MenHibrix® (Meningcoccal Groups C andY and Haemophilus B Tetanus Toxoid Conjugate Vaccine): Product and Clinical Data Overview

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MenHibrix® Adds Infant/Toddler Meningococcal Vaccination Against the Two Most Prevalent Non-B Serogroups†

- Given in a four-dose series according to the routine US vaccination schedule for Hib (2, 4, 6 and 12 to 15 months of age)
- Targets the two most important non-B serogroups in the US
- Allows initiation of vaccination against MenC and MenY as of age 6 weeks
- Provides an additional source of Hib conjugate vaccine for the US
  - Immune interference for the Hib antigen was not observed‡
- No immune interference observed with PCV7, DTaP-HepB-IPV, MMR, and varicella vaccines¶
- Safety profile similar to licensed controls in over 7500 children

†Cohn AC, MacNeil JR, Harrison LH, *et al*. Changes in *Neisseria meningitidis* disease epidemiology in the United States, 1998-2007: Implications for prevention of meningococcal disease. Clin Infect Dis 2010;50:184-91.

‡Bryant KA, Marshall GS, Marchant CD, *et al*. Immunogenicity and safety of *H influenzae* type b- *N meningitidis* C/Y conjugate vaccine in infants. Pediatrics 2011;127:e1375.

¶Marshall GS, Marchant CD, Blatter M, *et al*. Co-administration of a novel *Haemophilus influenzae* type b and *Neisseria meningitidis* serogroups C and Y-tetanus toxoid conjugate vaccine does not interefere with the immune response to antigens contained in the infant series routinely used in the United States. Human Vaccines 2011;7(2):258-264.

MenHibrix® Composition

- MenHibrix® contains:
  - PRP 2.5 µg
  - MenC 5 µg
  - MenY 5 µg
  - TT 18 µg
  - No adjuvant
  - No preservatives

MenHibrix®: Clinical Development Program

Development Phase (Study #)	N (Total)	N (MenHibrix®)	Key Immuno Objectives
I/IIa (001/002 and 003/004)	**797**	**160**	Proof of Concept Dose Range
II (005/006/013/014/015)	**756**	**287**	Non-inferiority to licensed Hib (PD3 and PD4) Co-administration with PCV7 5 year persistence
II (007/008)	**1103**	**661**	PD2 immunogenicity NI to licensed Hib (PD3) Co-administration with MMR and varicella
III (009/010 and 011/012)	**8571**	**6414***	Non-inferiority to licensed Hib (PD3 and PD4) Immunogenicity to MenC and MenY (PD3 and PD4) Co-administration with DTaP-HBV-IPV, MMR, and varicella Lot to lot consistency
Total Safety Database	**11,227**	**7521**	

NI: Non-inferiority PD: Post-dose PCV7: 7-valent pneumococcal vaccine

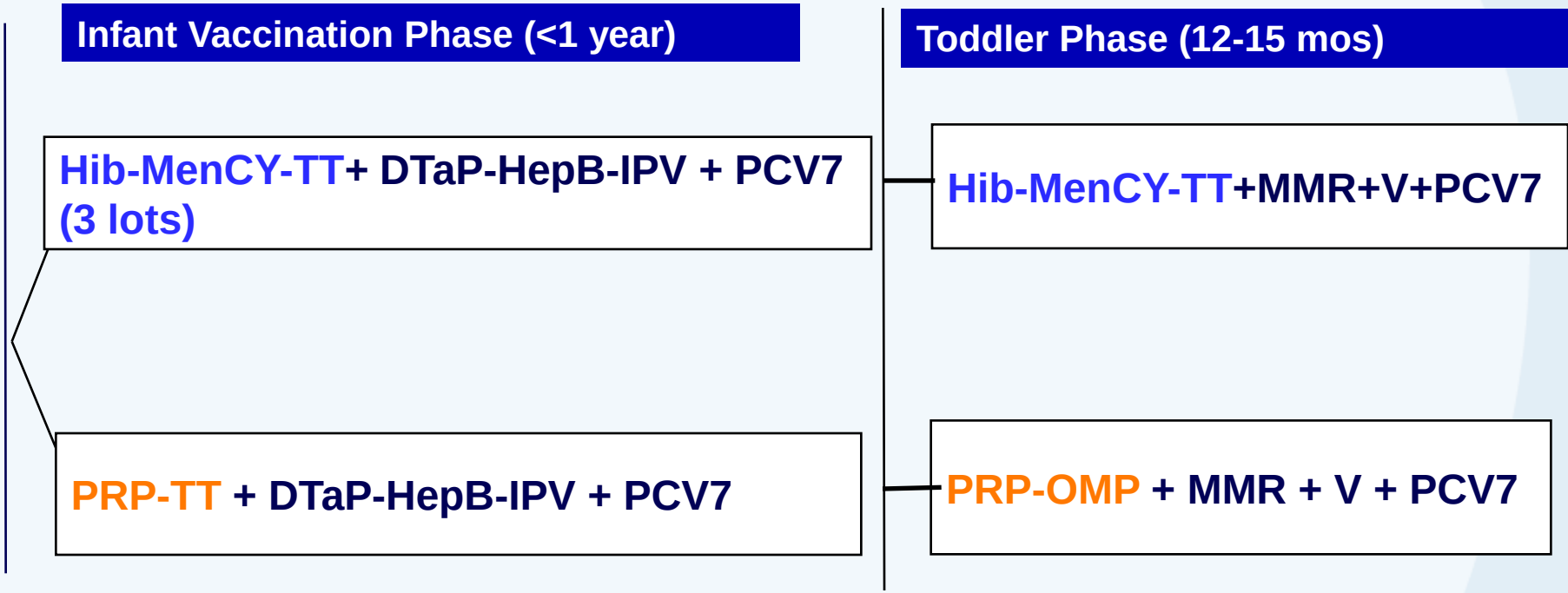
DTaP-HepB-IPV: Combined diphtheria, tetanus, acellular pertussis, hepatitis B and poliovirus vaccine

MMR: Combined measles, mumps, and rubella vaccine V: Varicella vaccine

*Note: in study 011, one subject was randomzied to receive MenHibrix® but did not receive any dose of study vaccine

Pivotal Phase 3 Study Design- Lot to Lot consistency and Non Inferiority

Randomization 3:1
Schedule: 2-4-6 and 12-15
N= 4180 safety; n= 695 immunogenicity



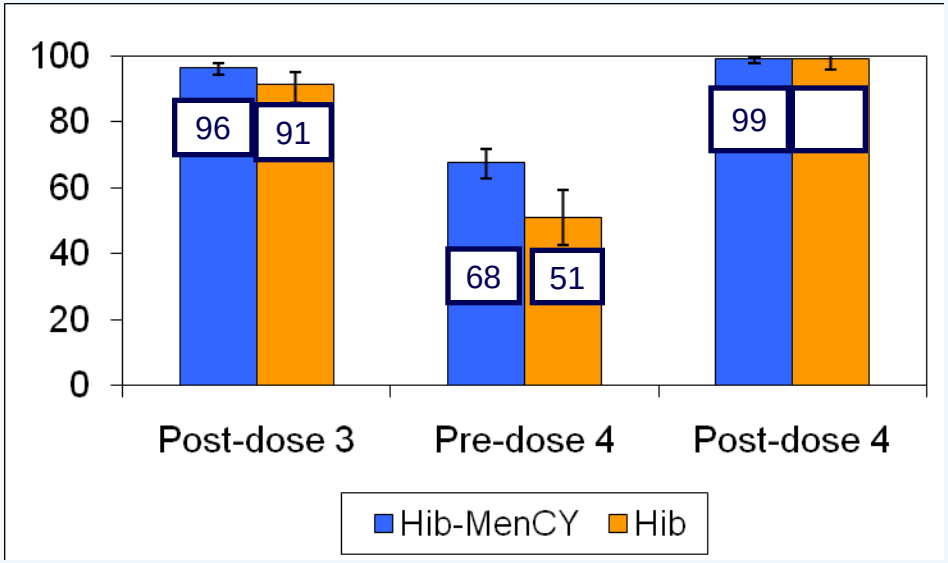
PRP-TT: ActHIB®
PRP-OMP: PedvaxHIB®
DTaP-HepB-IPV: Pediarix®
PCV7: Prevnar®
MMR: M-M-R_{II}®
V: Varivax®

‡Bryant KA, Marshall GS, Marchant CD, *et al*. Immunogenicity and safety of *H influenzae* type b- *N meningitidis* C/Y conjugate vaccine in infants. Pediatrics 2011;127:e1375.

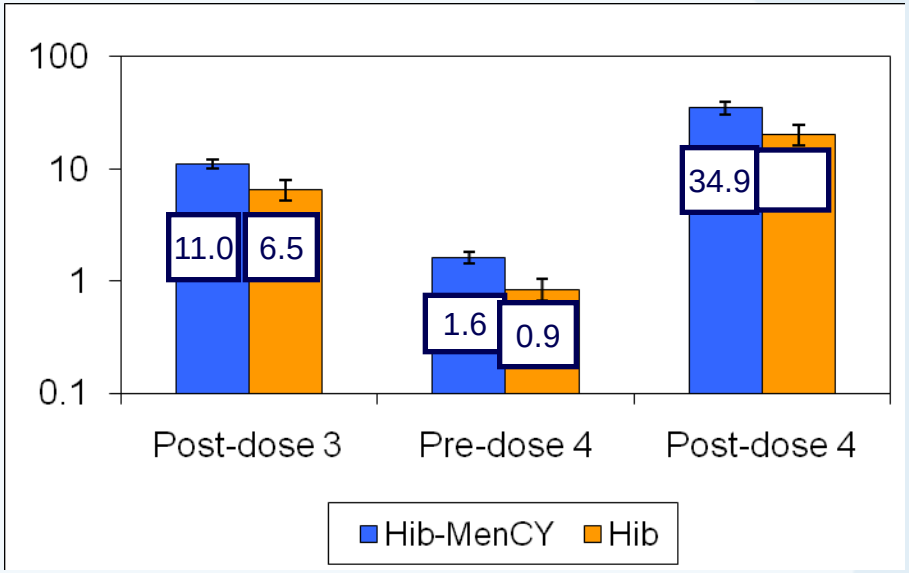
MenHibrix® is Non-inferior to Licensed Hib After Dose 3 and Dose 4

Study 009/010

% with concentrations ≥1.0 µg/mL



Anti-PRP GMCs µg/mL (Log_{10} Scale)



Non-inferiority criterion:

Lower limit of 95% CI for difference (Hib-MenCY-TT minus Hib) is ≥-10%

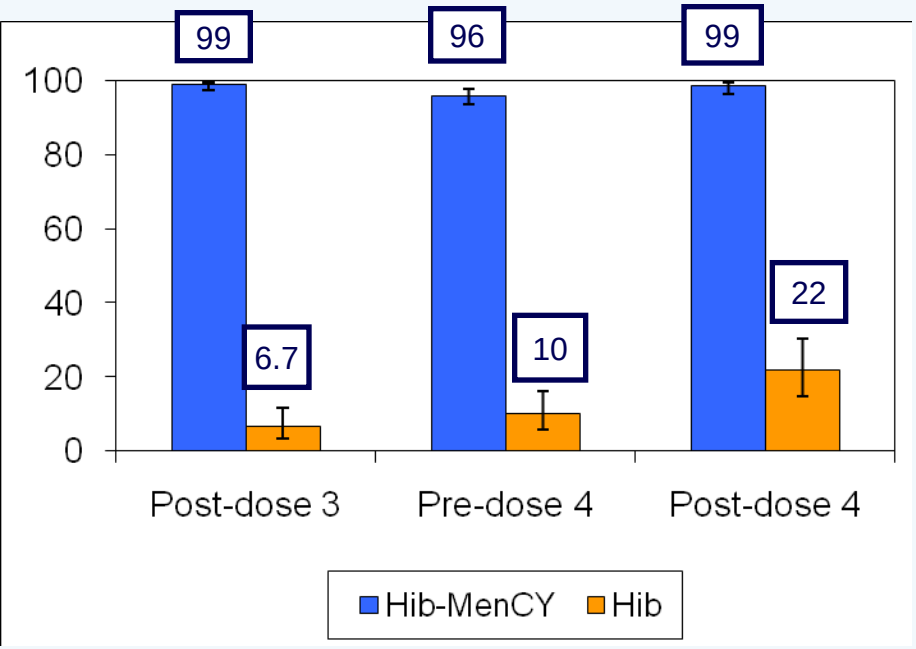
Note: subjects in control group received PRP-TT for dose 1, 2, and 3, and PRP-OMP for dose 4

Bryant K, et al. Immunogenicity and safety of *H. influenzae* type b- *N. meningitidis* C/Y conjugate vaccine in infants. Pediatrics June 2011;127:e1375

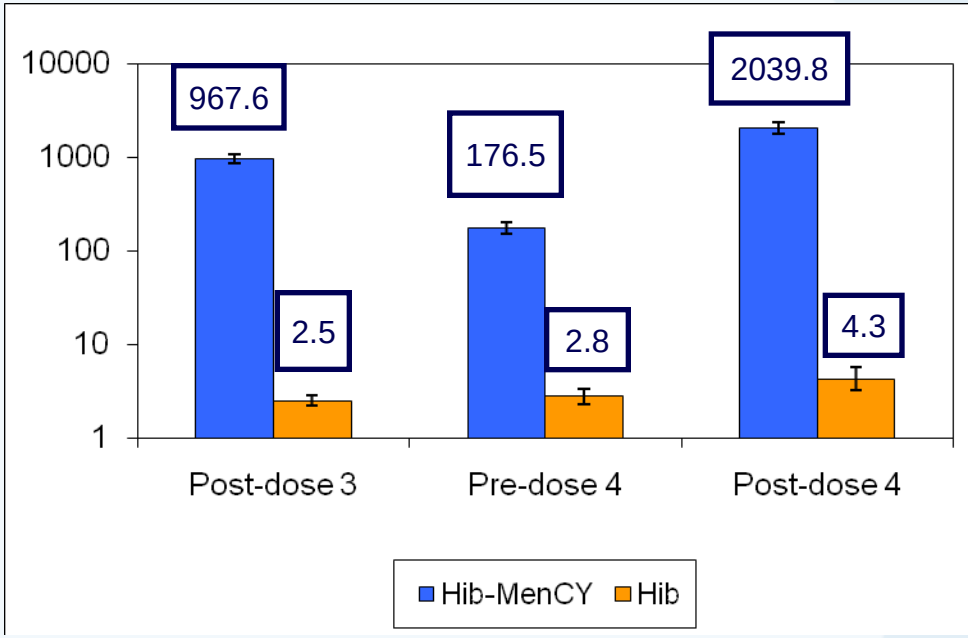
MenC: 99% Seroprotected After Dose 3 and Dose 4

Study 009/010

% with hSBA-MenC titers ≥1:8



hSBA-MenC GMTs (Log_{10} Scale)



12.0-fold increase in hSBA-MenC titers after dose 4

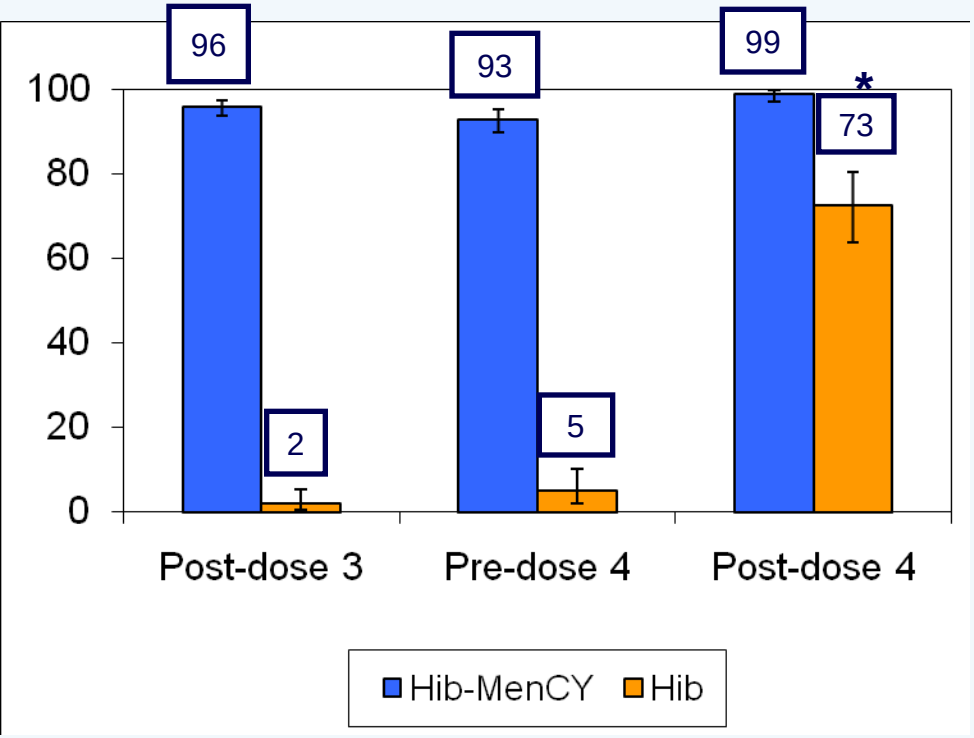
Note: subjects in control group received PRP-TT for dose 1, 2, and 3, and PRP-OMP for dose 4

Bryant K, et al. Immunogenicity and safety of *H. influenzae* type b- *N. meningitidis* C/Y conjugate vaccine in infants. Pediatrics June 2011;127:e1375

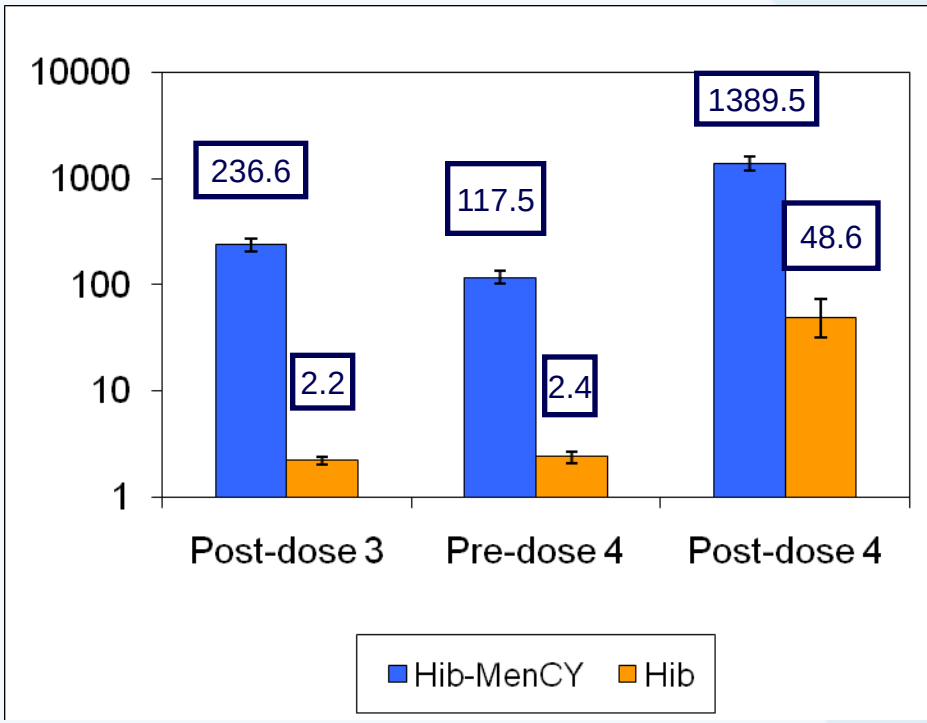
MenY: 96% Seroprotected After Dose 3 and 99% Protected After Dose 4

Study 009/010

% with hSBA-MenY titers ≥1:8



hSBA-MenY GMTs (Log_{10} Scale)



12-fold increase in hSBA-MenY titers after dose 4

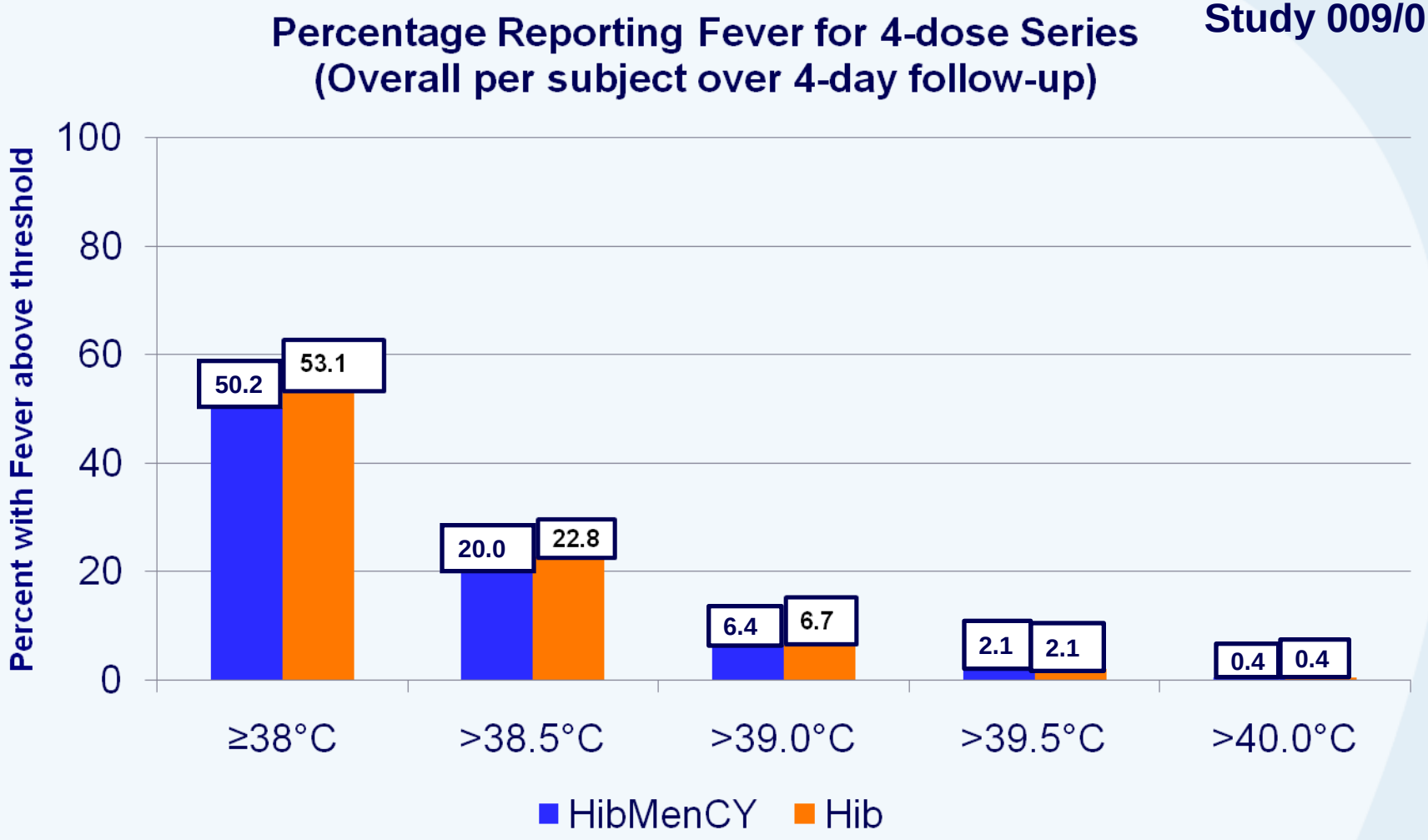
Note: subjects in the control group received PRP-TT for dose 1, 2, and 3, and PRP-OMP for dose 4

Bryant K, et al. Immunogenicity and safety of *H. influenzae* type b- *N. meningitidis* C/Y conjugate vaccine in infants. Pediatrics June 2011;127:e1375

*subjects in control group were seropostive after dose 4 due to cross-reactive antibody induced by PRP-OMP

Fever >39.5°C Non-Inferior to Hib Post-dose 3 and 4

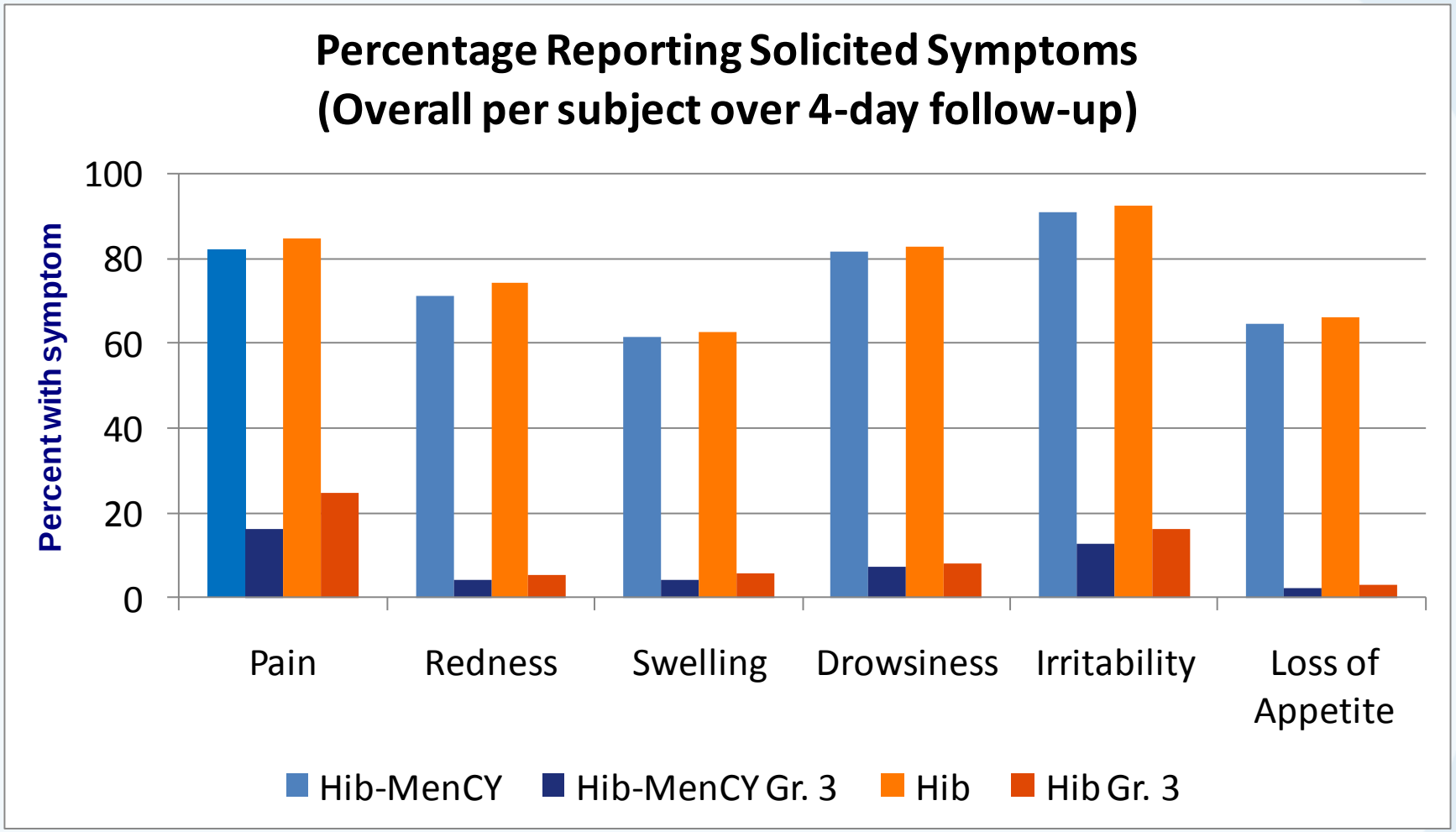
Study 009/010



Bryant K, et al. Immunogenicity and safety of *H. influenzae* type b- *N. meningitidis* C/Y conjugate vaccine in infants. Pediatrics June 2011;127:e1375

Safety Profile Comparable to Licensed Hib Vaccine over 4-dose Series

Study 009/010



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No Immune Interference Observed in Previous Clinical Trials

Endpoints and Criteria for Co-ad Vaccines

Antigen	Study	Endpoint	Criterion	Met?
Diphtheria/ Tetanus	009	Conc. ≥0.1 IU/ml	LL ≥ -10%	✓
Poliovirus types 1, 2, and 3	009	Titer ≥1:8	LL ≥ -10%	✓
Pertussis	005/009	GMCs	LL ≥ 0.67	✓
PCV7	005	GMCs	LL ≥ 0.5	✓
MMR	008/010	Measles: ≥150 mIU/ml Mumps: ≥28 ED_{50} Rubella: ≥10 mIU/ml	LL ≥ -5%	✓
Varicella	008/010	FAMA: ≥1:5	LL ≥ -10%	✓
Hepatitis B	009	Conc. ≥10 mIU/ml	descriptive	similar

N/A: specific hypothesis was not tested, but no significant differences between groups in exploratory analysis

Marshall, et al, Human Vaccines, 2011

Clinical Summary of MenHibrix®

- All meningococcal immunogenicity criteria met
- Anti-PRP responses are non-inferior to licensed monovalent Hib after dose 3 and dose 4
- No immune interference observed with PCV7, DTaP-HepB-IPV, MMR, and varicella
- Persistence of antibodies until six years of age in majority of recipients has been demonstrated for all three antigens
- Safety profile comparable to licensed monovalent Hib

***MenHibrix* has the potential to add protection against MenC and MenY to the pediatric vaccination schedule without adding shots or medical office visits**