Immunogenicity and Safety of Kinrix™: A Combination DTaP-IPV Vaccine in Children 4-6 Years of Age

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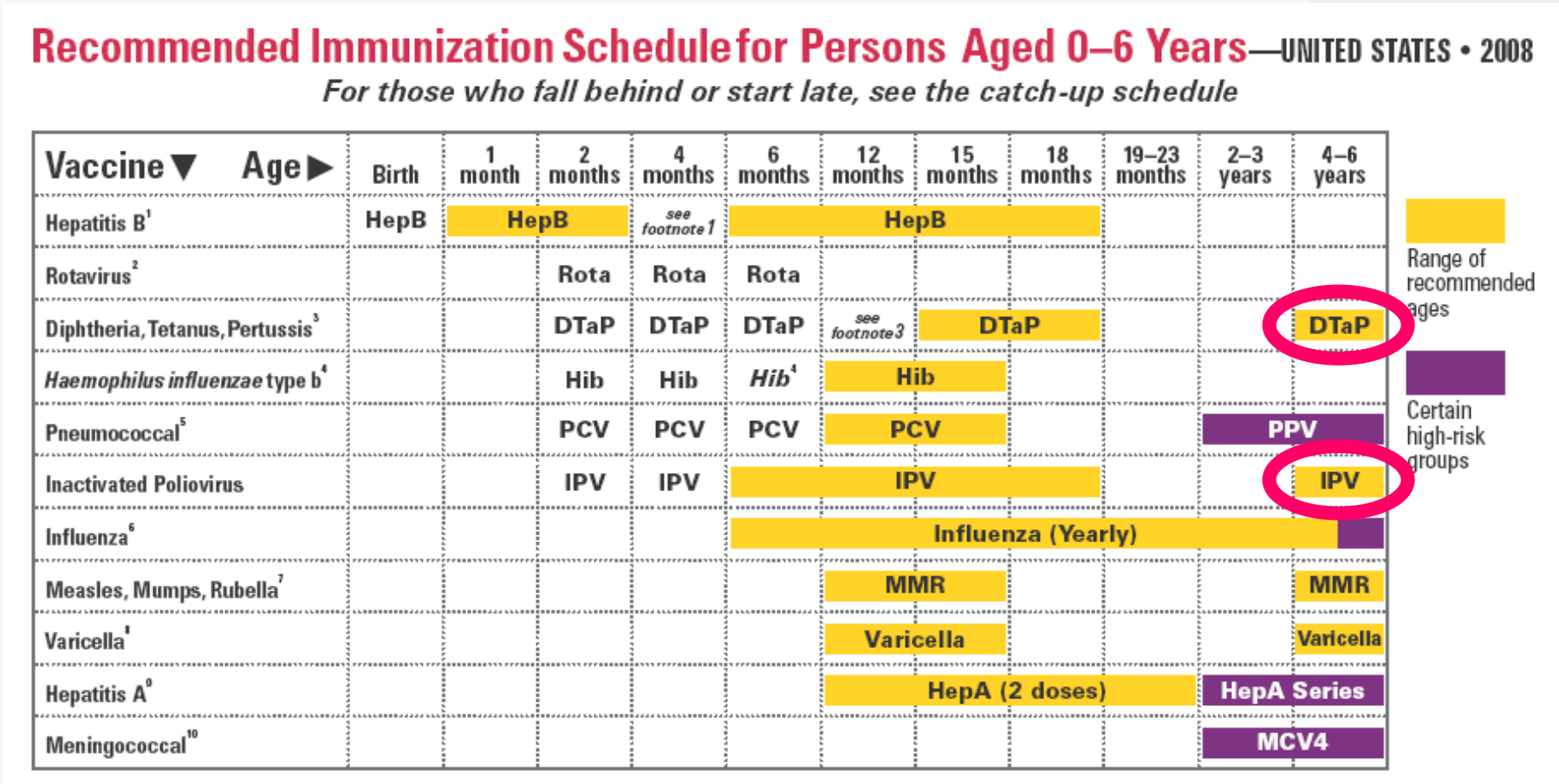
GlaxoSmithKline Biologicals

Kinrix: Intended Use



Combining DTaP and IPV into a single injectable vaccine reduces by 1 the number of injections required to provide all recommended immunizations to children 4-6 years of age

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Studies in support of licensure application

- Study 213503/048 (US)
  - Pivotal study
    - 3,156 children vaccinated with *Kinrix*
    - 997 with immunogenicity data
  - Primary objectives to assess safety, immunogenicity, and lot consistency
- Study 213503/047 (US)
  - Supportive study, 200 children vaccinated with *Kinrix*
  - Primary objectives to assess safety and immunogenicity
    - Provides information on coadministered MMR vaccine immunogenicity
- Study 213503/046 (Australia)
  - 181 children vaccinated with Kinrix
  - Provides supportive safety information

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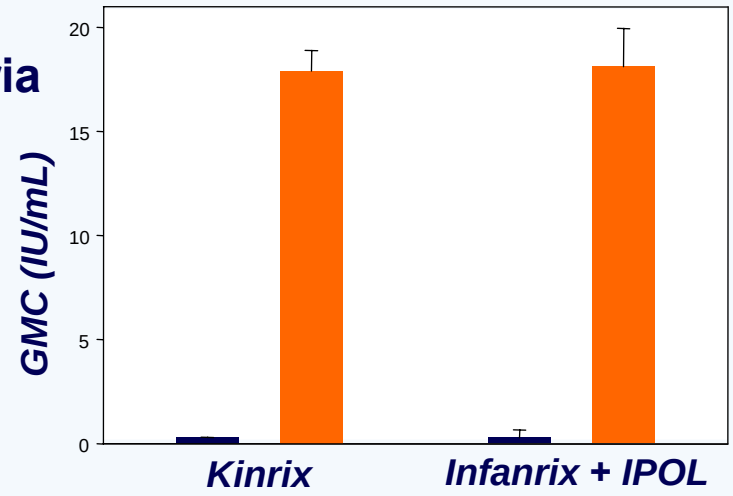
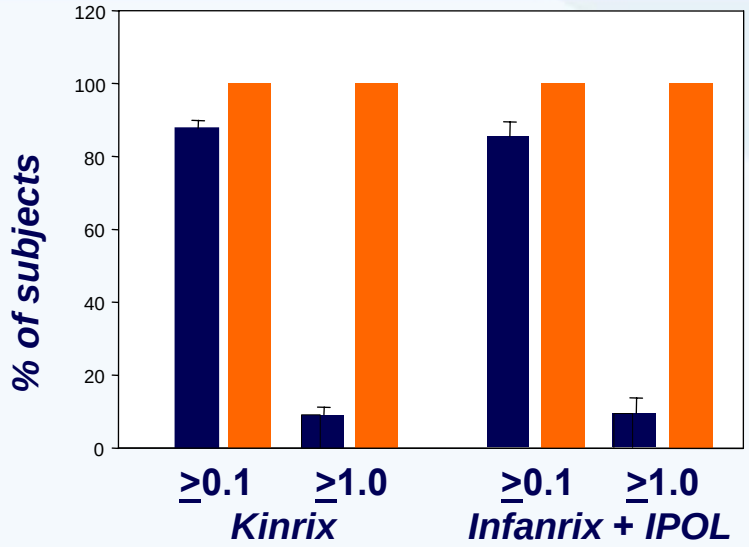
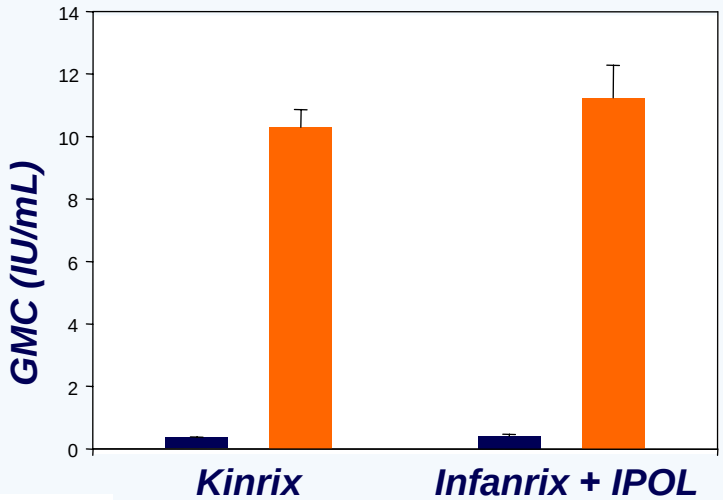
Increase in serum antibody concentrations after vaccination – Diphtheria and Tetanus, Study 048

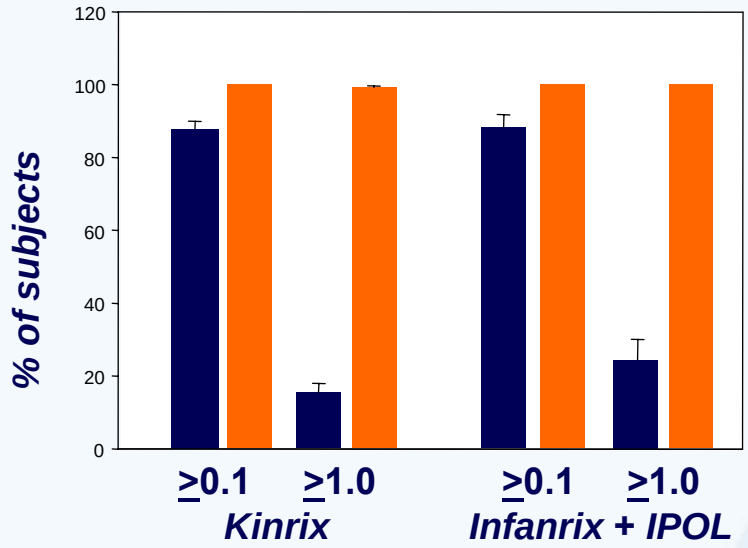
Diphtheria





Tetanus





Pre- vaccination

Post- vaccination

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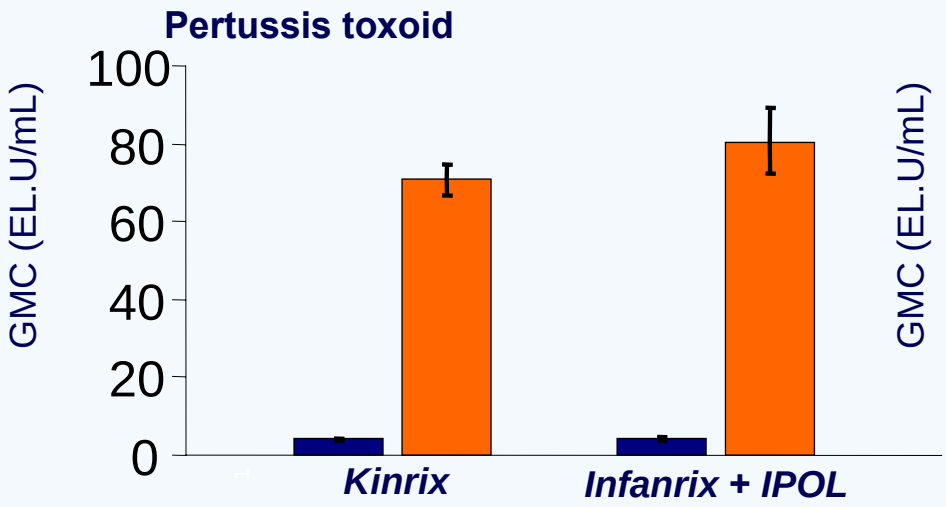
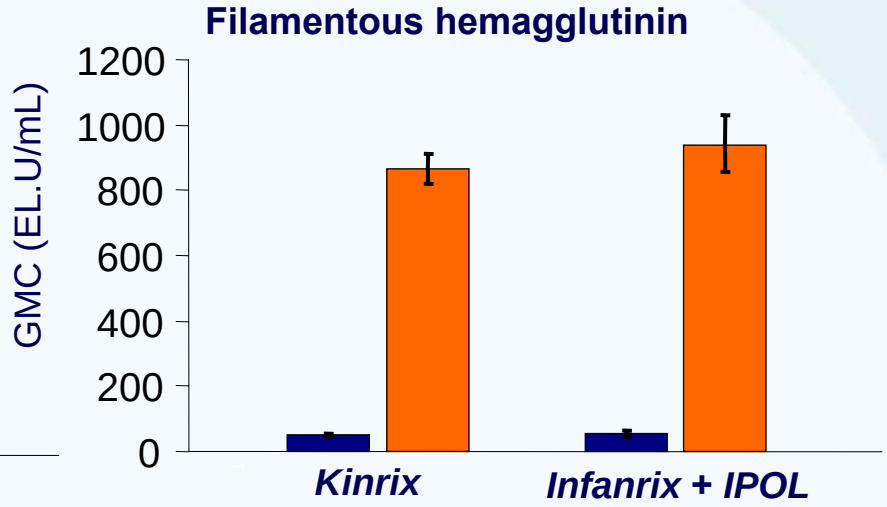
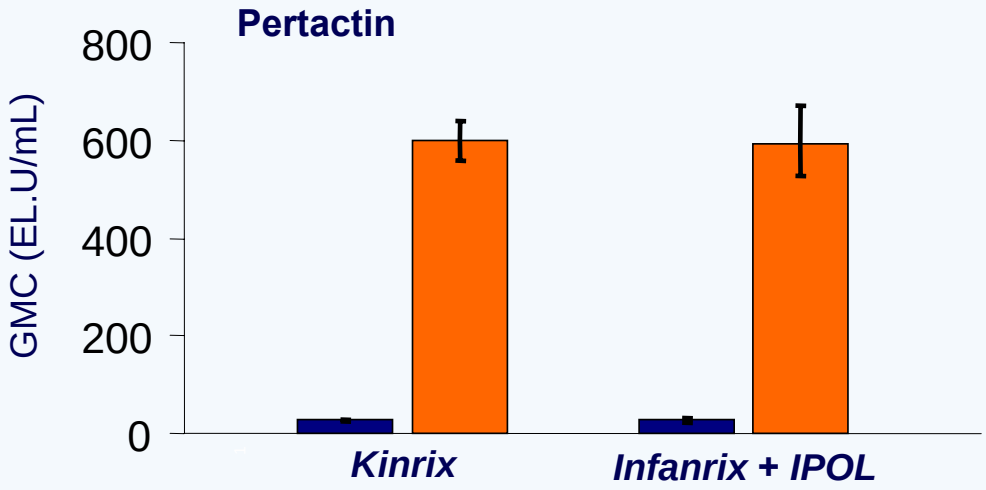
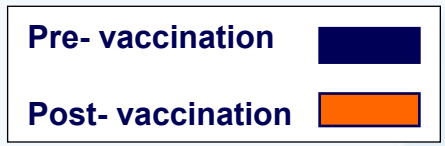
Increase in serum antibody concentrations after vaccination – Pertussis antigens, Study 048









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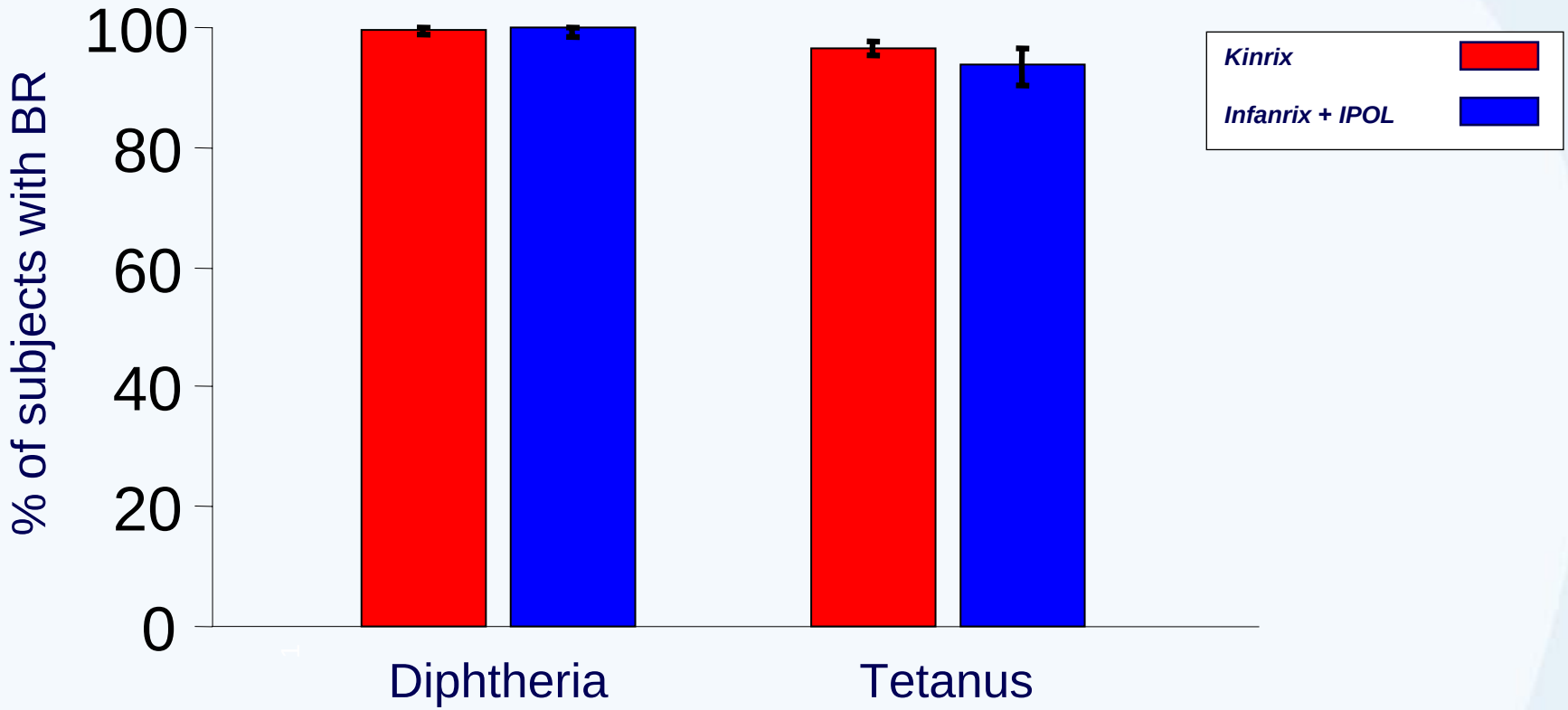
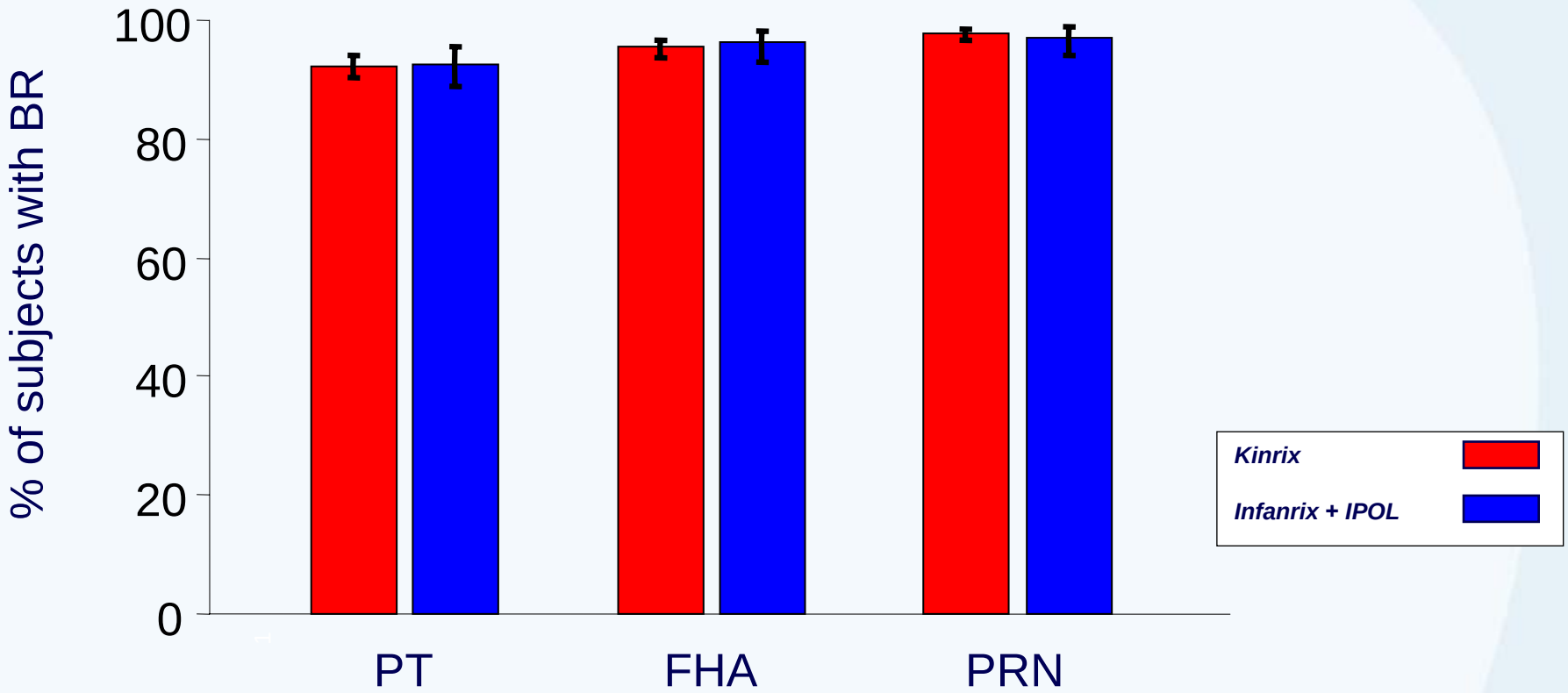
95%CI for the GM was obtained by exponential transfer of the 95%CI for the mean of the log-transformed titer

Percentage of subjects with post-vaccination booster responses – Diphtheria and Tetanus, Study 048



Booster response:
for initially seronegative subjects – post-vaccination Ab concentration ≥0.4IU/mL
for initially seropositive subjects, post-vaccination Ab concentration ≥4x initial concentration

Percentage of subjects with post-vaccination booster responses – Pertussis, Study 048



Booster response:
for initially seronegative subjects – post-vaccination Ab concentration ≥20EL.U/mL
for initially seropositive subjects w. pre-vaccination Ab concentration <20EL.U/mL, post-vaccination Ab concentration ≥4x initial concentration
for initially seropositive subjects w. pre-vaccination Ab concentration ≥20EL.U/mL, post-vaccination Ab concentration ≥2x initial concentration

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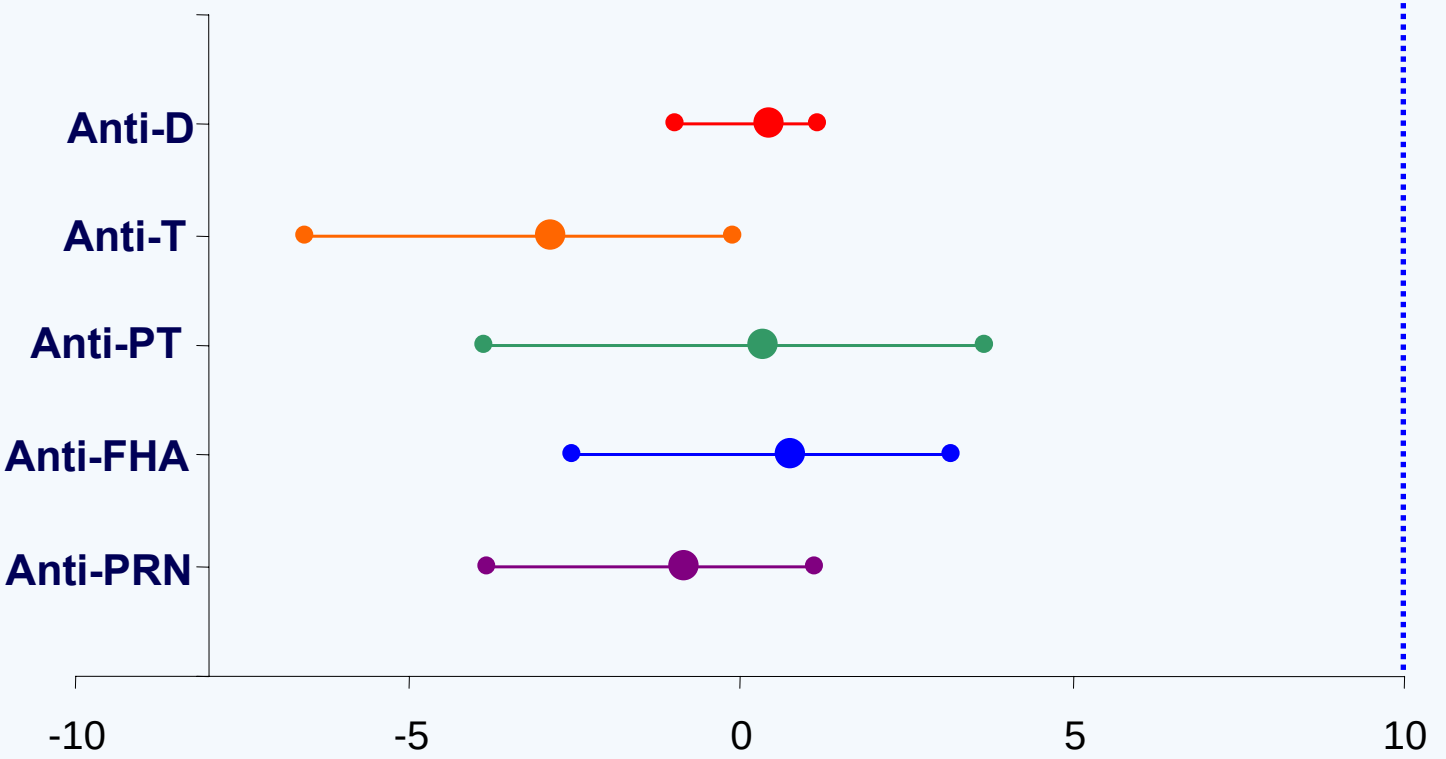
Kinrix is non-inferior to *Infanrix* with regard to DTaP booster responses, Study 048

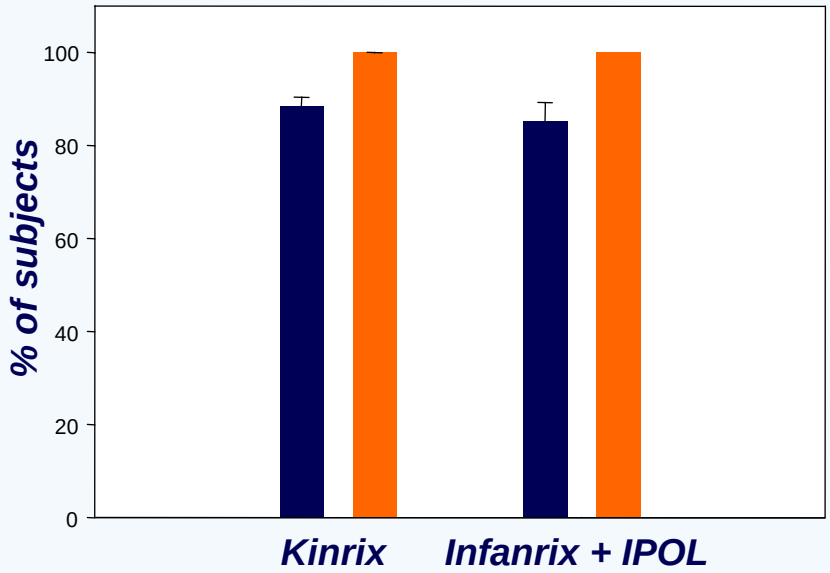
Non-inferiority criteria met if upper limit of 95% CI for group difference in booster response rate ≤10%



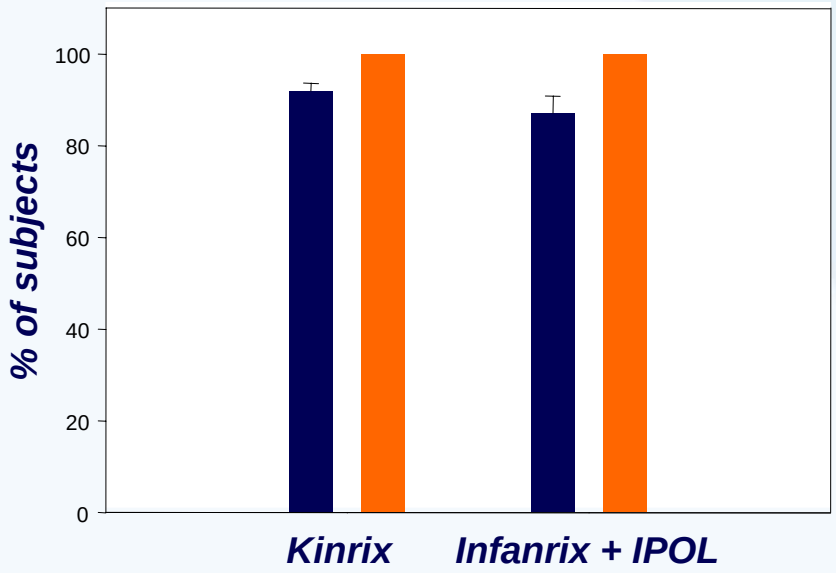
Obtained using an ANCOVA with vaccine group as fixed effect and pre-vaccination log-transformed titer as regressor

Increase in seroprotection after vaccination – Poliovirus, Study 048

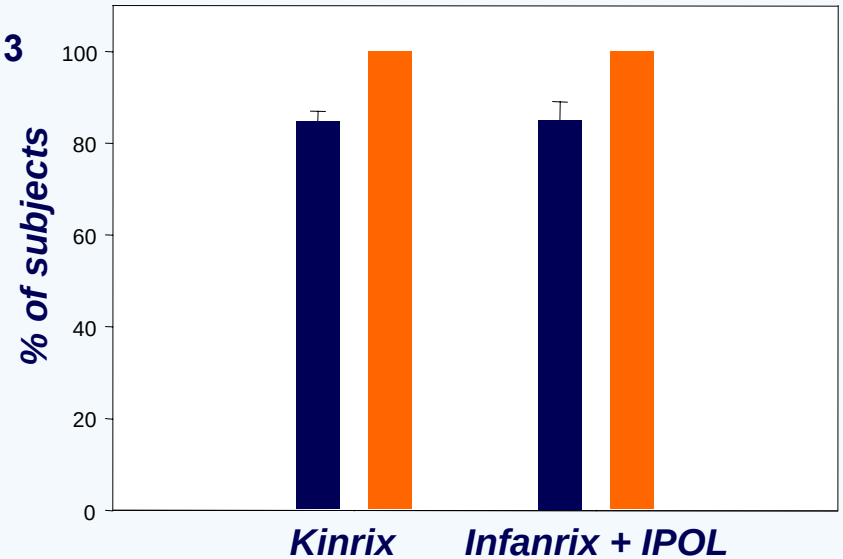
Poliovirus Type 1



Poliovirus Type 2



Poliovirus Type 3



Pre- vaccination

Post- vaccination

Seroprotection = antibody titer ≥ 1:8, one month after vaccination

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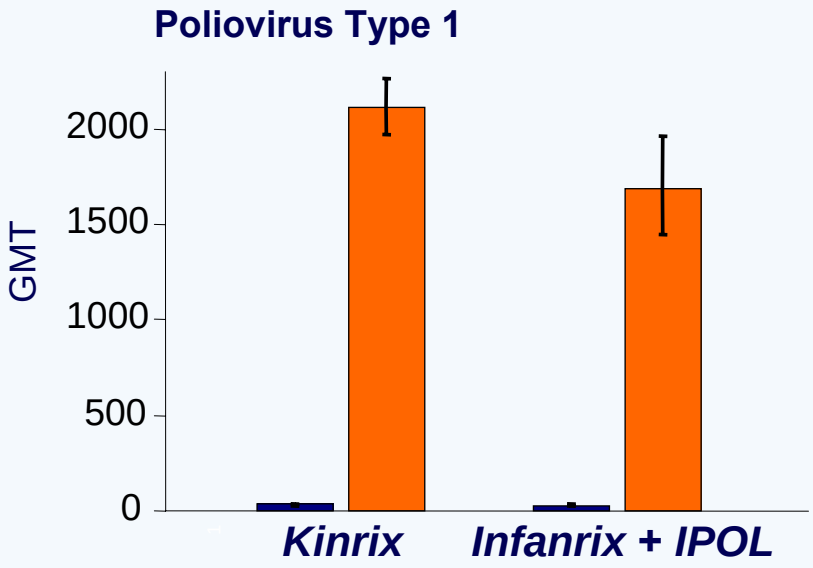
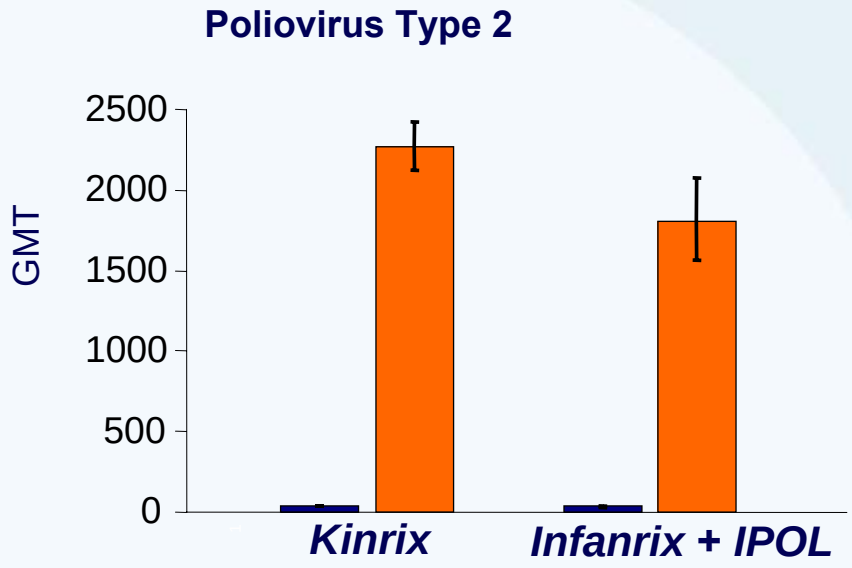
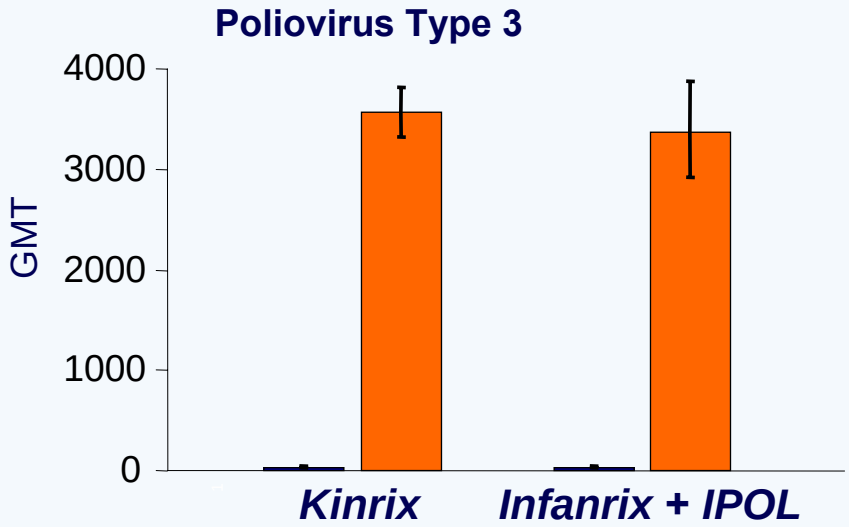
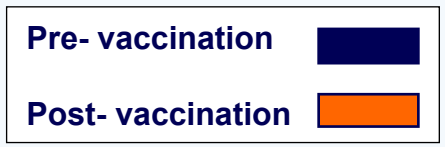
Increase in antibody GMTs after vaccination – Poliovirus, Study 048









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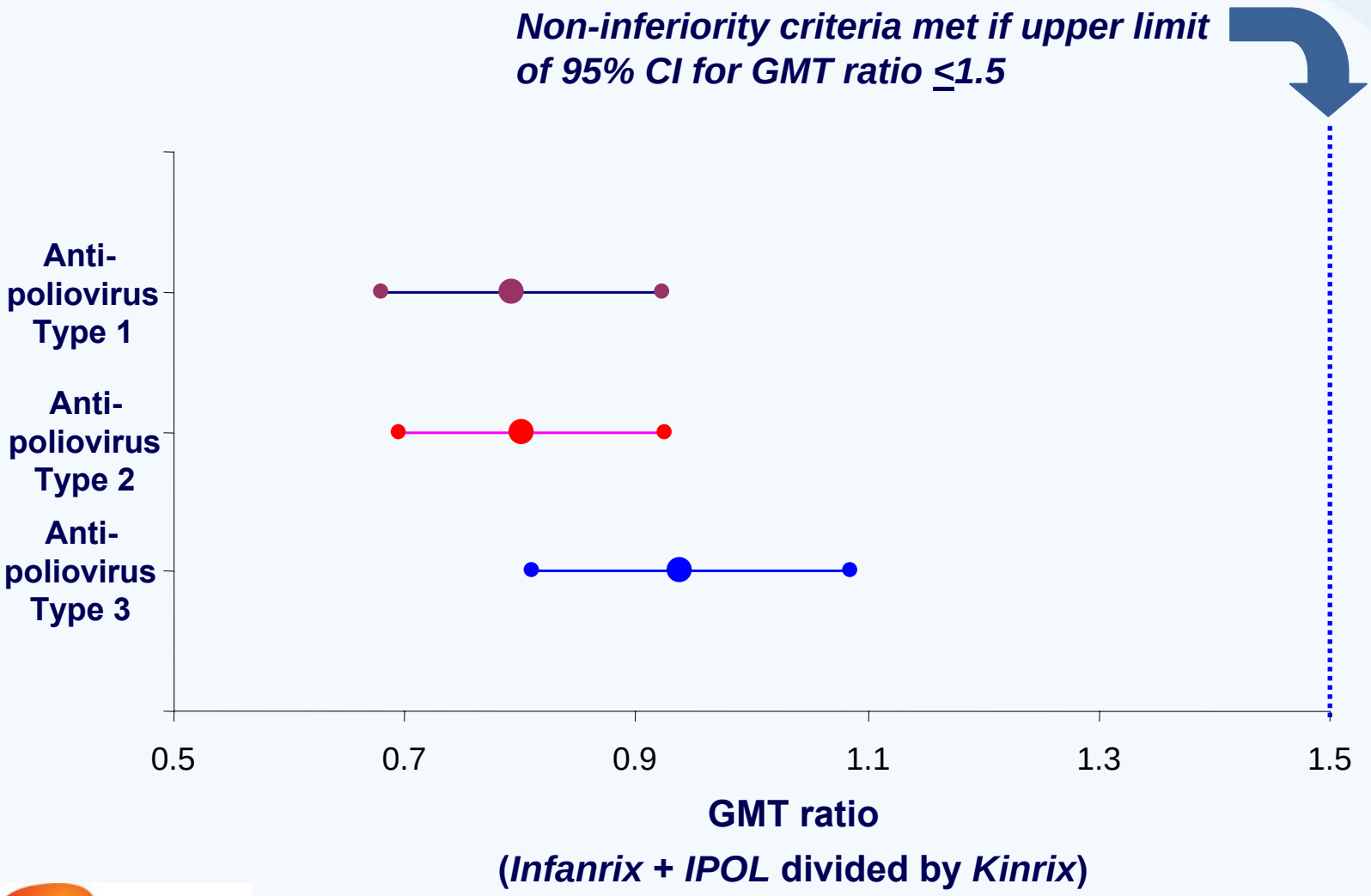
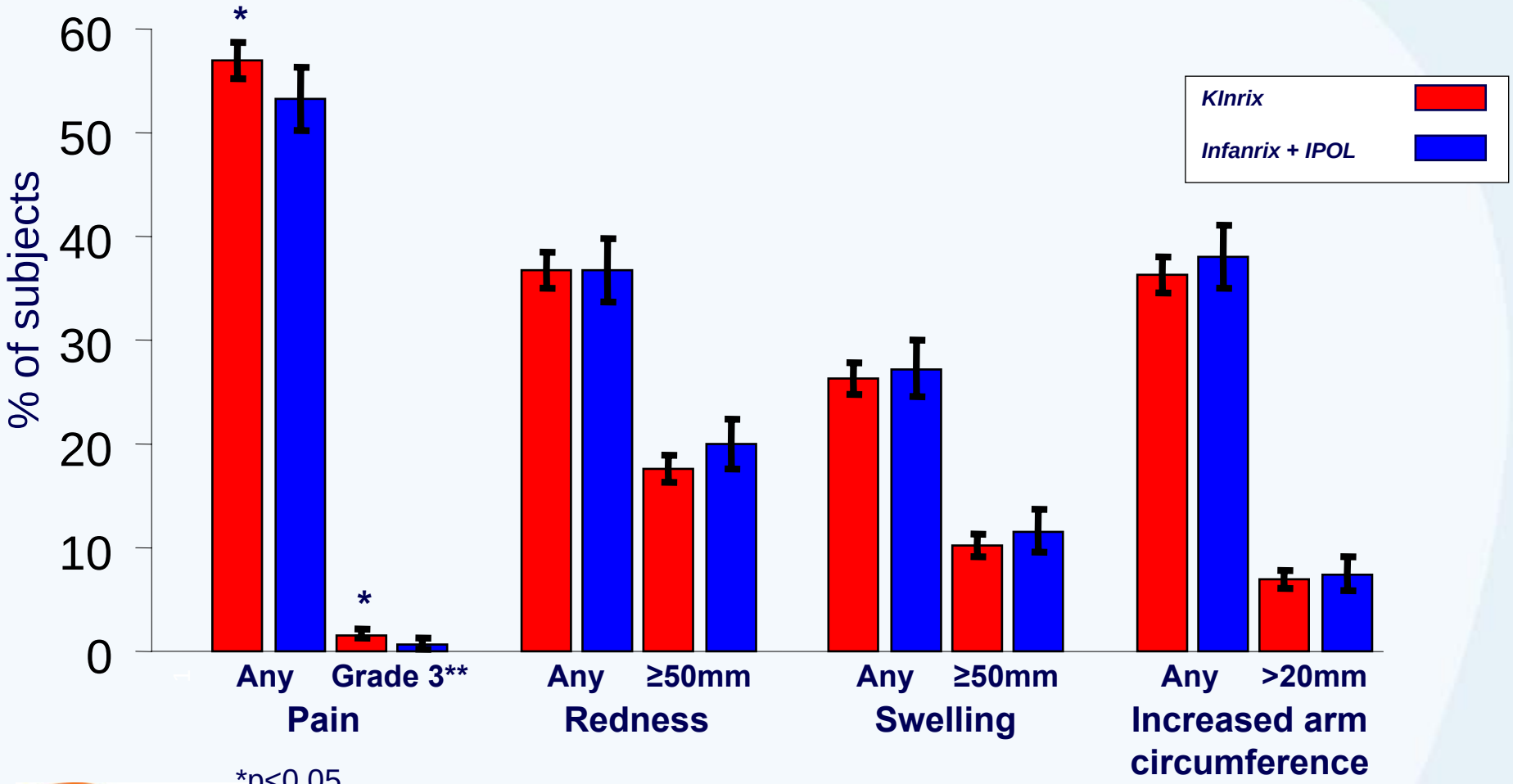
95%CI for the GM was obtained by exponential transfer of the 95%CI for the mean of the log-transformed titer

Kinrix is non-inferior to *IPOL* with regard to anti-poliovirus post-vaccination GMTs, Study 048



Obtained using an ANCOVA with vaccine group as fixed effect and pre-vaccination log-transformed titer as regressor

Solicited local symptoms occurring at DTaP injection site within 4 days (days 0-3) of vaccination, Study 048



*p<0.05

**Grade 3 pain – sufficient to prevent normal daily activities

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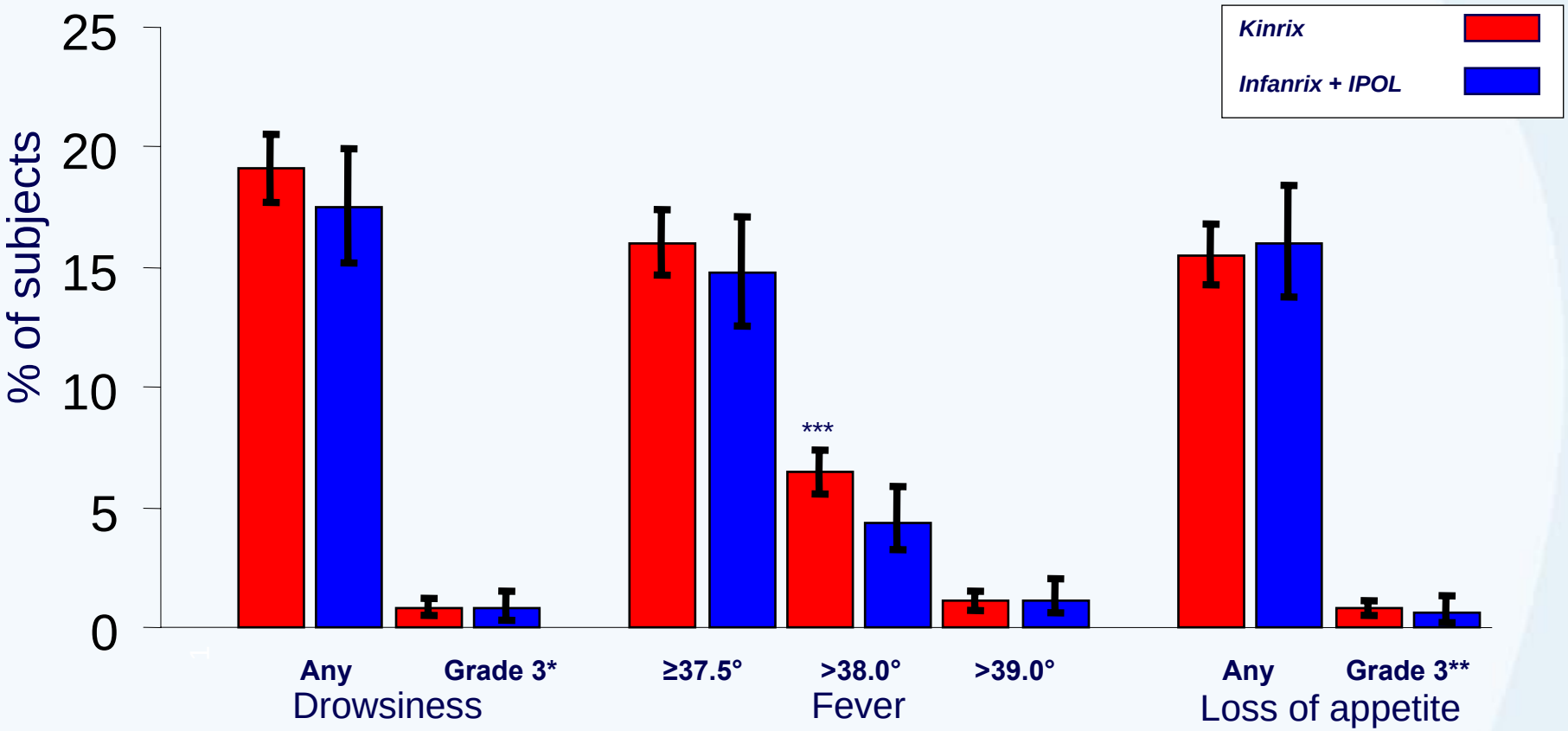
Solicited general symptoms within 4 days (days 0-3) of vaccination, Study 048



*Grade 3 drowsiness – preventing normal daily activities
**Grade 3 loss of appetite - not eating at all
***p<0.05

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Conclusions

- Immune responses and reactogenicity were comparable between *Kinrix* and *Infanrix* + *IPOL*
  - No apparent difference in immunogenicity of MMR vaccine coadministered with Kinrix or *Infanrix* + *IPOL*
- *Kinrix* is expected to provide protection comparable to *Infanrix* and *IPOL*, with one fewer injection required

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Additional slides

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Composition of *Kinrix*

Kinrix (DTaP-IPV)	GSK's *Infanrix*® (DTaP)	GSK's *Pediarix*® (DTaP-HepB-IPV)
Diphtheria toxoid 25 Lf Tetanus toxoid 10 Lf PT 25 µg FHA 25 µg PRN 8 µg Poliovirus type 1 (Mahoney) 40 D Ag units Poliovirus type 2 (MEF-1) 8 D Ag units Poliovirus type 3 (Saukett) 32 D Ag units	Diphtheria toxoid 25 Lf Tetanus toxoid 10 Lf PT 25 µg FHA 25 µg PRN 8 µg	Diphtheria toxoid 25 Lf Tetanus toxoid 10 Lf PT 25 µg FHA 25 µg PRN 8 µg HBSAg 10 µg Poliovirus type 1 (Mahoney) 40 D Ag units Poliovirus type 2 (MEF-1) 8 D Ag units Poliovirus type 3 (Saukett) 32 D Ag units

DTaP antigens identical to *Infanrix*, *Pediarix*
IPV antigens identical to *Pediarix*

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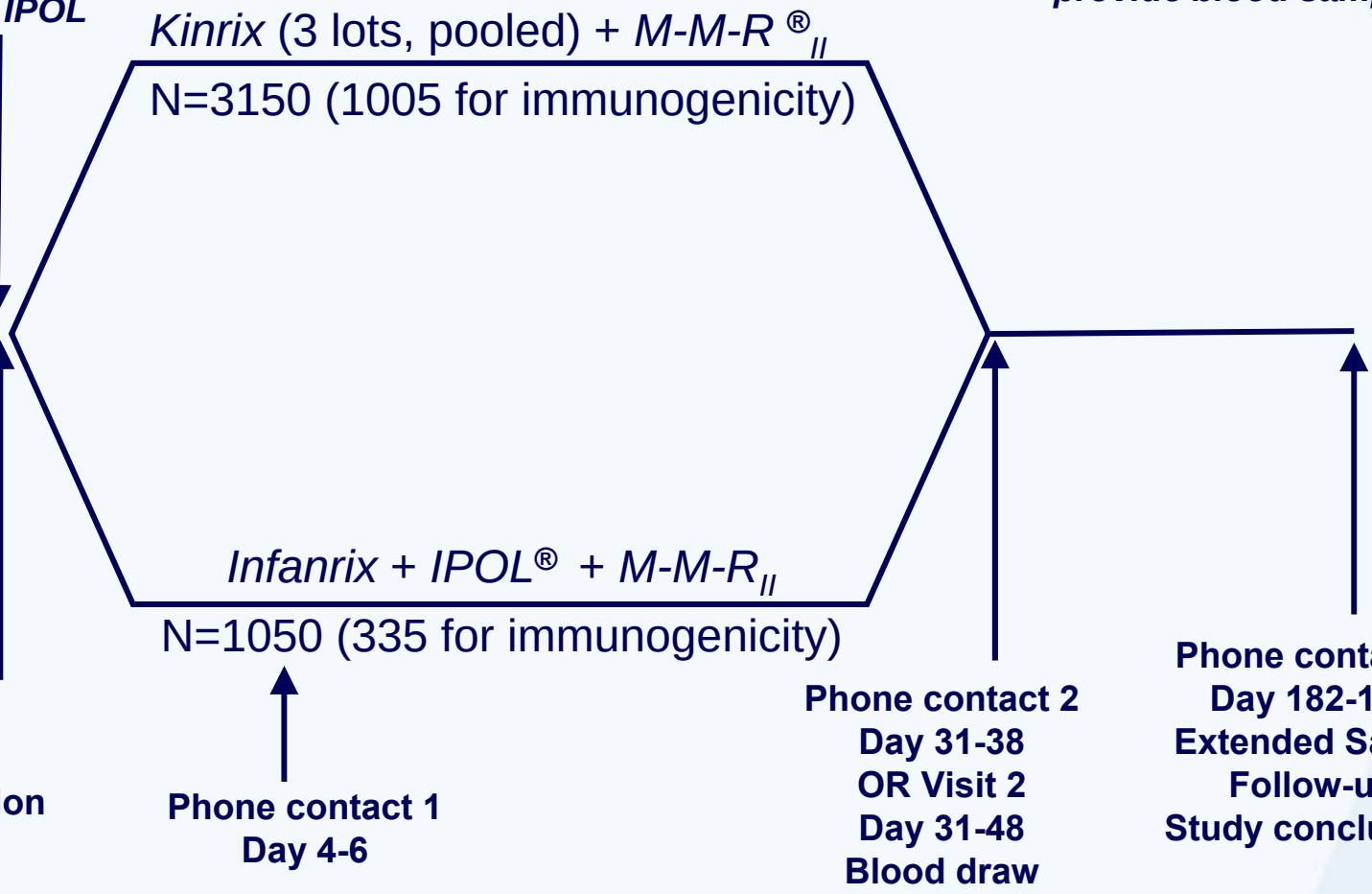
Clinical Study Design – 213503/048

Healthy children, 4-6yoa
4 prior DTaP
with Infanrix
3 prior IPV with IPOL

Safety/reactogenicity assessments conducted for all subjects

Immunogenicity assessments conducted on subset of subjects who agreed to provide blood samples



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Immunogenicity objectives in *Kinrix* studies

- Primary objectives
  - Non-inferiority of *Kinrix* to *Infanrix* + *IPOL*, with respect to:
    - Booster responses to DTaP antigens (all studies)
    - Post-vaccination GMTs for IPV antigens (all studies)
  - Lot-to-lot consistency for 3 manufacturing lots of *Kinrix* vaccine (study 048)
- Secondary objectives
  - Evaluation of booster responses and post-vaccination GMCs/GMTs for all *Kinrix* antigens, compared to *Infanrix* + *IPOL* (all studies)
  - Evaluation of immunogenicity of MMR vaccine coadministered with *Kinrix*, compared to coadministration with *Infanrix* + *IPOL* (study 047)

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Reactogenicity/safety objectives in *Kinrix* studies

- Primary objective (study 048)
  - Non-inferiority of *Kinrix* to *Infanrix* + *IPOL*, with respect to increased circumferential swelling at DTaP injection site
- Secondary objectives (all studies)
  - Evaluation of safety and reactogenicity in terms of
    - Solicited local events (injection site pain, swelling, redness, increased arm circumference)
    - Solicited general events (fever, drowsiness, loss of appetite)
    - Unsolicited adverse events
    - Serious adverse events

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Increased circumferential swelling Study 048

- Recorded within 4 days of vaccination
- Defined as swelling involving >50% of upper arm length AND with >30 mm increase in mid-upper arm circumference relative to baseline measurement
- Criteria for concluding non-inferiority:
  - Upper limit of 95% confidence interval for the between-group difference in percentage of subjects with increased circumferential swelling ≤2%

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Kinrix is non-inferior to *Infanrix* + *IPOL* with regard to increased circumferential swelling

Study 048

Incidence of ICS

Kinrix	0.6%
Infanrix +IPOL	1.0%

Group difference (95%CI) -0.41% (-1.26, 0.16)

Non-inferiority criteria met

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Unsolicited adverse events, Study 048

- Unsolicited AEs within 30 days of vaccination reported by 30.5% of *Kinrix* subjects; 28.8% of *Infanrix* + *IPOL* subjects
- SAEs within 6 months of vaccination reported by 0.4% of *Kinrix* subjects; 0.4% of *Infanrix* + *IPOL* subjects
- No fatalities reported among study subjects
- No clinically relevant differences between groups in reporting of unsolicited AEs

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