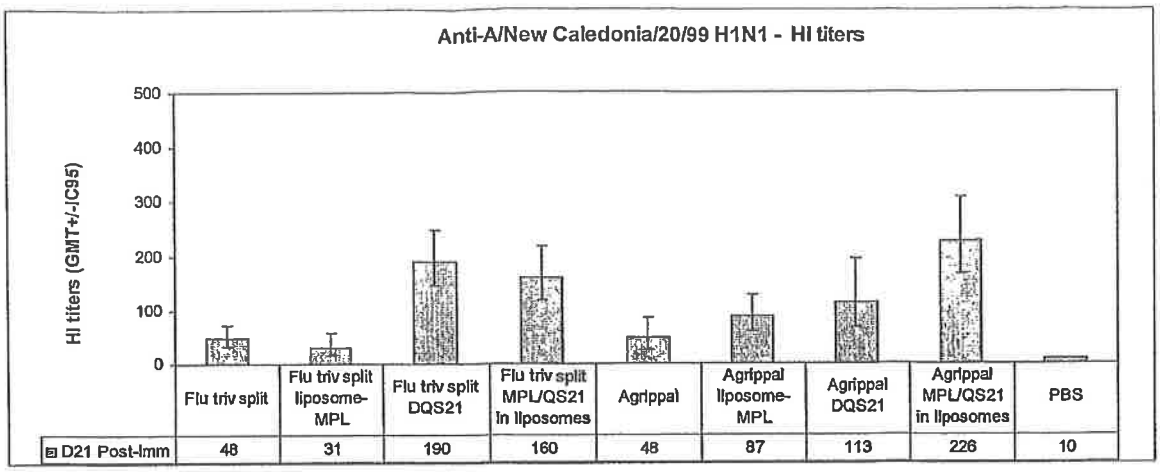

| | Trivalent Split Plain | Trivalent Split MPL/QS21 In liposomes |
|---|---|---|
| D-4 Pre Prim | 10 | 11 |
| D17 Post Prim | 11 | 10 |
| D21 Post Imm | 20 | 1437 |
| D13 Post Chall | 1437 | 2874 |

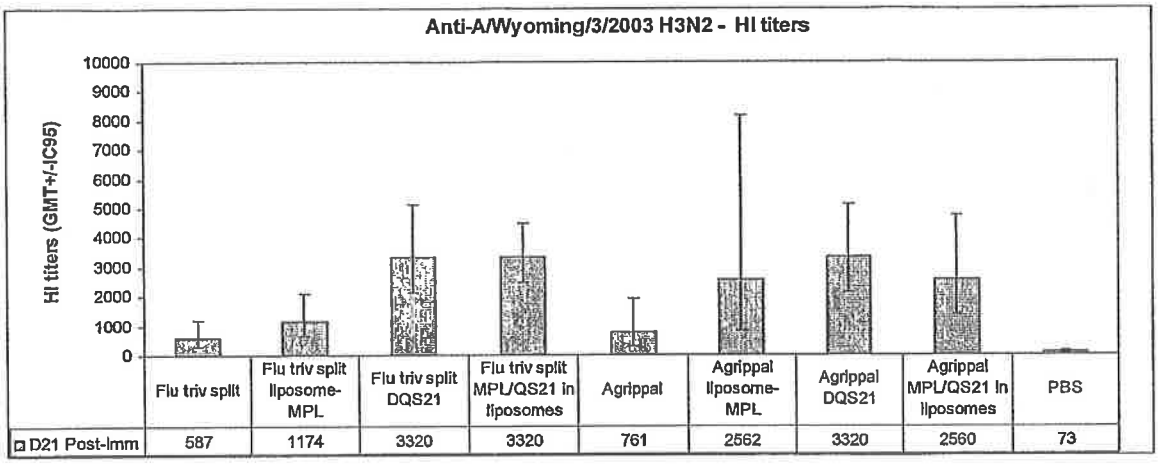
**Figure 3**




| | 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

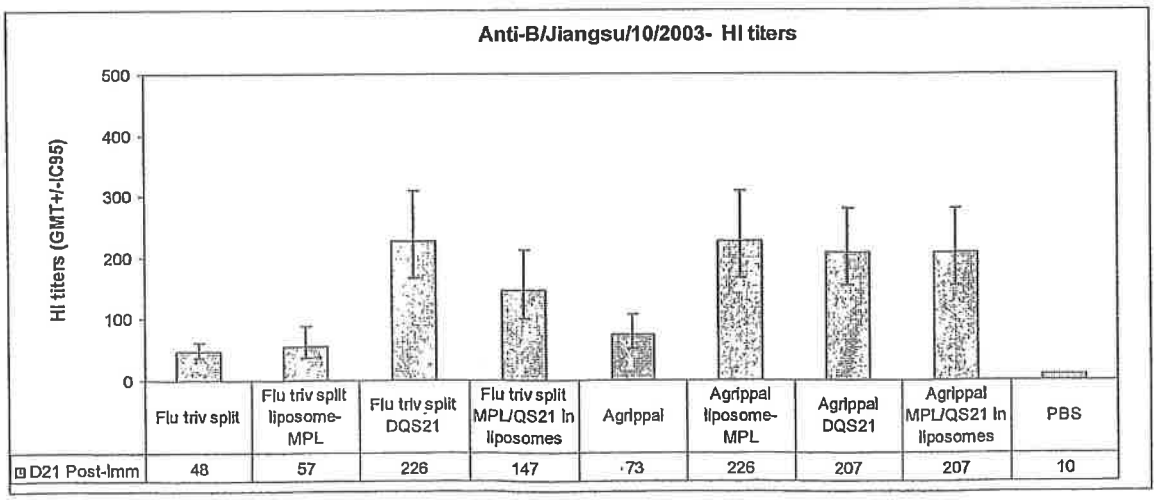
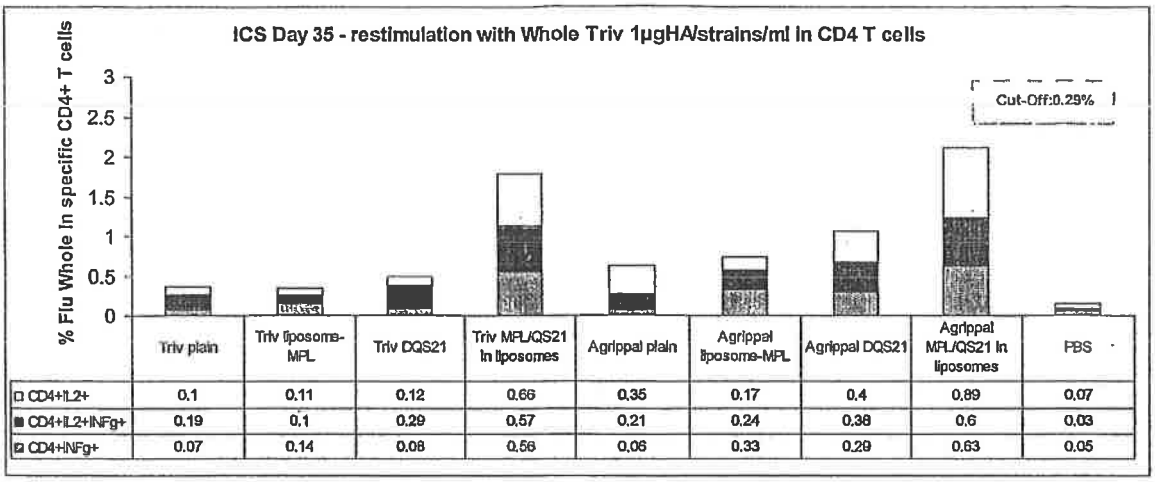

Anti-B/Jiangsu/10/2003- HI titers
HI titers (GMT+/-IC95)
500
400
300
200
100
0
Flu triv split
Flu triv split liposome-MPL
Flu triv split DQS21
Flu triv split MPL/QS21 in liposomes
Agrippal
Agrippal liposome-MPL
Agrippal DQS21
Agrippal MPL/QS21 in liposomes
PBS
D21 Post-Imm
48
57
226
147
73
226
207
207
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 0.57 0.21 0.24 0.38 0.6 0.03
CD4+INFg+ 0.07 0.14 0.08 0.56 0.06 0.33 0.29 0.63 0.05

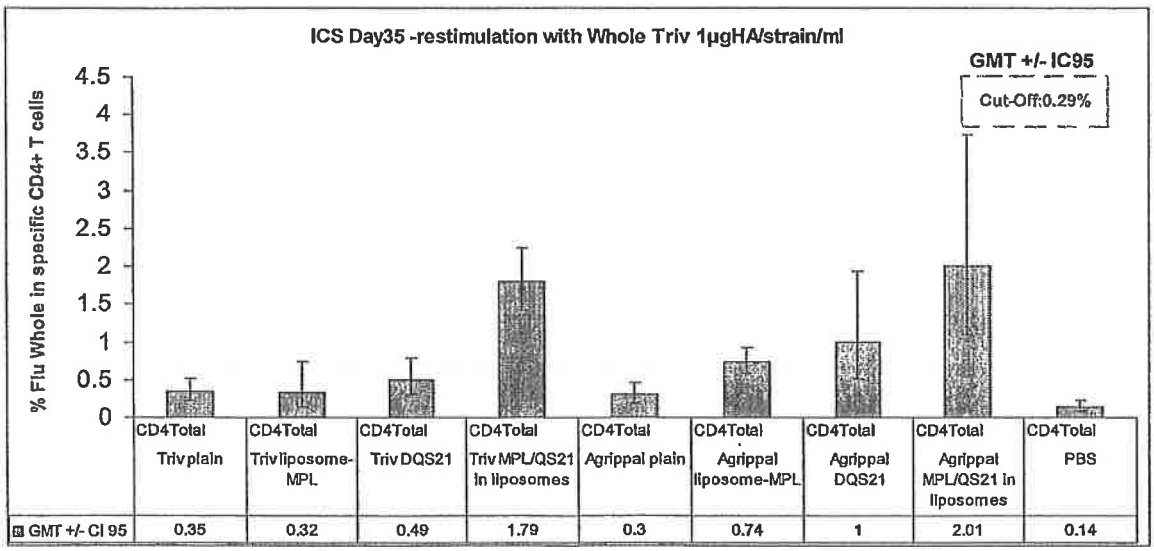

ICS Day35 -restimulation with Whole Triv 1µgHA/strain/ml
GMT +/- IC95
Cut-Off:0.29%
% Flu Whole in specific CD4+ T cells
CD4Total Triv plain
CD4Total Triv liposome-MPL
CD4Total Triv DQS21
CD4Total Triv MPL/QS21 in liposomes
CD4Total Agrippal plain
CD4Total Agrippal liposome-MPL
CD4Total Agrippal DQS21
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

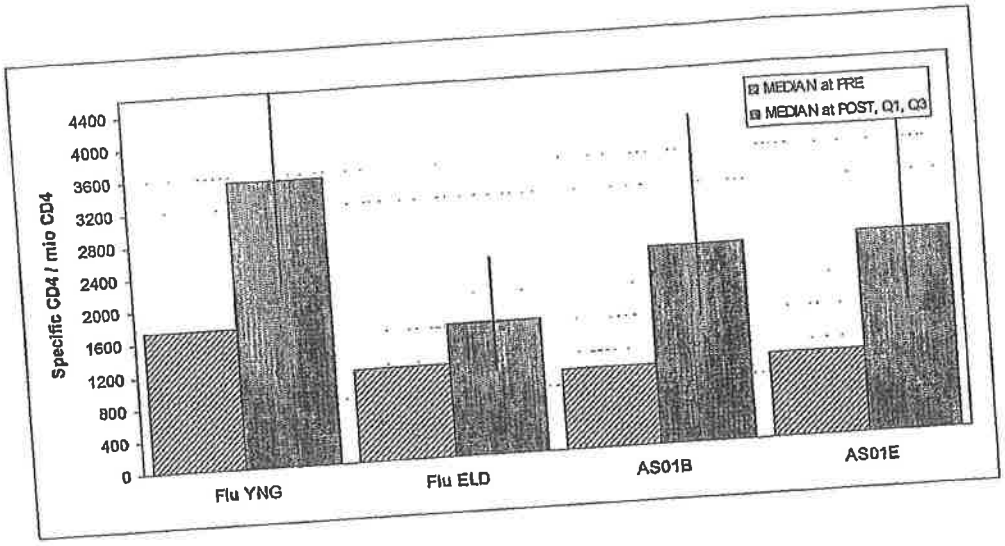



Figure 7

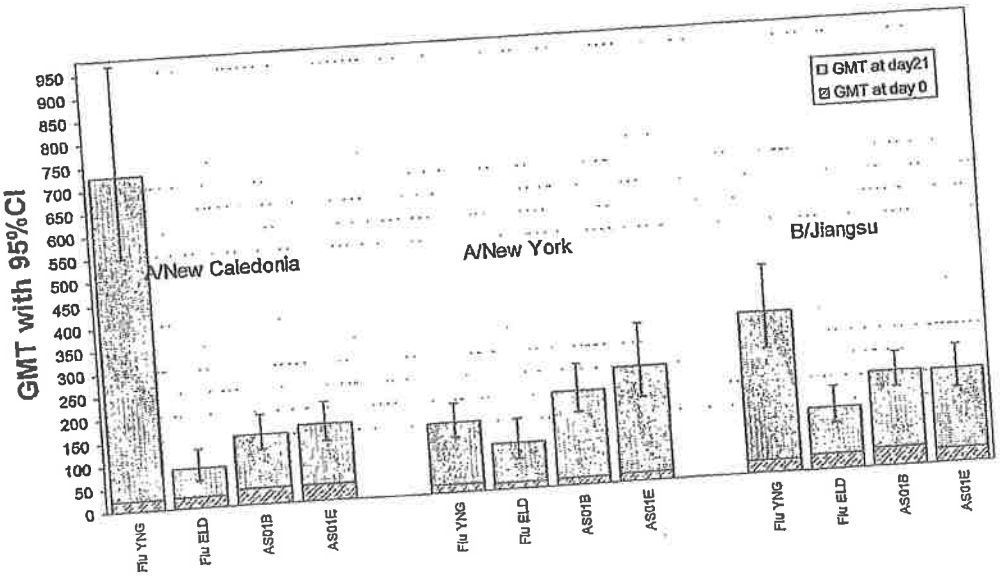


**Figure 8**

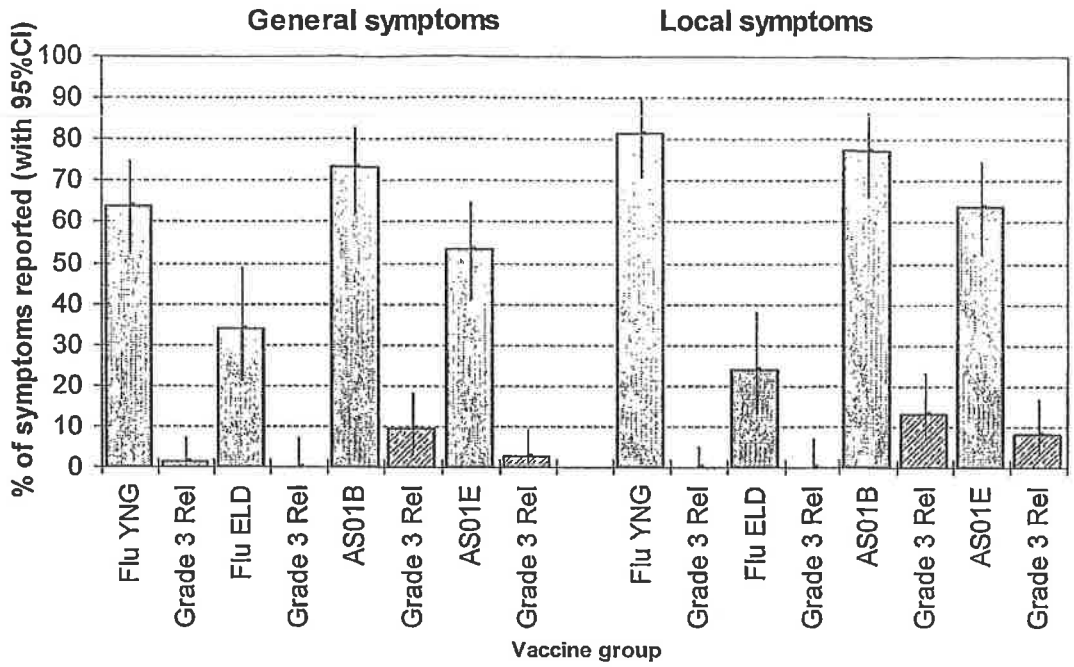

General symptoms
Local symptoms
% of symptoms reported (with 95%CI)
100
90
80
70
60
50
40
30
20
10
0
Flu YNG
Grade 3 Rel
Flu ELD
Grade 3 Rel
AS01B
Grade 3 Rel
AS01E
Grade 3 Rel
Flu YNG
Grade 3 Rel
Flu ELD
Grade 3 Rel
AS01B
Grade 3 Rel
AS01E
Grade 3 Rel
Vaccine group

Figure 9:

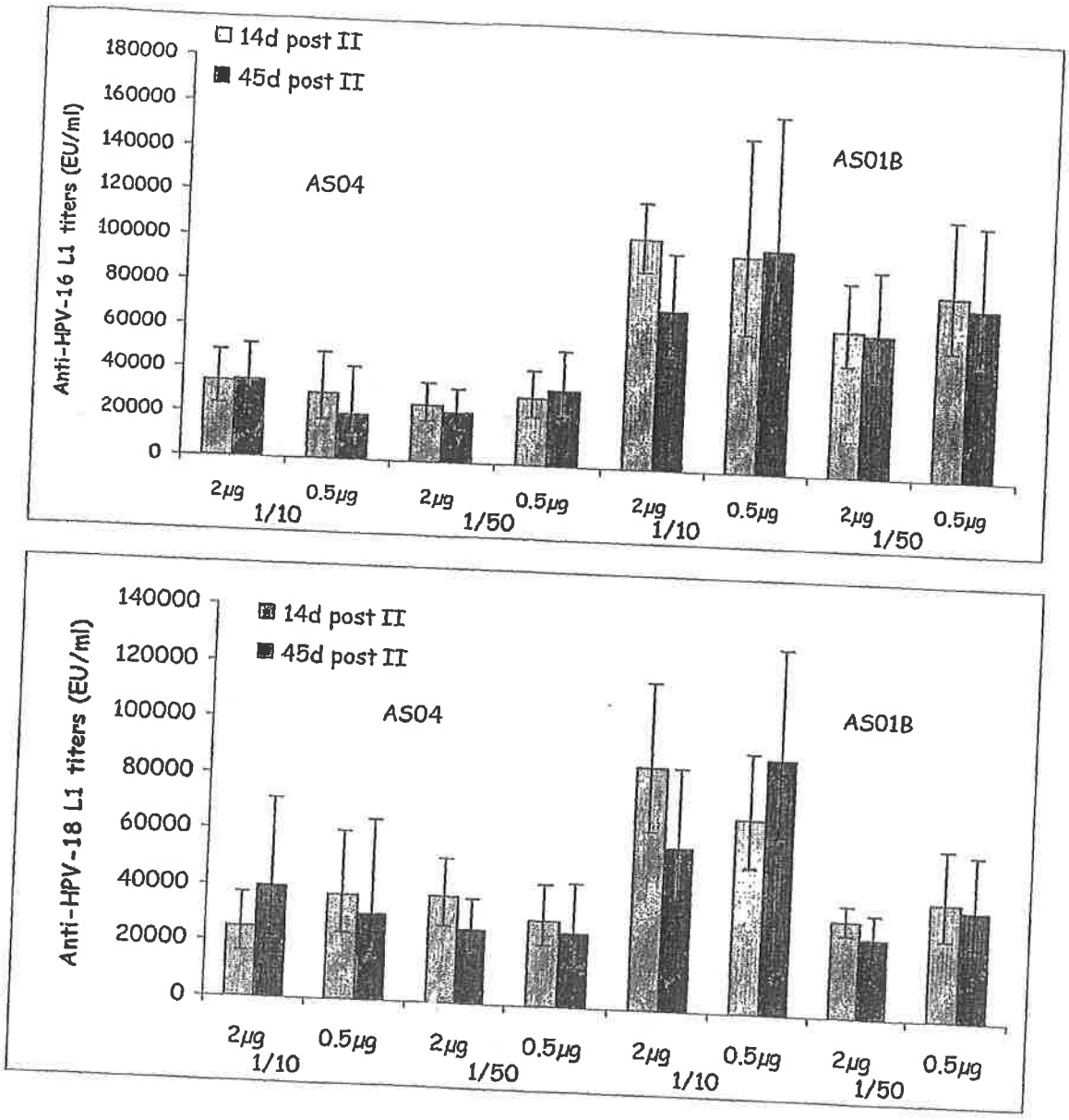
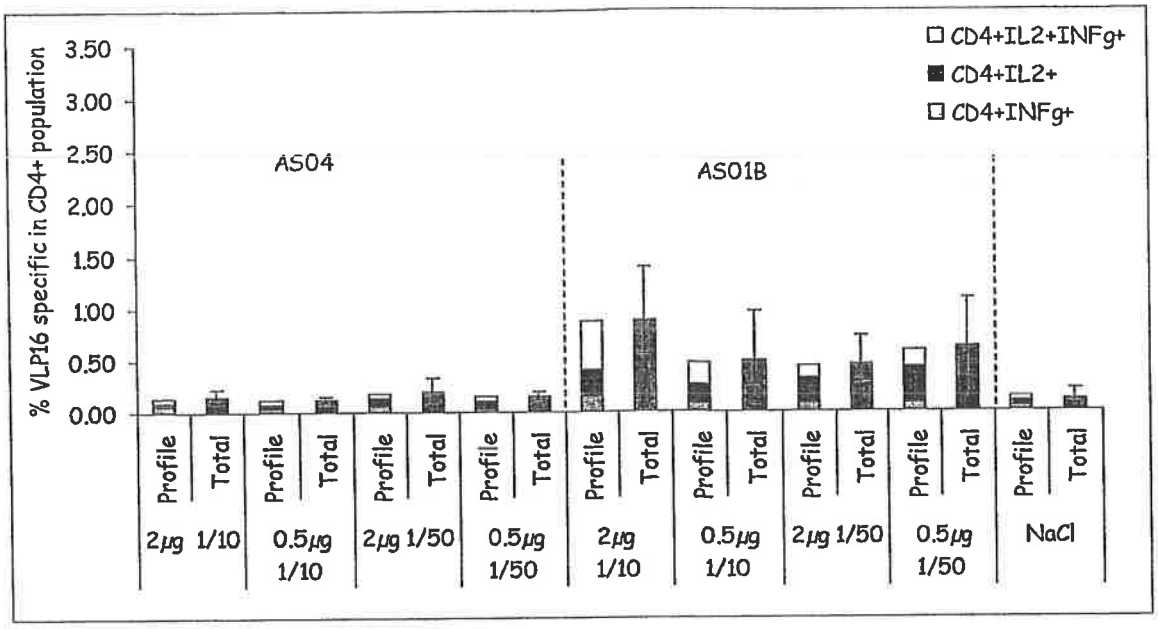

14d post II
45d post II
Anti-HPV-16 L1 titers (EU/ml)
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
AS04
AS01B
2µg
0.5µg
1/10
1/50
Anti-HPV-18 L1 titers (EU/ml)
140000
120000
100000
80000
60000
40000
20000
0

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

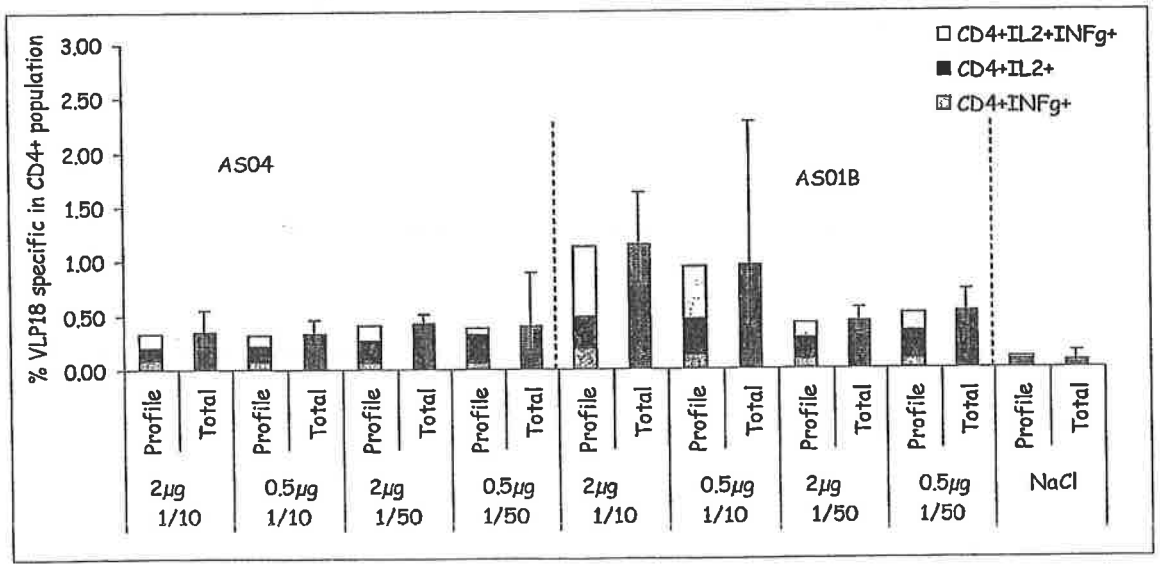
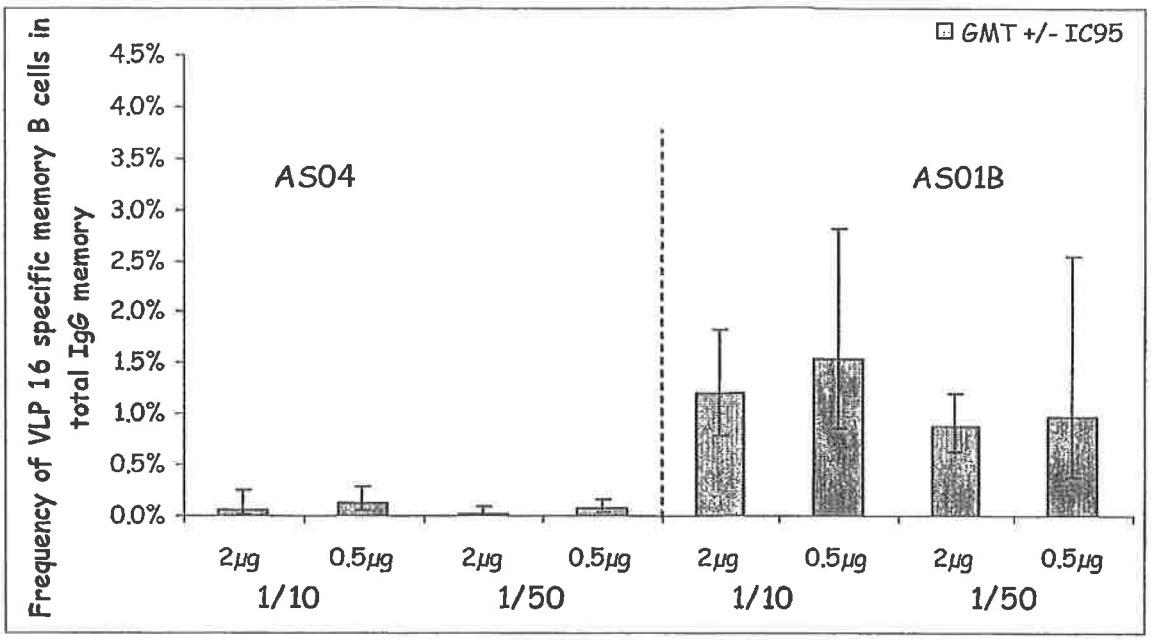

% VLP18 specific in CD4+ population
3.00
2.50
2.00
1.50
1.00
0.50
0.00
CD4+IL2+INFg+
CD4+IL2+
CD4+INFg+
AS04
AS01B
Profile
Total
2µg 1/10
0.5µg 1/10
2µg 1/50
0.5µg 1/50
2µg 1/10
0.5µg 1/10
2µg 1/50
0.5µg 1/50
NaCl

Figure 11:


GMT +/- IC95
Frequency of VLP 16 specific memory B cells in total IgG memory
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

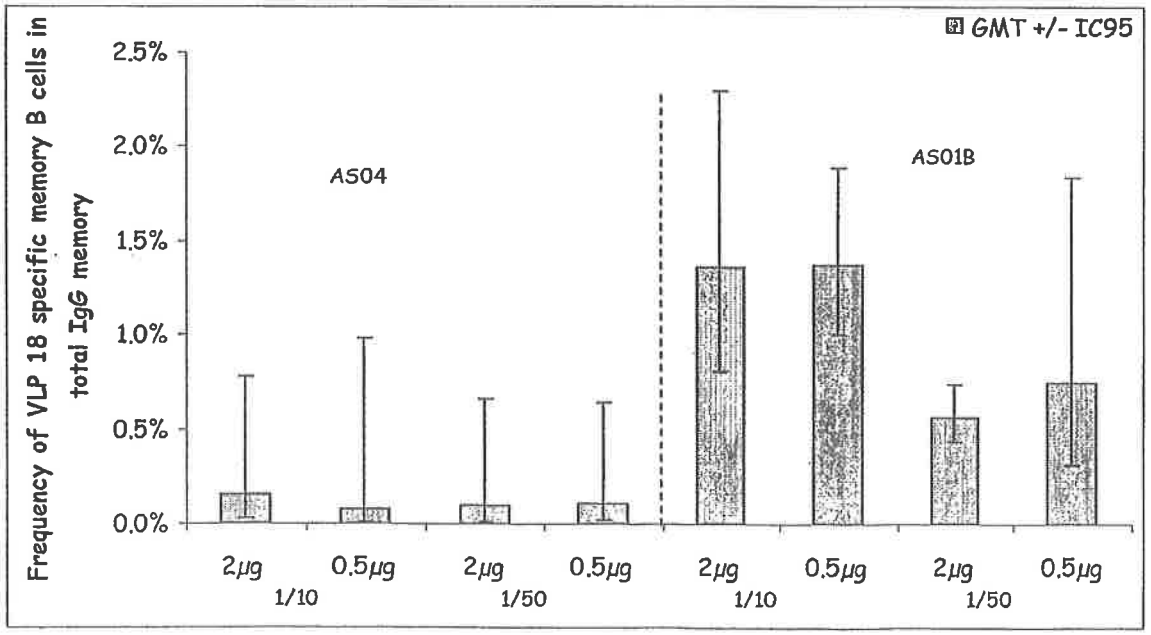

GMT +/- IC95
Frequency of VLP 18 specific memory B cells in total IgG memory
2.5%
2.0%
1.5%
1.0%
0.5%
0.0%
AS04
AS01B
2µg
0.5µg
2µg
0.5µg
2µg
0.5µg
2µg
0.5µg
1/10
1/50
1/10
1/50

Figure12 :

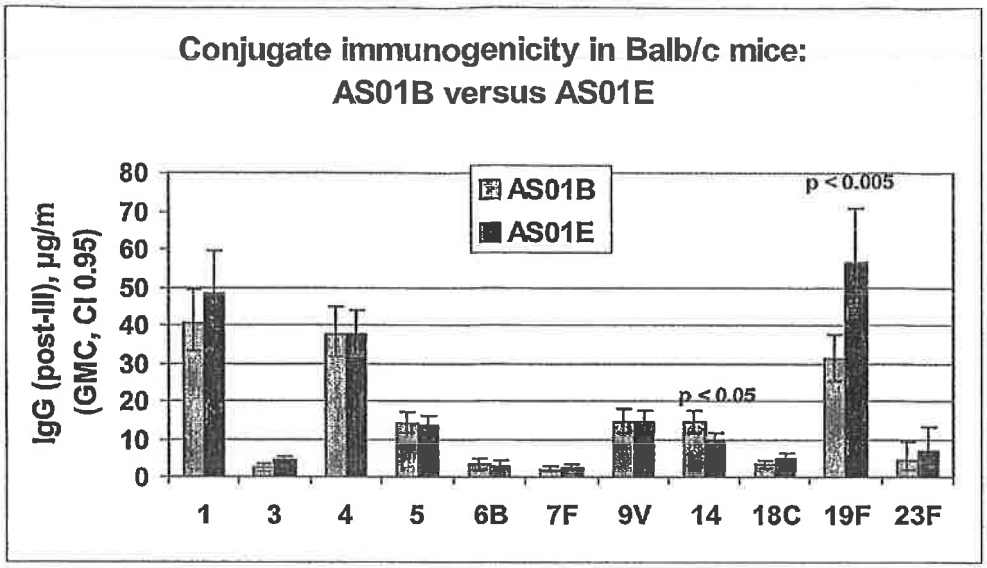

Conjugate immunogenicity in Balb/c mice:
AS01B versus AS01E
IgG (post-III), µg/m
(GMC, CI 0.95)
AS01B
AS01E
p < 0.005
p < 0.05
80
70
60
50
40
30
20
10
0
1
3
4
5
6B
7F
9V
14
18C
19F
23F

Figure 13:

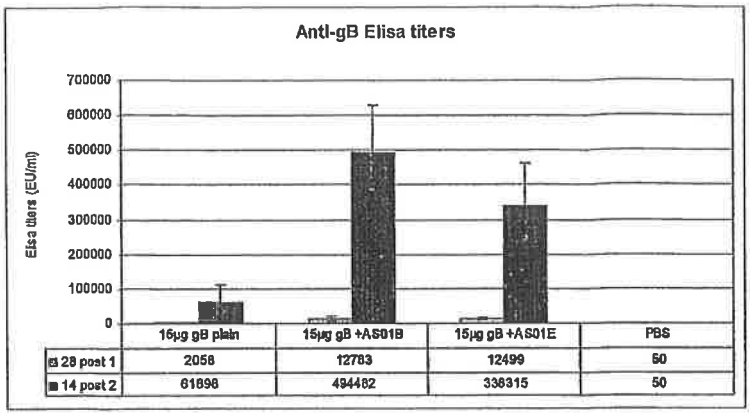



Figure 14:

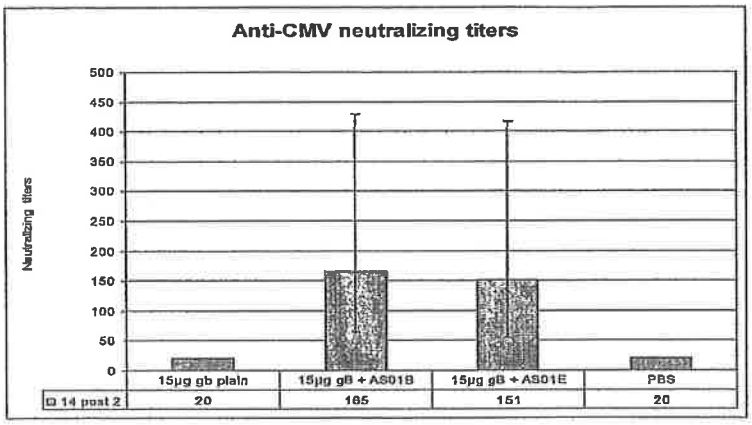


Figure 15:

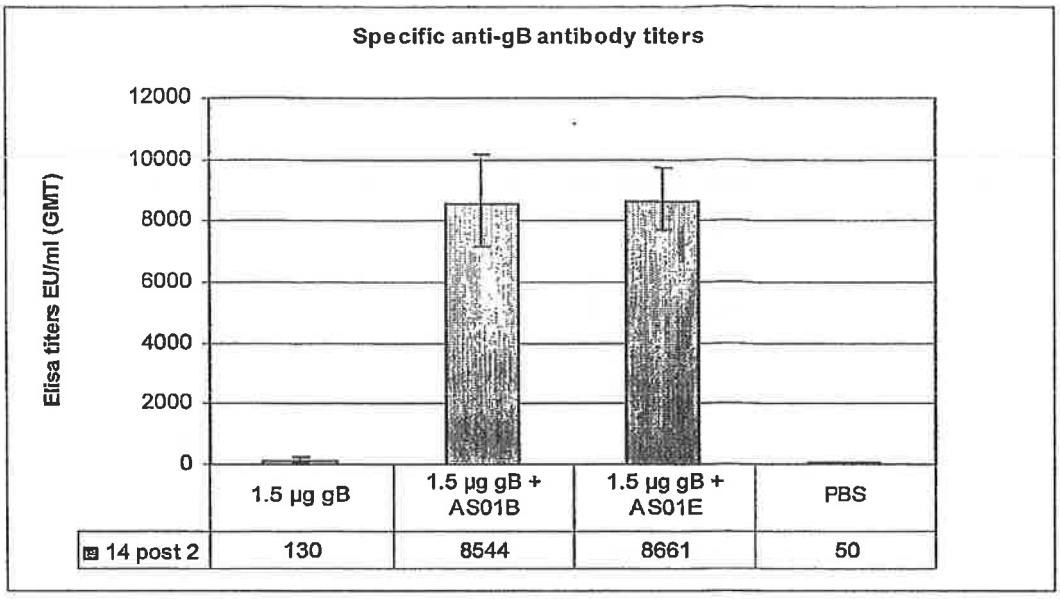



Figure 16:

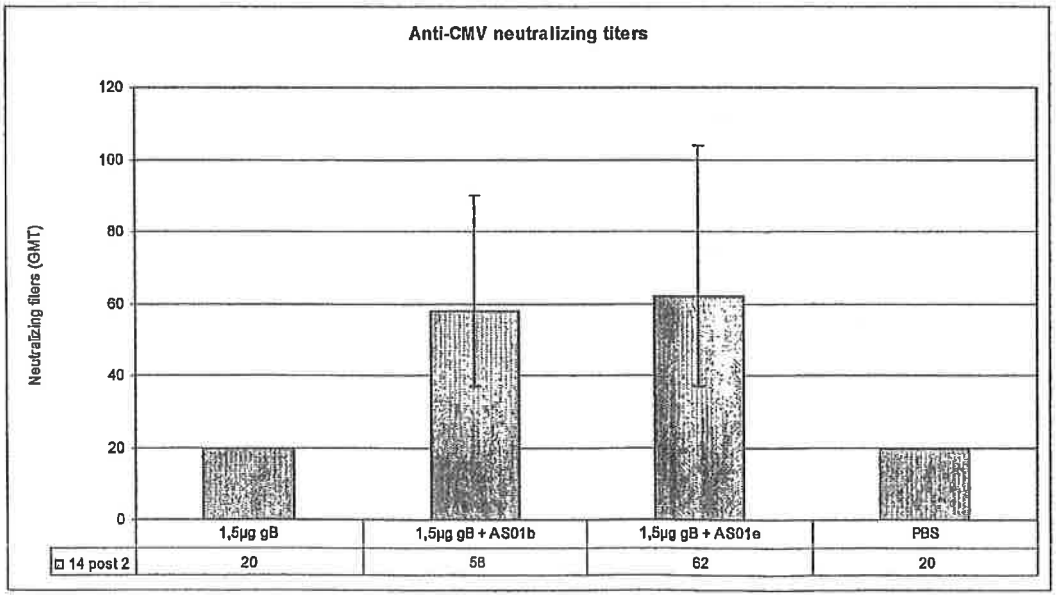
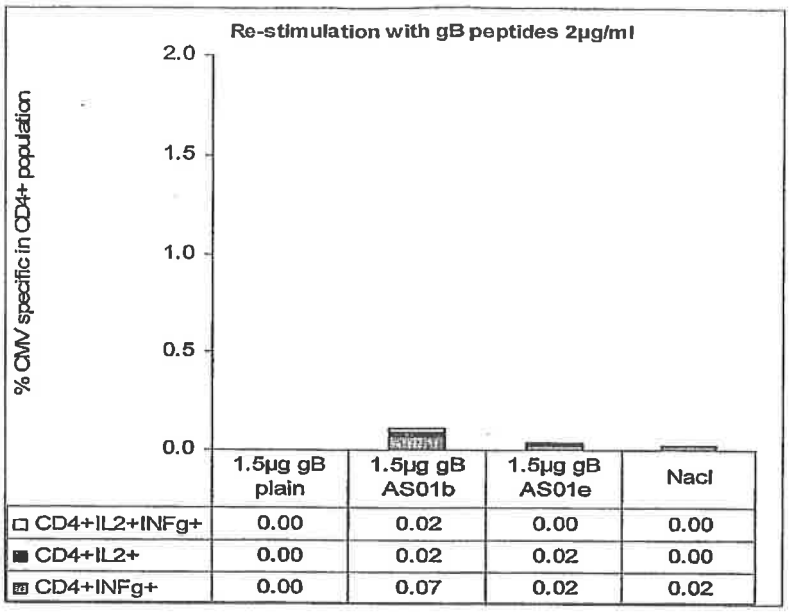
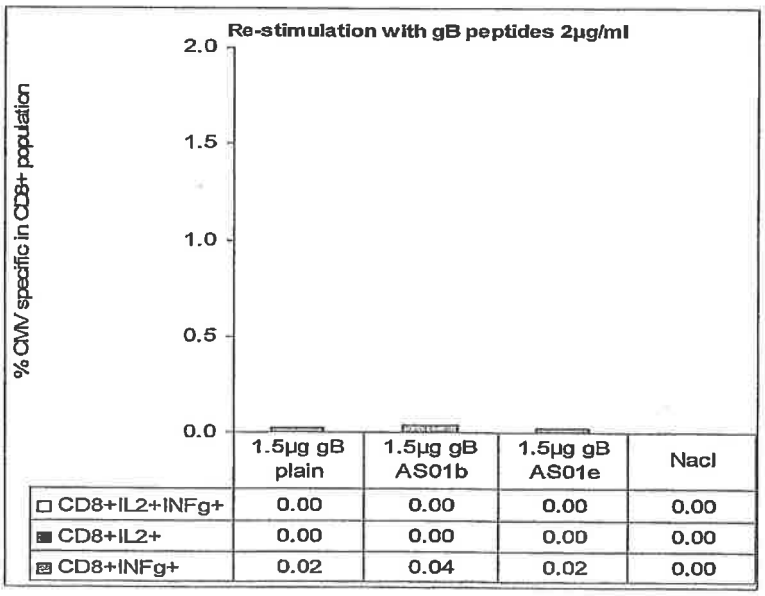


Figure 17:

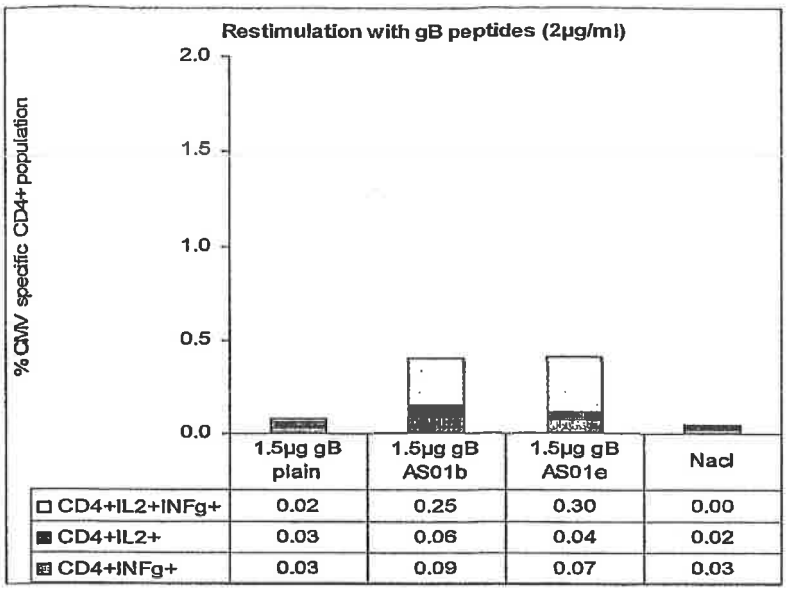



| | 1.5µg gB plain | 1.5µg gB AS01b | 1.5µg gB AS01e | Nacl |
|---|---|---|---|---|
| CD4+IL2+INFg+ | 0.00 | 0.02 | 0.00 | 0.00 |
| CD4+IL2+ | 0.00 | 0.02 | 0.02 | 0.00 |
| CD4+INFg+ | 0.00 | 0.07 | 0.02 | 0.02 |

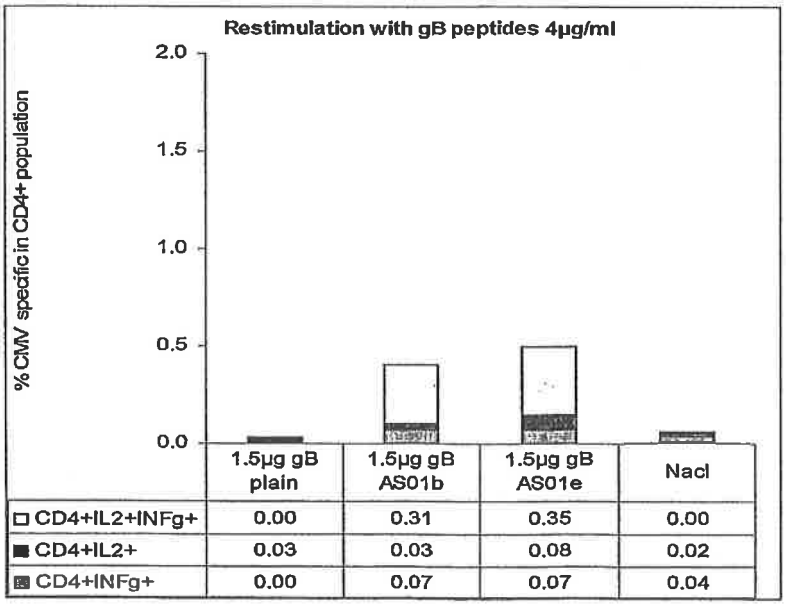



| | 1.5µg gB plain | 1.5µg gB AS01b | 1.5µg gB AS01e | Nacl |
|---|---|---|---|---|
| CD8+IL2+INFg+ | 0.00 | 0.00 | 0.00 | 0.00 |
| CD8+IL2+ | 0.00 | 0.00 | 0.00 | 0.00 |
| CD8+INFg+ | 0.02 | 0.04 | 0.02 | 0.00 |

Figure 18:

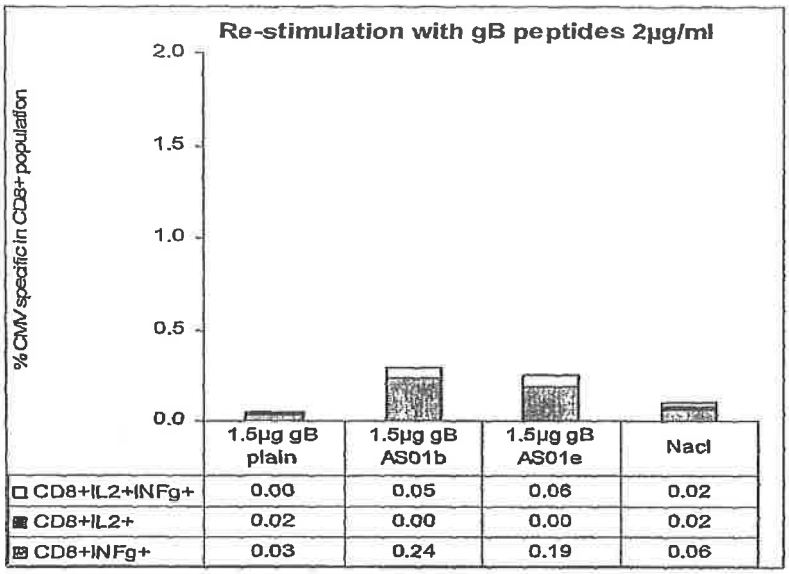



| | 1.5µg gB plain | 1.5µg gB AS01b | 1.5µg gB AS01e | Nacl |
|---|---|---|---|---|
| CD4+IL2+INFg+ | 0.02 | 0.25 | 0.30 | 0.00 |
| CD4+IL2+ | 0.03 | 0.06 | 0.04 | 0.02 |
| CD4+INFg+ | 0.03 | 0.09 | 0.07 | 0.03 |

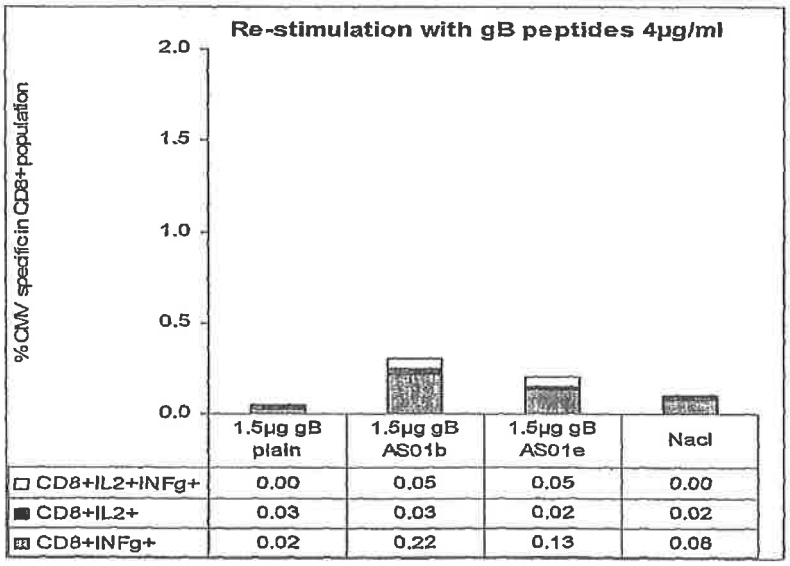



| | 1.5µg gB plain | 1.5µg gB AS01b | 1.5µg gB AS01e | Nacl |
|---|---|---|---|---|
| CD4+IL2+INFg+ | 0.00 | 0.31 | 0.35 | 0.00 |
| CD4+IL2+ | 0.03 | 0.03 | 0.08 | 0.02 |
| CD4+INFg+ | 0.00 | 0.07 | 0.07 | 0.04 |

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:

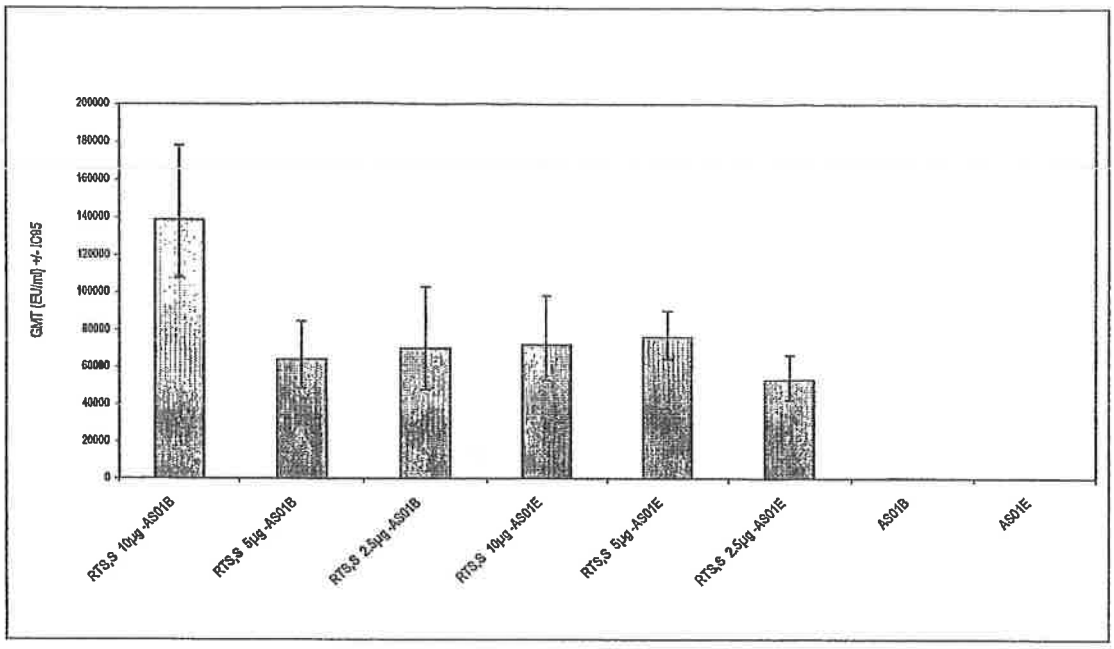



Figure 21:

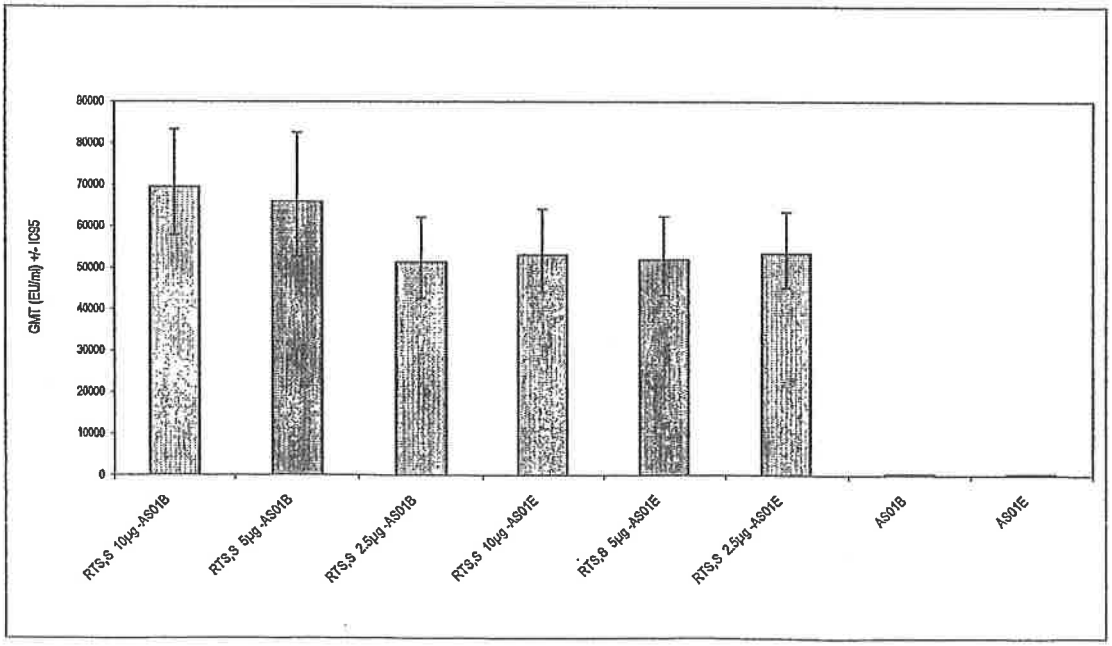
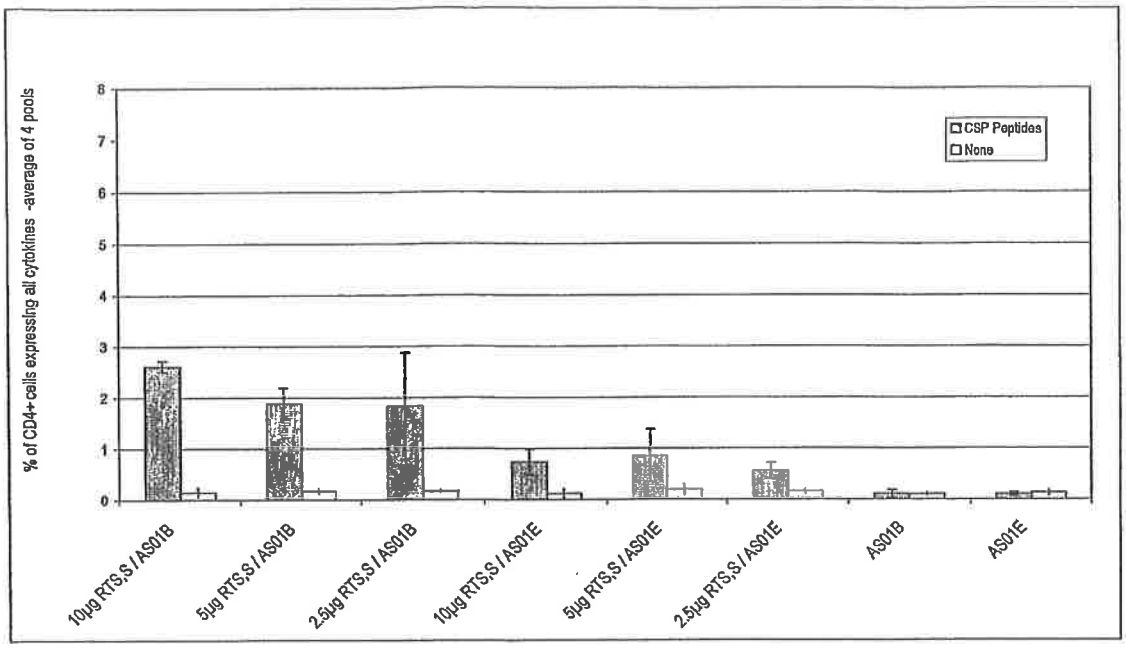


Figure 22:


% 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

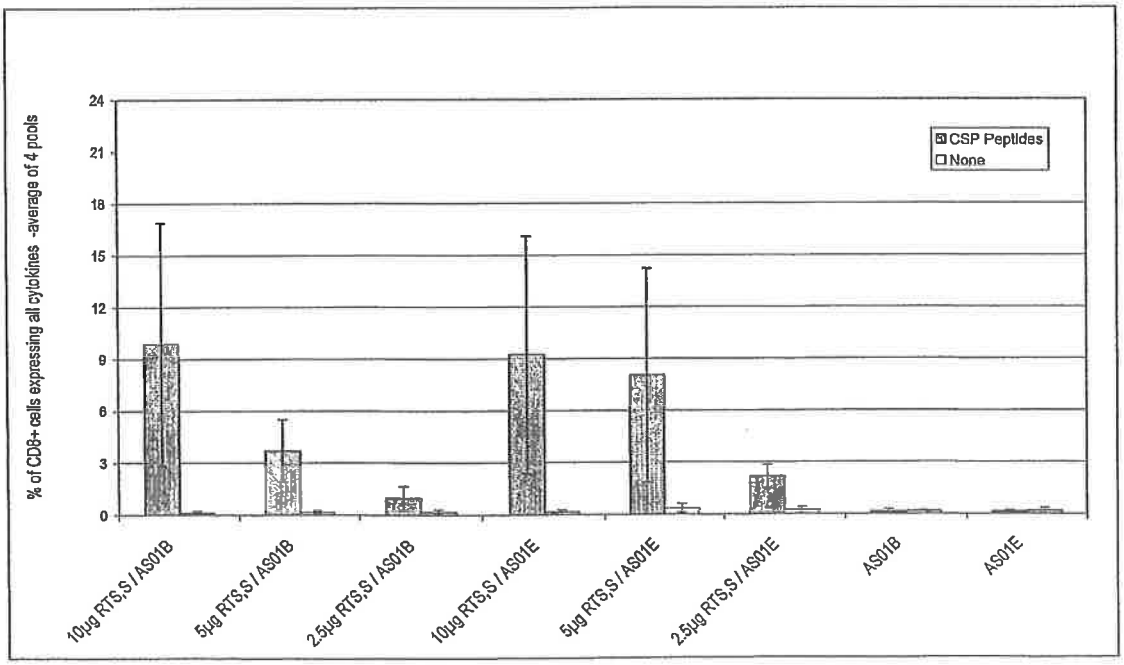
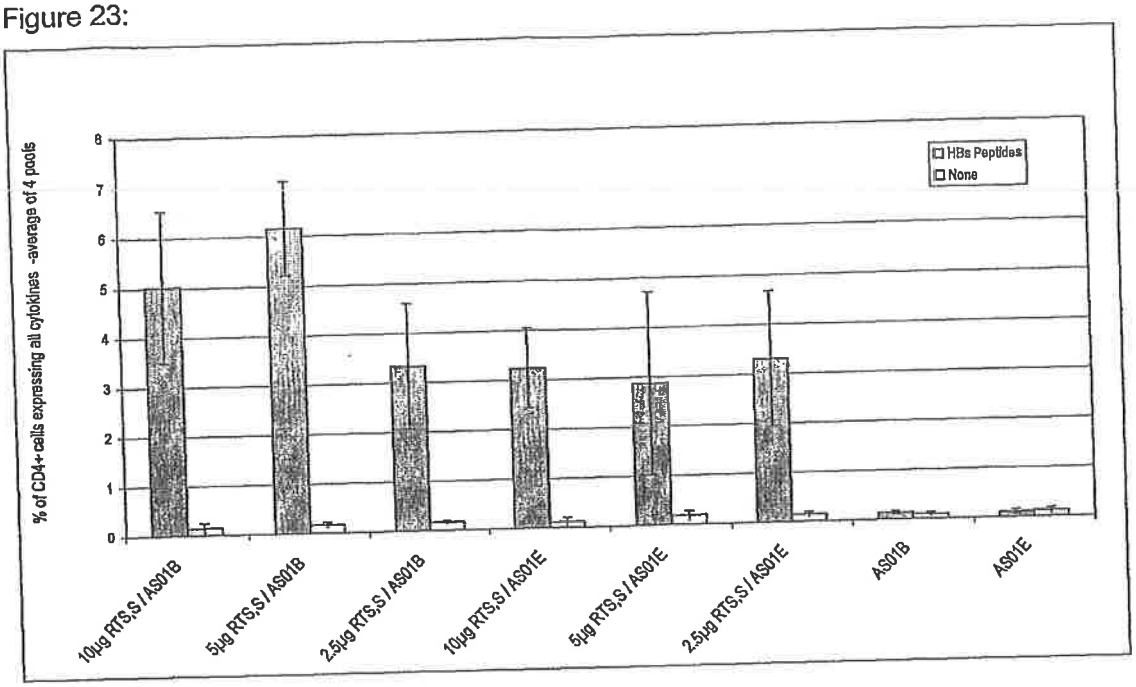

% of CD8+ cells expressing all cytokines -average of 4 pools
CSP Peptides
None
10µg RTS,S / AS01B
5µg RTS,S / AS01B
2.5µg RTS,S / AS01B
10µg RTS,S / AS01E
5µg RTS,S / AS01E
2.5µg RTS,S / AS01E
AS01B
AS01E

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

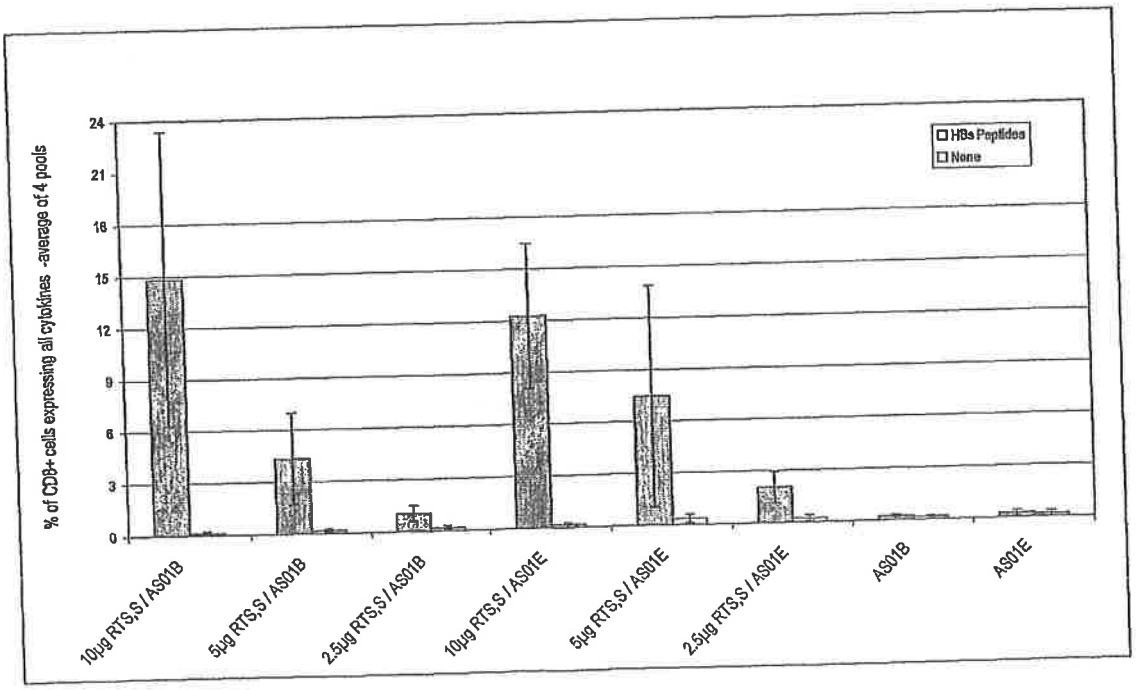
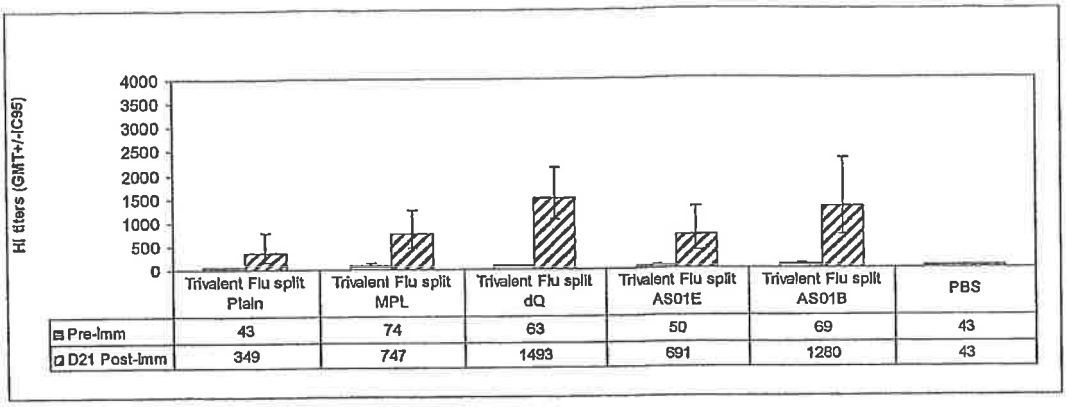
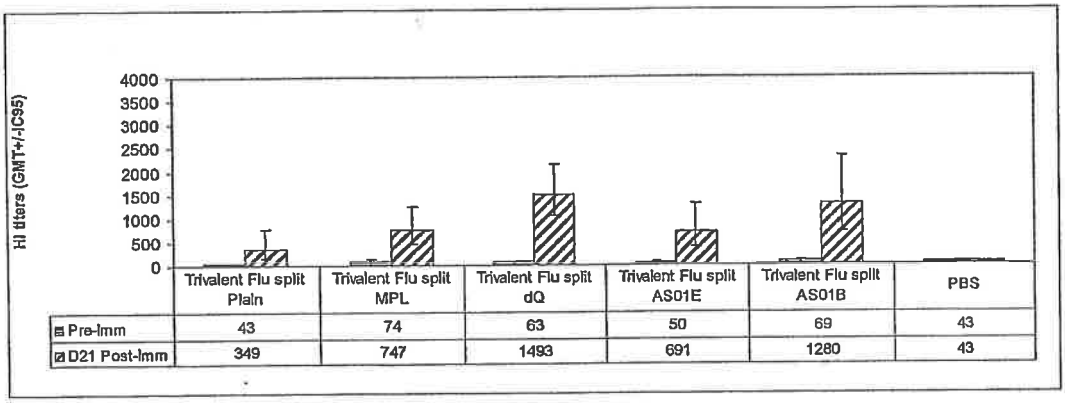

% of CD8+ cells expressing all cytokines -average of 4 pools
HBs Peptides
None
0
3
6
9
12
15
18
21
24
10µg RTS,S / AS01B
5µg RTS,S / AS01B
2.5µg RTS,S / AS01B
10µg RTS,S / AS01E
5µg RTS,S / AS01E
2.5µg RTS,S / AS01E
AS01B
AS01E

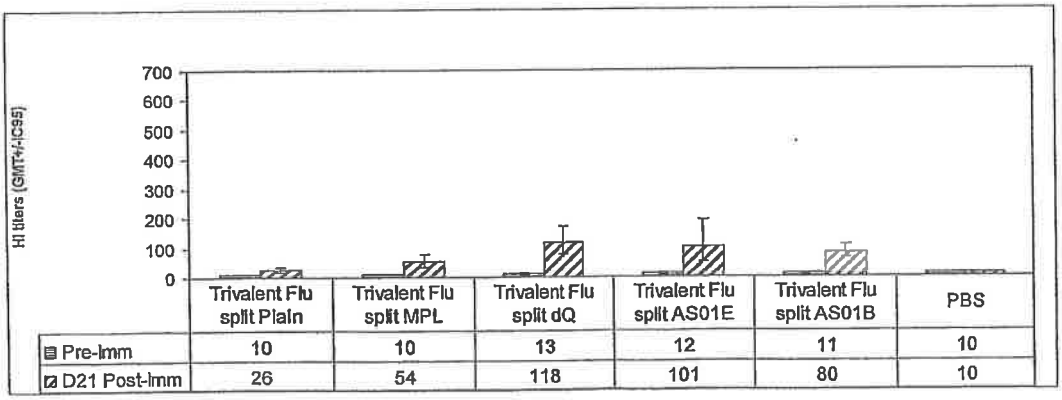
Figure 24:




| | 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 |

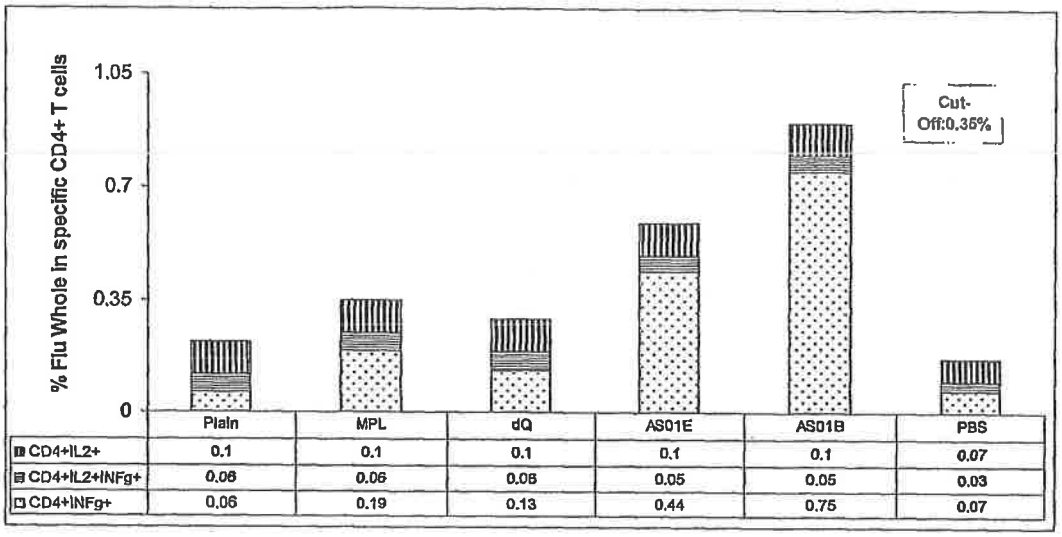



| | Trivalent Flu split Plain | Trivalent Flu split MPL | Trivalent Flu split dQ | Trivalent Flu split AS01E | Trivalent Flu split AS01B | PBS |
|---|---|---|---|---|---|---|
| Pre-Imm | 43 | 74 | 63 | 50 | 69 | 43 |
| D21 Post-Imm | 349 | 747 | 1493 | 691 | 1280 | 43 |



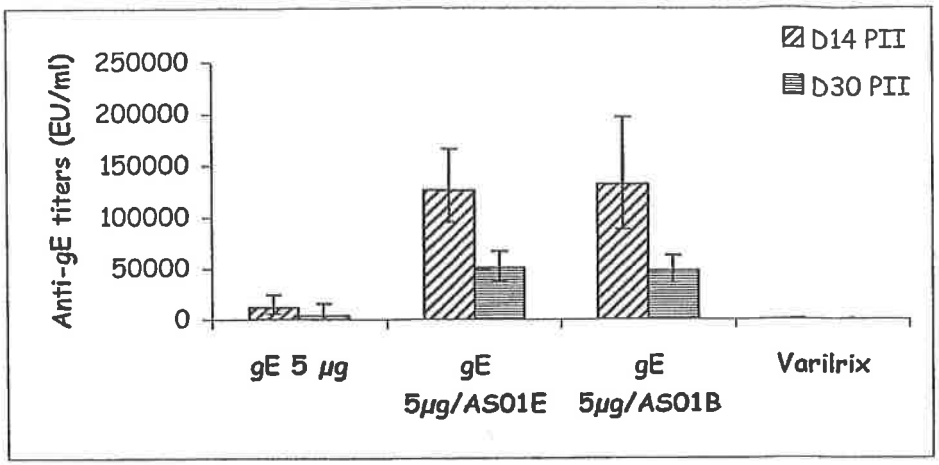

| | Trivalent Flu split Plain | Trivalent Flu split MPL | Trivalent Flu split dQ | Trivalent Flu split AS01E | Trivalent Flu split AS01B | PBS |
|---|---|---|---|---|---|---|
| Pre-Imm | 10 | 10 | 13 | 12 | 11 | 10 |
| D21 Post-Imm | 26 | 54 | 118 | 101 | 80 | 10 |

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+ | 0.06 | 0.06 | 0.06 | 0.05 | 0.05 | 0.03 |
| CD4+INFg+ | 0.06 | 0.19 | 0.13 | 0.44 | 0.75 | 0.07 |

Figure 26:


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

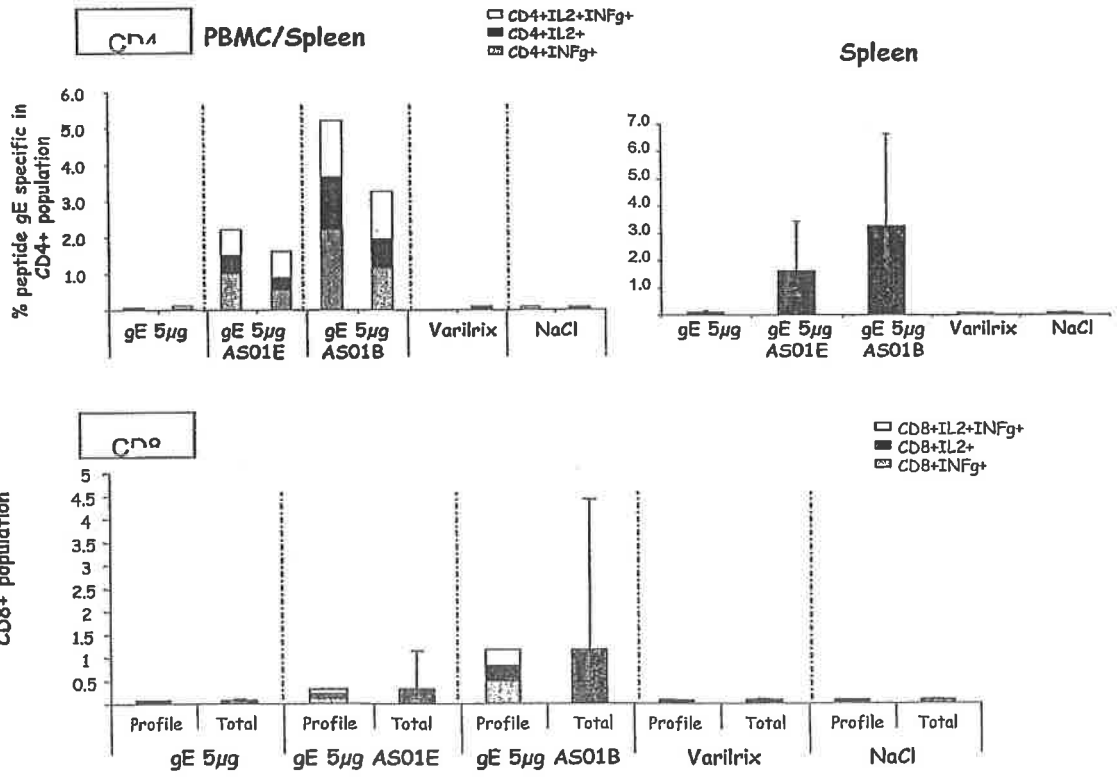

CD4
PBMC/Spleen
CD4+IL2+INFg+
CD4+IL2+
CD4+INFg+
% peptide gE specific in CD4+ population
gE 5µg
gE 5µg AS01E
gE 5µg AS01B
Varilrix
NaCl
Spleen
CD8
CD8+IL2+INFg+
CD8+IL2+
CD8+INFg+
% peptide gE specific in CD8+ population
Profile
Total
gE 5µg
gE 5µg AS01E
gE 5µg AS01B
Varilrix
NaCl

Figure 27

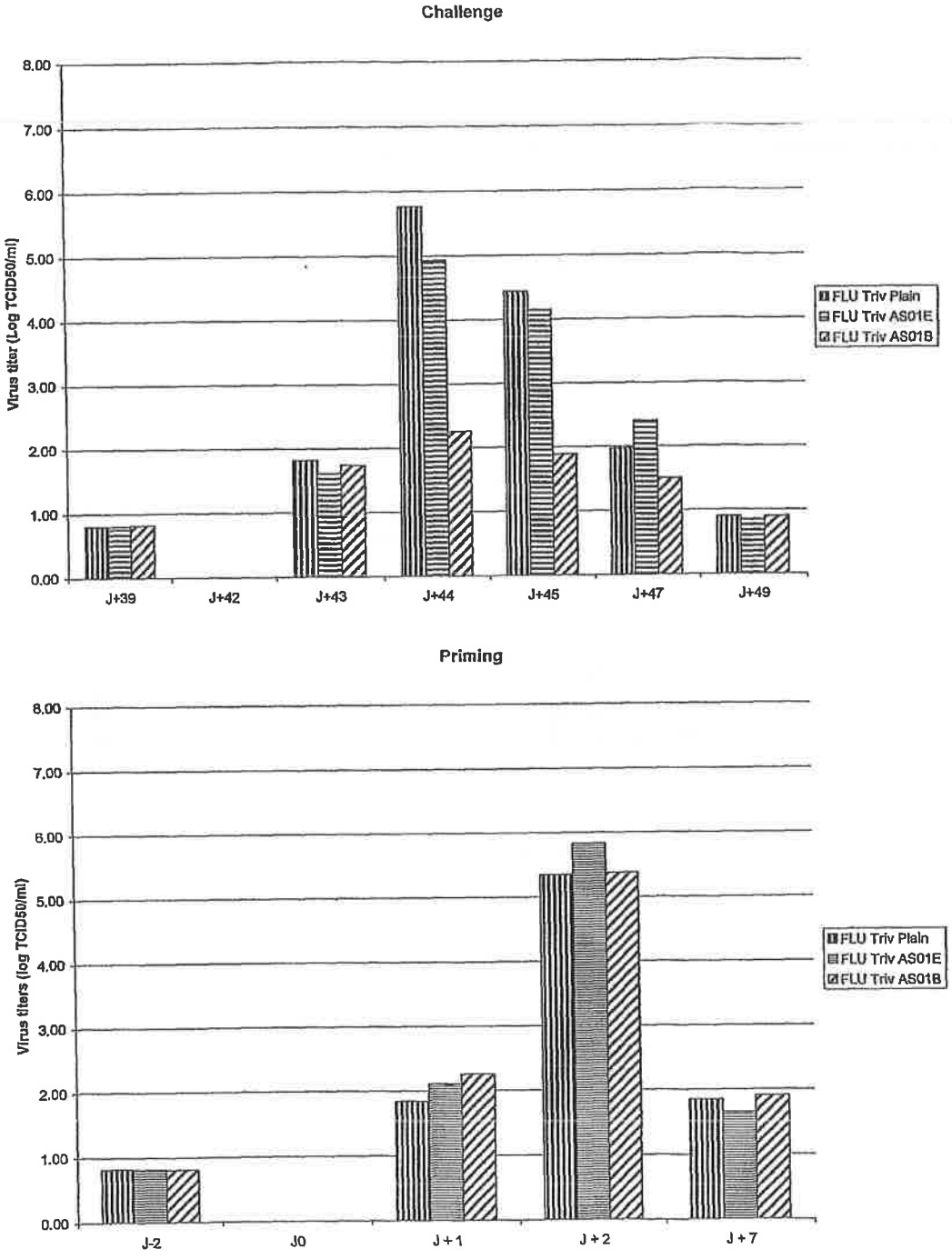
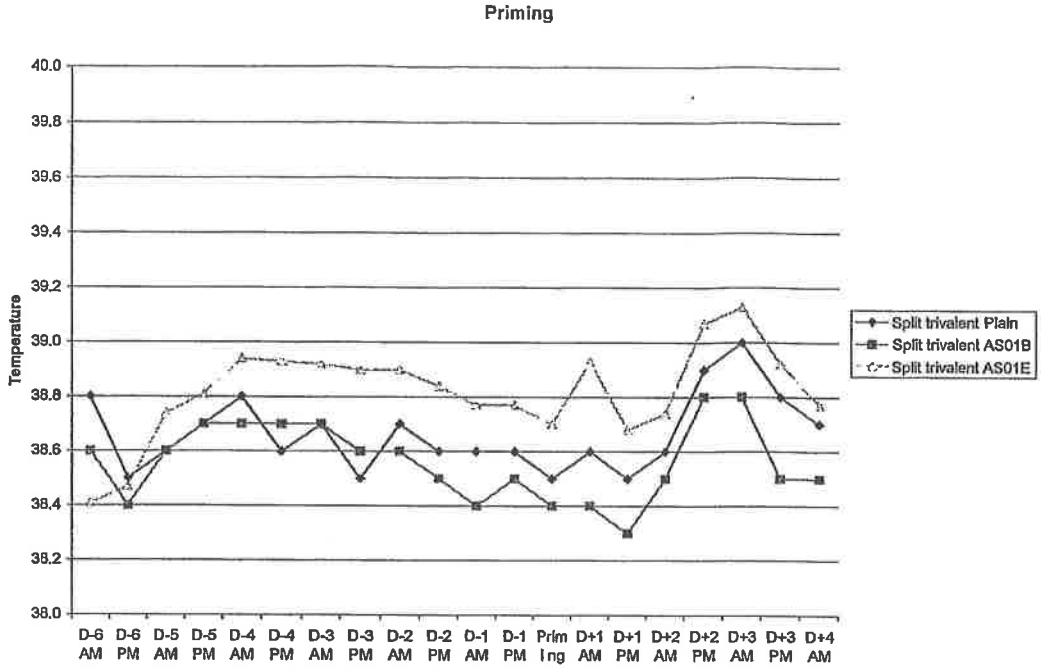

Challenge
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
Virus titer (Log TCID50/ml)
J+39
J+42
J+43
J+44
J+45
J+47
J+49
FLU Triv Plain
FLU Triv AS01E
FLU Triv AS01B
Priming
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
Virus titers (log TCID50/ml)
J-2
J0
J + 1
J + 2
J + 7
FLU Triv Plain
FLU Triv AS01E
FLU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

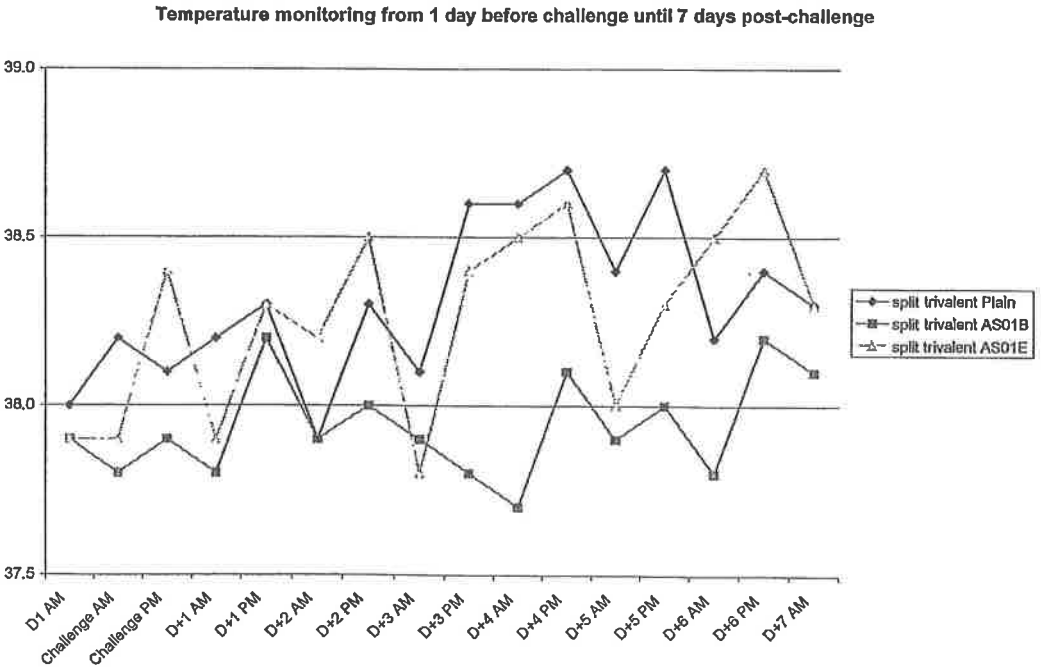
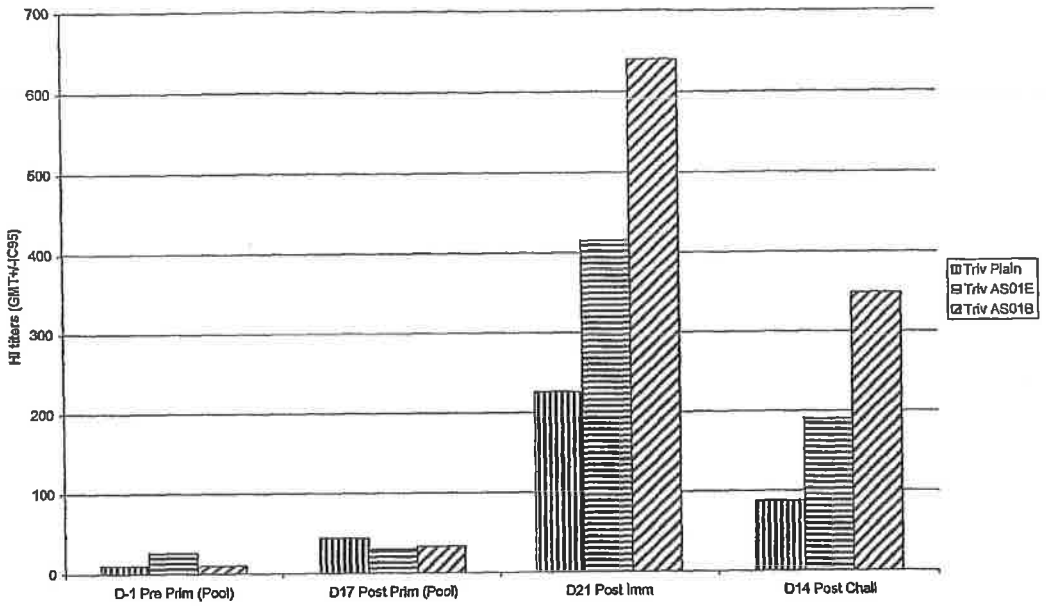

Temperature monitoring from 1 day before challenge until 7 days post-challenge
39.0
38.5
38.0
37.5
D1 AM
Challenge AM
Challenge PM
D+1 AM
D+1 PM
D+2 AM
D+2 PM
D+3 AM
D+3 PM
D+4 AM
D+4 PM
D+5 AM
D+5 PM
D+6 AM
D+6 PM
D+7 AM
split trivalent Plain
split trivalent AS01B
split trivalent AS01E

Figure 29:

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




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

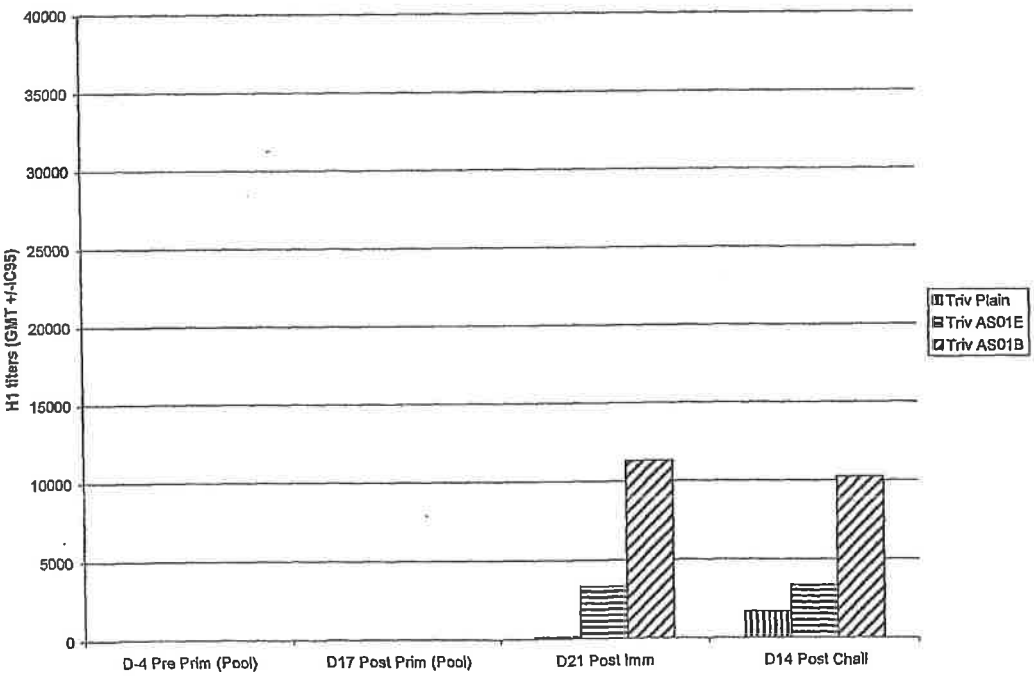
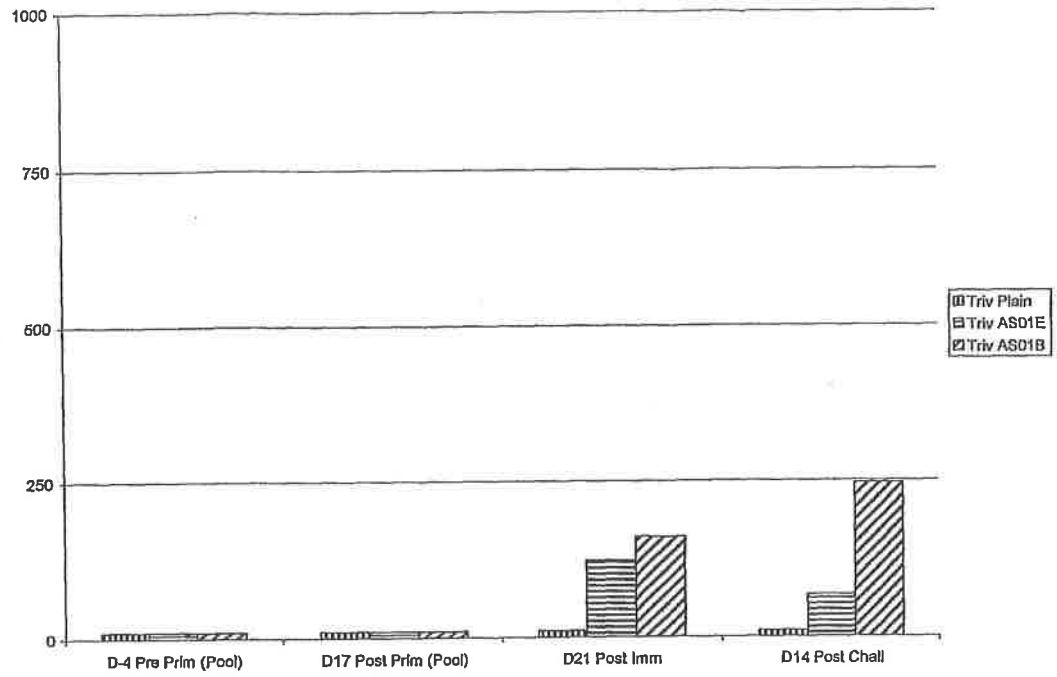


Figure 30:

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




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

