

**GSK's novel
Pneumococcal
non-typeable *Haemophilus influenzae* protein D
conjugate vaccine**

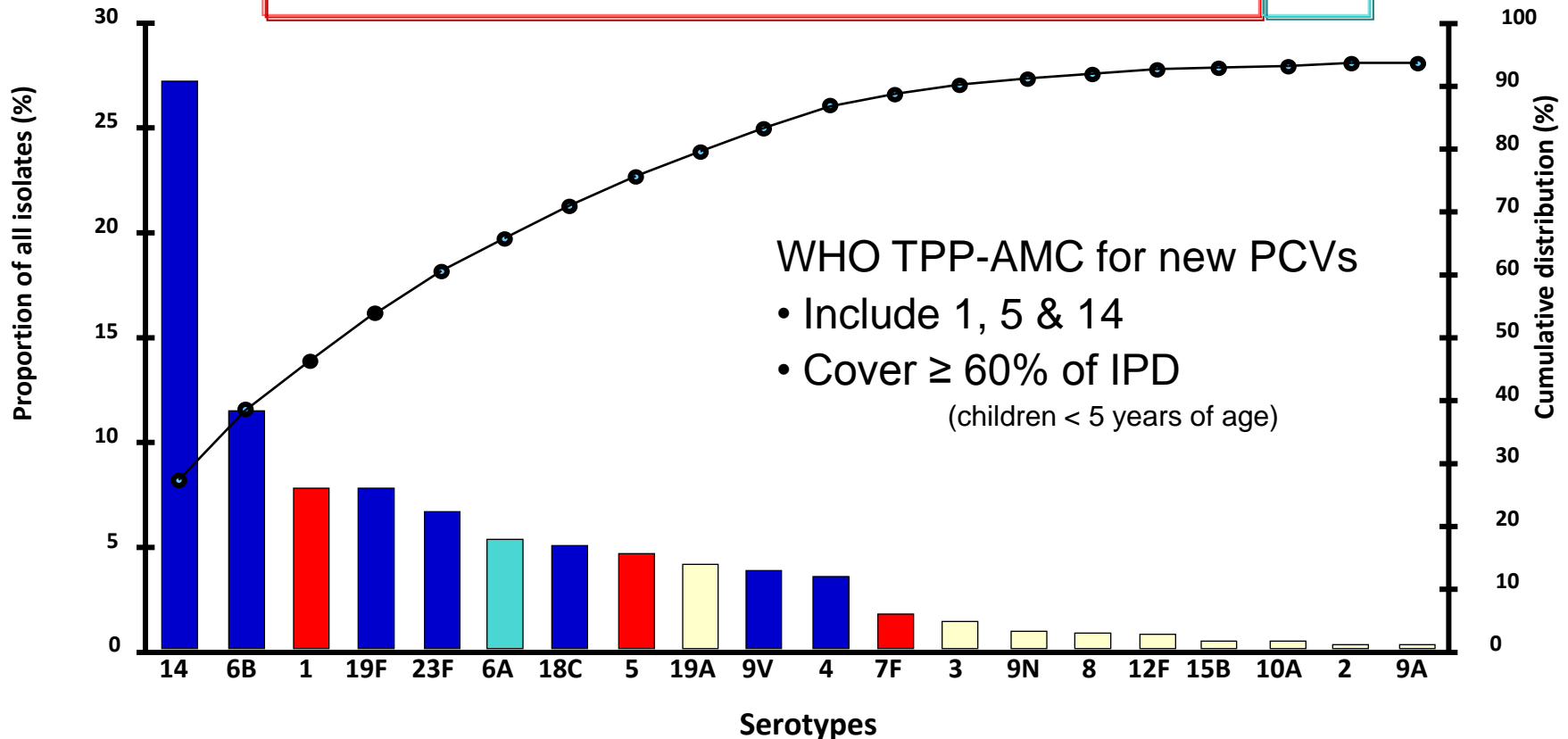
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GSK - Global Medical Affairs**

Serotypes covered by available PCV's

Serotype distribution of invasive disease-causing pneumococcal isolates in children < 5 years of age¹

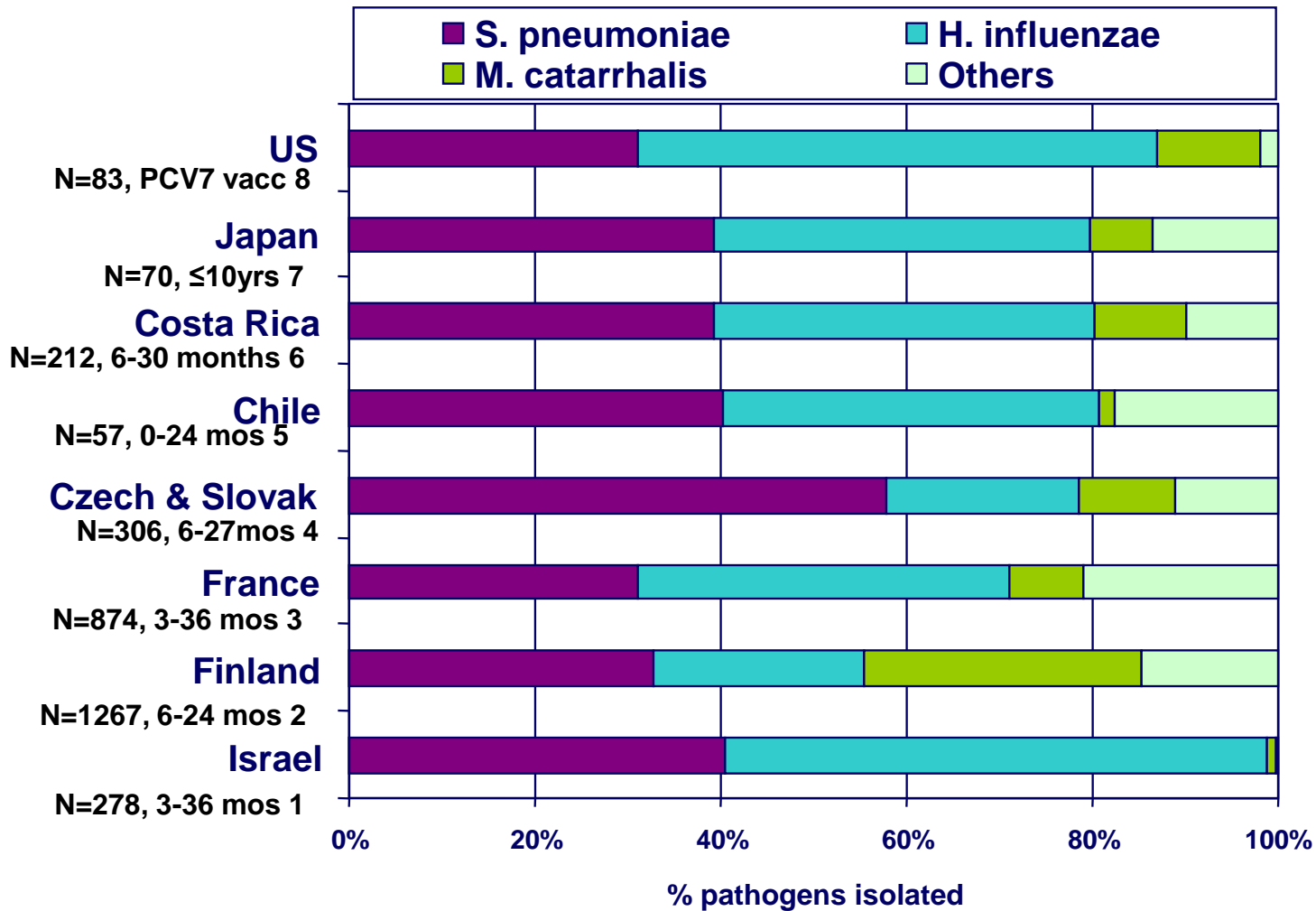
Global Distribution

PCV7-CRM	4	6B	9V	14	18C	19F	23F	6A*	
PHiD-CV	4	6B	9V	14	18C	19F	23F	1 5 7F	6A*



*Assumes 6A cross protection P^oHiD-CV and PCV-7 generate Immune response against STs 6A.

AOM Bacteriology in young children



S. pneumoniae
&
H. influenzae
=
the two major
bacterial AOM
pathogens

Vast majority of
H. influenzae
causing AOM are
non-typeable

N= Number of bacterial positive AOM episodes in infants

1. Liebovitz PIDJ 2003;
2. Eskola New Engl J Med 2001;
3. Gehanno PIDJ 2001;
4. Prymula Lancet 2006;
5. Rosenblut PIDJ 2001;
6. Arguedas PIDJ 2005;
7. Suzuki PIDJ 2005;
8. Block PIDJ 2004

Synflorix™ vaccine profile

PHiD-CV

Pneumococcal non-typeable *Haemophilus influenzae*-Protein D Conjugate Vaccine

1 4 5 7F 6B 9V 14 18C 19F 23F Protein D
18C-TT 19F-DT

- includes 10 pneumococcal serotypes (1,5 and 7F + PCV7 ST)
- minimize risk of interferences with co-administered vaccines by inclusion of a unique carrier protein (NTHi-Protein D) for 8 of the 10 serotypes
- potentially offers protection against NTHi by virtue of Protein D carrier protein (NTHi-Protein D), based on clinical experience*

S. pneumoniae

Meningitis

Sepsis

Pneumonia

Invasive infections

Immunogenicity profile

PHiD-CV clinical program was developed according to WHO and CHMP guidelines¹

Immunogenicity:

➤ ELISA (non-inferiority to PCV-7)

➤ Functional capacity (OPA) documentation

➤ Boostability demonstration



WHO & CHMP criteria

Co-administration with other paediatric vaccines

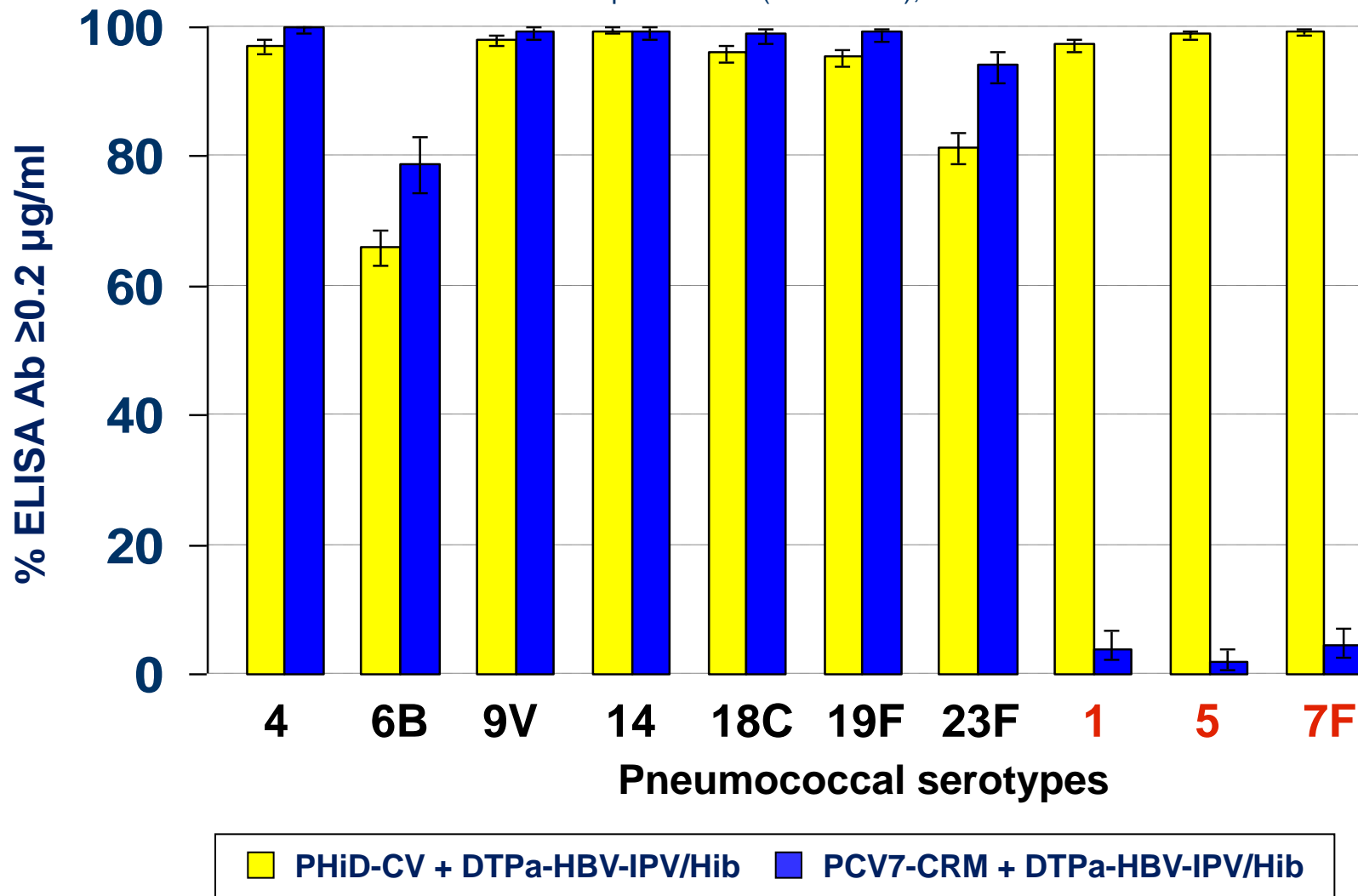
Safety & tolerability

Immunization schedules

➤ 2-3-4m; 3-4-5m; 2-4-6m; 3-5-11m; 6-10-14 wks

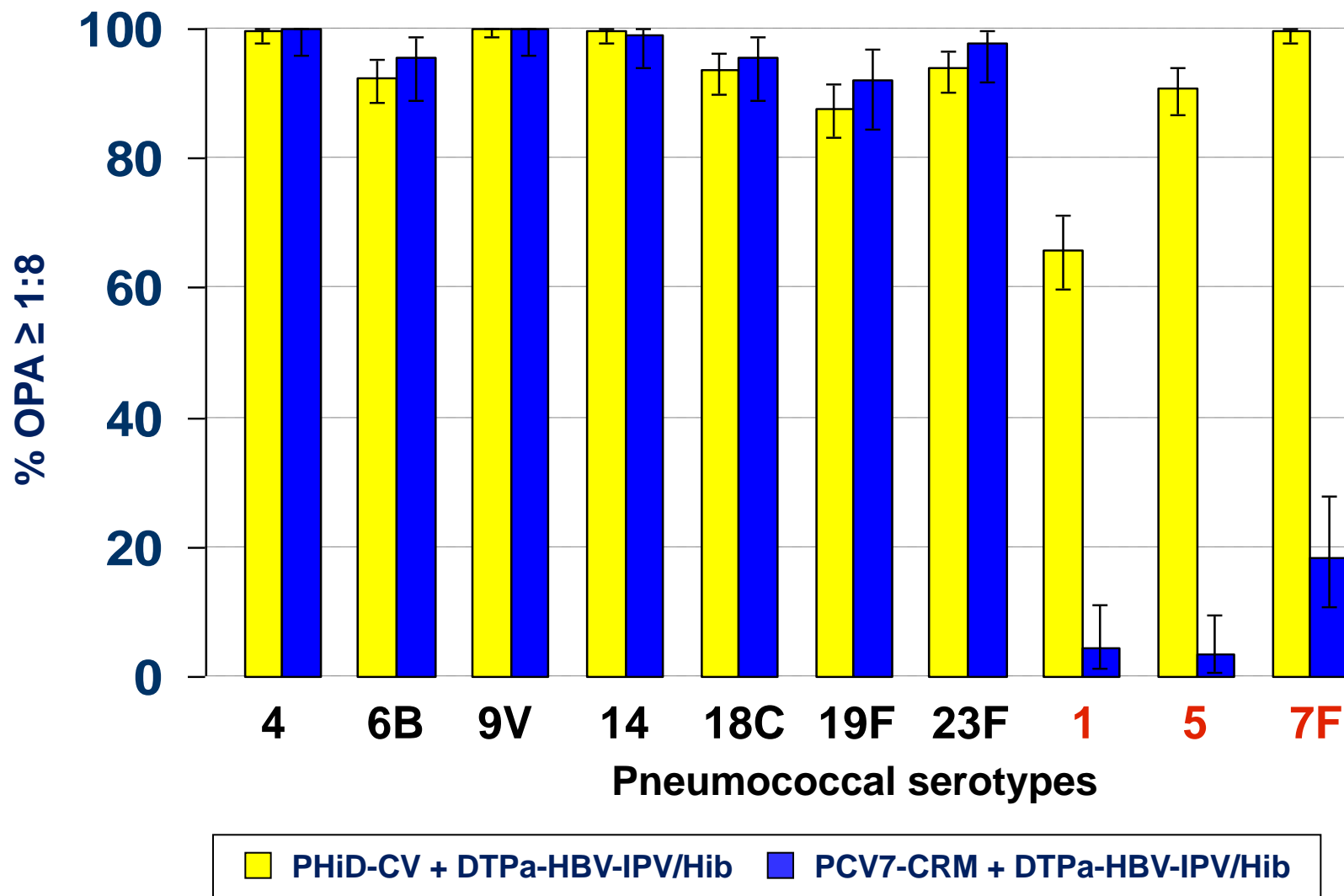
PHiD-CV is immunogenic for all serotypes (2-3-4 months schedule, DTPa combos co-administration)

Anti-pneumococcal serotype antibody % $\geq 0.2 \mu\text{g/ml}$
one month post-dose 3 (22F-ELISA); 2-3-4 mo



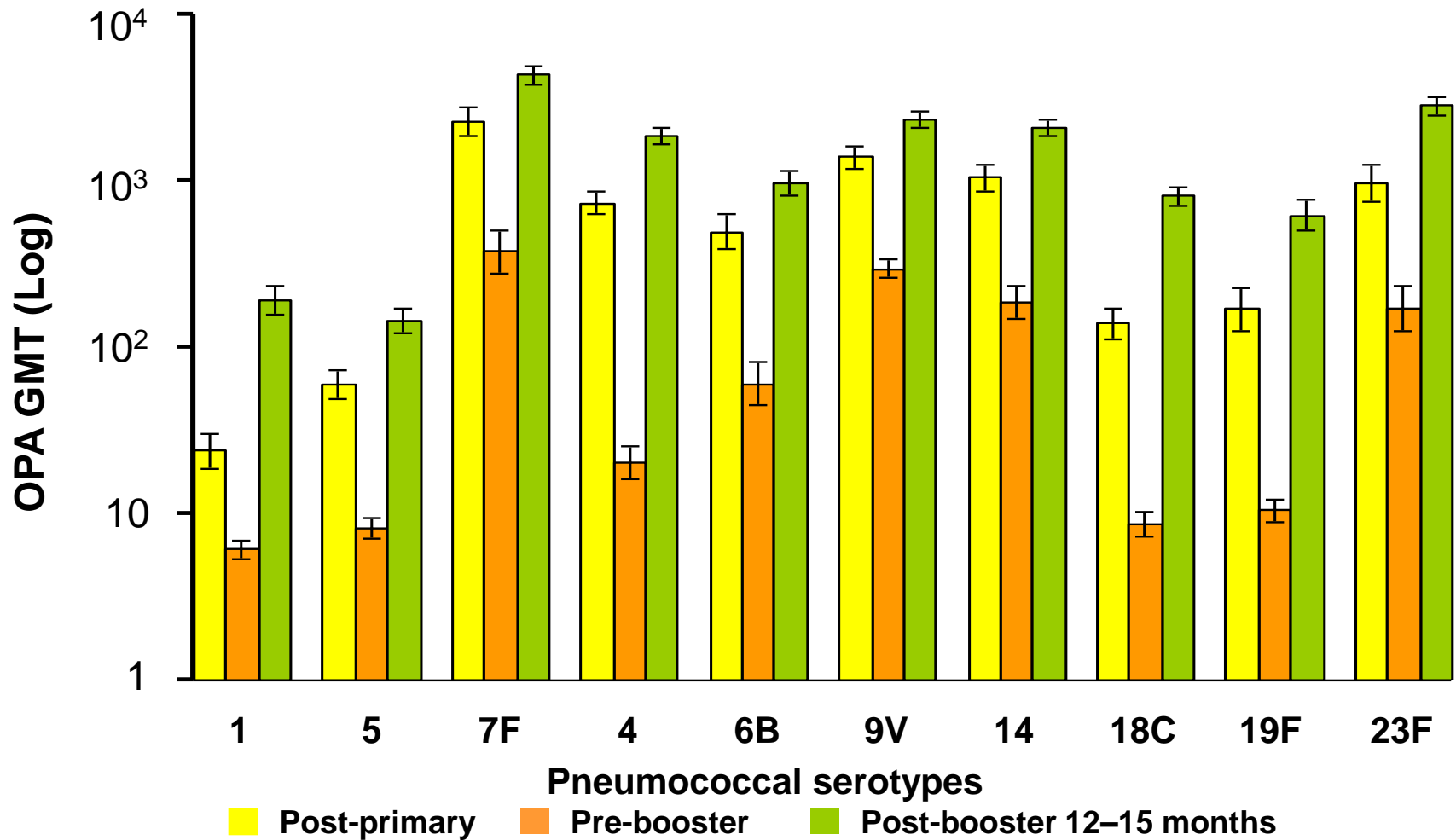
Anti-pneumococcal serotype OPA % \geq 1:8 one month post-dose 3; 2-3-4 mo

Study 10Pn-PD-DIT-001



Robust booster response observed for all serotypes by OPA and ELISA

Study 10Pn-PD-DIT-001&007



≥ 91.0% of subjects with OPA ≥ 8 post-booster

Booster Interchangeability: ELISA and OPA responses post-booster

	% subjects $\geq 0.2 \mu\text{g/mL}$			% subjects ≥ 8		
	PHiD-CV	PCV7 + PHiD-CV	PCV7	PHiD-CV	PCV7 + PHiD-CV	PCV7
4	99.7	100	100	100	100	100
6B	96.5	98.5	97.7	96.6	94.9	98.7
9V	100	100	100	100	100	100
14	99.1	100	100	100	100	100
18C	100	99.3	100	99.7	98.3	100
19F	99.4	97.8	100	94.9	98.3	92.5
23F	97.4	97.0	98.9	99.7	98.4	98.8
1	99.4	85.0	4.9	91.0	31.4	3.6
5	99.4	85.7	6.1	96.3	36.9	1.2
7F	100	95.5	7.1	99.7	98.3	31.1

PHiD-CV elicits antibody response and evidence of functional activity against vaccine related serotype 6A similar to PCV7

	PHiD-CV			PCV7		
	N	%> 8	GMT	N	%> 8	GMT
Post-primary						
DTPa combination coadministration						
2-3-4 mo (study 001/007)	260	58.0	40.9	89	68.5	83.3
2-4-6 mo (study 011/017) +Hib-MenC-TT	161a	74.0	100.9	156a	87.4	231.5
2-4 mo (study 011/017) (Post-dose2)	140 ^a	60.5^b		137a	26.8	
DTPw combination coadministration						
6-10-14 wks (study 012) +OPV	127	71.7	93.1	43	79.1	137.3
2-4-6 mo (study 012) +IPV	137	60.6	60.5	48	75.0	175.1
Post-booster (DTPa combination coadministration)						
After 2-3-4 mo (study 001/007)	327 ^a	85.0	254.8	84 ^a	94.4	872.7
After 2-4-6 mo (study 011/017) +Hib-MenC-TT	146 ^a	91.4	293.7	143 ^a	97.5	1166.4

PCV7-CRM: *Prevenar*™, Wyeth

PHiD-CV: Synflorix™, GSK Biologicals

^aThe actual number of subjects tested can slightly vary depending on the number of sera available for the present serotype

^b Synflorix™ groups pooled

Adapted from Vesikari et al. *Ped Infect Dis J* 2009;28(4), S66-76 ; Wysocki et al., *Ped Infect Dis J* 2009;28(4), S77-88; Bernal et al., *Ped Infect Dis J* 2009;28(4), S89-96

PHiD-CV elicits antibody response and evidence of OPA activity against vaccine related serotype 19A

	PHiD-CV			PCV7		
	N	%> 8	GMT	N	%> 8	GMT
Post-primary						
DTPa combination coadministration						
2-3-4 mo (study 001/007)	260	19.6	8.6	89	3.4	4.5
2-4-6 mo (study 011/017) +Hib-MenC-TT	161 ^a	19.8	7.1	156 ^a	1	4.1
2-4 mo (study 011/017) (Post-dose2)	146 ^a	4.3^b		137 ^a	0	
DTPw combination coadministration						
6-10-14 wks (study 012) +OPV	137	25.5	10.6	44	2.3	4.2
2-4-6 mo (study 012) +IPV	143	28.7	10.1	49	0	4
Post-booster (DTPa combination coadministration)						
After 2-3-4 mo (study 001/007)	327 ^a	48.8	29.2	84 ^a	27.6	11.1
After 2-4-6 mo (study 011/017) +Hib-MenC-TT	146 ^a	38.5	18.9	143 ^a	23.6	8.7

PCV7-CRM: *Prevenar*™, Wyeth

PHiD-CV: Synflorix™, GSK Biologicals

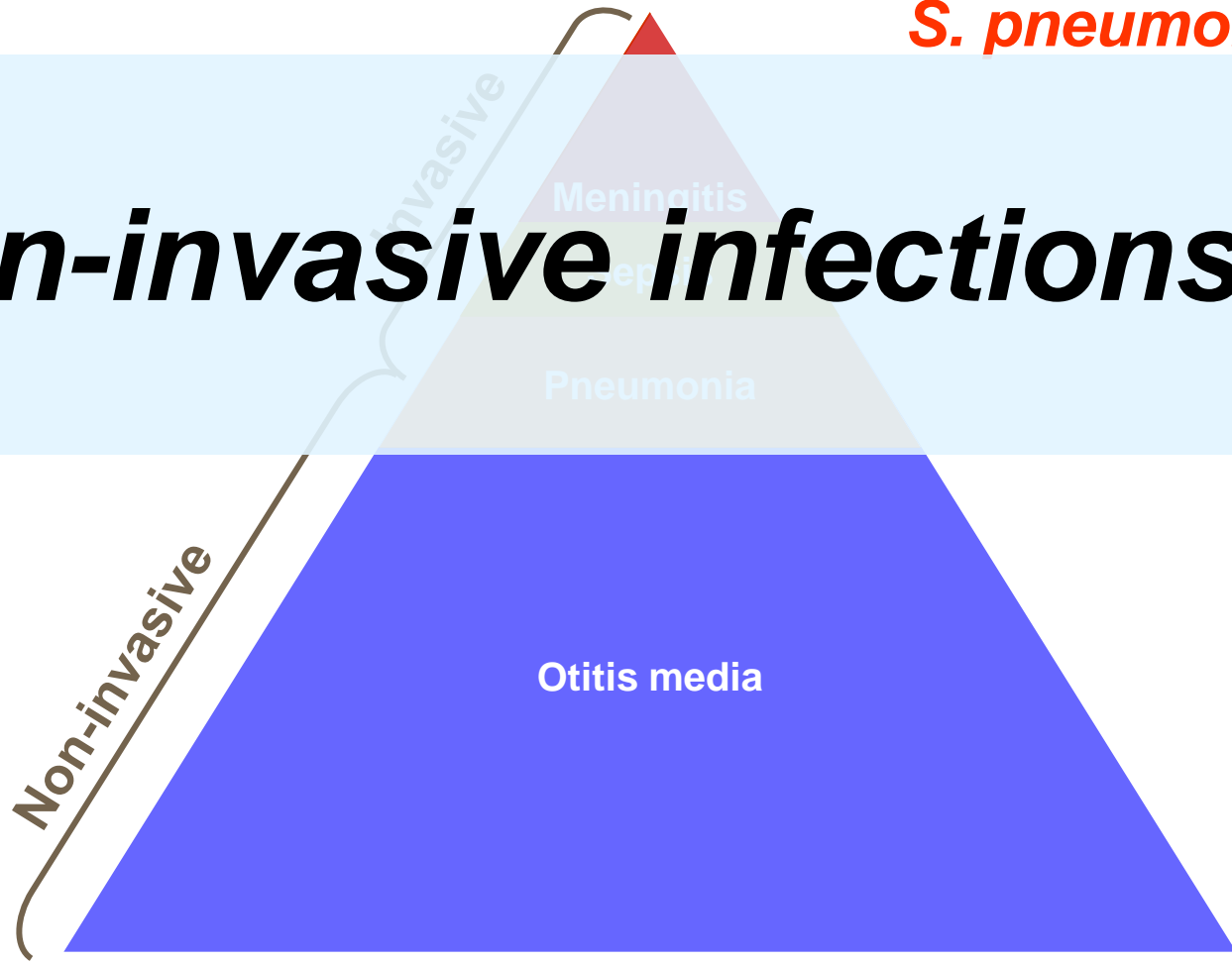
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S. pneumoniae

Non-invasive infections



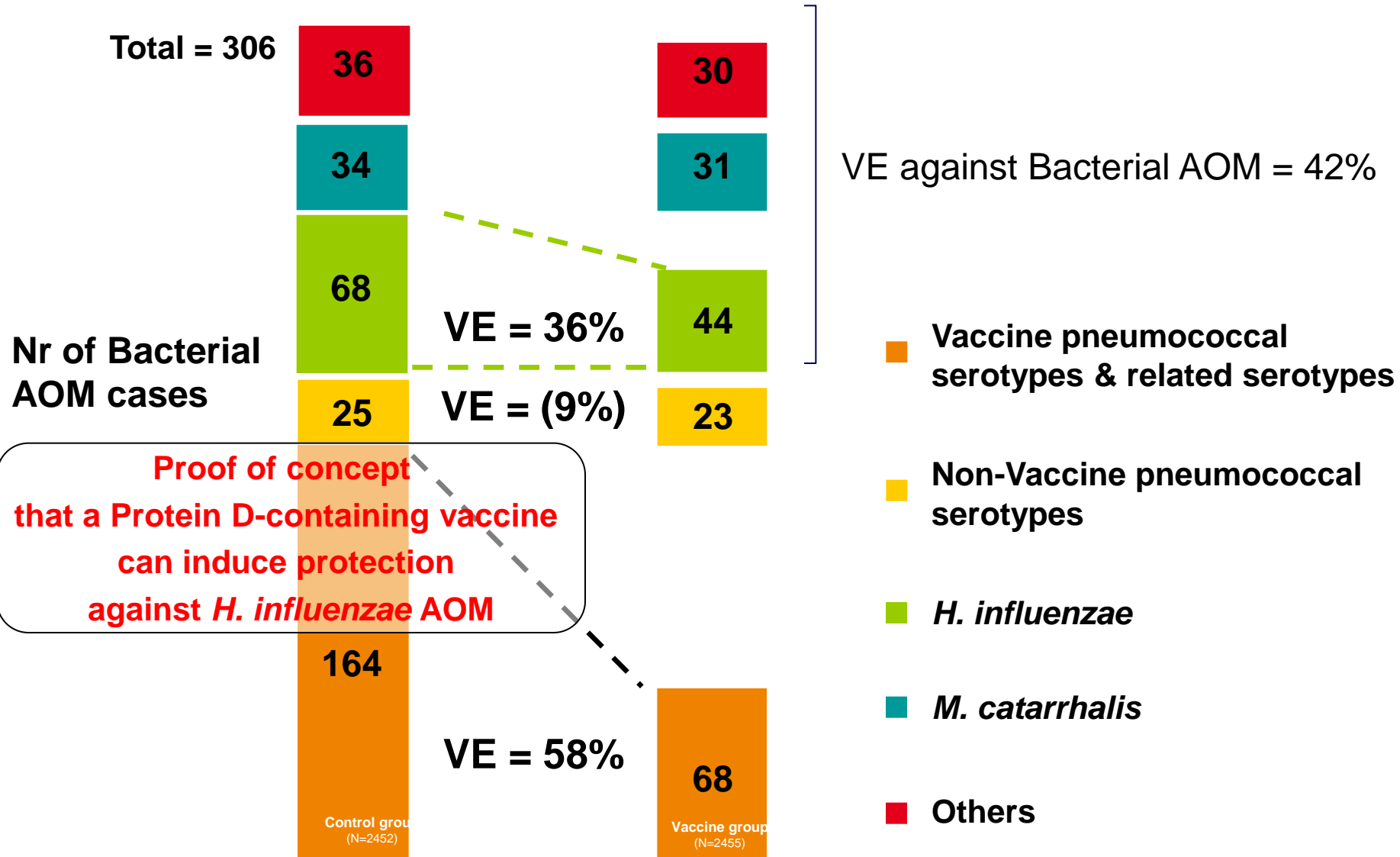
Pneumococcal Otitis media Efficacy Trial (POET)

Vaccine Efficacy Results against AOM

Conducted with experimental 11-valent vaccine, all serotypes Protein D conjugated

Endpoint	Number of episodes		Vaccine Efficacy	P value
	Pneumococcal vaccine	Control vaccine	% (95% CI)	
Clinical episodes*	333	499	33.6 (20.8 to 44.3)	<0.001
Culture confirmed bacterial episodes	178	306	42.1 (27.7 to 53.7)	<0.001
Recurrent AOM	8	18	55.6 (-1.9 to 80.7)	.052
Placement of PE Tubes	4	10	60.2 (-26.7 to 87.5)	.119

Vaccine Efficacy against Bacterial AOM



POET serotype specific AOM Efficacy

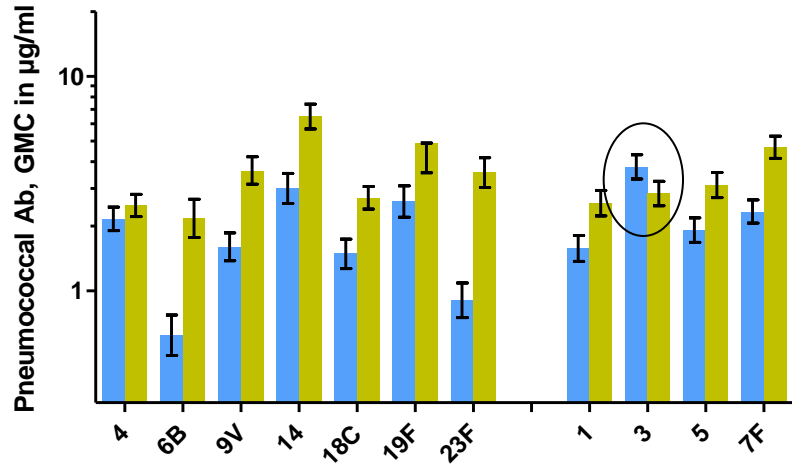
(Experimental 11 valent- vaccine)

	Control (N=2452)	11Pn-PD (N=2455)	VE (%)	95%CI	
4	3	0	100.0	-27.8	100.0
6B	24	3	87.6	58.4	96.3
9V	8	3	62.6	-40.8	90.1
14	22	1	95.5	66.0	99.4
18C	5	3	40.1	-176.6	87.0
19F	43	24	44.4	8.3	66.3
23F	18	5	72.3	24.8	89.8
PCV7 serotypes	122	39	68.2	53.5	78.2
1	1	1	0.2	-1495.0	93.8
3	17	20	-17.1	-126.5	39.5
5	0	0	-		
7F	1	0	100.0	-283.6	100.0
Any VT	141	60	57.6	41.4	69.3
6A	11	4	63.7	-13.9	88.4
19			67.4	-208.7	96.6
A			65.5	22.4	84.7

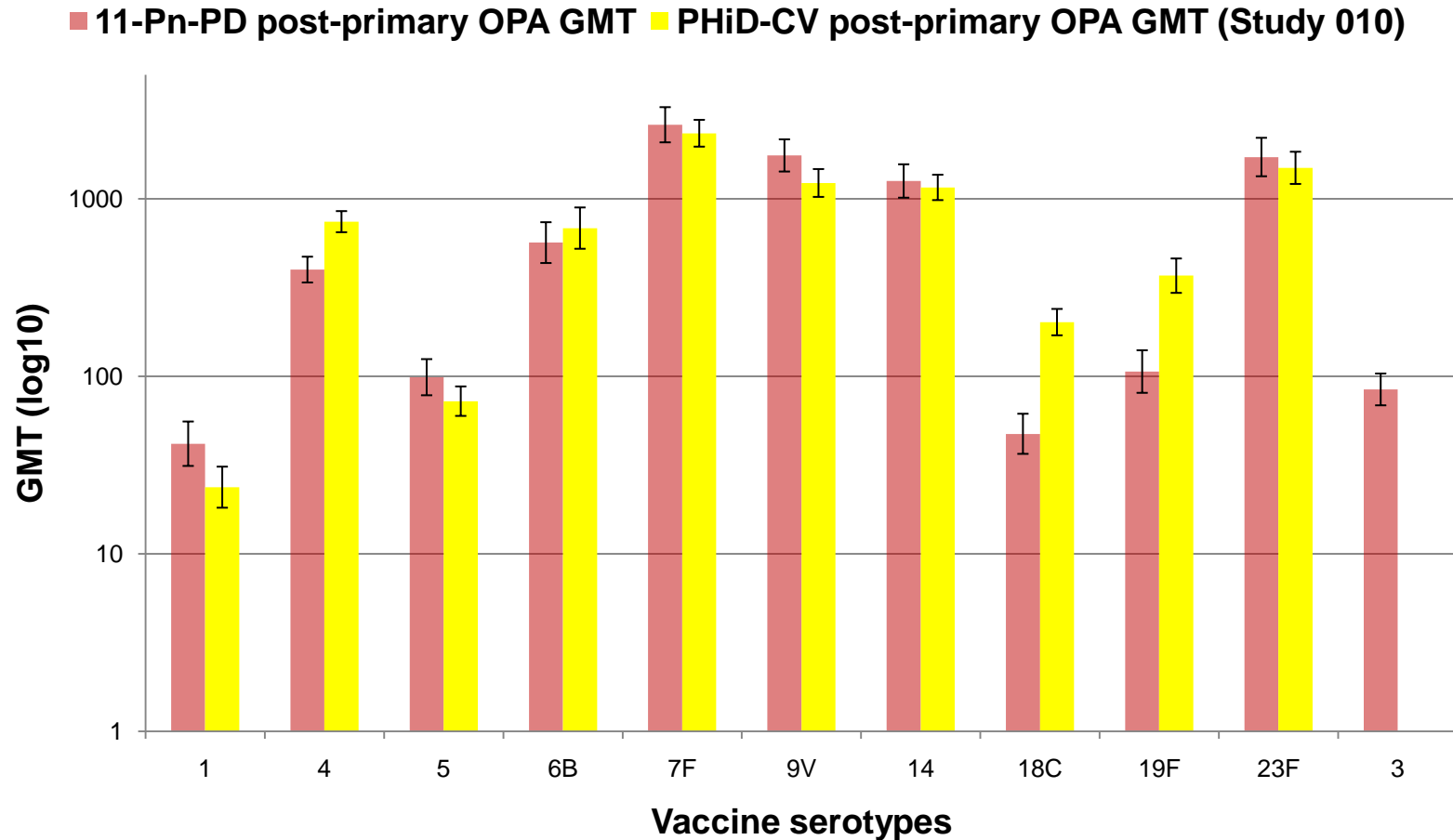
**No efficacy against serotype 3
despite high antibody levels**

Immune response with serotype 3 conjugate across different PCVs - No clear evidence of boostability observed

11-Pn-PD Czech & Slovak Republics 3+1
(Prymula et al., Lancet 2006)



Similarity of immunogenicity profiles between 11-Pn-PD and PHiD-CV post-primary vaccination: OPA GMT



*10Pn-PD-DiT groups without prophylactic paracetamol

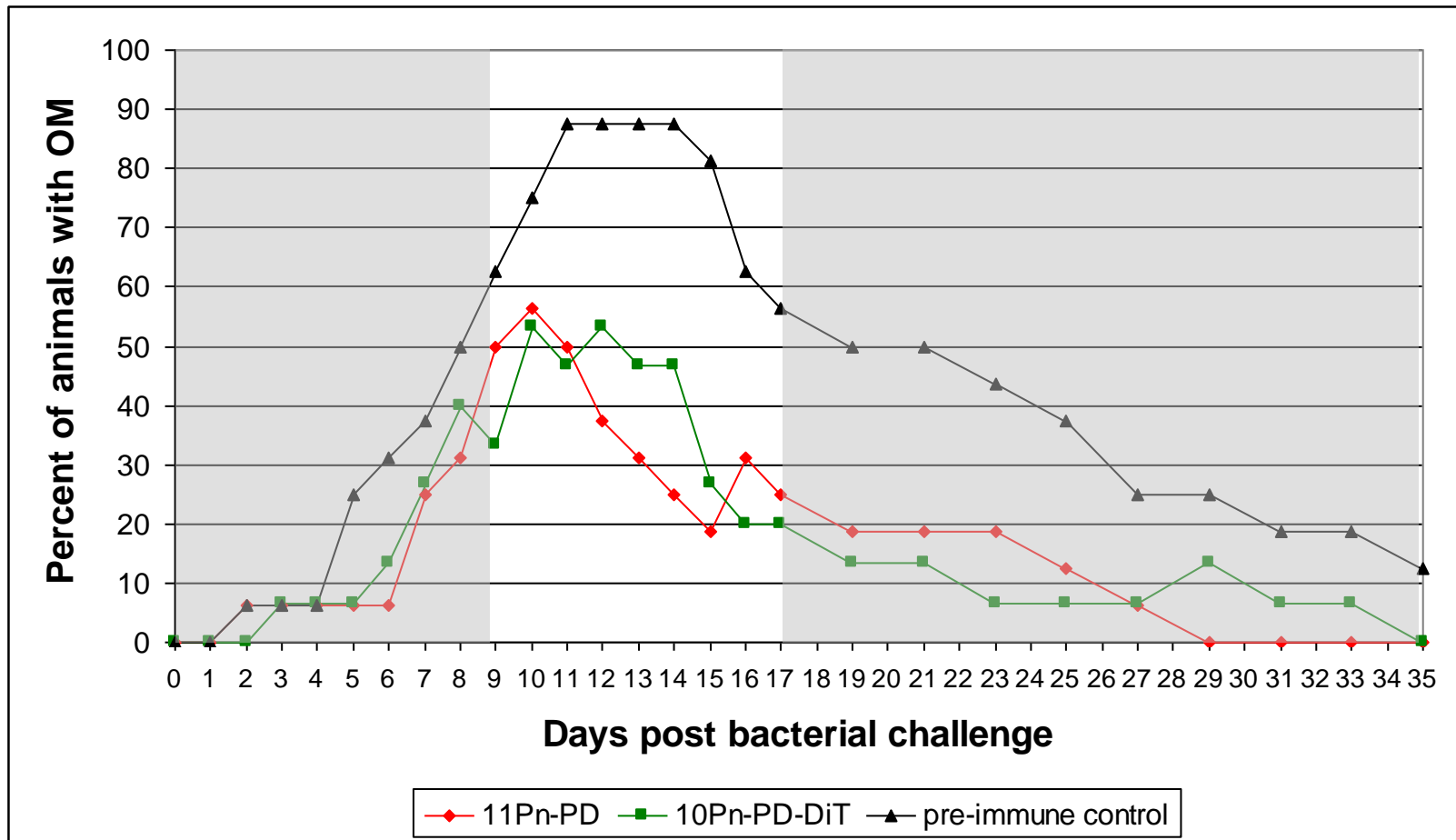
PHiD-CV - Pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine: *Synflorix*[™] and DTPa-HBV-IPV/Hib: *Infanrix hexa*[™] are trademarks of the GlaxoSmithKline group of companies

Both studies conducted in Czech Republic, according to a 3-4-5 month schedule, with *Infanrix hexa*[™] co-administered

Prymula, et al. Lancet 2006; 367: 740–48
Prymula et al., 2009; *Europaediatrics*, Moscow, Russia

Protein D immunization induces protection against infection

- Passive transfer of sera from infants immunized with 11Pn-PD (POET) or *Synflorix*TM (10Pn-PD-DiT) induce similar protection against NTHi OM in juvenile chinchilla's



Protection against pneumonia

- 🌿 No pneumonia efficacy data yet available with *PHiD-CV* or former formulation
- 🌿 Community Acquired Pneumonia encompasses invasive (bacteraemic) and non-invasive pneumonia
- 🌿 Protection against pneumonia likely mediated by antibodies against polysaccharide capsule [Austrian 1976, Smit 1977]
- 🌿 Reductions of mucosal infections by PCVs
 - pneumonia; consistently shown by 3 PCV formulations (PCV7-CRM, PCV9-CRM, PCV11-DT/TT) with VE ranging from 21 to 37%¹⁻³.
 - VST AOM; consistently shown by 3 PCV formulations (PCV7-CRM, PCV7-OMPC and 11-Pn-PD) with VE against ranging from 56 to 58%⁴⁻⁶.
 - VST carriage; (trends) shown by different PCV formulations (PCV4-DT, PCV7-CRM, PCV9-CRM)⁷

Vaccine Characteristics Associated with Efficacy against Pneumonia

Characteristic	PCV-7-CRM	PHiD-CV
IgG (Mucosal)	✓ 1	✓ 8-10
High GMC/GMT	✓ 2, 3, 4	✓ 8-10
Functionality by OPA	✓ 2	✓ 8-10
Prevention of AOM and/or colonisation (Strong supporting evidence)	✓ 5	✓ 9-11
Evidence of boostability	✓ 6, 7	✓ 8-11

Vaccines comparable in all these criteria are expected to protect against pneumonia in a similar manner



Summary

Summary on PHiD-CV

- 🌿 Functional & boostable responses against all serotypes included
 - IPD : Immunological Non-inferiority to PCV7-CRM ^{1,2}
Functional capacity (OPA)
Boostability
 - AOM : Immunological similarity (OPA) with POET formulation⁷
- 🌿 Similar results for different immunization schedules and co-administration regimens
 - 2-3-4m; 3-4-5m; 2-4-6m; 3-5-11m; 6-10-14 wks^{3,5,6}
 - Co-administration with other paediatric vaccines without affecting the safety and immunogenicity profiles²⁻⁵
 - No sign of interference with coadministered vaccines vs PCV7-CRM
- 🌿 Similar safety and reactogenicity profile as PCV7-CRM⁴
 - In range with DTPa and DTPw

Regulatory status

As of August 2009, **Synflorix™** is approved in more than 40 countries incl. Europe, Australia, New Zealand, Canada, Mexico, Colombia, Chile, UAE, Kenya and Turkey

- 🌿 **Synflorix™** is indicated for active immunisation against pneumococcal invasive disease and acute otitis media due to *S. pneumoniae*





Thank You