BOOSTRIX™

Vaccines and Related Biological Products
Advisory Committee
March 15, 2005

GlaxoSmithKline

GlaxoSmithKline Presentation

Vincent Ahonkhai, M.D. Vice President U.S. Regulatory Affairs, Vaccines	Introduction
Barbara Howe, M.D. Vice President & Director - Clinical R&D North America (Vaccines)	Epidemiology Clinical Development Plan
Leonard Friedland, M.D. Director – Clinical R&D North America (Vaccines)	Immunogenicity Safety
Vincent Ahonkhai, M.D.	Conclusion

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Proposed Names

Proprietary Name

Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed (Tdap)

Trade Name

BOOSTRIX™

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Proposed Indication

Single-dose, active booster immunization against diphtheria, tetanus, and pertussis (whooping cough) in individuals 10 through 18 years of age

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BOOSTRIX Vaccine Composition

Tetanus component
5 Lf

Diphtheria component
2.5 Lf

Pertussis components
8 mcg PT
8 mcg FHA
2.5 mcg PRN

Excipient
0.3 mg Al

Preservative Free
Thimerosal Free

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BOOSTRIX Vaccine Composition

Tetanus component
5 (10*) Lf

Diphtheria component
2.5 (25*) Lf

Pertussis components
8 (25*) mcg PT
8 (25*) mcg FHA
2.5 (8*) mcg PRN

Excipient
0.3 (0.5 / 0.7*) mg Al

*Infanrix®/Pediarix®

Preservative Free
Thimerosal Free

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Experience with individual components of BOOSTRIX (Tdap)

- **Individual components studied extensively and administered commercially**
  - *Infanrix* (DTaP) -51 million doses distributed in US (75 million worldwide)
  - *Pediarix* (DTaP-HepB-IPV) – 10 million doses in US

- **D, T and P included in similar DTaP-based combinations - 130 million doses outside of the US**

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BOOSTRIX – licensed outside US

- **Licensed in 1999; compared to US formulation:**
  - Identical: D, T and P antigen content
  - Differences:
    - contains 0.5 mg Al vs. 0.3 mg Al
    - Preservative (2-PE) vs. preservative-free
- **Licensed in numerous countries**
- **Over 1.9 million doses distributed**

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Basis for Licensure

- **Non-Inferiority:**
  BOOSTRIX (Tdap) vs. US-Licensed Td Vaccine
  - Immunogenicity and Safety
- **VRBPAC 1997: bridging to immunologic data from efficacy trials in children can be used to predict efficacy of pertussis vaccines in older populations**

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BOOSTRIX Main Results

- BOOSTRIX met pre-specified immunogenicity and safety criteria for non-inferiority
- BOOSTRIX is an alternative to Td vaccine with:
  - protection against pertussis
  - safety profile comparable to Td
  - no need for additional injection or office visit

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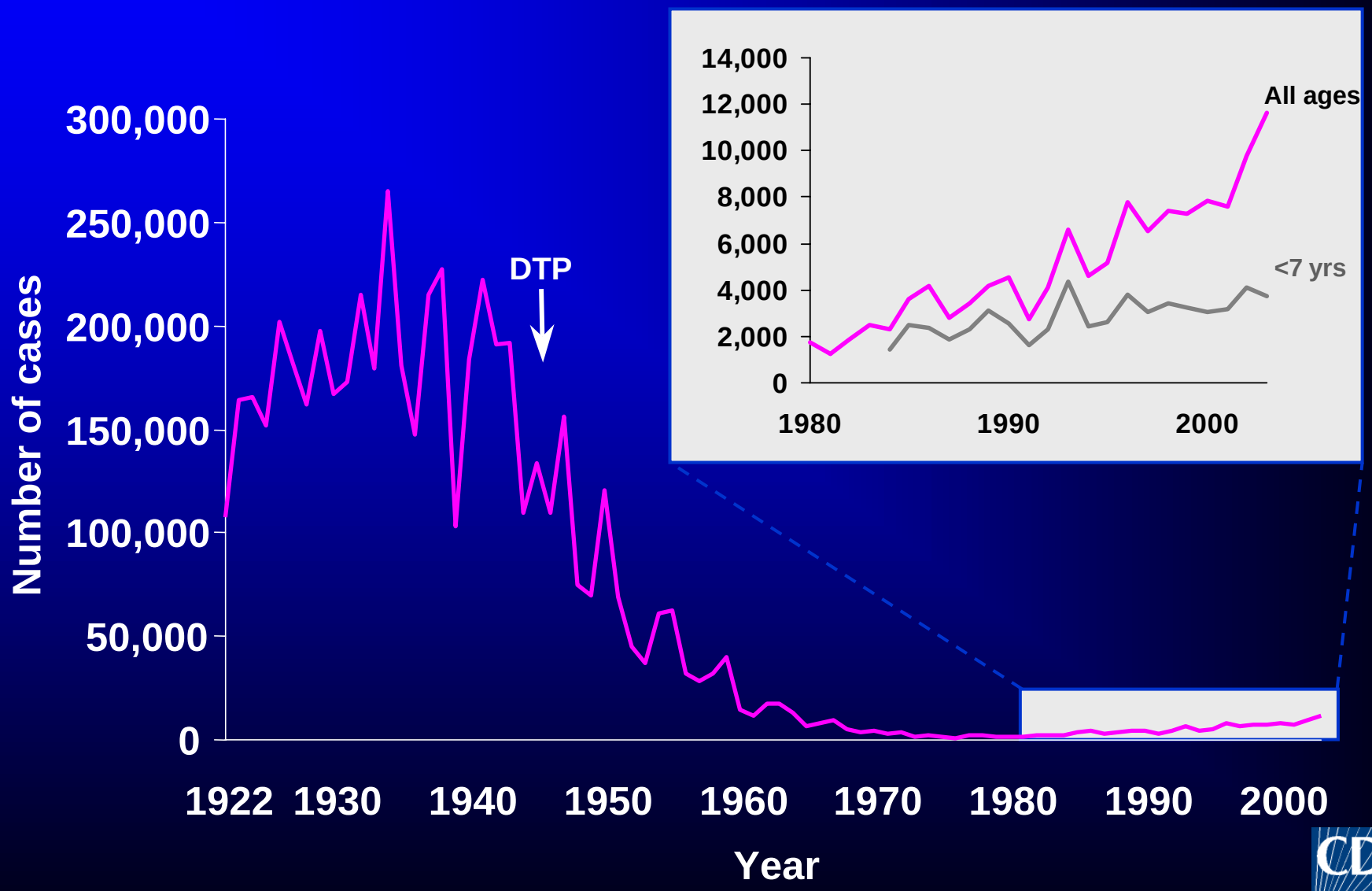
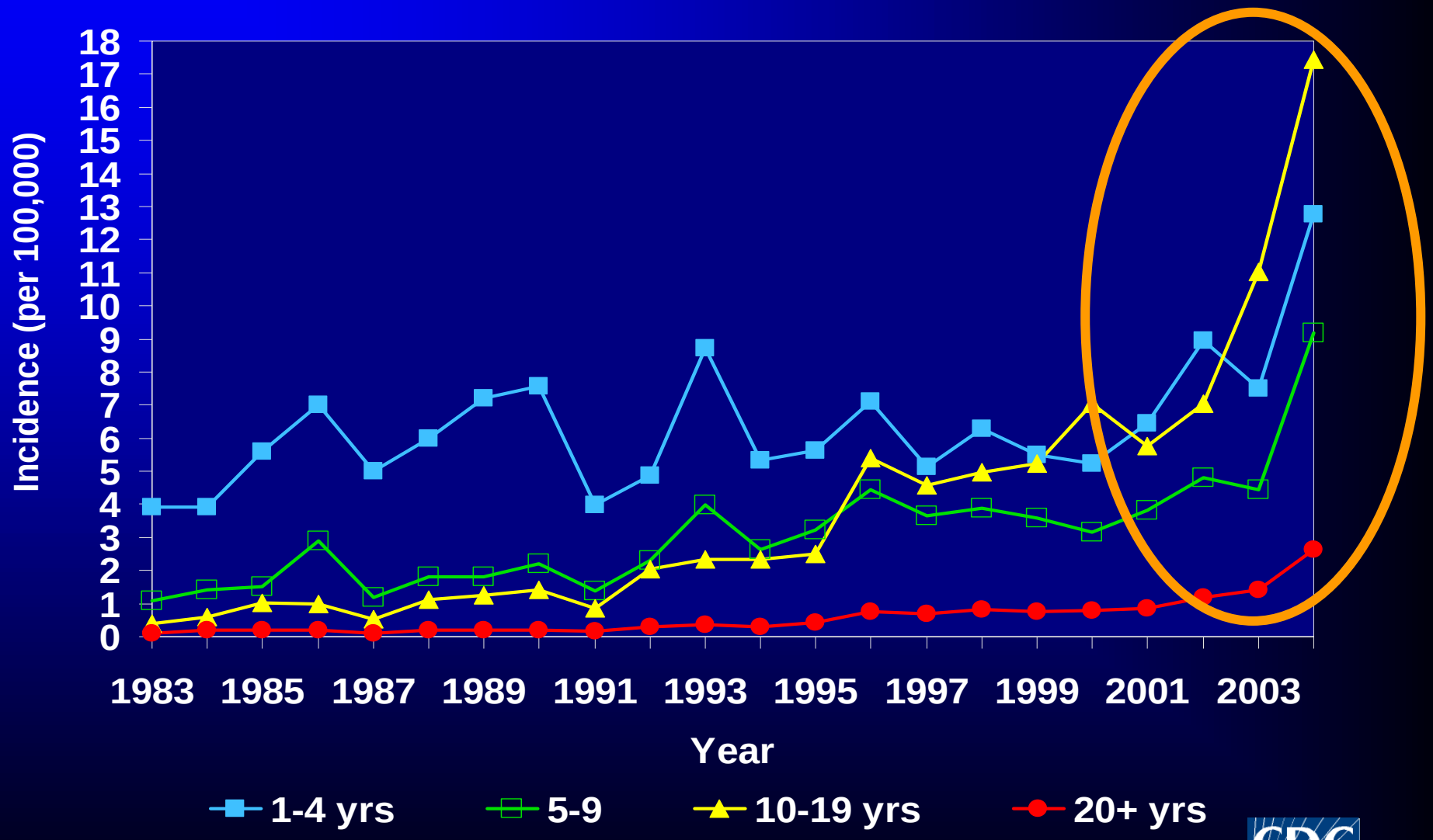
Reported Pertussis Cases-US,1922-2003

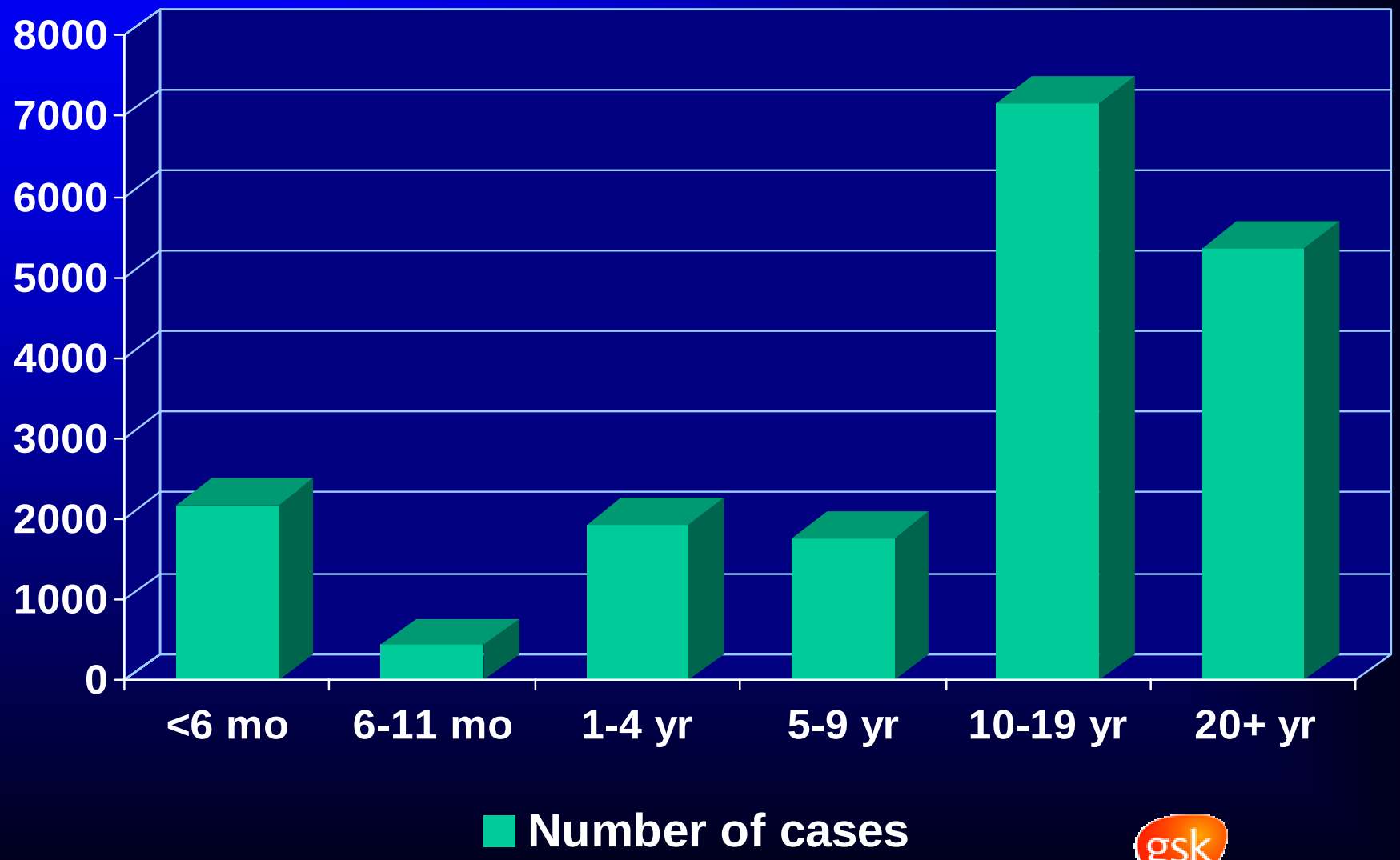


Reported Pertussis Incidence by Age Group 1983-2004*



* 2004 data are provisional

Age Distribution of Reported Pertussis Cases US 2004*



* 2004 data are provisional

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Why Adolescent Pertussis Vaccination?

- **High incidence of reported new cases (and growing)**
- **Under-recognized and under-reported**
- **Significant morbidity and public health impact**
- **Health economic specialists*: pertussis immunization of US adolescents could be beneficial and cost-effective**
- **Important reservoirs for infection**

* Caro J, et al. 43rd ICAAC abstracts, Sept 14-17, 2003: abstract G-1644
* Lee GM, et al. 2004 PAS abstracts, May 1-4, 2004: abstract 1795
* Purdy KW, et al. Clin Inf Dis 2004;39:20-8

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Adolescent Pertussis Vaccination: Fit with Current Schedule

- **Majority of routine Td boosters are administered to adolescents**
- **Current platform supports adolescent immunization**
  - Td recommended @ 11-12 years
  - Combining Td + ap = pertussis protection for adolescents without an additional injection

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Summary of Clinical Studies in BLA

Study Number	Category	Country	Age (yrs)	Objective(s)	BOOSTRIX 0. 133	BOOSTRIX 0.3	BOOSTRIX 0.5	Td	Other
001	Pivotal	USA	10 to 18	Consistency, Safety & Immuno		3080		1034	
004	Supportive	Finland	10 to 14	Safety & Immuno			450	60	
017/030	Supportive	Finland	13 to 17	Antibody persistence 3 and 5 yrs after 004			(267)	(36)	
029	Supportive	Belgium	10 to 18	Al dose ranging	214	209	224		
1, 2, 3, 7, 9, 10, 20, 28, 118	Safety synopses	Worldwide non-US	4 to 78	Safety			1341	569	409

Total (All Trials)

BOOSTRIX	5518
BOOSTRIX (0.3 mg Al)	3289
Td	1663
Other	409

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BOOSTRIX US Clinical Development Pivotal & Supportive Studies

- Randomized, blinded, prospective
- Healthy adolescents, up-to-date with DTP immunizations, last DTP ≥5 yrs earlier
- Immunogenicity evaluated one-month after vaccination (except persistence studies)
- Safety one-month after vaccination (except 6 month follow-up in study 001)
- Concomitant vaccine studies: not a requirement for licensure

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Clinical Trial Data to be Presented

Immunogenicity	Study
• Comparison to US-licensed Td	001
• Comparison to pertussis response in infants	001
• Lot consistency	001
• D, T and P antibody persistence	030

Safety	Study
• Comparison to US-licensed Td	001
• Limb swelling	001, 029
• Serious adverse events	All Studies

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Immunogenicity

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Immunological End-Points: D & T

- **Anti-D & anti-T seroprotection rates (≥0.1 IU/mL) and rates ≥1.0 IU/mL**
- **Anti-D & anti-T booster responses**
  - initially seroneg: post-vacc conc ≥ 4x cut-off (≥0.4)
  - initially seropos: post-vacc conc ≥ 4x pre-vacc conc
- **Antibody GMCs to D & T**

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Non-inferiority: BOOSTRIX vs US-licensed Td vaccine

Antibody	Assay	Parameter	Pre-specified limit (Δ) on difference
D	ELISA	Seroprotection (≥0.1 IU/mL)	10%
T	ELISA	Seroprotection (≥0.1 IU/mL)	10%
D	ELISA	Booster response (4-fold rise)	10%
T	ELISA	Booster response (4-fold rise)	10%

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Immunological End-Points: Pertussis

- **Anti-PT, anti-FHA & anti-PRN seropositivity rates (≥5 EL.U./mL)**
- **Anti-PT, anti-FHA & anti-PRN booster responses**
  - initially seroneg: post-vacc Ab conc ≥4x cut-off (≥20)
  - initially seropos (≥5 and <20): post-vacc conc ≥4x pre
  - initially seropos (≥20): post-vacc conc ≥2x pre
- **Antibody GMCs to PT, FHA & PRN**

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Non-inferiority: BOOSTRIX vs INFANRIX

Antibody	Assay	Parameter	Pre-specified limit (Δ) on difference
PT	ELISA	GMC ratio	1.5
FHA	ELISA	GMC ratio	1.5
PRN	ELISA	GMC ratio	1.5

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Clinical Trial Data to be Presented

Immunogenicity	Study
• Comparison to US-licensed Td	001
• Comparison to pertussis response in infants	001
• Lot consistency	001
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Safety	Study
• Comparison to US-licensed Td	001
• Limb swelling	001, 029
• Serious adverse events	All Studies

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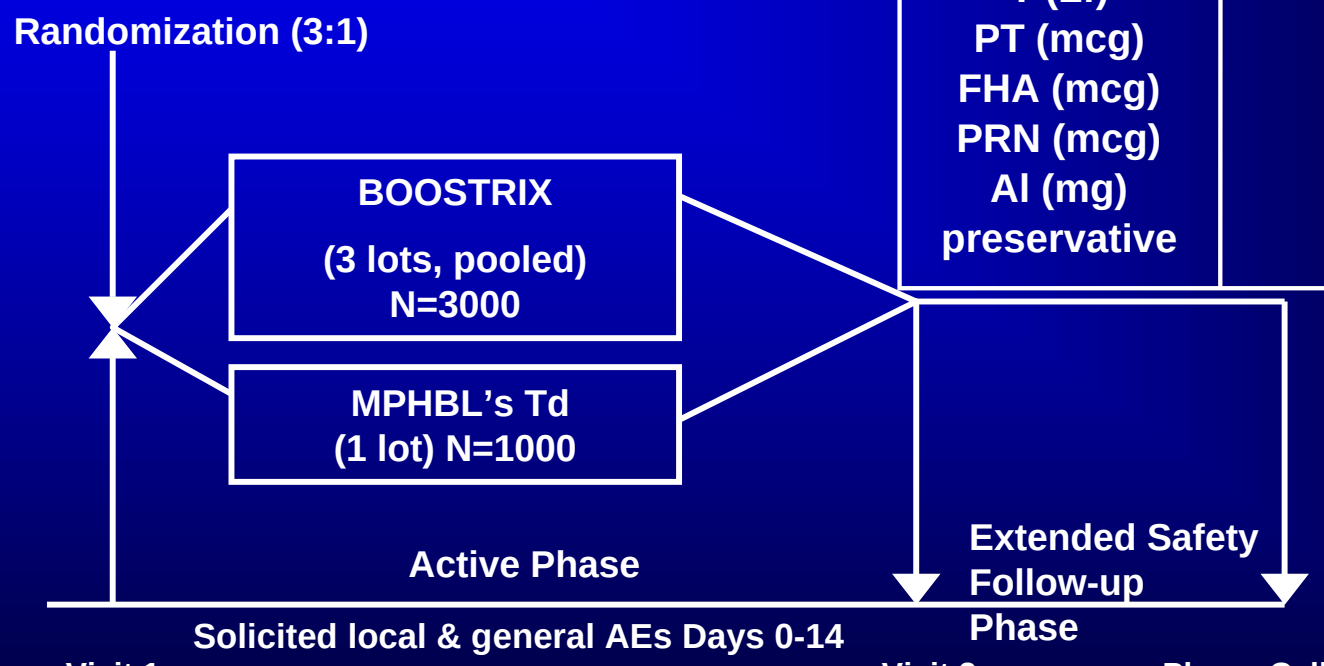
Pivotal Study 001 Design: randomized, observer-blinded, 45 U.S. centers

Composition (per 0.5 mL dose)	BOOSTRIX	Td (MPHBL)
D (Lf)	2.5	2
T (Lf)	5	2
PT (mcg)	8	-
FHA (mcg)	8	-
PRN (mcg)	2.5	-
Al (mg)	0.3	0.45
preservative	--	thio



Visit 1
Day 0
(10-18 years)
10-14 years = 3000
15-18 years = 1000

Visit 2
Month 1
End of Active Phase

Phone Call
Month 6
Study Conclusion

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Study 001:
Similar age, gender, race in both groups

Total Cohort

Characteristics	Parameters Or Categories	BOOSTRIX N= 3080	Td N= 1034
Age	Mean	12.9 yrs	12.9 yrs
	9-14 yrs	75.9%	72.9%
	15-18 yrs	24.1%	27.1%
Gender	Male	51.6%	53.6%
	Female	48.4%	46.4%
Race	White	85.8%	85.4%
	Black	5.7%	5.4%
	Hispanic	5.6%	6.0%
	Oriental	0.8%	0.9%
	Other	2.1%	2.3%

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Study 001: Vaccination History BOOSTRIX & Td

- Similar whole cell and acellular pertussis priming history in both groups
- Majority in both groups whole cell primed
- ~ 85% in each group received their last DT-containing vaccine within the last 5 – 10 years

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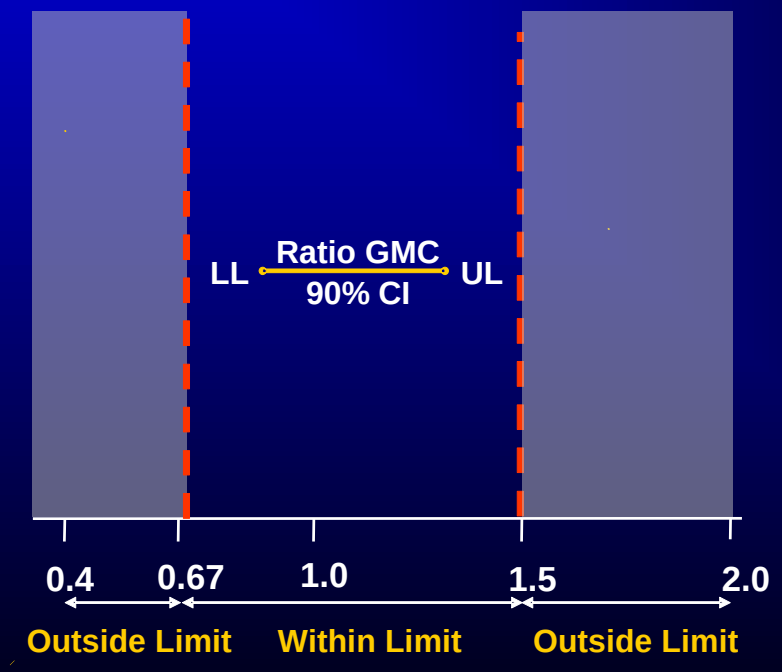
Study 001: primary objective # 1

Lot-to-lot consistency of three production lots of BOOSTRIX in terms of immunogenicity of each antigen, one month post-vaccination

Criteria for Success:



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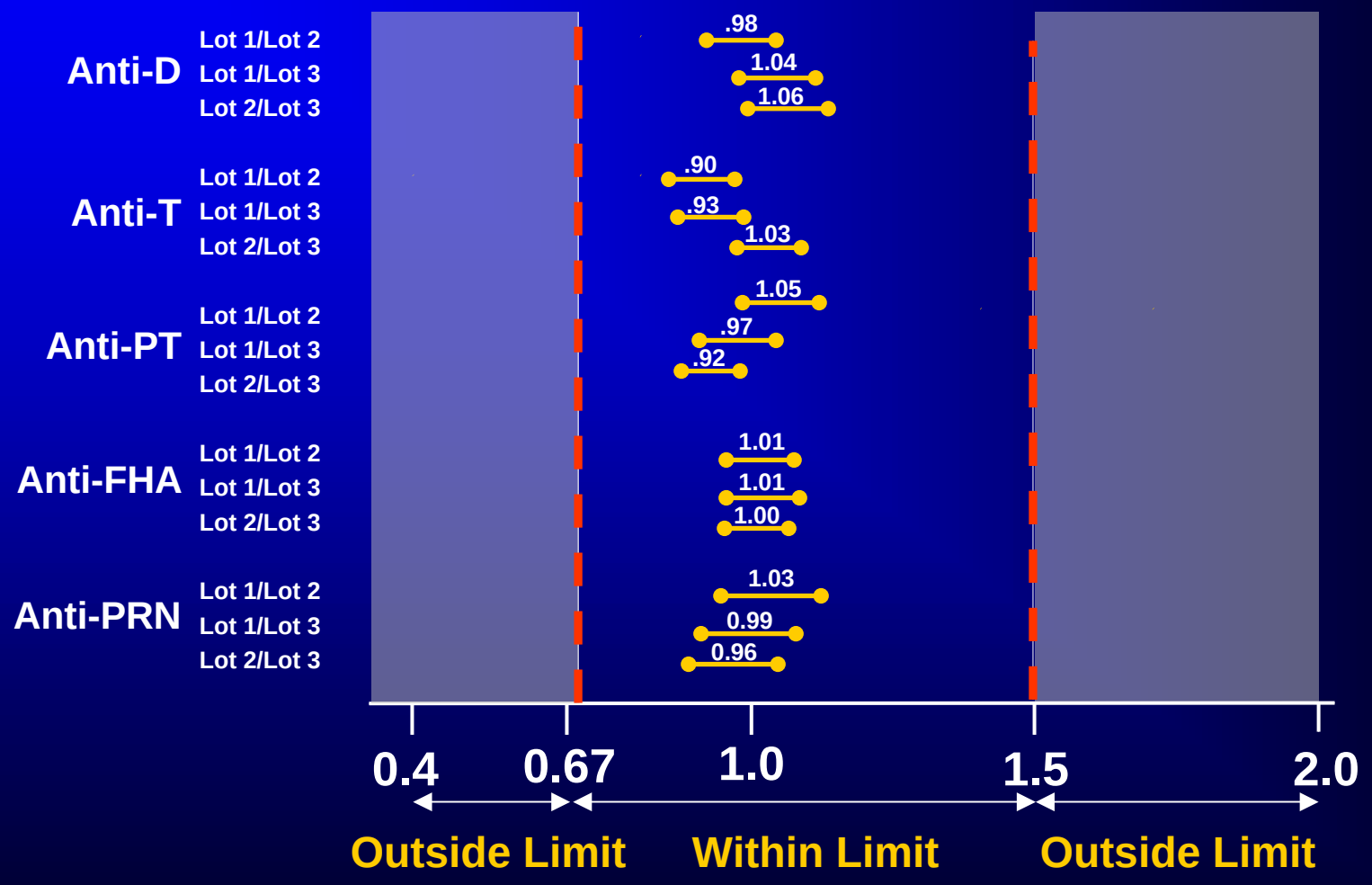
Study 001: Equivalence Testing Ratio of GMCs
90% CI on Ratio (Lot 1/Lot 2, Lot 1/Lot 3, Lot 2/Lot 3)



All Lot Consistency Criteria Met

LL — Ratio GMC — UL
90% CI

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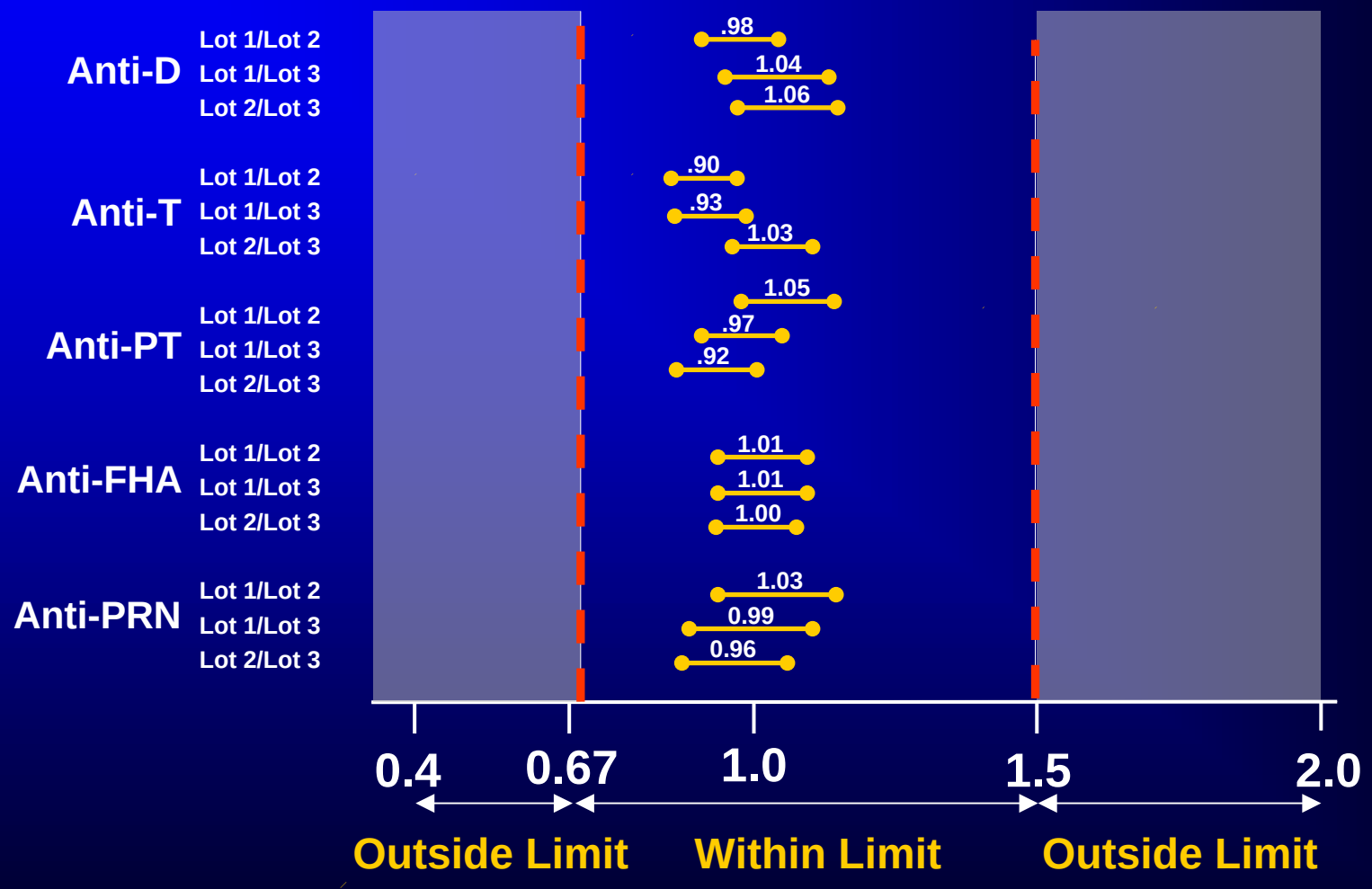
Study 001: Equivalence Testing Ratio of GMCs
95% CI on Ratio (Lot 1/Lot 2, Lot 1/Lot 3, Lot 2/Lot 3)



All Lot Consistency Criteria Met

LL — Ratio GMC — UL
95% CI

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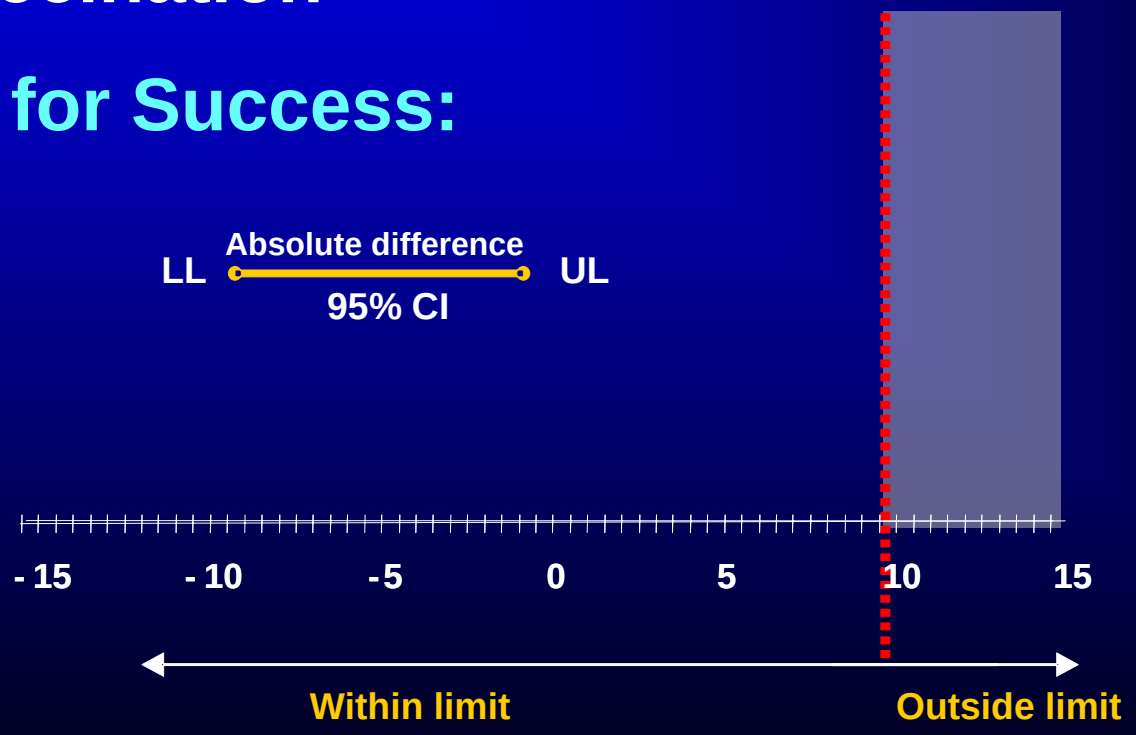
Study 001: primary objectives # 2 & 3

Non-inferiority BOOSTRIX compared to Td, with respect to anti-D and anti-T seroprotection rates (≥0.1 IU/mL) and booster responses, one month post-vaccination

Criteria for Success:



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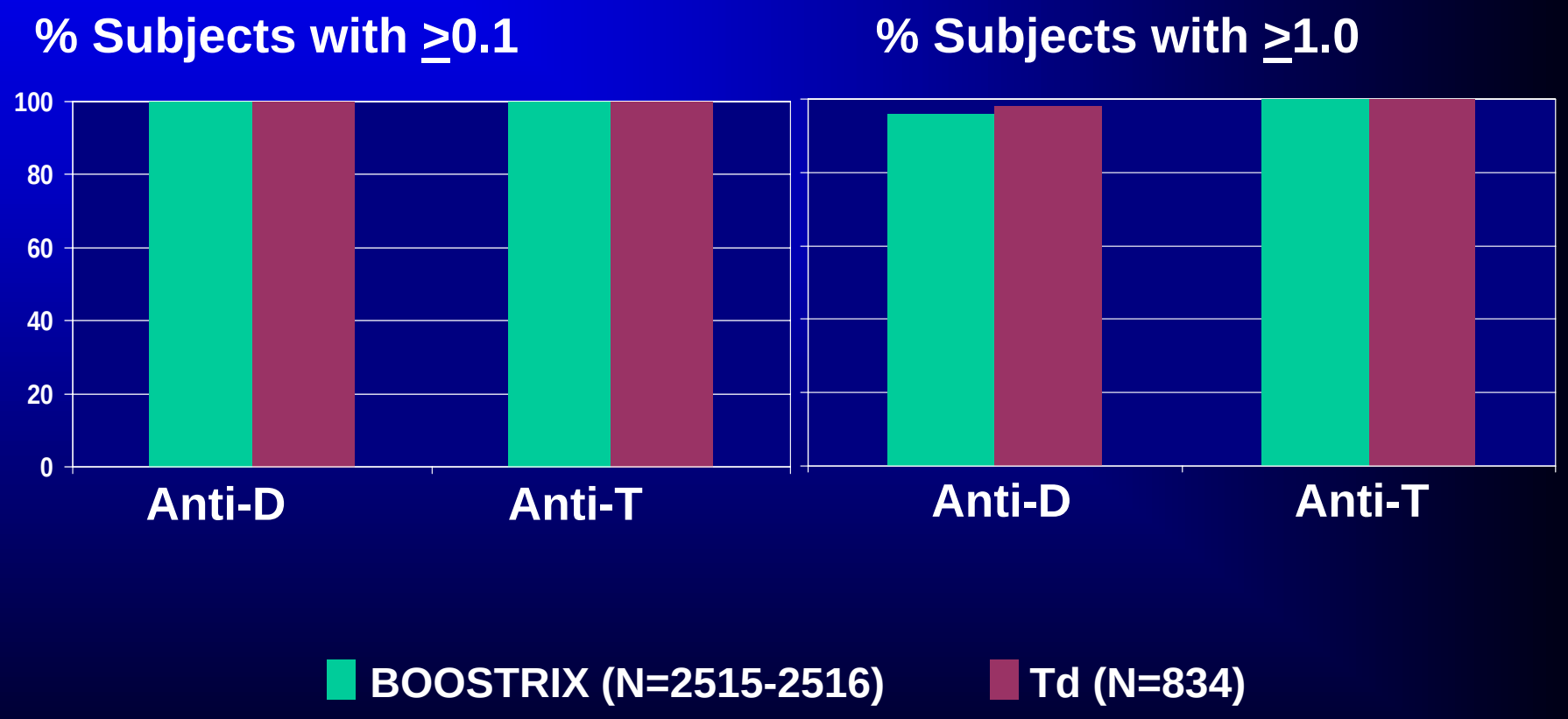
Study 001: D & T Seroprotection Rates (≥0.1 IU/mL) and 10X Seroprotection Rates (≥1.0 IU/mL)



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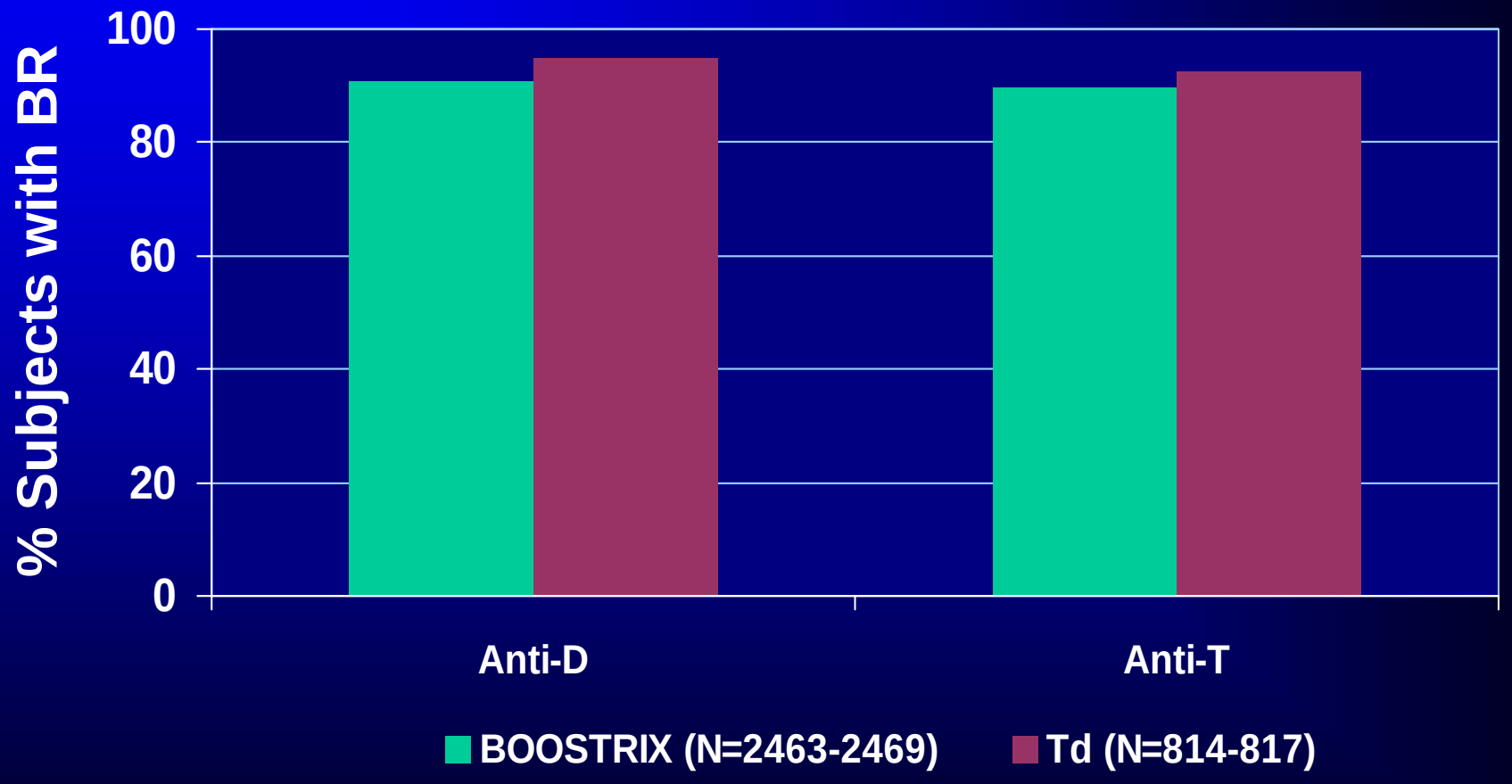
Study 001: D and T Booster Response* Rates



* initially seroneg: post-vacc conc ≥4x cut-off (≥0.4)
initially seropos: post-vacc conc ≥4x pre

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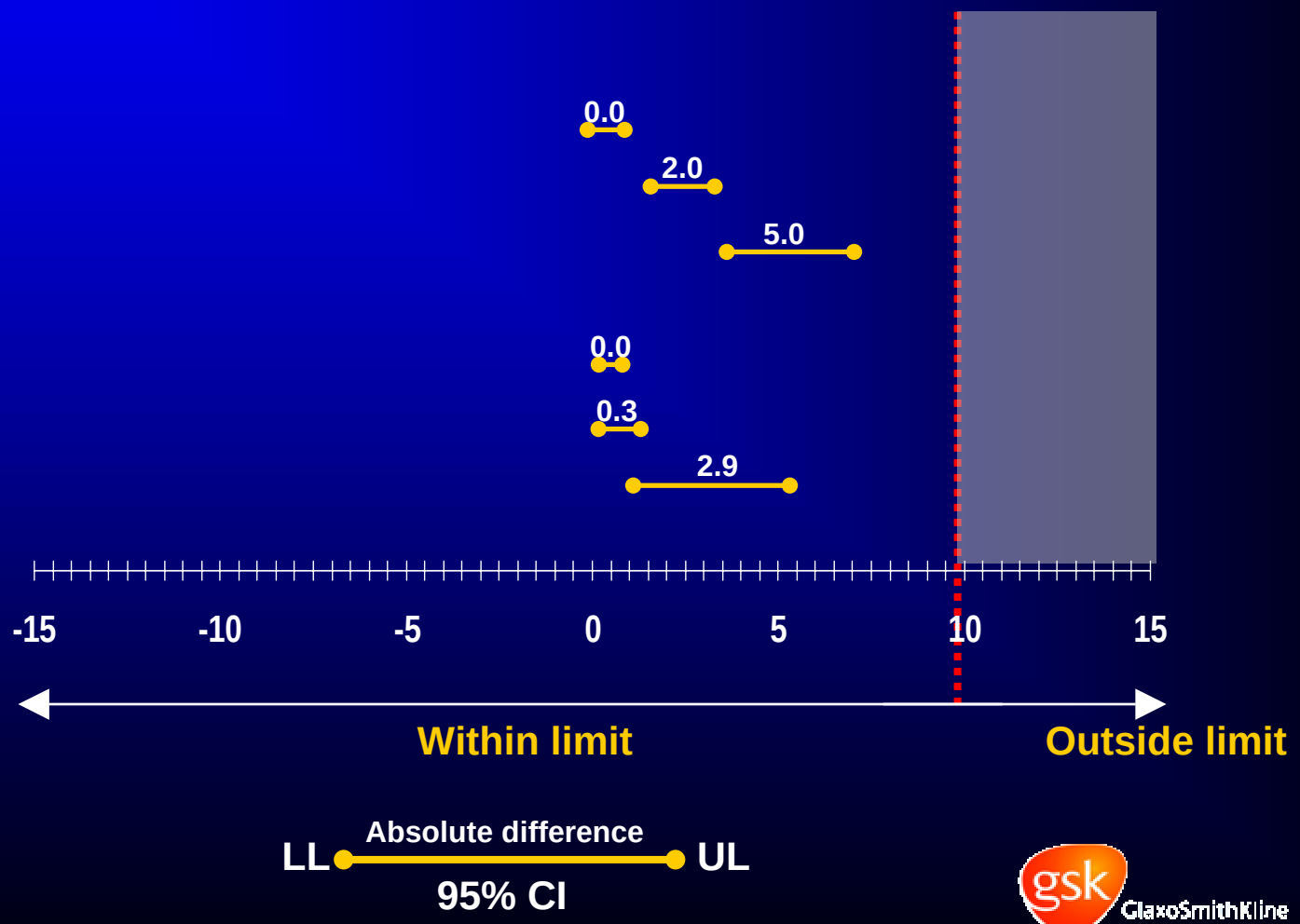
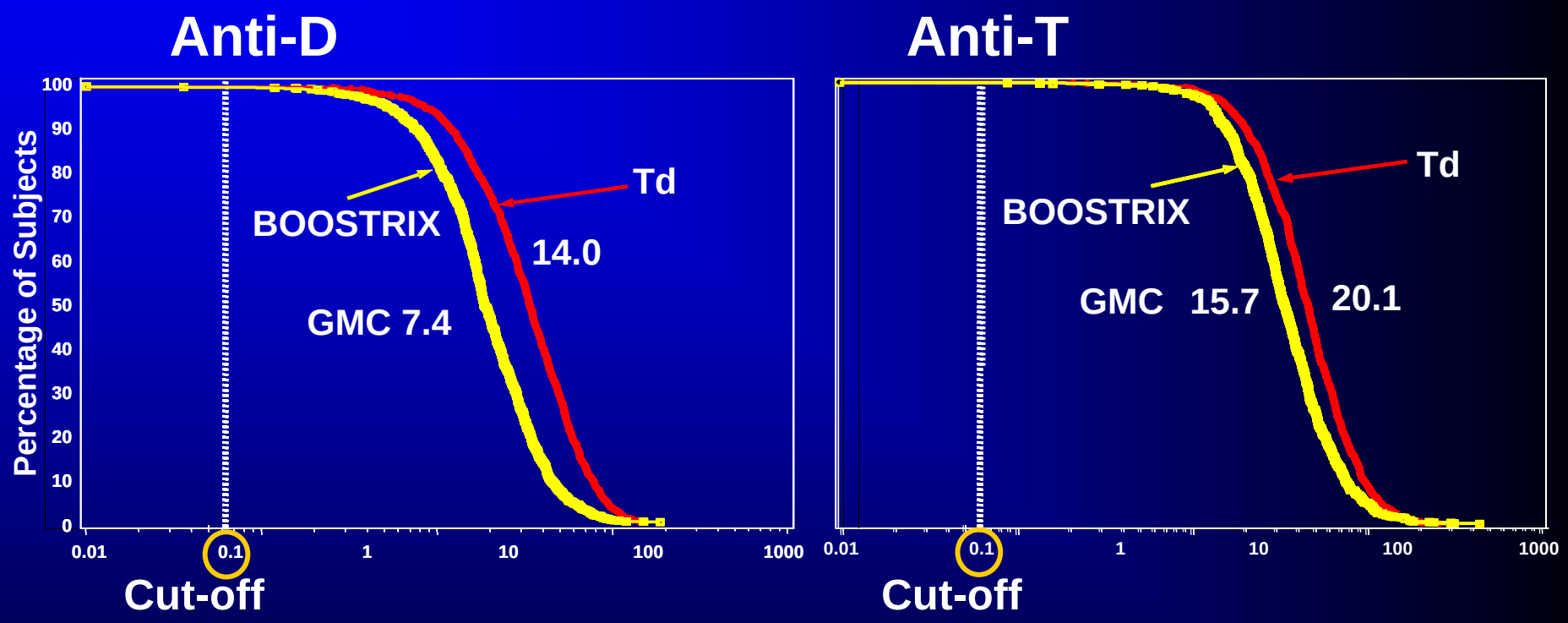
Study 001: D & T Non-inferiority Testing (Td minus BOOSTRIX) ≥0.1 IU/mL, ≥1.0 IU/mL, & Booster Response

All Non-inferiority Criteria Met



Study 001: Anti-D and Anti-T RCCs one month post-vaccination



Boostrix RCCs far to the right of protective level

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Study 001: primary objective # 4

Anti-PT, anti-FHA and anti-PRN booster responses in at least 80% of vaccinees administered BOOSTRIX, one month post-vaccination

Criteria for Success:

LL of 95% CI in proportion of subjects with booster response to each pertussis antigen in BOOSTRIX group is $\geq$80%

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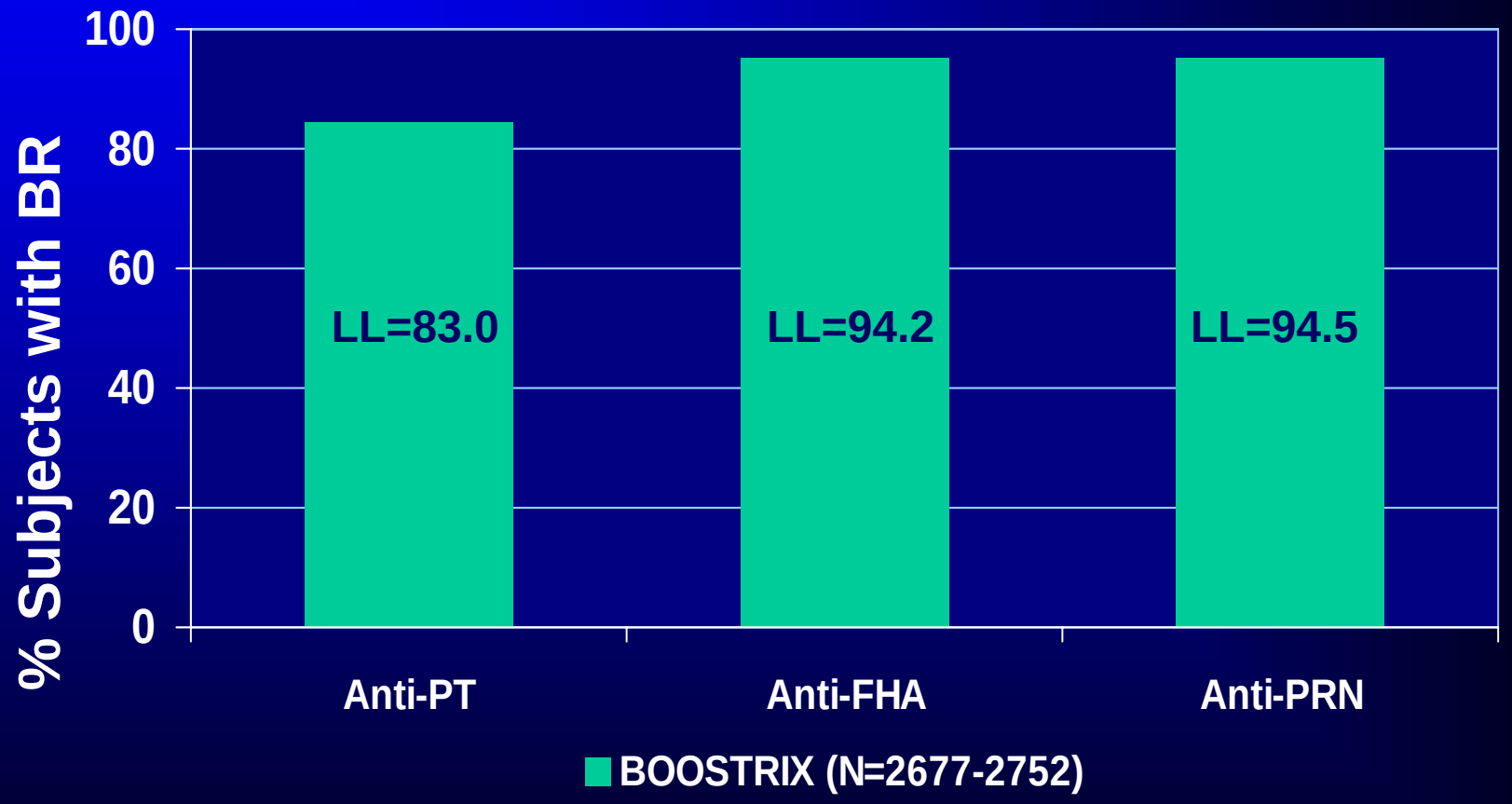
Study 001: Pertussis Booster Response* Rates

All Criteria Met



* initially seroneg: post-vacc Ab conc ≥4x cut-off (≥20)
initially seropos (≥5 and <20): post-vacc conc ≥4x pre
initially seropos (≥20): post-vacc conc ≥2x pre

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Pertussis: Immuno Bridge to Efficacy

- **pa responses in study 001 compared to those in INFANRIX (DTaP) immunogenicity Study 039[1]**
- **Further evaluation of Study 039 subjects in a household contact study demonstrated efficacy against pertussis[2]:**
  - WHO; 21 days spasmodic cough: 88.7% (95%CI 76.6-94.6)
  - Milder; 7 days spasmodic cough: 81.3% (95%CI 68.4-88.9)
- **Non-inferiority criteria: UL of the 95% CI on the GMC ratio INFANRIX over BOOSTRIX <1.5**

[1] Schmitt, HJ et al. J Pediatr 1996;129: 695-701

[2] Schmitt, HJ et al. JAMA 1996;275:37-41

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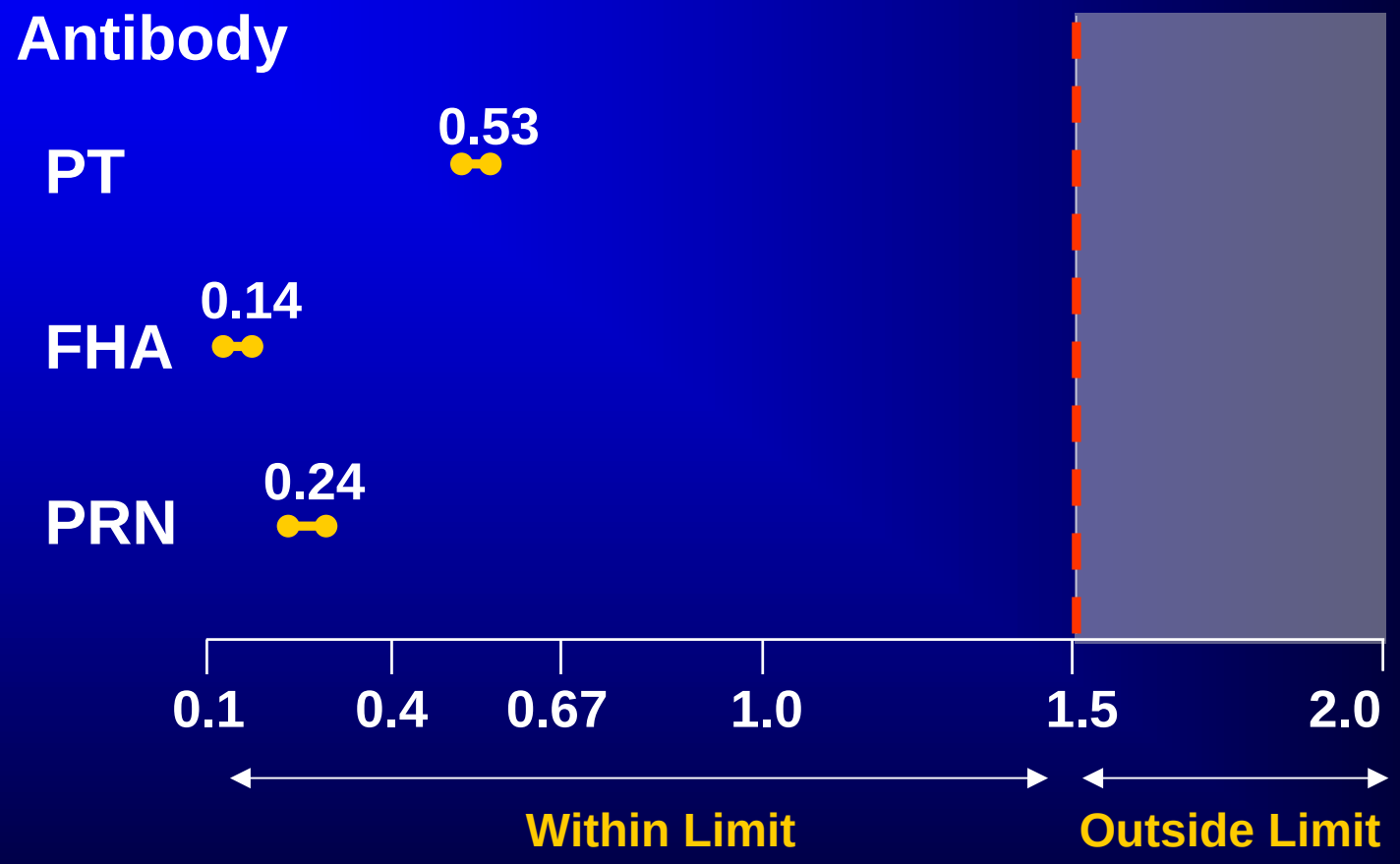
Non-inferiority Testing Ratio of GMCs

INFANRIX post-dose 3 in Infants (039) / BOOSTRIX post-dose 1 in Adolescents (001)

Total Cohort



All Non-inferiority Criteria Met

Ratio GMC

LL — UL

95% CI

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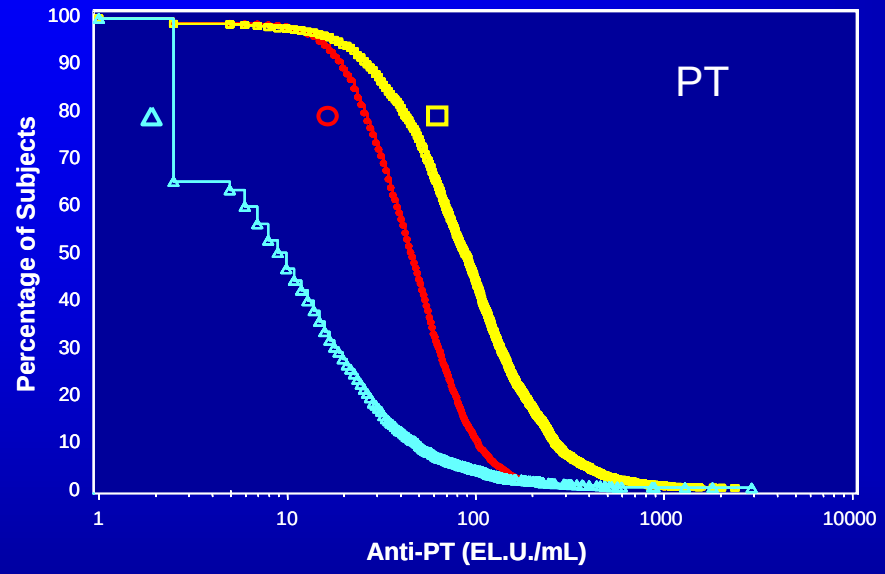
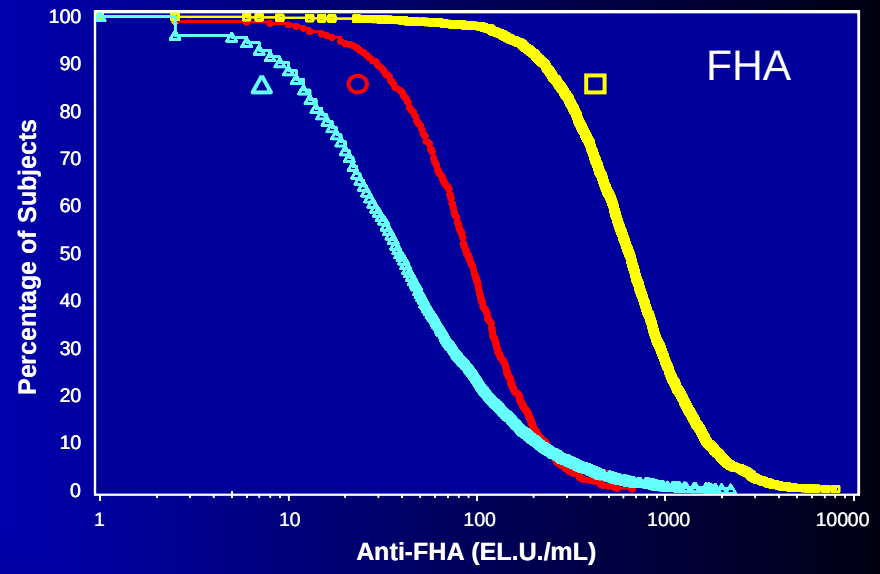
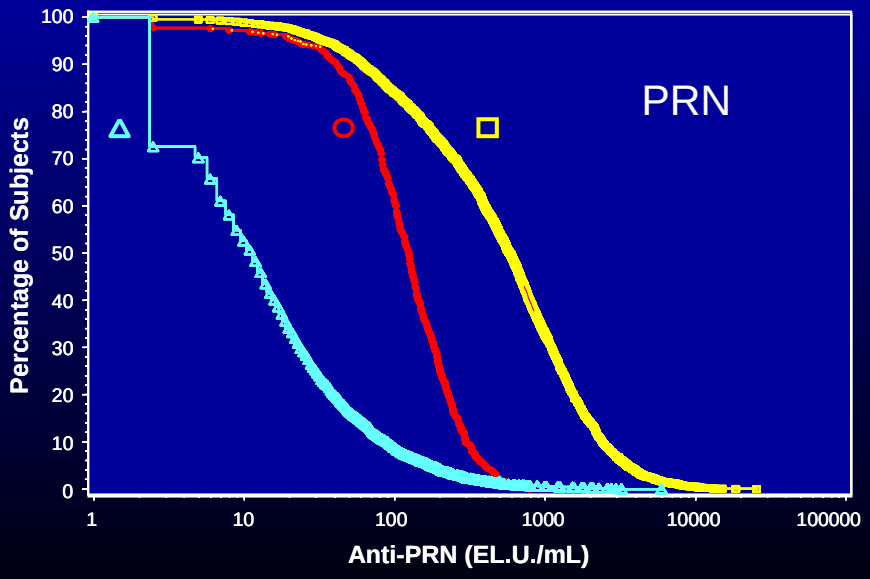
RCCs comparing PT, FHA & PRN Antibody Concentrations in INFANRIX Study 039 (Infants) and BOOSTRIX Study 001 (Adolescents) Total Cohort







BOOSTRIX pre-vaccination
INFANRIX post dose 3
BOOSTRIX post-vaccination

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Study 001: Conclusions

All Criteria Met

- **Diphtheria and Tetanus:**
  Non-inferiority: BOOSTRIX vs. US-Licensed Td
- **Pertussis antibody response:**
  Booster response achieved for all pertussis antigens
  Non-inferiority: BOOSTRIX vs. INFANRIX
- **Lot consistency:**
  Equivalence: BOOSTRIX 3 production lots

Clinical Trial Data to be Presented

Immunogenicity	Study
• Comparison to US-licensed Td	001
• Comparison to pertussis response in infants	001
• Lot consistency	001
• D, T and P antibody persistence	030

Safety	Study
• Comparison to US-licensed Td	001
• Limb swelling	001, 029
• Serious adverse events	All Studies

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Supportive Study 030

- **5 year serologic follow-up of Study 004**
  - Study 004: Finland, N = 510 healthy 10-14 year olds
    - 450 BOOSTRIX (0.5 mg Al)
    - 60: Td (Lederle) + investigational pa vaccine 1 month later
- **Subjects in Study 030: BOOSTRIX = 267, Td + pa = 36 (ages 15-17)**
- **Objective: evaluate antibody persistence 5 years after BOOSTRIX vaccination in adolescents**

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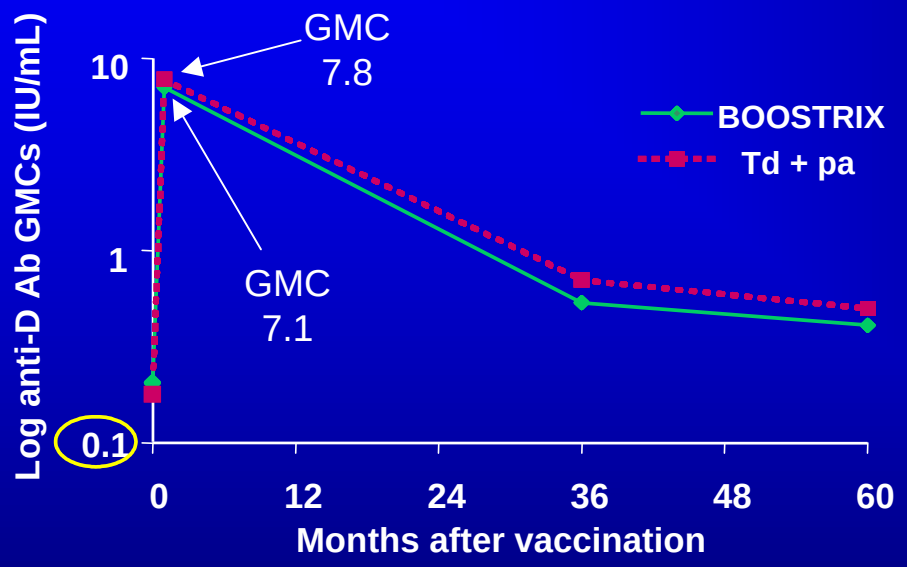
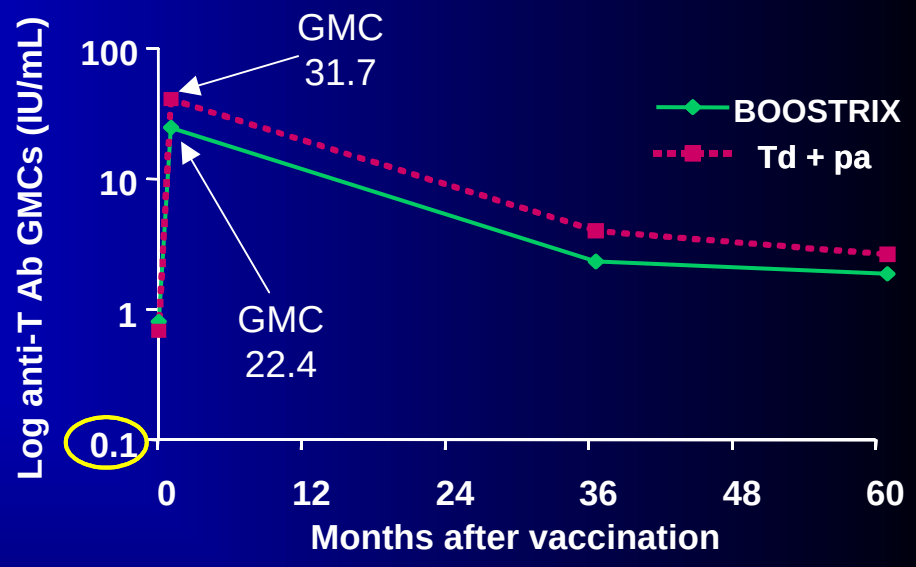
Study 030: Evolution of anti-D & anti-T GMCs over 60 months





anti-D **anti-T**

Boostrix GMCs remain well above protective level

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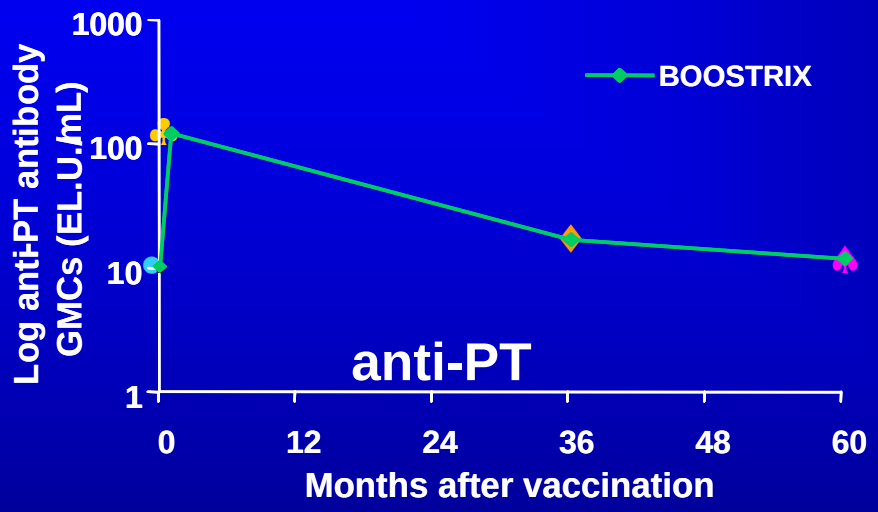
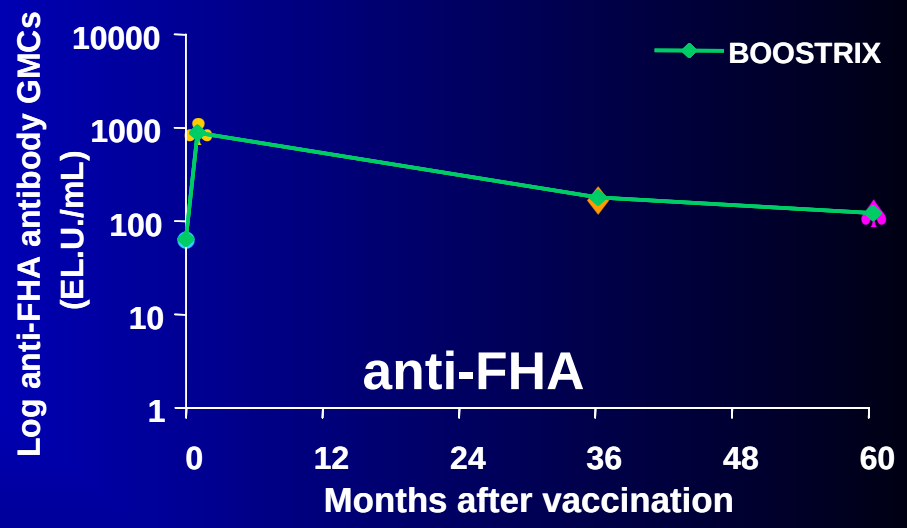
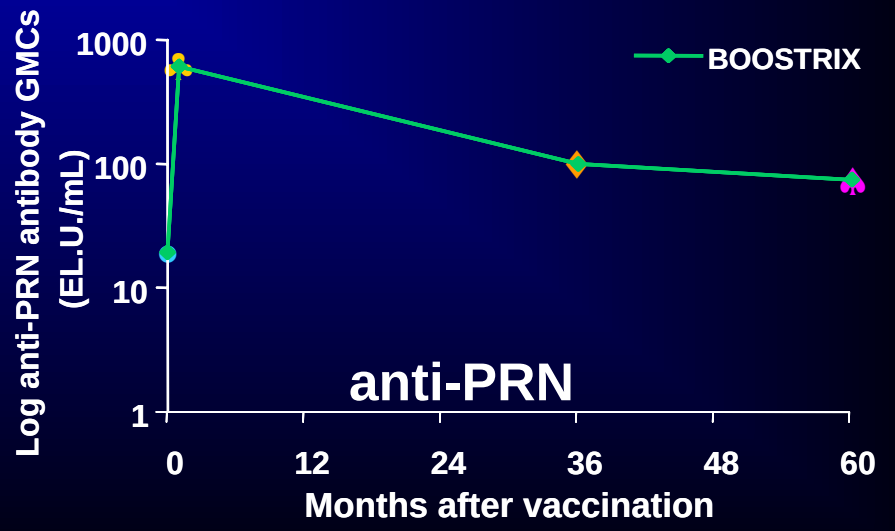
Study 030: Evolution of anti-PT, anti-FHA & anti-PRN GMCs over 60 months





- Pre vaccination
- Post 1 mo
- Post 3 yr
- Post 5 yr



Duration of Protection
Study 030

- At 5 years:
  - GMCs to D, T, FHA and PRN remained higher than at pre-vaccination levels; GMC to PT approached pre-vaccination level
  - Anti-D and anti-T remained above seroprotective levels

INFANRIX Italian Efficacy Follow-up

- Efficacy against pertussis following primary series with no booster sustained to at least 6 yrs of age (86%, 95%CI 79-91%)
  (Salmaso, Pediatrics 2001;108:e81)

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Immunogenicity: Overall Conclusions

All Objectives Met

- **Diphtheria and Tetanus:**
  Non-inferiority: BOOSTRIX vs. US-Licensed Td
- **Pertussis antibody response:**
  Booster response achieved for all pertussis antigens
  Non-inferiority: BOOSTRIX vs. INFANRIX
- **Lot consistency:**
  Equivalence: BOOSTRIX 3 production lots
- **Antibody persistence through 5 years**

Safety

BOOSTRIX – Clinical Experience in U.S. File

Population	Clinical Studies	Persons Receiving BOOSTRIX
Adolescents - U.S.	1	3080 (BOOSTRIX 0.3 mg Al)
Adolescents – Finland	1	450 (BOOSTRIX 0.5 mg Al)
Adolescents – Belgium	1	209 (BOOSTRIX 0.3 mg Al)
		224 (BOOSTRIX 0.5 mg Al)
		214 (BOOSTRIX 0.133 mg Al)
All Ages - worldwide	9	1341 (BOOSTRIX 0.5 mg Al)
TOTAL	12	5518
		3289 Adolescents (0.3 mg Al)

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Objectives of Clinical Trials

Immunogenicity	Study
• Comparison to US-licensed Td	001
• Comparison to pertussis response in infants	001
• Lot consistency	001
• D, T and P antibody persistence	030

Safety	Study
• Comparison to US-licensed Td	001
• Limb swelling	001, 029
• Serious adverse events	All Studies

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Safety Data Collected

- **Solicited local and general adverse events:**
  through Day 15
- **Unsolicited adverse events:**
  all AEs: through Day 31
  specific AEs: through Month 6 (Study 001)
- **Serious adverse events:**
  duration of study

US Pivotal Study 001

- **Multi-center, randomized, controlled study: 4114 healthy 10-18 year olds**
  - 3080: BOOSTRIX (0.3 mg Al)
  - 1034: Td (US-licensed MPHBL)
- **Overall Objective: compare safety profile to Td**

Study 001

- **Primary safety objective:**

  Non-inferiority of BOOSTRIX compared to Td for Grade 3 pain at the injection site

Criteria for Success

UL of 95% CI for difference in frequency Grade 3 pain over 15-day period, BOOSTRIX minus Td, is $\leq$4%

Grade 3 pain = spontaneously painful and/or prevented activities

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Study 001: Non-inferiority Testing on Percentage of Subjects with Grade 3 Pain
15 Day follow-up period

BOOSTRIX (N=3032) %	Td (N=1013) %	BOOSTRIX minus Td Difference	95% CI LL	95% CI UL
4.58	4.04	0.54	- 1.01	1.87*

*** Upper limit below clinical limit (4%) for non-inferiority**

Criterion Met

Grade 3 pain = spontaneously painful and/or prevented activities

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Study 001: Incidence (%) of solicited local events 15-Day follow-up period

		BOOSTRIX (N=3032)	Td (N=1013)	p-value
Pain	Any	75.3	71.7	0.022
	Grade 2 or 3	51.2	42.5	<0.001
	Grade 3	4.6	4.0	0.538
Redness	Any	22.5	19.8	0.087
	>20 mm	4.1	3.9	0.855
	≥50 mm	1.7	1.6	0.888
Swelling	Any	21.1	20.1	0.532
	>20 mm	5.3	4.9	0.744
	≥50 mm	2.5	3.2	0.258
Increased mid-upper arm circumference (vaccinated arm)	Any	28.3	29.5	0.470
	>20 mm	2.0	2.2	0.700
	>40 mm	0.5	0.3	0.587

Grade 2 pain = when limb moved
Grade 3 pain = spontaneously painful and/or prevented activities

Study 001: Incidence (%) of solicited general events 15-Day follow-up period

		BOOSTRIX (N=3030)	Td (N=1013)	p-value
Fever	≥99.5	13.5	13.1	0.831
	>100.4	5.0	4.7	0.739
	≥102.4	1.4	1.0	0.421
Headache	Any	43.1	41.5	0.379
	Grade 2 or 3	15.7	12.7	0.022
	Grade 3	3.7	2.7	0.135
Fatigue	Any	37.0	36.7	0.851
	Grade 2 or 3	14.4	12.9	0.251
	Grade 3	3.7	3.2	0.493
Gastrointestinal	Any	26.0	25.8	0.901
	Grade 2 or 3	9.8	9.7	0.903
	Grade 3	3.0	3.2	0.751

Grade 2 = interfered with activities
Grade 3 = prevented activities

Study 001: Safety in Specific Subpopulations

- **Exploratory analyses**
  - Age (10-14 and 15-18 yrs)
  - Gender
  - Race
  - Vaccination history (4 or 5 prior DTP doses)
  - Type previous DTP (all DTPw, mixture DTPw/DTaP, unknown)
- **Results between BOOSTRIX and Td groups consistent with those of the overall total cohort**

Injection Site Swelling

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Injection Site Swelling

- **ISS after repeat vaccination with DTaP, DTPw and Td have been well described**
- **Rennels[1]: entire proximal limb swelling occurs in 2% to 6% of children with 4th & 5th consecutive DTaP doses**
- **Studies 001 and 029 prospectively solicited large swelling**
  - 001 included daily mid-arm circumference
  - most subjects primed with at least 3 doses of DTPw

[1] Rennels Sem Ped Inf Dis 2003;14:196-198

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Large Injection Site Swelling (LISS) Criteria

- **Study 029:**
  - Swelling >100 mm
  - Diffuse swelling or noticeable increase in limb circumference
- **Study 001:**
  - Swelling >100 mm
  - >50 mm increase in mid-upper arm circumference compared to pre-vaccination baseline
  - Diffuse swelling that interfered or prevented normal activities (e.g., writing, computer use, school attendance, sleeping)

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Study 001 LISS Reports: N=2/4047

Swelling (mm)	Redness (mm)	Pain Intensity	Functional Impairment	Increase mid-upper arm circumference (mm)	Onset	Joint Involvement	Duration
BOOSTRIX: 1/3034 (0.03%)							
90	90	Grade 3	Grade 3	8	Day 2	None	3 Days
Td: 1/1013 (0.1%)							
102	80	Grade 1	None	13	Day 3	None	Unknown

Pain Intensity Grade 1 = painful on touch
Pain Intensity Grade 3 = spontaneously painful and/or prevented activities
Functional Impairment Grade 3 = prevented activities

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Study 029 LISS Reports: N=5/647 (0.8%)

Swelling (mm)	Redness (mm)	Pain Intensity	Functional Impairment	Onset	Joint Involvement	Duration
BOOSTRIX 0.3 mg Al						
125	125	Grade 2	Grade 2	Day 2	None	4 Days
110	110	Grade 3	Grade 3	Day 2	None	2 Days
110	100	Grade 2	Grade 2	Day 2	None	2 Days
127	125	Grade 3	Grade 3	Day 1	None	3 Days
BOOSTRIX 0.5 mg Al						
120	120	Grade 2	Grade 2	Day 2	None	2 Days

Pain Intensity Grade 2 = painful when limb moved
Pain Intensity Grade 3 = spontaneously painful
Functional Impairment Grade 2 = interferes with activities
Functional Impairment Grade 3 = prevents activities

Note: no Td comparator in Study 029

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LISS Summary, Next Steps

- Low incidence in studies 029 and 001 (0.03-0.8%)
- LISS events do not signal a new or unexpected safety issue
- US adolescents primed throughout life with DTaP vaccine not evaluable until 2007
- Post-approval, a study report will be submitted on a cohort of 300 German adolescents who recently completed a clinical study where they received a 6th consecutive dose of acellular-pertussis containing vaccine

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Study 001: Unsolicited AEs Reported in at Least 1% of Subjects, Day 0-30

WHO Preferred Term	BOOSTRIX (N=3034) %	Td (N=1013) %
At least one AE	25.4	24.5
Pharyngitis	4.6	4.3
URI	4.3	4.8
Rhinitis	2.7	0.7
Injury	2.2	1.8
Coughing	1.8	1.6
Injection site reaction	1.7	1.6
Pain	1.6	1.1
Dysmenorrhea	1.2	0.7

Study 001: Unsolicited AEs Day 31 - Month 6

Category	BOOSTRIX (N=3005) %	Td (N=1003) %	p-value
At least one AE	5.5	4.3	0.161
Onset chronic illness	0.7	0.9	0.677
Emergency Room Visit	3.4	2.5	0.209
Physician Office Visit	1.7	1.6	0.888
SAE	0.5	0.2	0.386

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All Studies: Serious Adverse Events Day 0-30

Pivotal Study 001: None

Supportive studies: 10 subjects reported 10 SAEs

Study	Onset	Age/Sex	Vaccines administered	SAE	Related to vaccine
004	20 D	11/F	BOOSTRIX 0.5	Diabetes Mellitus	No
004	23 D	10/F	BOOSTRIX 0.5	Appendicitis	No
029	21 D	13/M	BOOSTRIX 0.5	Cerebral concussion 2° vasovagal syncope and fall	No
029	37 D	11/F	BOOSTRIX 0.5	Diabetic coma	No
029	28 D	14/F	BOOSTRIX 0.3	Alcohol intoxication	No
01	0 D	12/F	BOOSTRIX 0.5	Syncope	No
02	7 D	49/F	BOOSTRIX 0.5	Uveitis	No
02	3 D	44/M	pa	Chest pain	No
118	29 D	6/F	BOOSTRIX 0.5	Adenoidectomy	No
118	24 D	6/M	Td	Burn	No

Study 001: Serious Adverse Events Day 31 – Month 6

16 subjects reported 22 SAEs (all reported as unrelated to vaccine)

- 14 subjects (0.5%) received BOOSTRIX 0.3 (20 SAEs)
  - injury x4, drug overdose x 2, depression, ADHD, headache, cholecystitis, spontaneous abortion, menorrhagia, anemia, pleural effusion, pneumothorax, pulmonary bulla, sinusitis, anisocoria, migraine, drug abuse
- 2 subjects (0.2%) received Td (2 SAEs)
  - appendicitis, tooth abscess

In addition: No deaths, 4 pregnancies
(1 possibly in the initial 31 days after vaccination)

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Safety and Reactogenicity: Conclusions

- 3289 subjects BOOSTRIX 0.3
- 2229 subjects BOOSTRIX 0.5 or 0.133
- Non-inferiority demonstrated BOOSTRIX compared to Td: Grade 3 pain at the injection site
- BOOSTRIX safety profile comparable to US-licensed Td

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GlaxoSmithKline Presentation

Vincent Ahonkhai, M.D. Vice President U.S. Regulatory Affairs, Vaccines	Introduction
Barbara Howe, M.D. Vice President & Director - Clinical R&D North America (Vaccines)	Epidemiology Clinical Development Plan
Leonard Friedland, M.D. Director – Clinical R&D North America (Vaccines)	Immunogenicity Safety
Vincent Ahonkhai, M.D.	Conclusion

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Adequacy of Efficacy Data

- **Met all agreed non-inferiority criteria**
- **For Diphtheria and Tetanus antigens, at least as immunogenic as US-licensed Td vaccines**
- **Pertussis booster response induced and immune response at least as immunogenic as *Infanrix***

Adequacy of Safety Data

- Extensive clinical and marketing experience with individual antigens
- Safety demonstrated in ~5500 subjects
- Safety profile comparable to US-licensed Td vaccine
- BOOSTRIX met all agreed non-inferiority criteria

BOOSTRIX Risk/Benefit

- Safety and reactogenicity profile comparable to US-licensed Td vaccine
- Immunogenicity is comparable to Td
- Confers protection against pertussis
- Offers needed protection against pertussis with no additional injection
- Fits ACIP-recommended 11-12 year preadolescent visit

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BOOSTRIX™

Vaccines and Related Biological Products
Advisory Committee
March 15, 2005

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