

ACIP Meeting, CDC, Atlanta

June 25, 2008

Pentacel®

DTaP-IPV/Hib

**Diphtheria and Tetanus Toxoids and Acellular Pertussis
Adsorbed, Inactivated Poliovirus and Haemophilus b
Conjugate (Tetanus Toxoid Conjugate) Vaccine**

sanofi pasteur

The vaccines division of sanofi-aventis Group

Outline

- **Clinical Development Program**
- **Safety**
- **Immunogenicity**
 - **Pertussis**
 - **Hib**
- **Conclusions**

Pentacel Clinical Studies for US Licensure

Study	Purpose	N	Pentacel
P3T06	Pentacel vs Standard US Vaccines (Daptacel, IPOL, ActHIB)	1939	485
M5A10	Pentacel vs Standard US Vaccines (Daptacel, IPOL, ActHIB)	2167	1083
494-01	Lot consistency, Pentacel vs Formulation Components (HCPDT, Poliovax, ActHIB)	3538	2506
M5A07	Interaction with Prevnar (Infant Series)	1166	1166
494-03	Interaction with Prevnar, MMR and Varivax vaccines (4th Dose)	1207	1207
5A9908	Administration at 15-16 vs 17-18 months of age	1782	1782

Composition of Pentacel Vaccine

Antigen	Pentacel	Standard US Single Entity Vaccines		
		Daptacel	IPOL	ActHIB
Diphtheria Toxoid	15 Lf	15 Lf		
Tetanus Toxoid	5 Lf	5 Lf		
PT	20 µg	10 µg		
FHA	20 µg	5 µg		
PRN	3 µg	3 µg		
FIM 2 & 3	5 µg	5 µg		
Poliovirus Type 1	40 DAU		40 DAU	
Poliovirus Type 2	8 DAU		8 DAU	
Poliovirus Type 3	32 DAU		32 DAU	
PRP-T	10 µg			10 µg

Safety

Pentacel Clinical Studies: Comparison with Single Entity Vaccines

3 randomized, blinded, controlled, comparative trials

■ P3T06 (N=1939)

- Safety and immunogenicity comparison with licensed vaccines
- Control vaccines: Daptacel, IPOL, ActHIB
- Schedule: 2, 4, 6, and 15-16 months of age

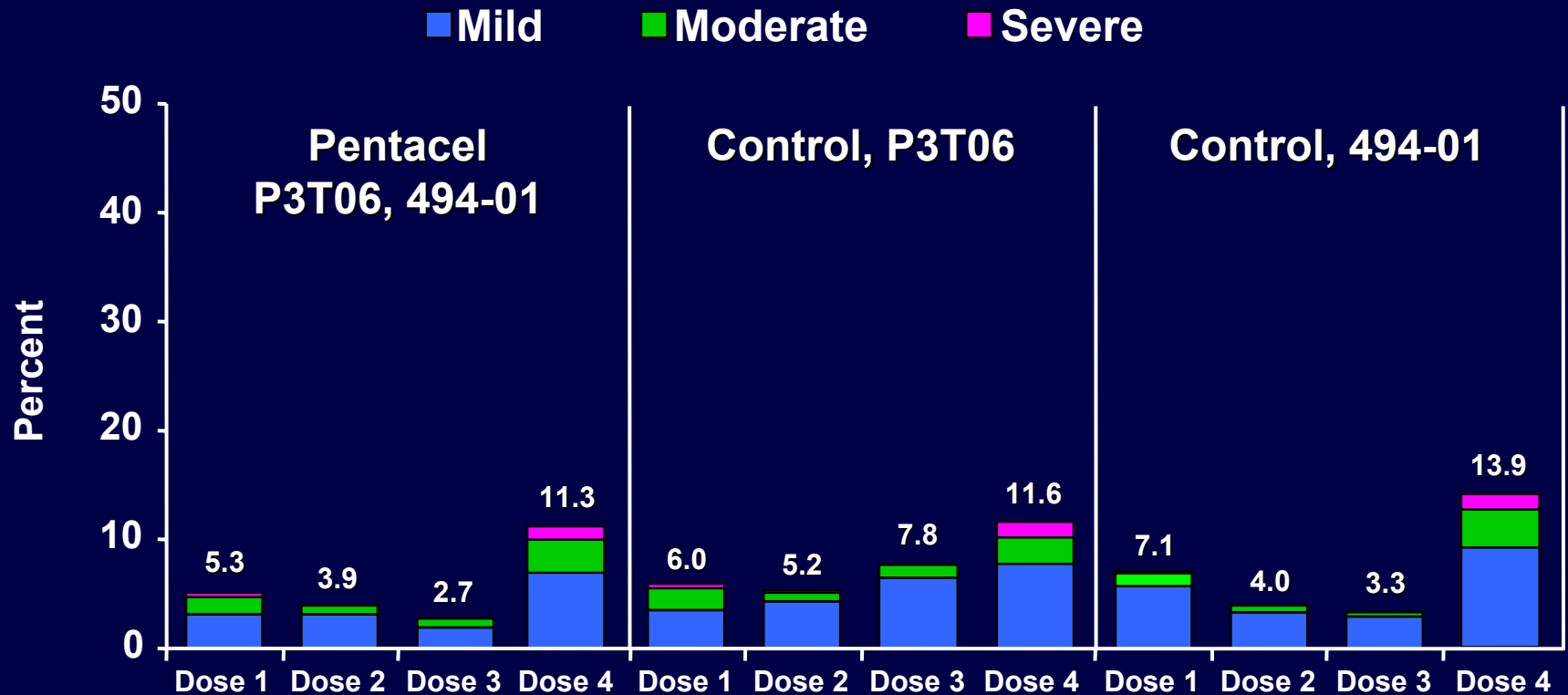
■ 494-01 (N= 3538)

- Lot consistency study; comparison with components
- Control products: HCPDT, Poliovax, ActHIB
- Schedule: 2, 4, 6, and 15 months of age

■ M5A10 (N= 2167)

- Immunogenicity comparison with licensed vaccines
- Control vaccines: Daptacel, IPOL, ActHIB
- Schedule: 2, 4, 6 months of age (15-16 month vaccination ongoing)

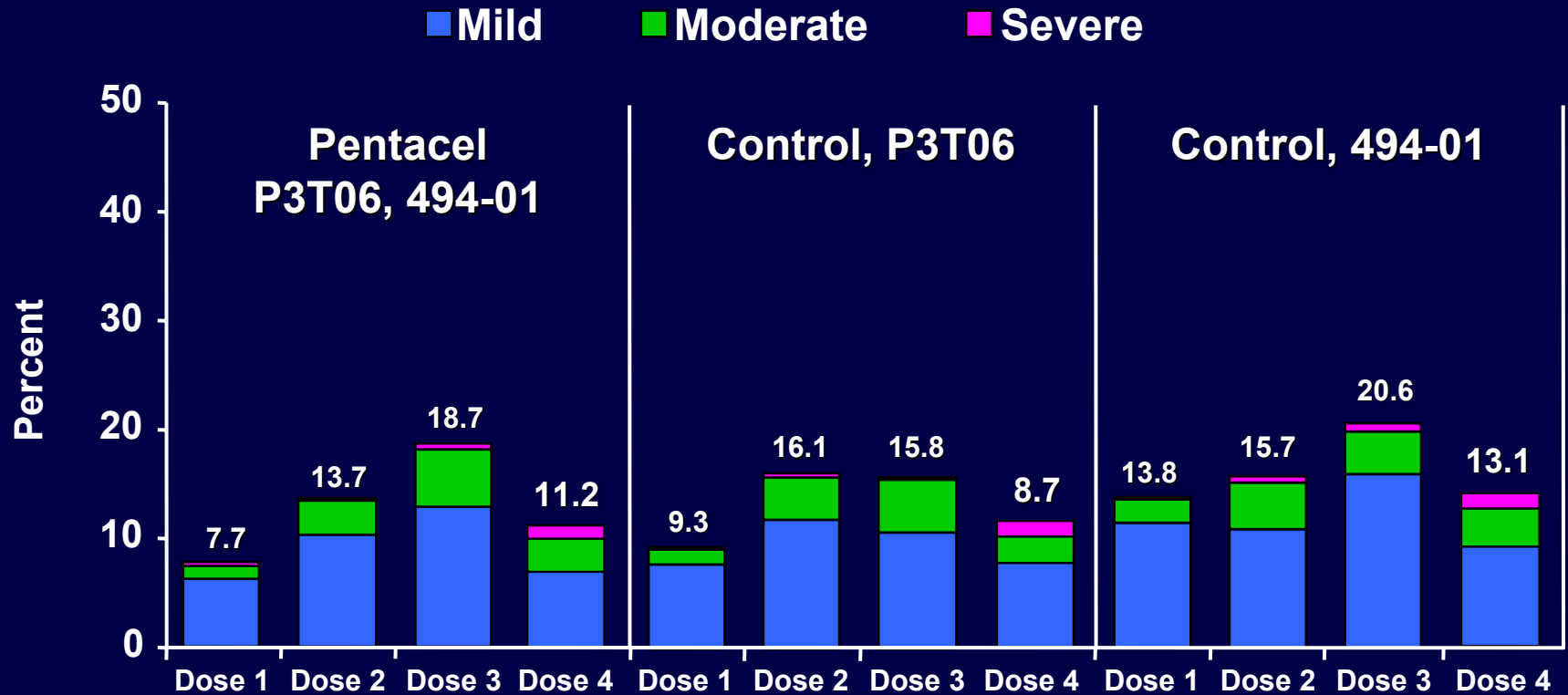
Doses 1-4: Solicited Local Swelling, Days 0-3, Comparison to Controls[†] by Dose



	Dose 1	Dose 2	Dose 3	Dose 4	Dose 1	Dose 2	Dose 3	Dose 4	Dose 1	Dose 2	Dose 3	Dose 4
Any	5.3	3.9	2.7	11.3	6.0	5.2	7.8	11.6	7.1	4.0	3.3	13.9
Mild	3.2	3.1	2.0	6.9	3.6	4.3	6.5	7.7	5.8	3.4	3.0	9.2
Moderate	1.6	0.8	0.7	3.2	2.0	0.9	1.2	2.6	1.2	0.5	0.3	3.5
Severe	0.4	0.0	0.0	1.2	0.4	0.1	0.1	1.3	0.1	0.1	0.0	1.3

[†]Percentages are based on the most severe reaction at any of the vaccination sites for the individual control vaccines

Doses 1-4: Solicited Fever, Days 0-3, Comparison to Controls by Dose



Any	7.7	13.7	18.7	11.2	9.3	16.1	15.8	8.7	13.8	15.7	20.6	13.1
Mild	6.2	10.4	12.9	8.1	7.7	11.8	10.7	5.5	11.5	10.8	16.0	9.1
Moderate	1.1	3.1	5.1	2.5	1.5	3.9	4.8	2.4	2.2	4.3	3.9	3.5
Severe	0.4	0.2	0.7	0.6	0.1	0.4	0.3	0.8	0.1	0.6	0.7	0.5

†Percentages are based on the most severe reaction at any of the vaccination sites for the individual control vaccines

Unsolicited Adverse Events

■ Non-serious

- No difference in rates between Pentacel and control groups for frequently reported and rare events
- Most events were common childhood conditions such as URI, otitis media, teething and nasal congestion
- Majority assessed as non-related by the investigators

■ Serious Adverse Events

- SAE rates identical for Pentacel and Control
- No SAEs were reported as related to Pentacel
- A total of 5 deaths, all considered unrelated.
 - 4 Pentacel: suffocation, day 9; auto accident, day 22; SIDS, day 52; neuroblastoma, diagnosis day 95.
 - 1 Control: ependymoma, diagnosis day 54.

Pentacel: Clinical Safety Conclusions

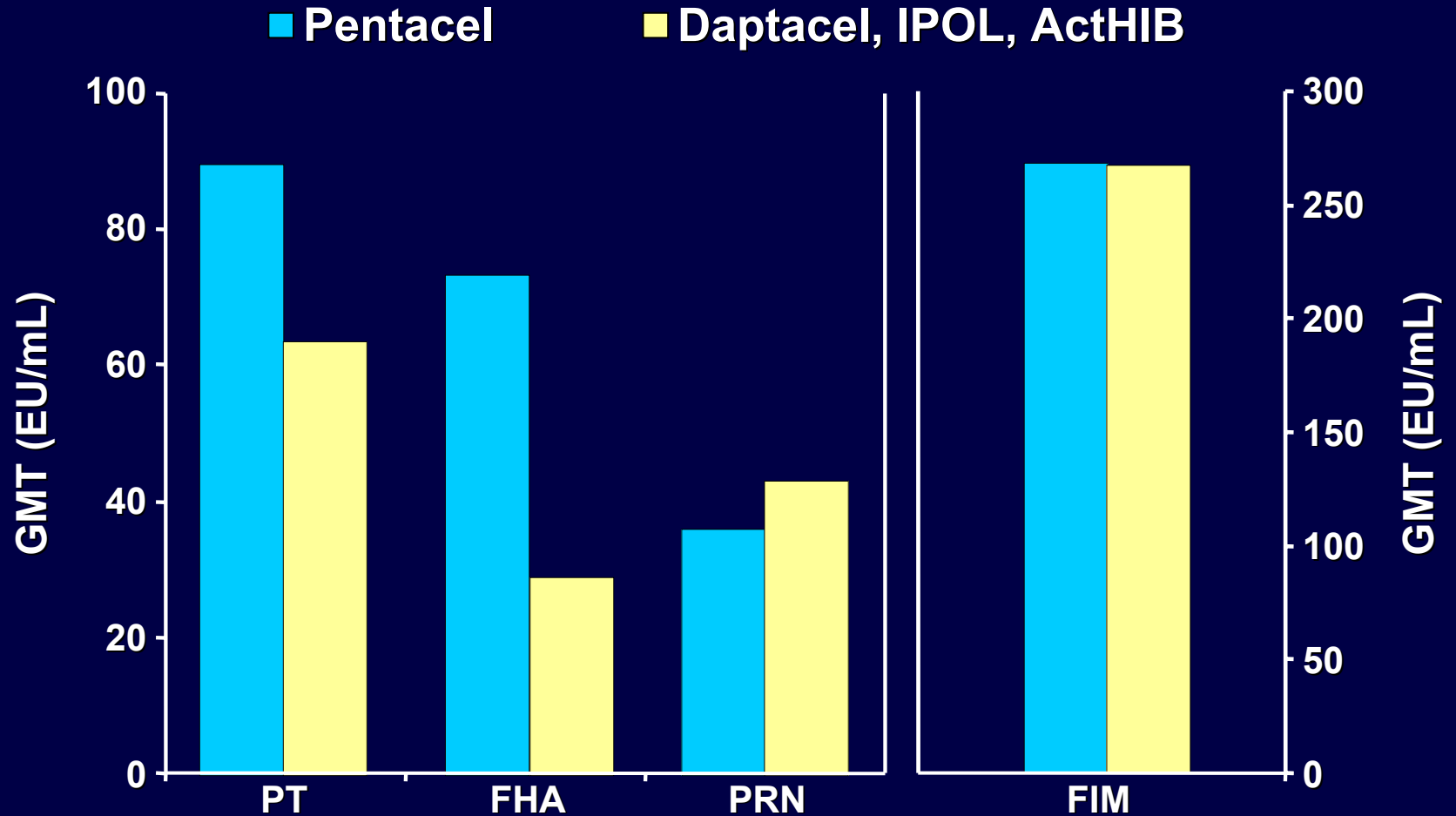
- **Safety profile of Pentacel is similar to that of separate administration of standard US vaccines (Daptacel, IPOL, and ActHIB)**
- **Pentacel is safe when administered alone or concomitantly with other age-recommended vaccines**

Immunogenicity

- **Pertussis Immunogenicity**
- Hib (PRP) Immunogenicity

P3T06: Pentacel vs Daptacel, IPOL, ActHIB

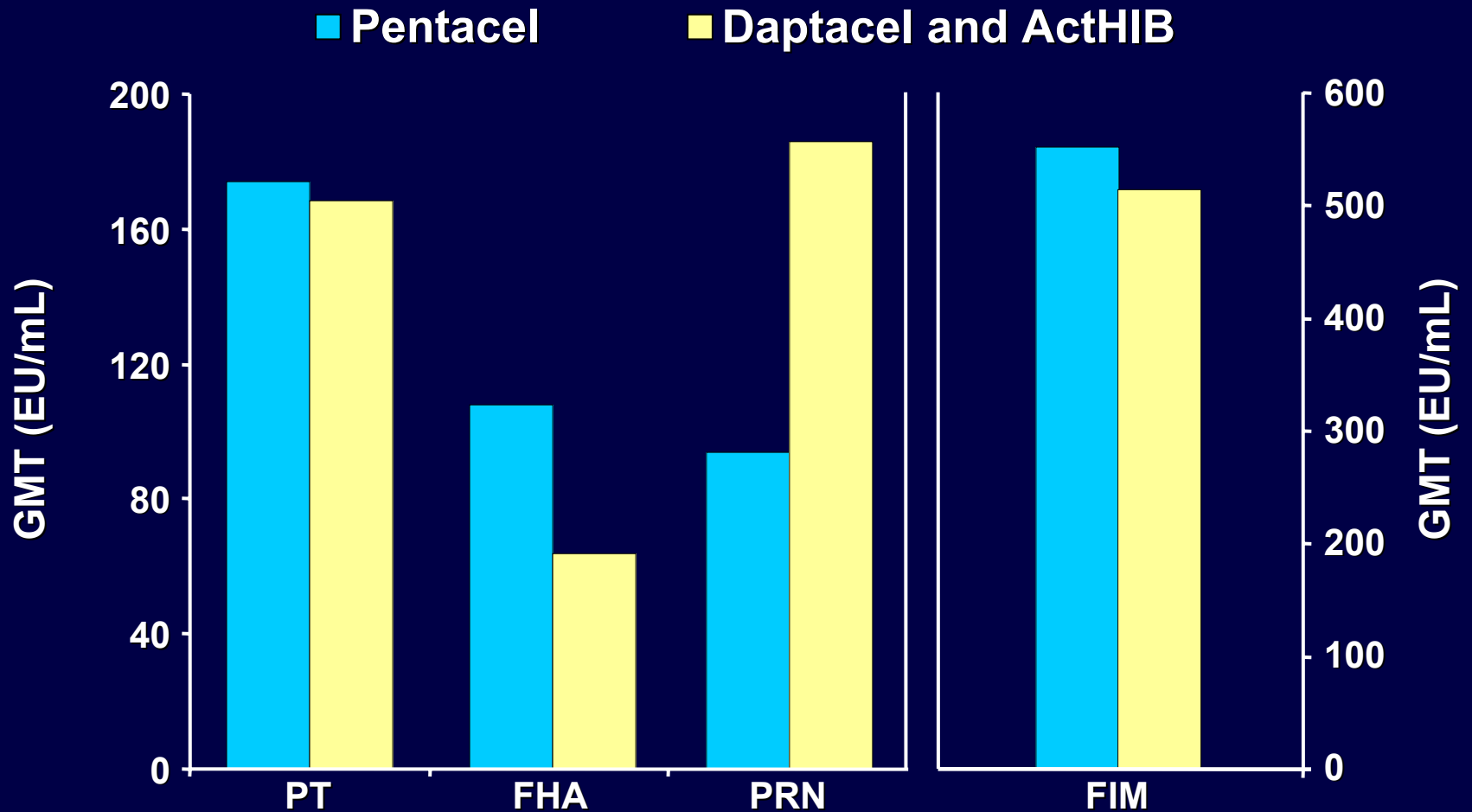
Post-Dose 3: Pertussis GMTs



Pentacel	90.0	73.7	36.1	268.2
Control	63.8	29.2	43.3	267.2

P3T06: Pentacel vs Daptacel, IPOLO, ActHIB

Post-Dose 4: Pertussis GMTs



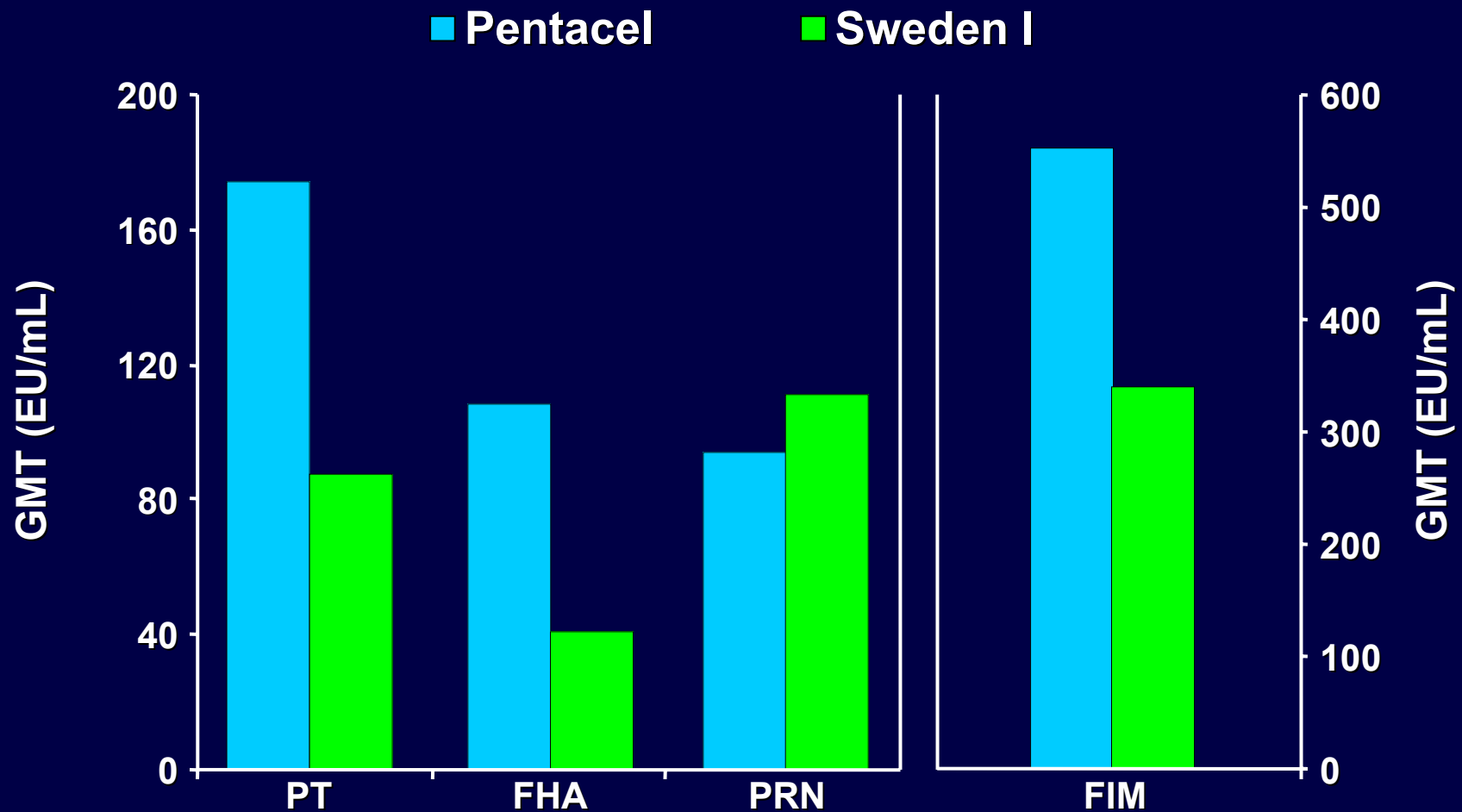
Pentacel	174.0	107.9	93.6	553.4
Control	168.5	64.0	186.1	513.5

Pentacel Bridge to Efficacy

P3T06 vs Sweden I Efficacy Trial

- **NIH-sponsored efficacy trial in Sweden 1992-1995**
 - Infants received Daptacel at 2, 4, 6 months of age
 - 85% efficacy vs WHO-defined classic pertussis
 - 78% efficacy vs any pertussis (lab-confirmed, ≥ 1 day of cough)
- **Pertussis antibody levels in Sweden I Efficacy Trial were compared to those following 4 doses of Pentacel in US pivotal trials P3T06 and 494-01**
- **Sera from P3T06, 494-01 and the Sweden I Efficacy Trial were tested contemporaneously in same laboratory, under same conditions, using the same validated assay**

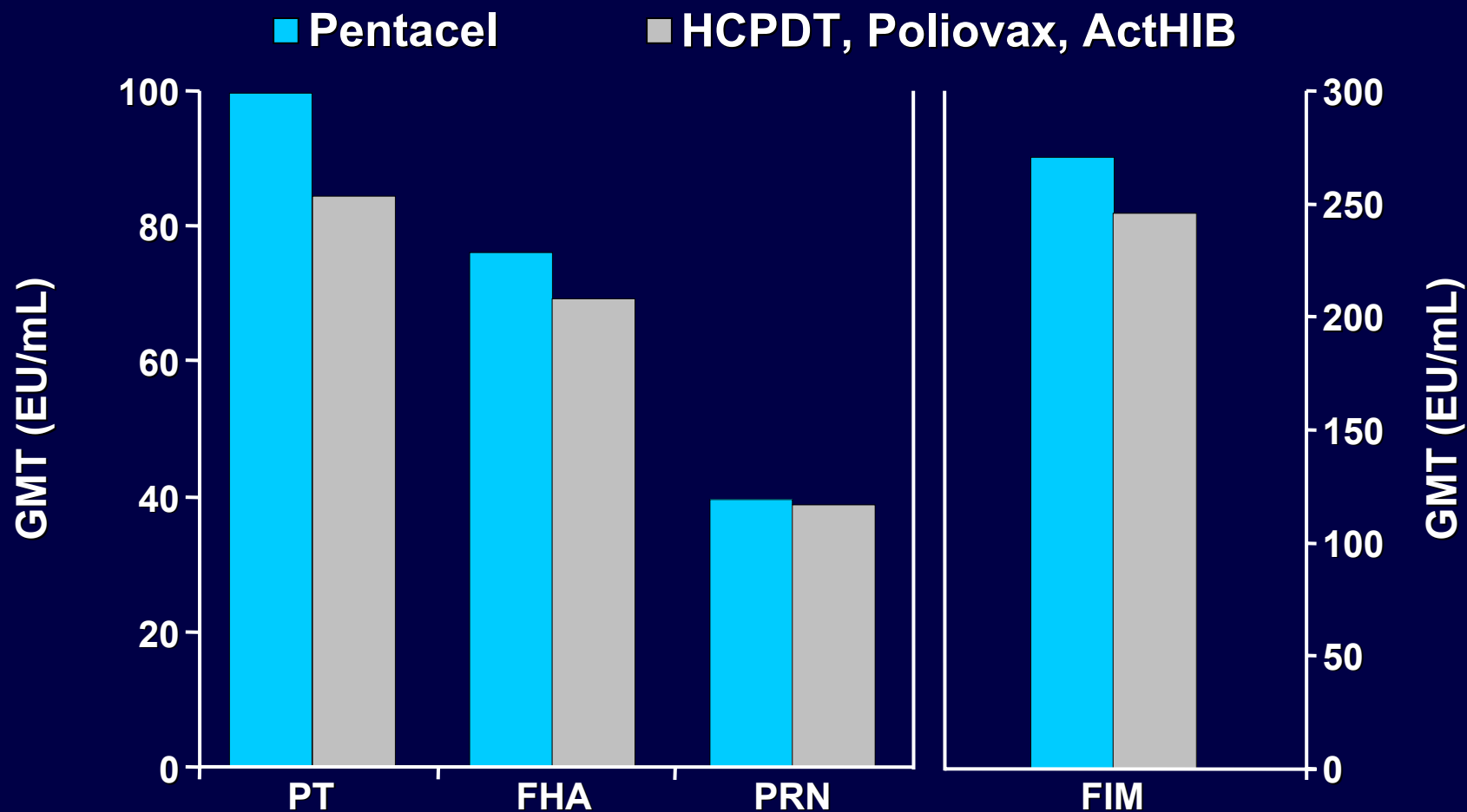
P3T06: Pentacel vs Sweden I (Bridge to Efficacy) GMTs



Pentacel	174.0	107.9	93.6	553.4
Sweden I	87.5	40.7	111.3	339.3

494-01: Pentacel vs HCPDT, Poliovax, ActHIB

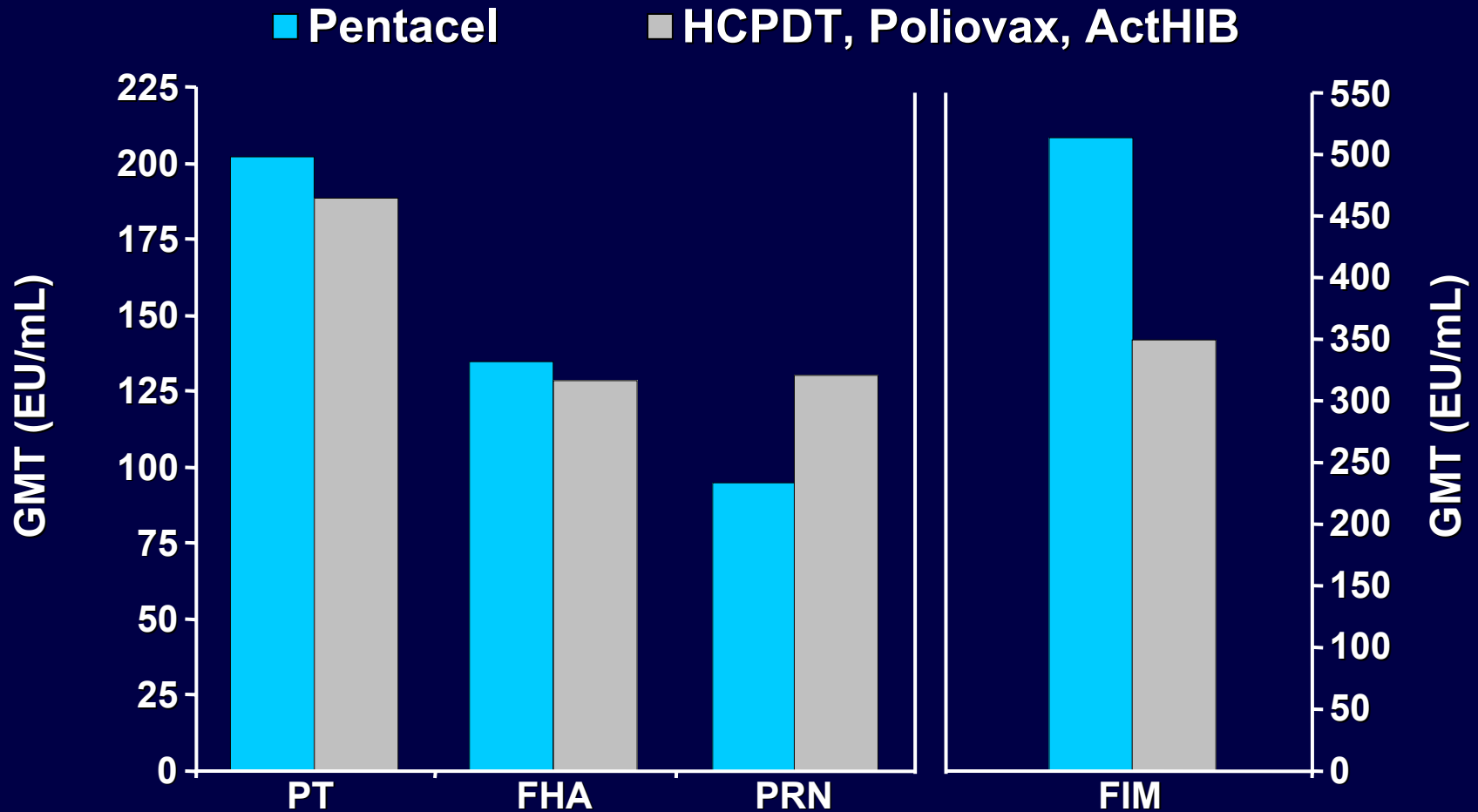
Post-Dose 3: Pertussis GMTs



Pentacel	99.7	76.2	39.6	270.3
Control	84.5	69.2	38.6	246.0

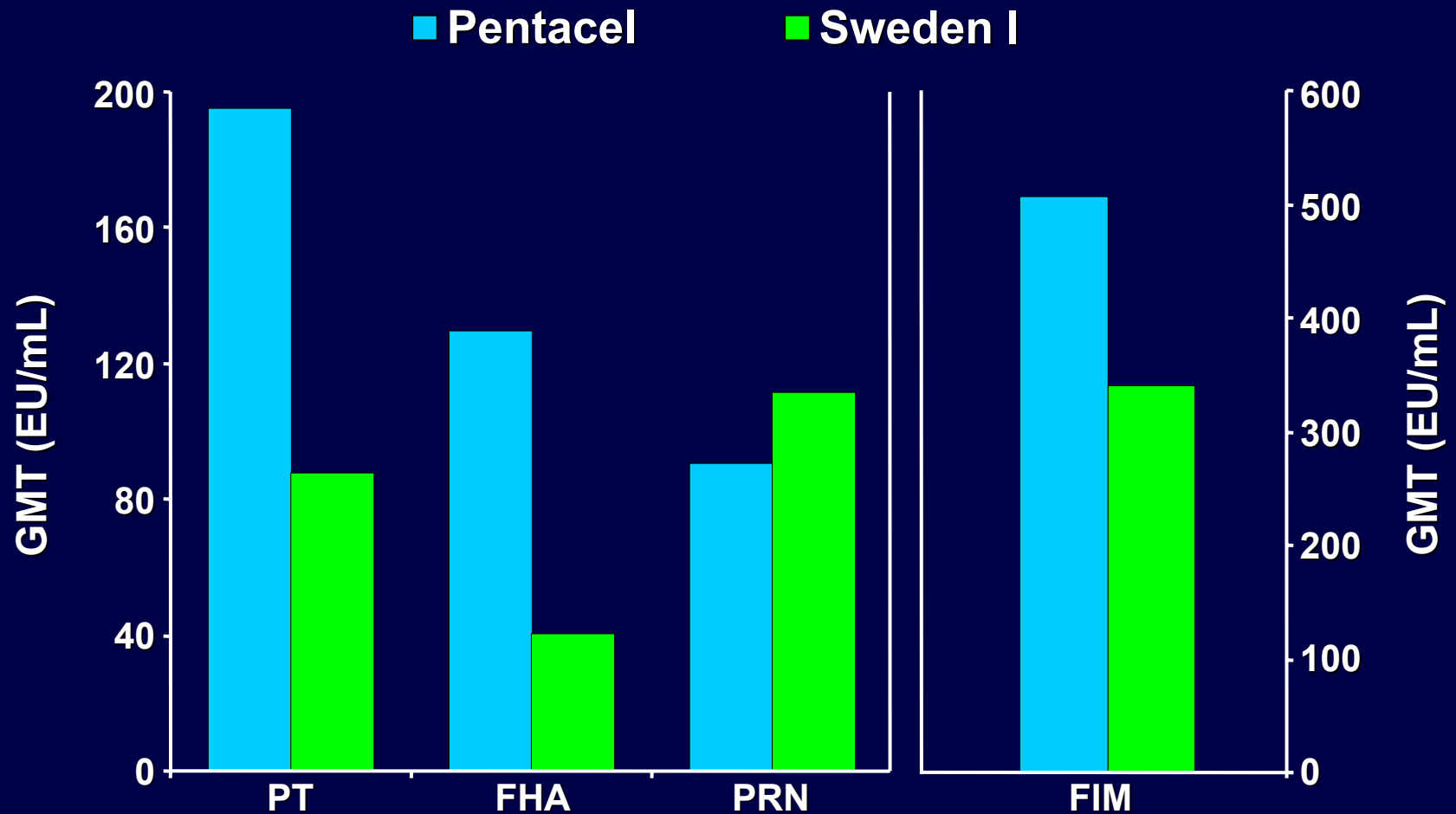
494-01: Pentacel vs HCPDT, Poliovax, ActHIB

Post-Dose 4: Pertussis GMTs



Pentacel	202.2	134.6	94.9	514.2
Control	188.6	128.3	129.9	350.3

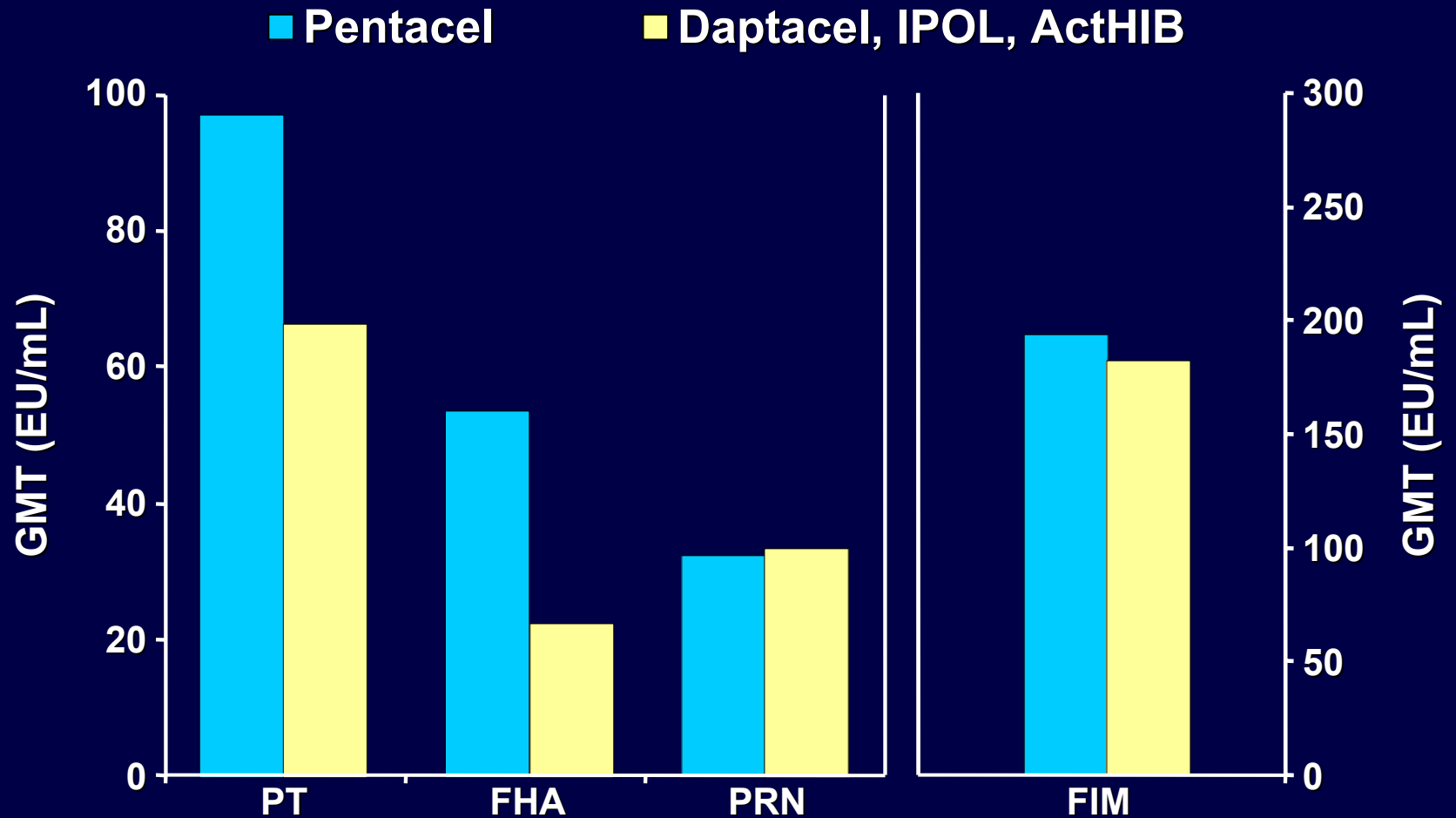
494-01: Pentacel vs Sweden I (Bridge to Efficacy) GMTs



Pentacel	195.1	129.9	90.8	506.6
Sweden I	87.5	40.7	111.3	339.3

M5A10: Pentacel vs Daptacel, IPOL, ActHIB

Post-Dose 3: Pertussis GMTs

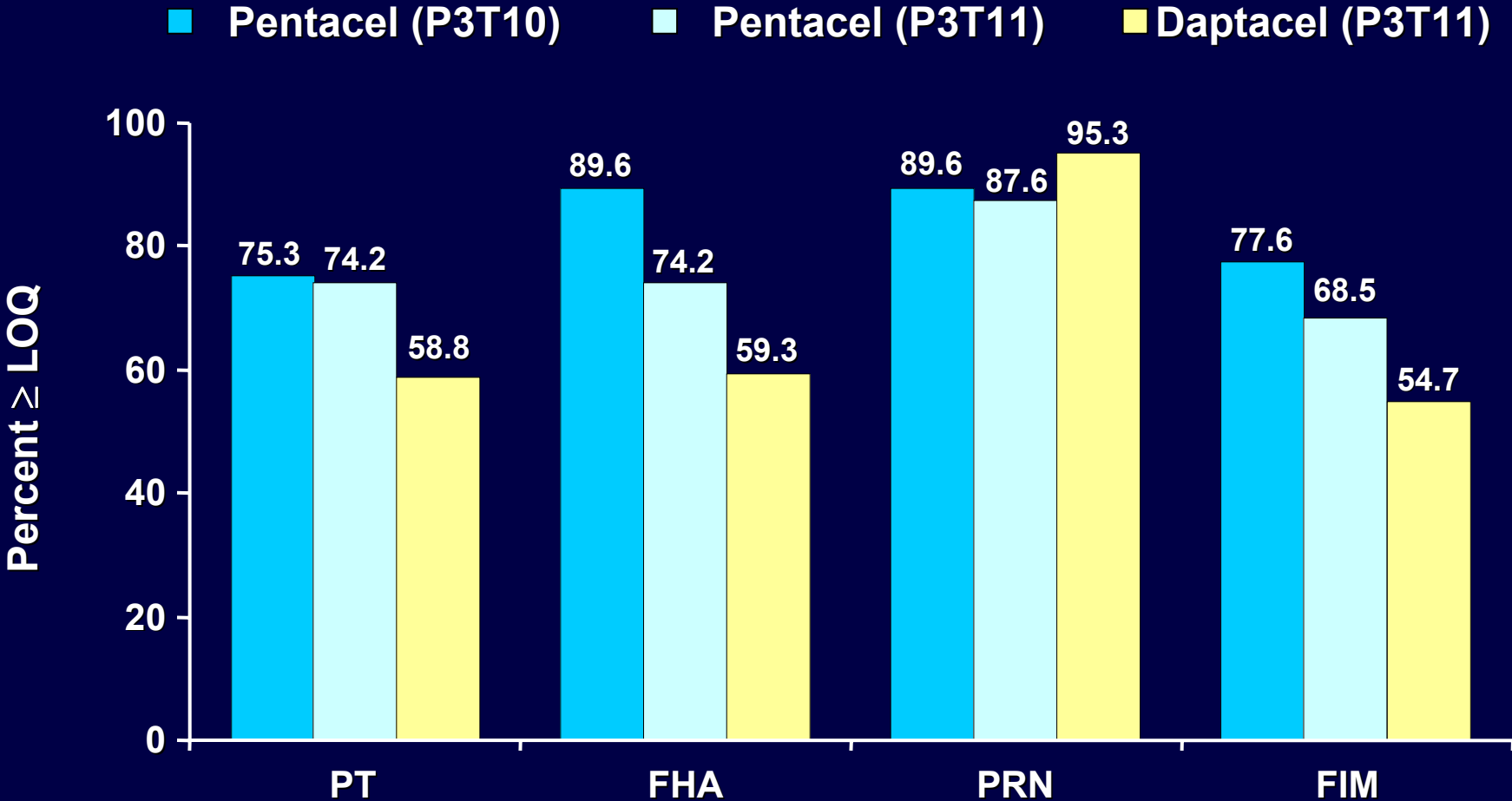


Pentacel	97.3	53.6	32.5	193.8
Control	66.5	22.5	33.6	181.7

5th Dose Follow-up Studies to 494-01, P3T06: Studies P3T10 and P3T11

- **Multi-center, randomized, open-label studies**
- **Solicited all Pentacel or Daptacel recipients in P3T06 and 494-01 to participate at 4-6 yrs of age**
- **Sample size for pertussis immunogenicity**
 - 259 in P3T10
 - 363 in P3T11 (89 primed with Pentacel, 274 primed with Daptacel)
- **Blood obtained for serology immediately prior to 5th dose**

Percent Seropositive* at *Pre-Dose 5*, By Study and Pertussis Antigen



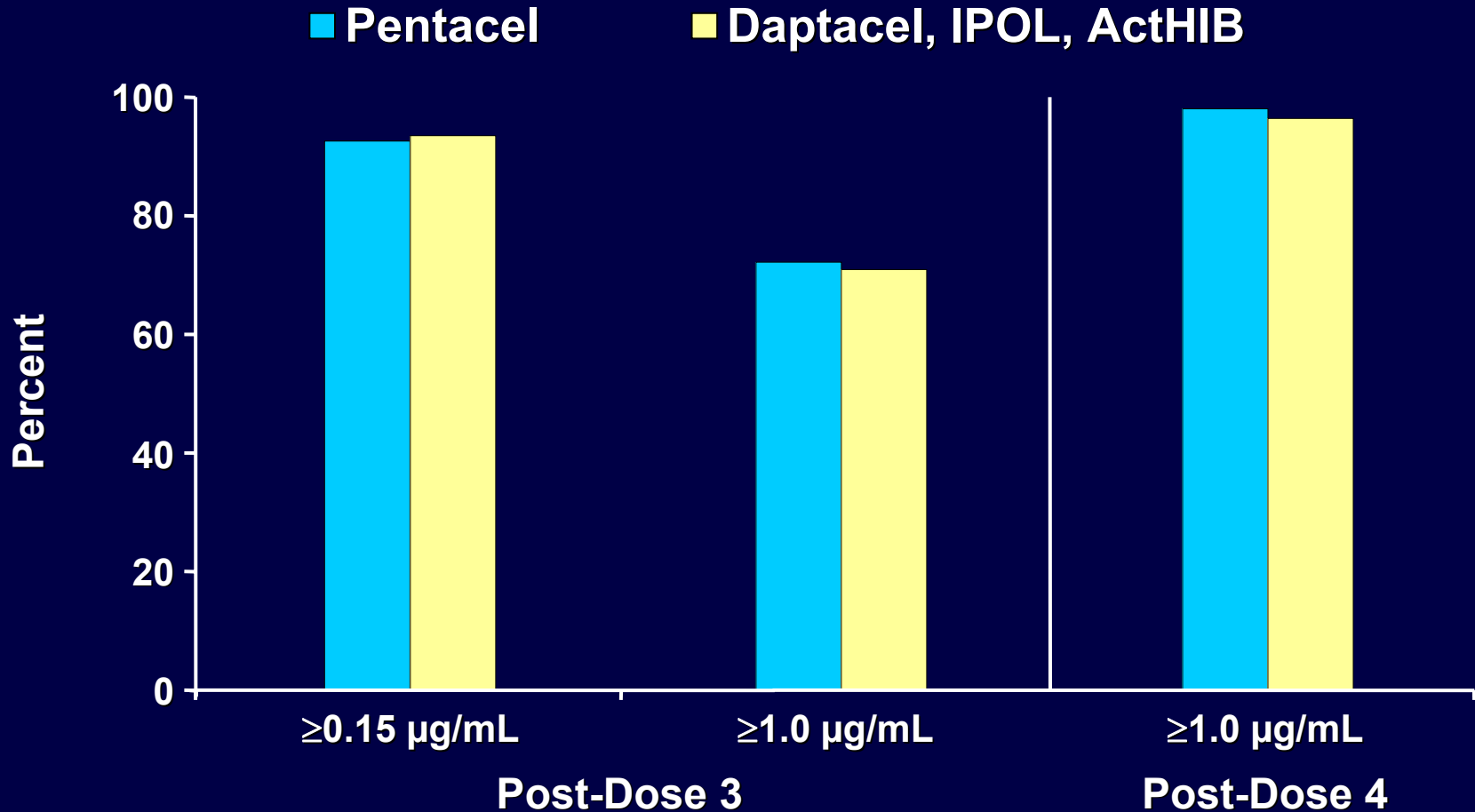
*≥LOQ: PT, 5; FHA, 3; PRN, 3; FIM, 17

Immunogenicity

- Pertussis Immunogenicity
- Hib (PRP) Immunogenicity

P3T06: Pentacel vs Daptacel, IPOL, ActHIB

Post-Doses 3 and 4: Hib Seroprotection Rates



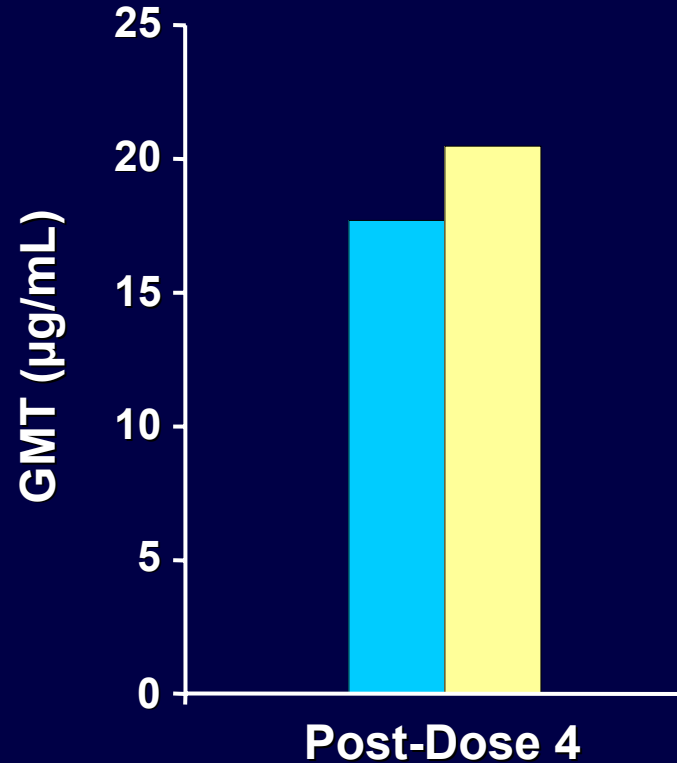
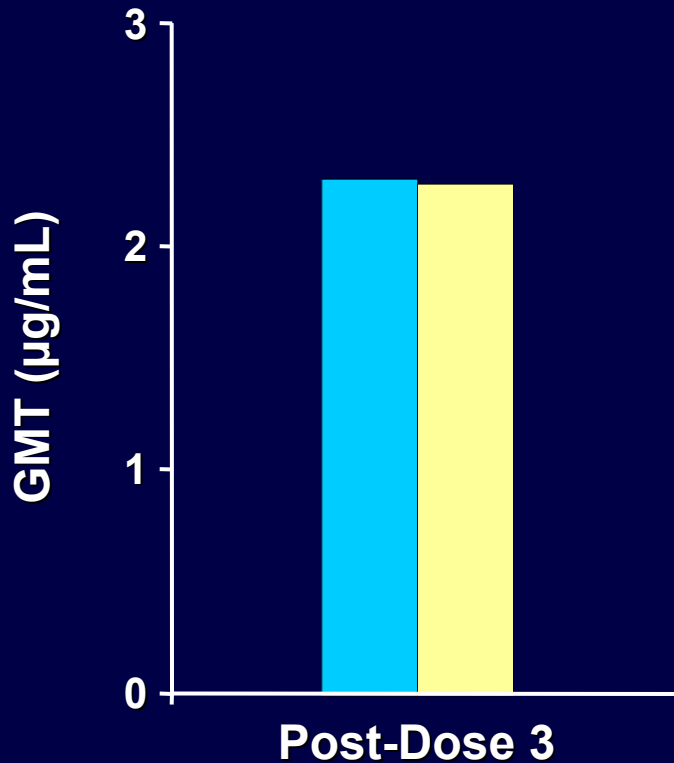
Pentacel	92.3	72.1	97.8
Control	93.3	70.8	95.9

P3T06: Pentacel vs Daptacel, IPOL, ActHIB

Post-Doses 3 and 4: Hib GMTs

■ Pentacel

■ Daptacel, IPOL, ActHIB

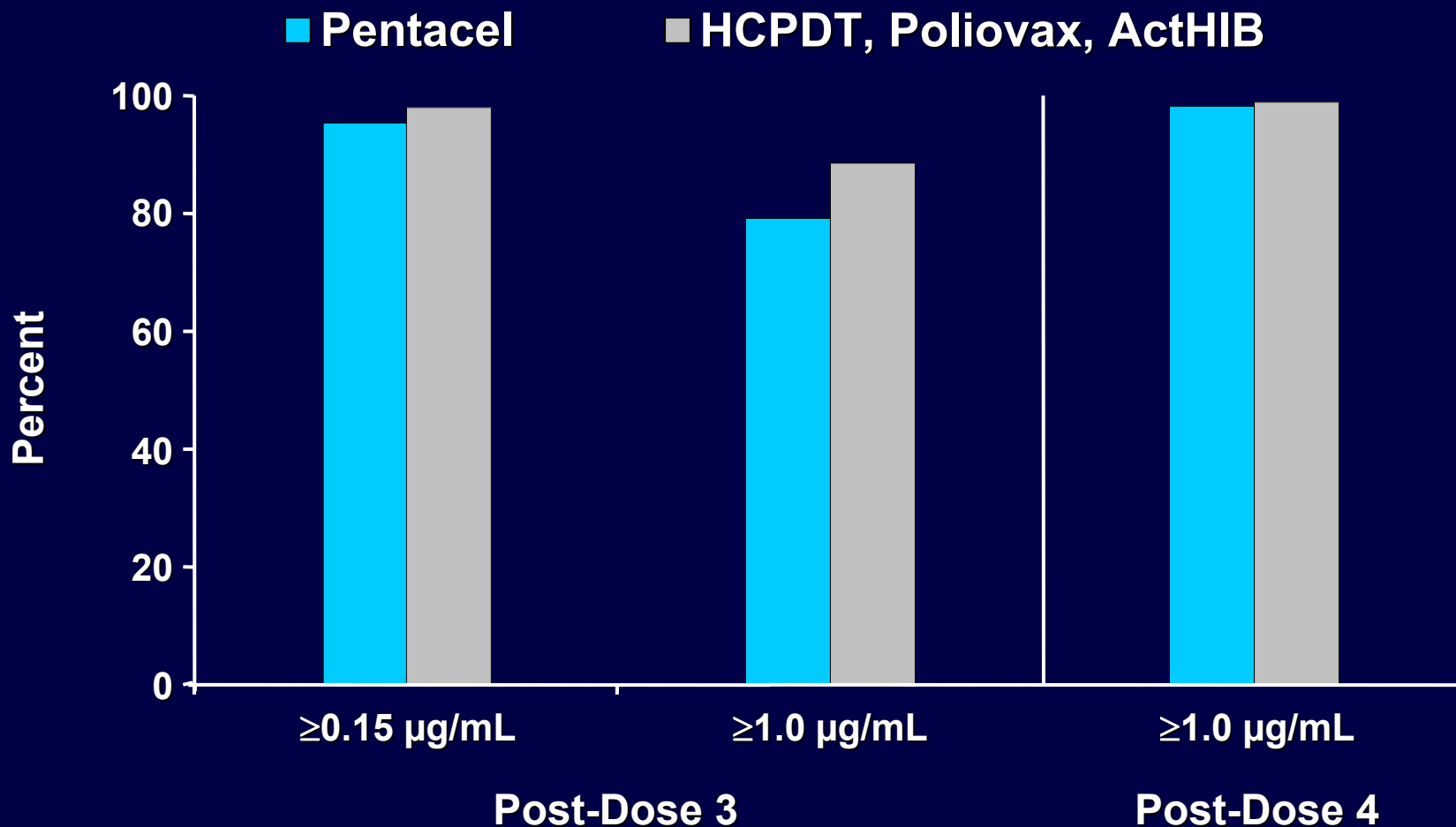


Pentacel	2.31
Control	2.29

17.71
20.49

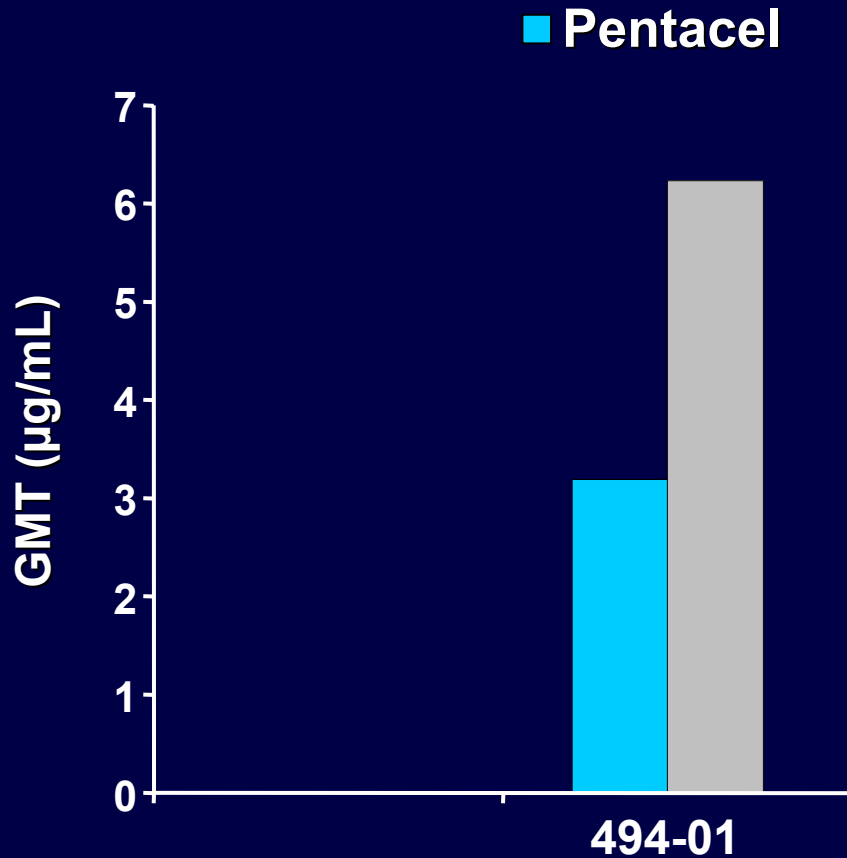
494-01: Pentacel vs HCPDT, Poliovax, ActHIB

Post-Doses 3 and 4: Hib Seroprotection Rates

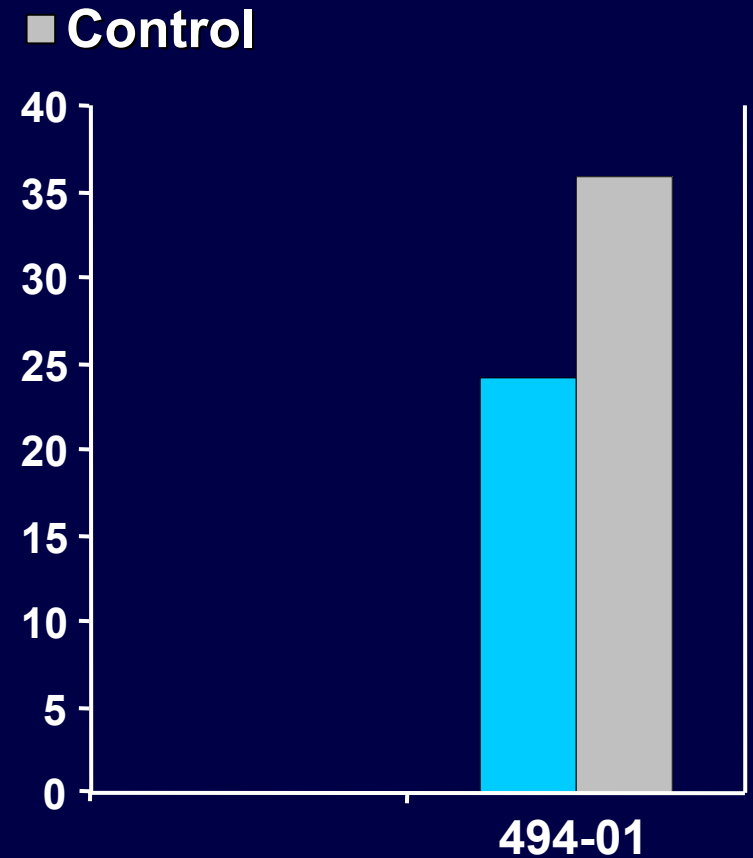


Pentacel	95.4	79.1	98.2
Control	98.3	88.8	99.0

P3T06 and 494-01: Comparison of Hib GMTs *Post-Doses 3 and 4*



Post-Dose 3

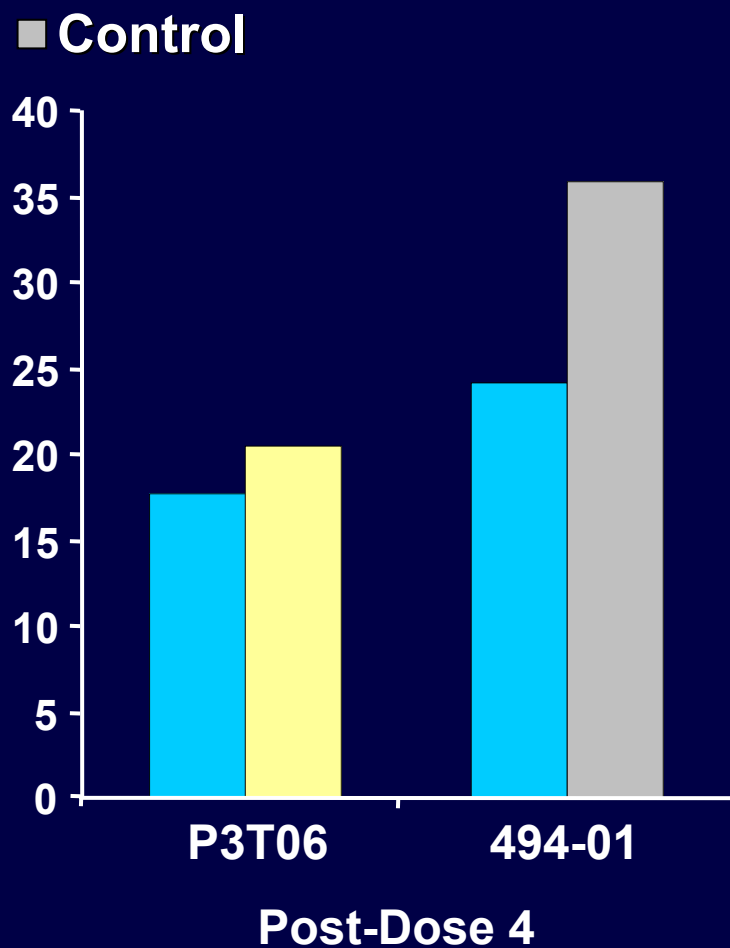
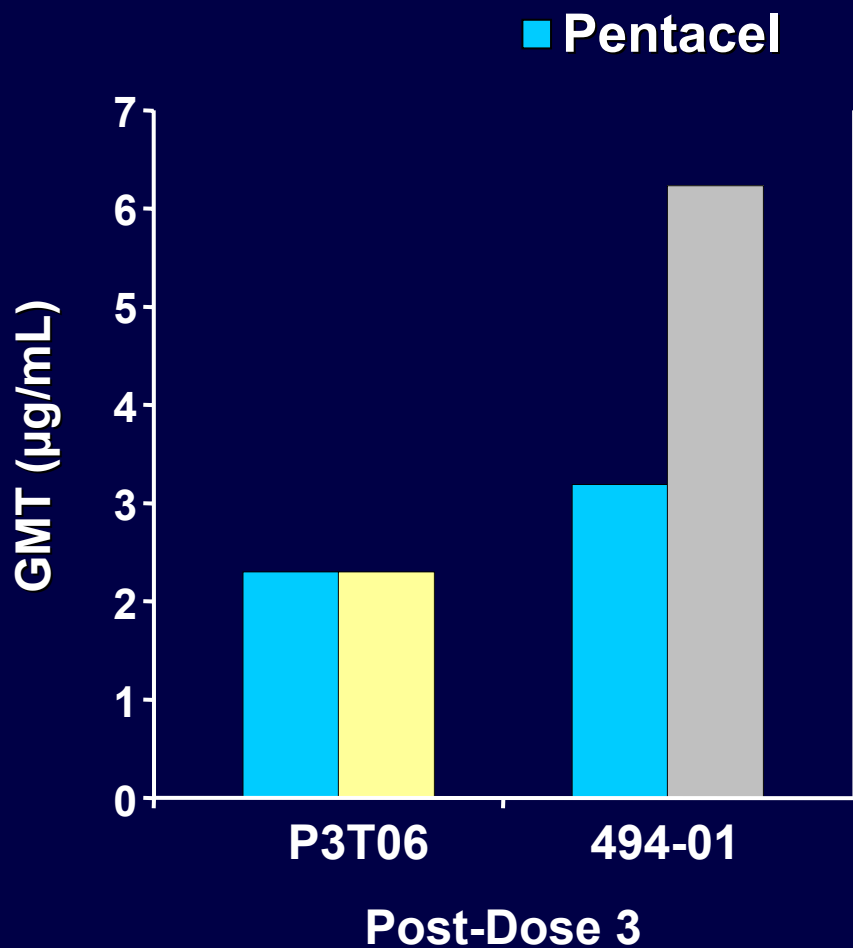


Post-Dose 4

Pentacel		3.19
Control		6.23

		24.12
		35.90

P3T06 and 494-01: Comparison of Hib GMTs *Post-Doses 3 and 4*

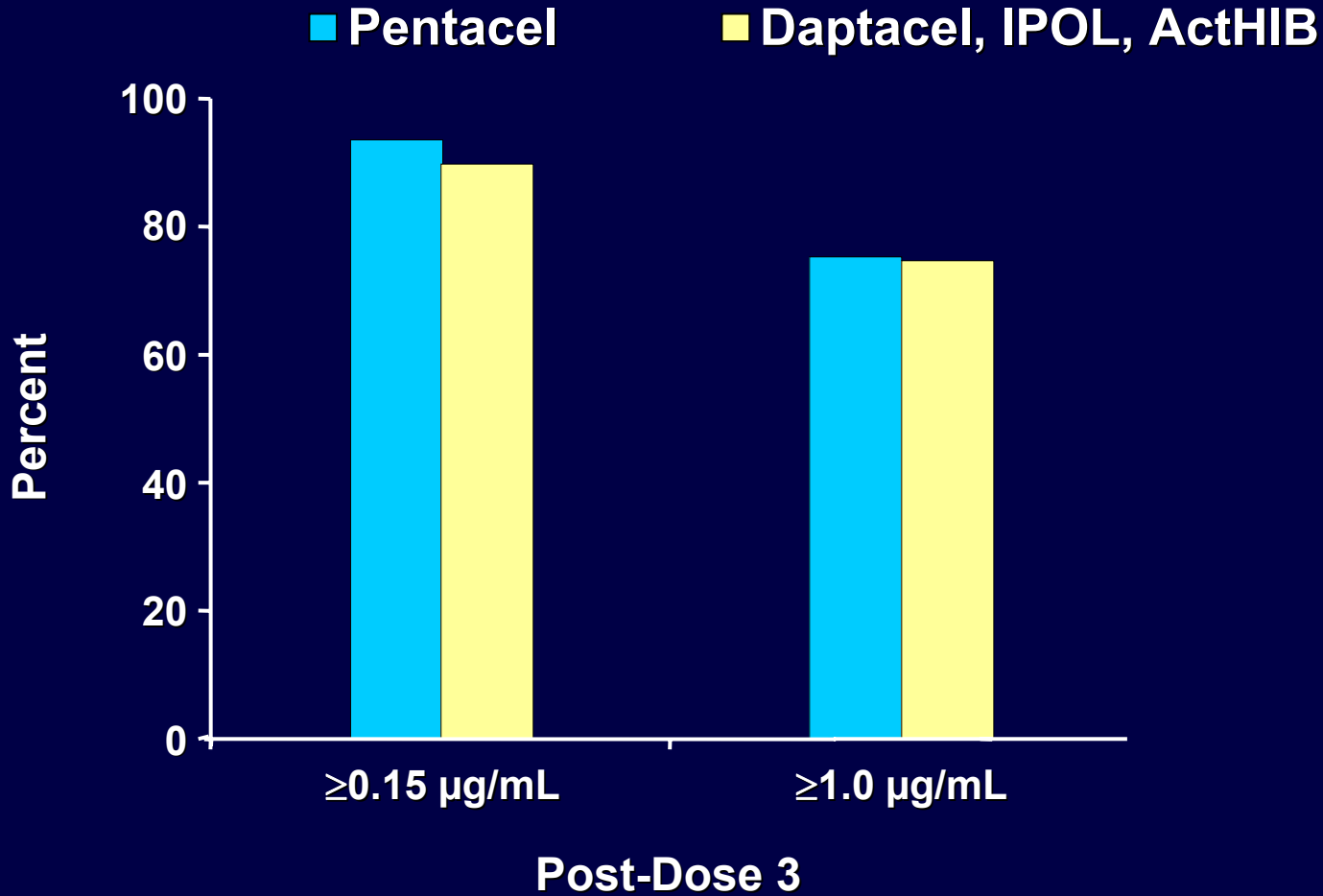


Pentacel	2.31	3.19
Control	2.29	6.23

17.71	24.12
20.49	35.90

M5A10: Pentacel vs Daptacel, IPOL, ActHIB

Post-Dose 3: Hib Seroprotection Rates

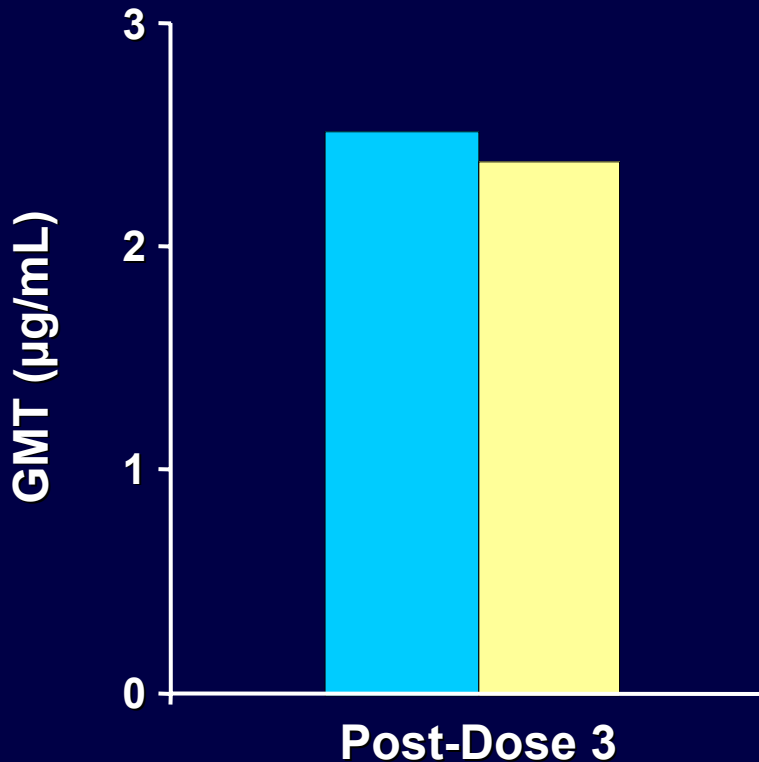


Pentacel	93.8	75.1
Control	90.3	74.8

M5A10: Pentacel vs Daptacel, IPOL, ActHIB

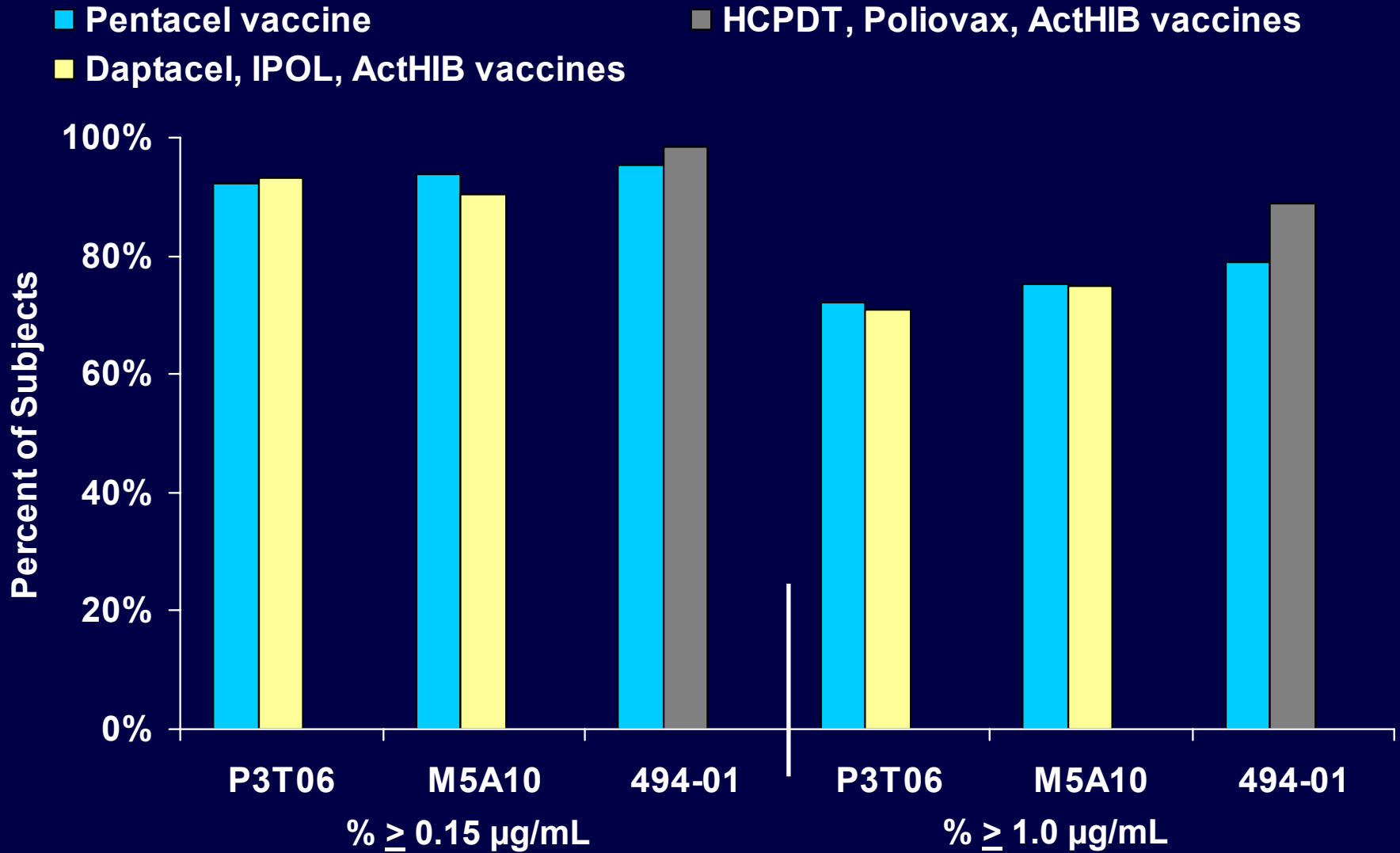
Post-Dose 3: Hib GMTs

■ Pentacel ■ Daptacel, IPOL, ActHIB

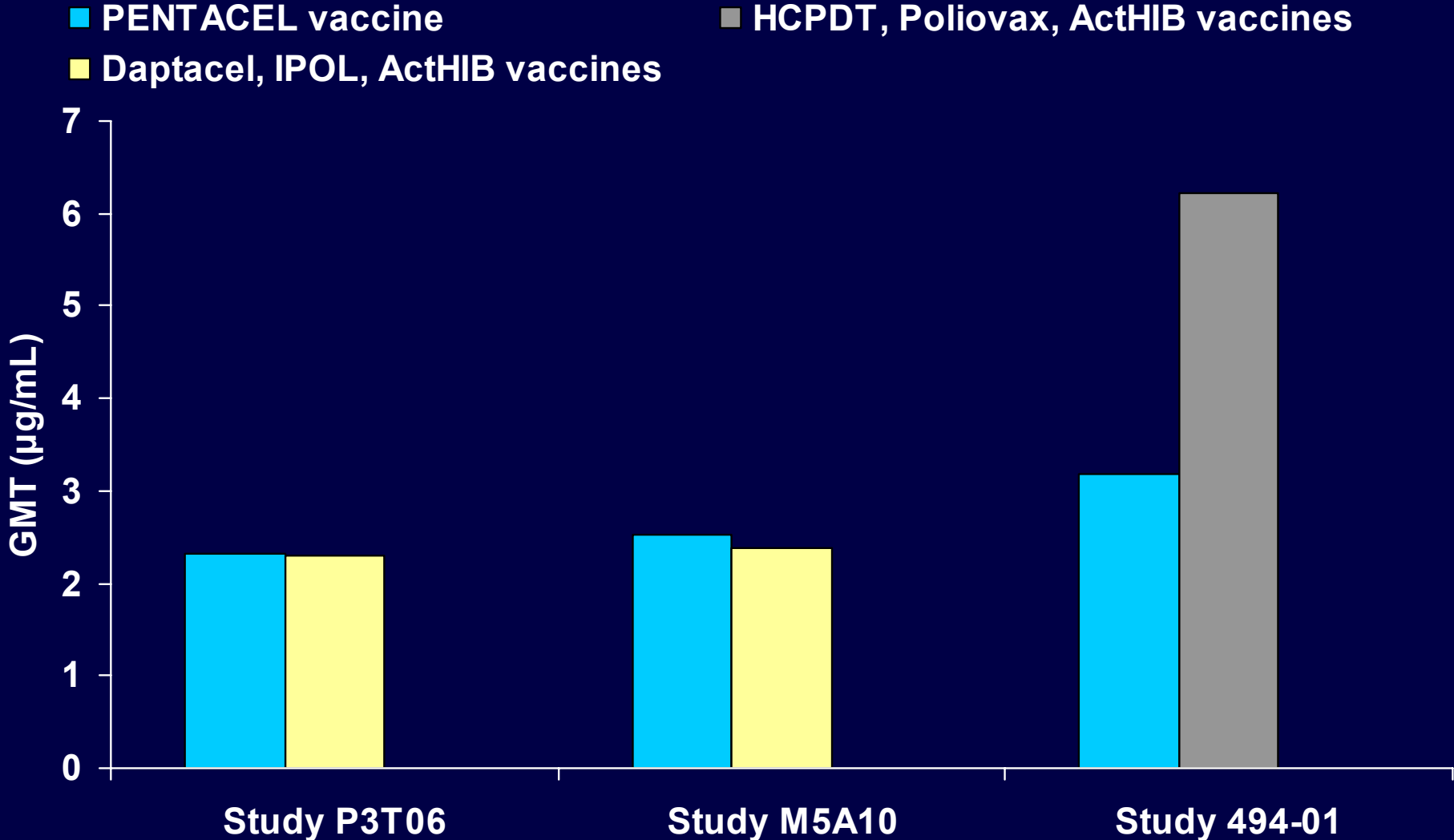


Pentacel	2.52
Control	2.38

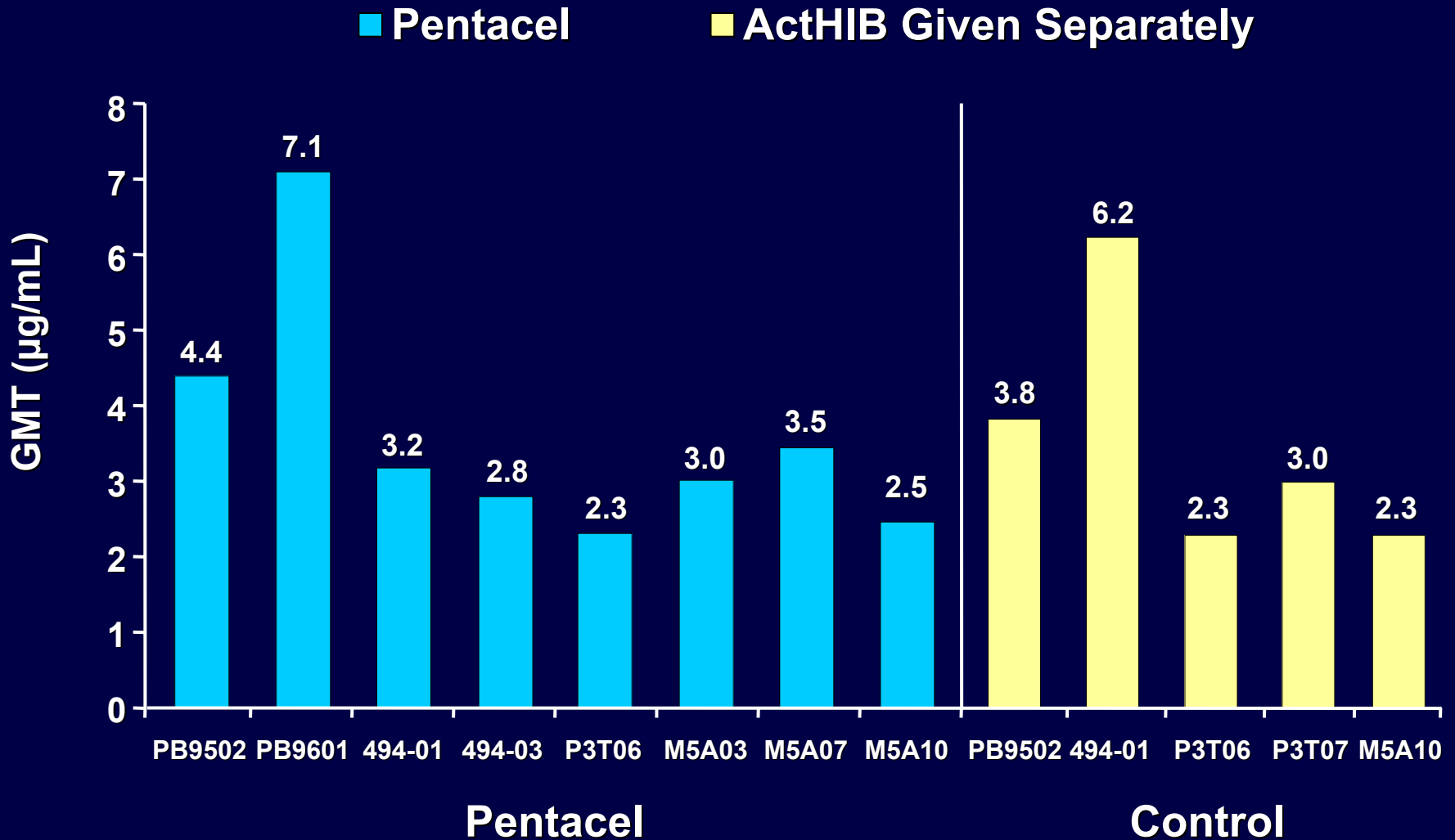
Hib Seroprotection Rates, Post-Dose 3



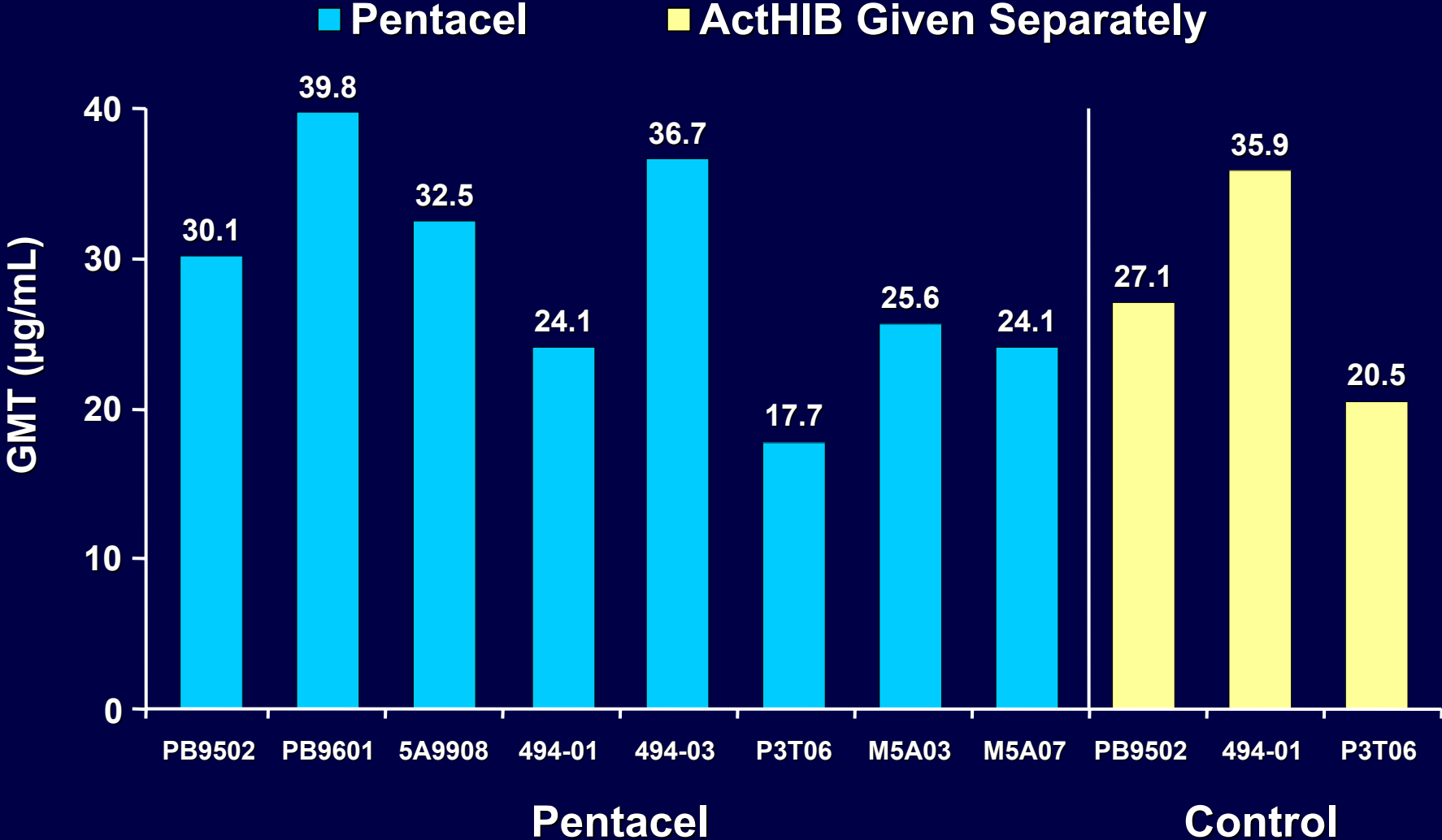
Hib GMTs, Post-Dose 3



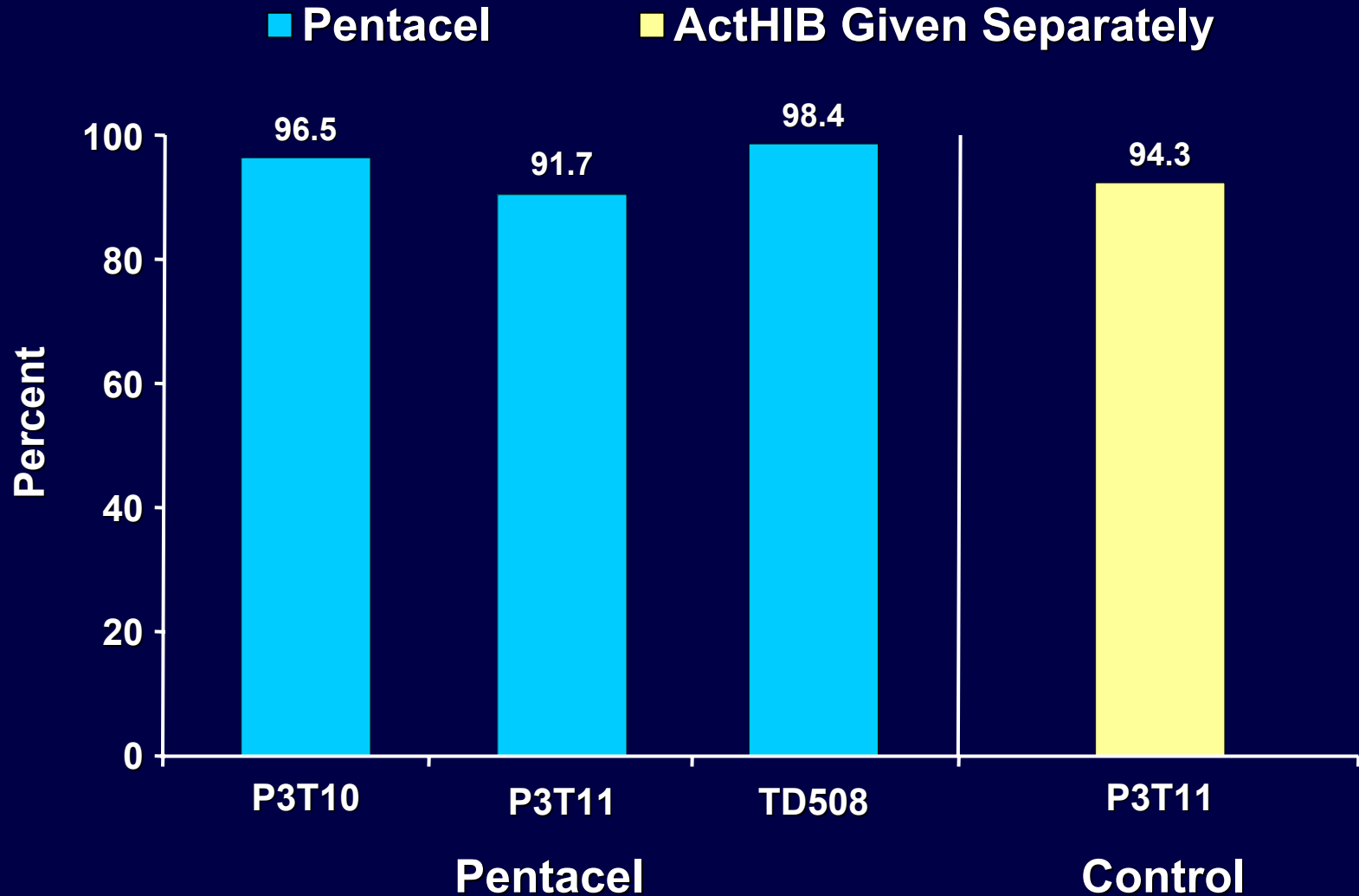
Hib GMTs at *Post-Dose 3*, By Study



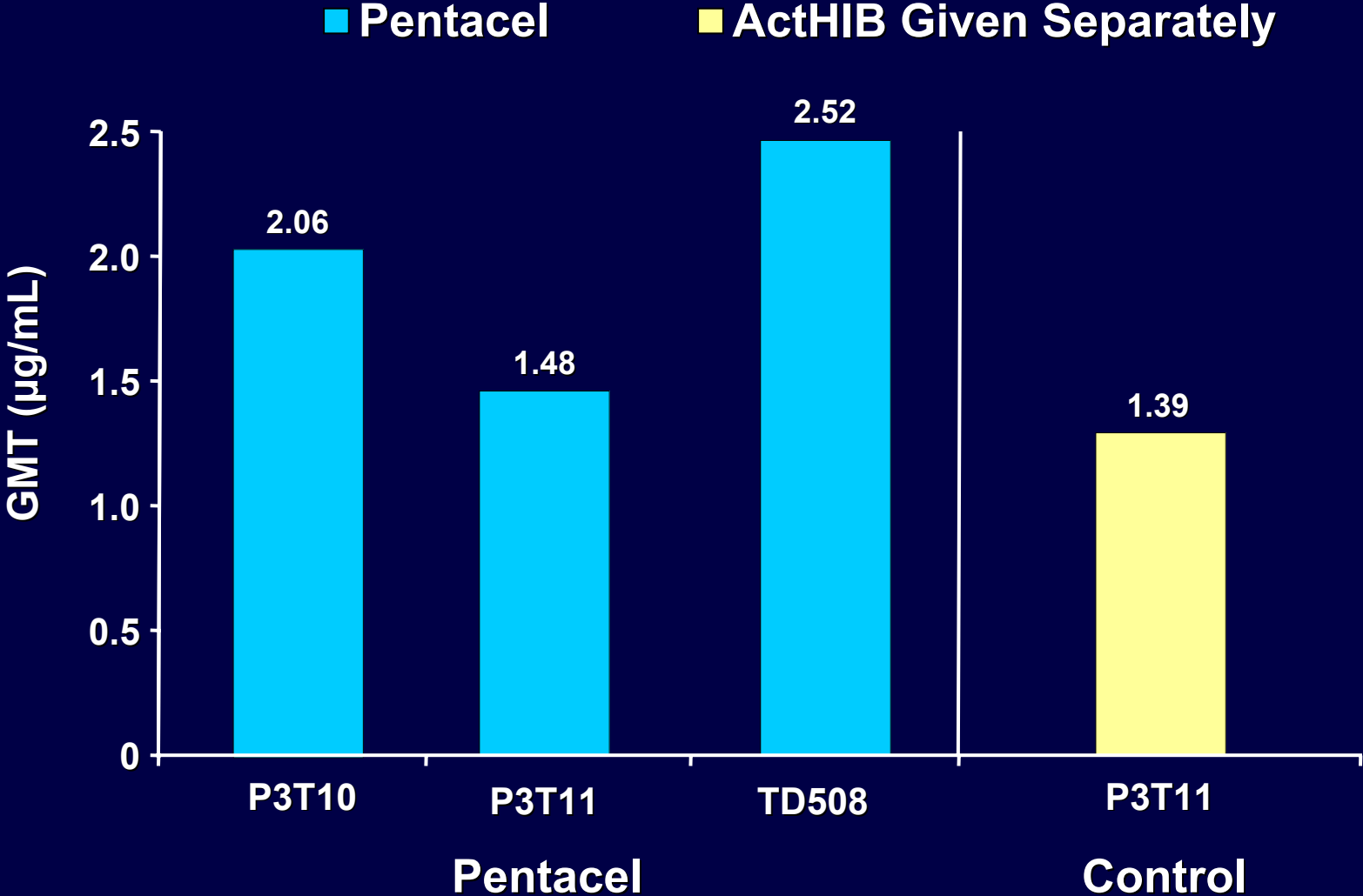
Hib GMTs at *Post-Dose 4*, By Study



Hib Seroprotection ($\geq 0.15 \mu\text{g/mL}$) at *Pre-Dose 5*, By Study



Hib GMTs at *Pre-Dose 5*, By Study



Pentacel Immunogenicity Conclusions

- **Pentacel efficacy against Pertussis can be concluded based on serological bridge to the Sweden I Efficacy Trial**
- **Pentacel produced Hib GMTs and seroprotection rates that were comparable to separately administered standard US vaccines**
- **Immune responses were similar when Pentacel was administered alone or concomitantly with other vaccines**

2008 Recommended Childhood Immunization Schedule: Birth – 18 Months

Vaccine ▼	Age ►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months
Hepatitis B ¹		HepB	HepB			HepB			
Rotavirus ²				Rota	Rota	Rota			
Diphtheria, Tetanus, Pertussis ³				DTaP	DTaP	DTaP		DTaP	
<i>Haemophilus influenzae</i> type b ⁴				Hib	Hib	Hib⁴	Hib		
Inactivated Poliovirus				IPV	IPV	IPV			
Pneumococcal ⁵				PCV	PCV	PCV	PCV		
Influenza ⁶						Influenza (Yearly)			
Measles, Mumps, Rubella ⁷							MMR		
Varicella ⁸							Varicella		
Hepatitis A ⁹							HepA (2 doses)		

Pentacel: First DTaP-IPV-Hib Combination Vaccine in the US

Unique Benefits for Entire Immunization Community

■ Patient Benefits

- Maximum shot reduction
- Well established safety profile including 10 years of exclusive use in Canada

■ Health Care Provider Benefits

- Optimizes implementation of immunization recommendations
- Simplifies administration

■ Public Health Benefits

- May improve vaccination coverage rates and timeliness
- Improves combination and Hib vaccine supply