GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	A phase IV, open-label, non-randomised, multicentre study to assess the immunogenicity and safety of *Infanrix hexa*™ administered as primary vaccination in healthy infants born to mothers vaccinated with *Boostrix*™ during pregnancy or immediately post-delivery.
eTrack study number and Abbreviated Title	201330 [DTPA (BOOSTRIX)-048 PRI]
Scope:	All analyses as planned per protocol and for study report
Date of Statistical Analysis Plan	16-Jul-2018 Final
Co-ordinating author:	PPD
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APP 9000058193 Statistical Analysis Plan Template (Effective date: 14 April 2017)	

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LIST OF ABBREVIATIONS

AE	Adverse event
Anti-HBs	Antibodies against hepatitis B surface antigen
ATP	According-To-Protocol
CI	Confidence Interval
CRDL	Clinical Research and Development Lead
CRF	Case Report Form
CSR	Clinical Study Report
CTRS	Clinical Trial Registry Summary
dTpa	Combined reduced antigen content diphtheria-tetanus-acellular pertussis vaccine
DTPa	Diphtheria-Tetanus-acellular Pertussis
eCRF	electronic Case Report Form
Eli Type	Internal GSK database code for type of elimination code
ELISA	Enzyme-linked immunosorbent assay
EOS	End of study
EPAR	European Public Assessment Report
FHA	Filamentous Haemagglutinin
GMC	Geometric mean antibody concentration
GMT	Geometric mean antibody titer
GSK	GlaxoSmithKline
HBs	Hepatitis B surface antigen
HBV	Hepatitis B Virus
Hib	Haemophilus influenzae type b
IDMC	Independent Data Monitoring Committee
IM	Intramuscular

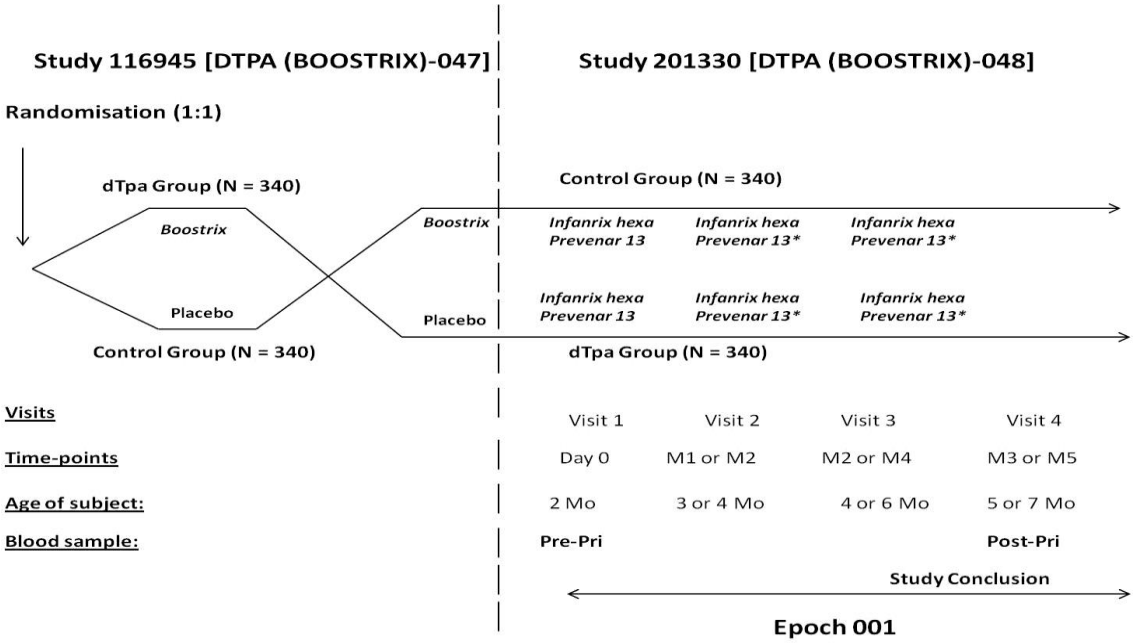
IMP	Investigational Medicinal Product
IPV	Inactivated Poliovirus Vaccine
IU/ml	International units per milliliter
LAR	Legally Acceptable Representative
LL	Lower Limit of the confidence interval
MedDRA	Medical Dictionary for Regulatory Activities
NA	Not Applicable
PRN	Pertactin
PRP	Hib capsular polysaccharide Polyribosyl-Ribitol Phosphate
PT	Pertussis Toxoid
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBIR	GSK Biological's Internet Randomization System
SD	Standard Deviation
SR	Study Report
SRT	Safety Review Team
TFL	Tables Figures and Listings
TOC	Table of Content
TVC	Total Vaccinated Cohort
UL	Upper Limit of the confidence interval
WHO	World Health Organization

1. DOCUMENT HISTORY

Date	Description	Protocol Version
16-JUL-2018	Final Version	Amendment 1 Final - 06-SEP-2016

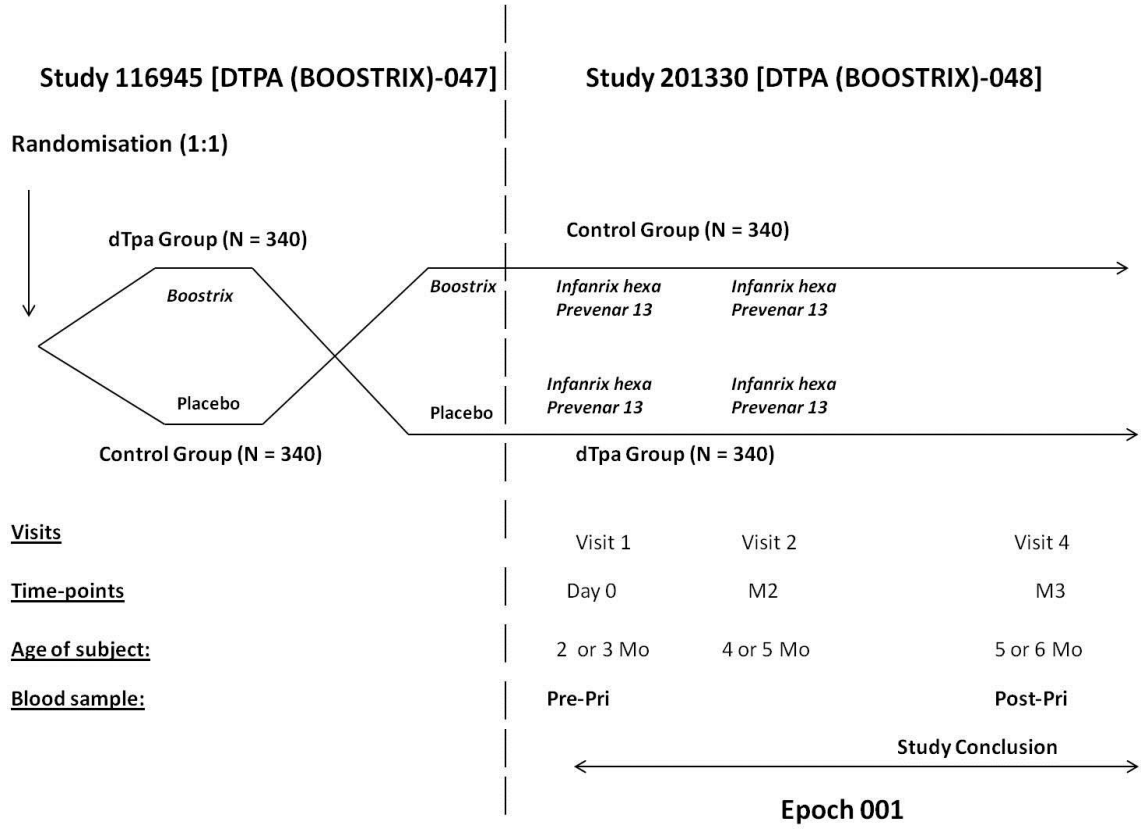
2. STUDY DESIGN

Figure 1 Study design diagram for infants receiving a 3-dose schedule of *Infanrix hexa*



N: Maximum number of subjects planned to be enrolled
M = Month, Mo = age in months
Timepoints have been numbered based on the different vaccination schedules. D0, M1, M2 and M3 timepoints reflect for subjects who will be vaccinated according to the 2, 3 and 4 month schedule while D0, M2, M4 and M5 timepoints reflect for subjects who will be vaccinated according to the 2, 4 and 6 month schedule.
* In some countries/regions with an *Infanrix hexa* 3-dose schedule, *Prevenar 13* is given as a 2-dose schedule at 2 and 4 months of age as a part of the routine immunisation programme
Pre-Pri = Blood sample to be collected before the first dose of the primary vaccination course
Post-Pri = Blood sample to be collected one month after the last dose of the primary vaccination course

Figure 2 Study design diagram for infants receiving a 2-dose schedule of *Infanrix hexa*



N: Maximum number of subjects planned to be enrolled
M = Month, Mo = age in months
Pre-Pri = Blood sample to be collected before the first dose of the primary vaccination course
Post-Pri = Blood sample to be collected one month after the last dose of the primary vaccination course
Subjects will be vaccinated either at 2 and 4 months of age or 3 and 5 months of age, according to the routine national immunisation schedule

Protocol waivers or exemptions are not allowed with the exception of immediate safety concerns. Therefore, adherence to the study design requirements, including those specified in the outline of study procedures (Section 5.5 of the protocol), are essential and required for study conduct.

- Experimental design: Phase IV, open-label, non-randomised, multi-centric, multi-country study with two parallel groups.
- Duration of the study: The intended duration of the study is approximately 3 months, per subject, for subjects vaccinated according to the 2 and 4, the 3 and 5 or the 2, 3 and 4 months schedule and approximately 5 months, per subject, for those vaccinated according to 2, 4 and 6 month schedule.

- Epoch 001: Primary starting at Visit 1 (Day 0) and ending at Visit 4 (Month 3 or 5, depending on the vaccination schedule).
- End of study (EOS): Last testing results released of samples collected at Visit 4.
- Study groups: The study groups and epoch foreseen in the study are presented in Table 1.

Table 1 Study groups and epoch foreseen in the study

Study Groups	Number of subjects	Age (Min - Max)*	Epoch
			Epoch 001
dTpa Group	340	6-**14** weeks	x
Control Group	340	6-**14** weeks	x

*Up to and including 14 weeks and 6 days of age.

The study groups and treatment foreseen in the study are presented in Table 2.

Table 2 Study groups and treatments foreseen in the study

Treatment names	Vaccine name	Study Groups	
		dTpa Group	Control Group
Infanrix hexa	DTP**a**-HBV-IPV	x	x
	Hib	x	x
Prevenar 13	Prevenar 13	x	x

- Control: uncontrolled
- Vaccination schedules: All subjects will receive either 3 doses of *Infanrix hexa* co-administered with *Prevenar* 13* at 2, 4 and 6 months or 2, 3 and 4 months, either 2 doses of *Infanrix hexa* co-administered with *Prevenar* 13 at 3 and 5 months or 2 and 4 months, depending on the immunisation schedule of the country.

  *In some countries/regions with an *Infanrix hexa* 3 doses routine national immunisation schedule, *Prevenar* 13 could be administered as 2-doses or 3-doses primary vaccination schedule (according to the routine national immunisation schedule).
- Treatment allocation: non-randomised. All subjects will receive *Infanrix hexa* co-administered with *Prevenar* 13.
- Blinding: Open-label. Note: The study personnel operating GSK Biologicals' randomisation system on internet (SBIR) and the site staff will remain blinded towards the treatment allocation to subjects in study 116945 [DTPA (BOOSTRIX)-047].
- The blinding of study epoch is presented in Table 3.

Table 3 Blinding of study epoch

Study Epoch	Blinding
Epoch 001	open

- Sampling schedule: Blood samples will be drawn from all subjects at the following timepoints:
  - Pre-Pri: Before the first *Infanrix hexa* vaccine administration, a volume of approximately 2 mL of whole blood (to provide approximately 0.7 mL of serum) will be collected from all study participants.
  - Post-Pri: One month after the last dose of *Infanrix hexa* primary vaccination, approximately 5 mL of whole blood (to provide approximately 1.7 mL of serum) will be collected from all study participants.
- Type of study: extension of other protocol(s) 116945 [DTPA (BOOSTRIX)-047].
- Data collection: Electronic Case Report Form (eCRF).
- Safety monitoring: An independent data monitoring committee (IDMC) (including paediatrician and statistician) will be put in place to oversee the safety of infants born to mothers who were vaccinated with Boostrix during pregnancy in the clinical study 116945 [DTPA (BOOSTRIX)-047] i.e. each SAE/incidence of grade 3 local and general solicited AEs, unsolicited AEs will be reviewed by this committee as per IDMC approved charter.

3. OBJECTIVES

3.1. Primary objective

- To assess the immunological response to *Infanrix hexa* in terms of seroprotection status for diphtheria, tetanus, hepatitis B, poliovirus and Hib antigens, and in terms of vaccine response to the pertussis antigens, one month after the last dose of the primary vaccination in infants born to mothers vaccinated with Boostrix during pregnancy or immediately post-delivery.

Refer to Section 4.1 for the definition of the primary endpoint.

3.2. Secondary objectives

- To assess persistence of antibodies against diphtheria, tetanus and pertussis antigens, before the first dose of *Infanrix hexa* in infants born to mothers vaccinated with Boostrix during pregnancy or immediately post-delivery.
- To assess the immunological response to *Infanrix hexa* and *Prevenar 13* in terms of antibody concentrations or titres against all antigens, one month* after the last dose of the primary vaccination in infants born to mothers vaccinated with Boostrix during pregnancy or immediately post-delivery.
- To assess the immunological response to *Infanrix hexa* in terms of seropositivity rates against pertussis antigens, one month after the last dose of the primary vaccination in infants born to mothers vaccinated with Boostrix during pregnancy or immediately post-delivery.
- To assess the safety and reactogenicity of *Infanrix hexa* and *Prevenar 13* in terms of solicited and unsolicited symptoms and serious adverse events (SAEs).

  *In some countries/regions with an *Infanrix hexa* 3-dose vaccination schedule, *Prevenar* 13 could be administered as 2-doses or 3-doses primary vaccination schedule (according to the routine national immunisation schedule). In such an instance, the evaluation will be performed one month after the last *Infanrix hexa* dose regardless of *Prevenar* 13 vaccination. In the countries/regions with an *Infanrix hexa* 2-dose schedule, *Prevenar* 13 is co-administered at the same time as *Infanrix hexa.*

Refer to Section 4.2 for the definition of the secondary endpoints.

4. ENDPOINTS

4.1. Primary endpoints

- Immunogenicity with respect to components of *Infanrix hexa*.
  - Anti-diphtheria, anti-tetanus, anti-HBs, anti-poliovirus type 1, anti-poliovirus type 2, anti-poliovirus type 3 and anti-polyribosyl-ribitol phosphate (anti-PRP) seroprotection status, one month after the last dose of primary vaccination.

    A seroprotected subject is a subject whose antibody concentration/titre is greater than or equal to the level defining clinical protection. The following seroprotection thresholds are applicable:
    - Anti-diphtheria antibody concentrations ≥ 0.1 IU/mL.
    - Anti-tetanus antibody concentrations ≥ 0.1 IU/mL.
    - Anti-HBs antibody concentrations ≥ 10 mIU/mL.
    - Anti-poliovirus types 1, 2 and 3 antibody titres ≥ 8.
    - Anti-PRP antibody concentrations ≥ 0.15 µg/mL.
  - Vaccine response to PT, FHA and PRN antigens, one month after the last dose of primary vaccination.

    Vaccine response to the PT, FHA and PRN antigens, is defined as:
    - appearance of antibodies in subjects who were initially seronegative (i.e., with concentrations <cut-off value).
    - at least maintenance of pre-vaccination antibody concentrations in subjects who were initially seropositive (i.e., with concentrations ≥cut-off value).

4.2. Secondary endpoints

- Persistence of antibodies before the first dose of Infanrix hexa.
  - Anti-diphtheria and anti-tetanus seroprotection status, anti-PT, anti-FHA, anti-PRN seropositivity status and antibody concentrations.
- Immunogenicity with respect to components of *Infanrix hexa* and Prevenar 13.
  - Anti-diphtheria, anti-tetanus, anti-poliovirus type 1, anti-poliovirus type 2, anti-poliovirus type 3, anti-HBs, anti-PRP, anti-PT, anti-FHA, anti-PRN and anti-pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) antibody concentrations or titres, one month after the last dose of primary vaccination.
- Immunogenicity with respect to components of *Infanrix hexa*.
  - Anti-PT, anti-FHA, anti-PRN antibody seropositivity status, one month after the last dose of primary vaccination.

- Solicited local and general symptoms.
  - Occurrence of solicited local/general symptoms during the 4-day (Day 0-Day 3) follow-up period after each vaccination.
- Unsolicited adverse events.
  - Occurrence of unsolicited symptoms during the 31-day (Day 0-Day 30) follow-up period after each vaccination.
- Serious adverse events.
  - Occurrence of SAEs from first vaccination dose to study end.

5. ANALYSIS SETS

5.1. Definition

5.1.1. All enrolled subjects

- All subjects for whom study invasive procedure has been achieved and informed consent has been obtained.

5.1.2. Total vaccinated cohort (TVC)

The TVC will include all vaccinated subjects for whom data are available.

- A safety analysis based on the TVC will include all subjects with at least one vaccine administration documented.
- An immunogenicity analysis based on the TVC will include vaccinated subjects for whom data concerning immunogenicity endpoint measures are available.

5.1.3. ATP cohort for analysis of safety

The ATP cohort for analysis of safety will include all subjects from the TVC who complied with the vaccine administration:

- who have received at least one dose of study vaccines according to their random assignment.
- for whom administration route and site of study vaccines is known and according to the protocol.
- who have not received a vaccine not specified or forbidden in the protocol.

5.1.4. ATP cohort for analysis of immunogenicity

The ATP cohort for immunogenicity will include all evaluable subjects from the ATP cohort for safety:

- who meet all eligibility criteria;
- who comply with the procedures and intervals defined in the protocol.
- who do not meet any of the criteria for elimination from an ATP analysis (refer to Section 6.7.2 of the protocol) during the study;
- who do not receive a product leading to exclusion from an ATP analysis as listed in Section 6.7.2 of the protocol;
- who do not present with a medical condition leading to exclusion from an ATP analysis as listed in Section 6.8 of the protocol;
- who are born full term (full term is defined ≥ 37 weeks of gestation);
- for whom data concerning immunogenicity endpoint measures are available. This will include subjects for whom assay results are available for antibodies against at least one study vaccines antigen component.

The interval between the last vaccination visit and post-primary blood sampling, considered for inclusion of a subject will be 21–48 days.

5.2. Criteria for eliminating data from Analysis Sets

Elimination codes are used to identify subjects to be eliminated from analysis. Detail is provided below for each sets.

5.2.1. Elimination from Total vaccinated cohort (TVC)

Code 1030 (Study vaccine not administered at all) and code 900 (invalid informed consent or fraud data) will be used for identifying subjects eliminated from TVC.

5.2.2. Elimination from ATP cohort for safety

5.2.2.1. Excluded subjects

All eliminations from the primary study 116945 [DTPA(BOOSTRIX)-047] will be applicable for this follow up study except for the visit specific elimination codes (2090, 2100 and 2120) in other words the code 1050, 1060, 1070 assigned to the mother in study 116945 [DTPA(BOOSTRIX)-047] will be inherited to the infant.

A subject will be excluded from the ATP cohort for safety and immunogenicity under the following conditions

Code	Decode => Condition under which the code is used
900	Questionable subject => Invalid informed consent or fraudulent data. In case informed consent is obtained retrospectively the subject is not eliminated.
1030	Study vaccine dose not administered at all but subject number allocated => subjects enrolled but not vaccinated
1040	Administration of vaccine(s) forbidden in the protocol Concurrently participating in another clinical study, at any time during the study period, in which the subject has been or will be exposed to an investigational or a non-investigational vaccine/product (pharmaceutical product or device). A vaccine not foreseen by the study protocol administered during the period starting from 30 days before each dose of vaccine and ending 30 days after*, with the exception of inactivated influenza vaccine and other vaccines given as a part of the national/regional immunisation schedule, that are allowed at any time during the study period. *In case an emergency mass vaccination for an unforeseen public health threat (e.g.: a pandemic) is organised by the public health authorities, outside the routine immunisation program, the time period described above can be reduced if necessary for that vaccine provided it is licensed and used according to its SPC or package insert (PI) and according to the local governmental recommendations and provided a written approval of the Sponsor is obtained.
1050	Randomisation failure (subject who received a vaccine not compatible with randomization) This code is inherited from the mother.
1060	Randomisation code broken at the investigator site OR at GSK Safety department. This code is inherited from the mother.
1070	Incomplete vaccination course before treatment withdrawal: =>for instance only part of the multiple planned administrations at one visit has been administered. For instance, Prevenar not administered while *Infanrix hexa* is. when no study vaccination at a visit, no other study vaccination can occur up to conclusion/drop-out (Ex. No vaccination at visit 2, but vaccinations at visits 1 and 3 would lead to assignment of code 1070). Note that the code would not be proposed for a subject who had vaccination as planned but missed the last vaccination(s) due to drop-out. In the example given previously, the code would not be proposed if the subject had missed also the vaccination at visit 3). This code is also inheritated from the mother Site or route of study vaccine administration wrong or unknown.
1080	Vaccine temperature deviation (vaccine administration not as per protocol) => *Infanrix hexa* vaccine administered despite a Good Manufacturing Practices (GMP) no-go temperature deviation
1090	Expired vaccine administered (vaccine administration not as per protocol)=> Subjects who received an expired Infanrix hexa

5.2.3. Elimination from ATP cohort for immunogenicity

5.2.3.1. Excluded subjects

All eliminations from the primary study 116945 [DTPA(BOOSTRIX)-047] will be applicable for this follow up study except for the visit specific elimination codes (2090, 2100 and 2120).

A subject will be excluded from the ATP cohort for immunogenicity when he/she is excluded from the ATP cohort for safety (see Section 5.1.3)

The following additional codes will be used:

Code	Decode => Condition under which the code is used
2010	Protocol violation (inclusion/exclusion criteria) including age and excluding codes mentioned below. A male or female between, 6 and 14 weeks of age (including 6 weeks and up to and including 14 weeks and 6 days of age) at the time of the first vaccination. Healthy subjects as established by medical history and clinical examination before entering into the study. This code is also inheritated from the mother
2040	Administration of any medication forbidden by the protocol=> Immunosuppressants or other immune-modifying drugs administered chronically (i.e. more than 14 days) since birth. For corticosteroids, this will mean prednisone $\geq$ 0.5 mg/kg/day, or equivalent. Inhaled and topical steroids are allowed. Long-acting immune-modifying drugs administered at any time during the study period (e.g. infliximab). This code is also inheritated from the mother
2050	Underlying medical condition forbidden by the protocol => Subjects may be eliminated from the ATP cohort for immunogenicity if, during the study, they incur a condition that has the capability of altering their immune response (e.g. any confirmed or suspected immunosuppressive or immunodeficient condition) or are confirmed to have an alteration of their initial immune status.
2080	Vaccination done but: noncompliance with vaccination schedules (dates of vaccination not corresponding to protocol intervals or unknown vaccination dates) Intervals between study visits for subjects vaccinated with *Infanrix hexa* at 2, 4 and 6 months of age is 42-104 days from birth to visit 1, 52-78 days from visit 1 to visit 2, 52-78 days from visit 2 to visit 3. Intervals between study visits for subjects vaccinated with *Infanrix hexa* at 2, 3 and 4 months of age is 42-104 days from birth to visit 1, 21-48 days from visit 1 to visit 2, 21-48 days from visit 2 to visit 3. Intervals between study visits for subjects vaccinated with *Infanrix hexa* at 2 and 4 months of age is 42 to 104 days from birth to visit 1, 52-78 days from visit 1 to visit 2. Intervals between study visits for subjects vaccinated with Infanrix hexa at 3 and 5 months of age is 42 to 104 days from birth to visit 1, 52-78 days from visit 1 to visit 2.
2090	Blood sample taken but: noncompliance with blood sampling schedules (dates of blood sampling not corresponding to adapted protocol intervals or unknown blood sample/vaccination dates) => 21-48 days from last vaccination visit to visit 4
2100	Serological results not available for antigens POST vaccination (including lost samples, blood sample not done, unable to test, absence of parallelism) => no immunogenicity results available at visit 4.
2120	Obvious incoherence, abnormal serology evolution or error in data (incoherence between CRF and results, wrong sample labelling)

6. STATISTICAL ANALYSES

Note that standard data derivation rule and stat methods are described in annex 1 (see Section 11) and will not be repeated below.

6.1. Demography

6.1.1. Analysis of demographics/baseline characteristics planned in the protocol

Demographic characteristics (age in weeks, race, height [cm], weight [kg], head circumference [cm], body mass index in [kg/m^2]), cohort description and withdrawal status will be summarised by group using descriptive statistics:

- Frequency tables will be generated for categorical variables such as race;
- Mean, median and standard deviation will be provided for continuous data such as age.

The distribution of subjects enrolled among the study sites will be tabulated as a whole and per group.

6.1.2. Additional considerations

Gender, country, schedule of vaccination will also be summarised by group using above mentioned descriptive statistics.

All demography summaries will be generated for the TVC. The summary of age, height, weight, head circumference, gender will also be provided for the ATP cohort for immunogenicity.
Number and reason for elimination from ATP cohorts will be tabulated by group.

Quartile 1 and quartile 3 will be provided for continuous data such as age in weeks, race, height [cm], weight [kg], head circumference [cm], body mass index in [kg/m^2].

6.2. Exposure.

6.2.1. Analysis of exposure planned in the protocol

NA

6.2.2. Additional considerations

The number of doses administered will be summarized by vaccine.

6.3. Immunogenicity

6.3.1. Analysis of immunogenicity planned in the protocol

The primary analysis will be based on the ATP cohort for analysis of immunogenicity. If in any vaccine group, the percentage of enrolled subjects excluded from this ATP cohort is more than 5%, a second analysis based on the TVC will be performed to complement the ATP analysis. All analyses will be descriptive. For each group, at each timepoint that a blood sample result is available:

- Seropositivity rates against PT, FHA and PRN antigens and pneumococcal antigens (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) with exact 95% CI [Clopper, 1934] will be calculated.
- Seroprotection rates against diphtheria toxoid, tetanus toxoid, HBs, PRP antigen and poliovirus types 1, 2, 3 antigens (with exact 95% CI [Clopper, 1934]) will be calculated.
- Percentage of subjects with anti-pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) antibody concentrations, depending on the GSK laboratory or WHO reference laboratory assay cut-offs, will be calculated along with its exact 95% CI [Clopper, 1934].
- Percentage of subjects with anti-D and anti-T antibody concentrations ≥ 1.0 IU/mL will be calculated along with its exact 95% CI [Clopper, 1934].
- Percentage of subjects with anti-PRP antibody concentrations ≥ 1.0 µg/mL and anti-HBs antibody concentrations ≥ 100 mIU/mL will be calculated along with its exact 95% CI [Clopper, 1934].
- GMC/GMT with 95% CI will be tabulated for antibodies against each antigen.

For serology results one month after last vaccination dose:

- The vaccine response rates to PT, FHA and PRN (with exact 95% CI) will be calculated.
- The distribution of antibody concentrations/titres for each antigen will be displayed using reverse cumulative distribution curves (RCCs).
- The distribution of antibody concentrations or titres of each antigen will be tabulated.

Additional summaries will be provided based on country.

Handling of missing data:

For a given subject and a given immunogenicity measurement, missing or non-evaluable measurements will not be replaced. Therefore, an analysis will exclude subjects with missing or non-evaluable measurements.

6.3.2. Additional considerations

Considering that RCC are available and the percentage of subjects with titres/concentration above key thresholds are available, the distribution of antibody concentrations or titres of each antigen will not be tabulated.

In addition to the percentage of seroprotected or seropositive subjects, the percentage of subjects above the following cut-off will be summarized

- Anti-PRP antibody concentrations ≥ 1.0 µg/mL.
- Anti-diphtheria antibody concentrations ≥ 1.0 IU/mL.
- Anti-tetanus antibody concentrations ≥ 1.0 IU/mL.
- Anti-HBs antibody concentrations ≥ 100 mIU/mL.
- Anti-pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) ≥ 0.35 µg/mL.

In light of the number of subjects enrolled in each country, the analysis by country will be replaced with analysis by schedule (2 doses ie 2,4 months combined with 3,5 months versus 3 doses i.e. 2,3,4 months combined with 2,4,6 months).

In addition subgroups analysis according to gestational age (27-32 weeks and 33-36 weeks) and age of the mother (18-24 year, 25-34 year and 35-45 year) will be performed.

The sub-group analyses will be limited to descriptive tables of GMT/GMC and the percentage of subjects with titres/concentration above key thresholds for ATP cohort of immunogenicity.

SCHEDULE_TXT(Element Text) country(CTY_NAM)

Frequency Percent Row Pct Col Pct	Australia	Canada	Czechia	Finland	Italy	Spain	Total
Age group(2, 3, 4 Months)	0 0.00 0.00 0.00	0 0.00 0.00 0.00	71 11.81 100.00 100.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	71 11.81
Age group(2, 4 Months)	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	7 1.16 100.00 2.48	7 1.16
Age group(2, 4, 6 Months)	38 6.32 8.32 100.00	144 23.96 31.51 100.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	275 45.76 60.18 97.52	457 76.04
Age group(3, 5 Months)	0 0.00 0.00 0.00	0 0.00 0.00 0.00	0 0.00 0.00 0.00	52 8.65 78.79 100.00	14 2.33 21.21 100.00	0 0.00 0.00 0.00	66 10.98
Total	38 6.32	144 23.96	71 11.81	52 8.65	14 2.33	282 46.92	601 100.00

Deviations from specifications for age and intervals between study visits for subjects vaccinated with *Infanrix hexa* by dose schedule (2 dose schedule and 3 dose schedule separately) will be tabulated.

6.4. Analysis of safety

6.4.1. Analysis of safety and reactogenicity planned in the protocol

The primary analysis will be based on the TVC. If more than 5% of enrolled subjects are excluded from the ATP cohort for analysis of safety, then a second analysis based on this ATP cohort will be performed to complement the TVC analysis. All analyses will be descriptive.

- The percentage of doses and of subjects with at least one local symptom (solicited or unsolicited), with at least one general symptom (solicited or unsolicited) and with any symptom (solicited or unsolicited) during the 4-day (Day 0-Day 3) solicited follow-up period will be tabulated with exact 95% CI [Clopper, 1934] after each vaccine dose and overall. The same calculations will be done for symptoms (solicited or unsolicited) rated as grade 3 in intensity, for symptoms (solicited or unsolicited) leading to medical advice and for symptoms (solicited or unsolicited) assessed as causally related to vaccination.

- The percentage of doses and of subjects reporting each individual solicited local and general symptom during the 4-day (Day 0-Day 3) solicited follow-up period will be tabulated after each vaccine dose and overall, with exact 95% CI [Clopper, 1934]. The same calculations will be done for each individual solicited symptom rated as grade 3 in intensity and for each individual solicited symptom assessed as causally related to vaccination.
- All computations mentioned above will be done for grade ≥2 (solicited symptoms only) and grade 3 symptoms, for symptoms considered related to vaccination (general symptoms only) and for symptoms that resulted in a medically-attended visit.
- Occurrence of fever and related fever will be reported per 0.5°C cumulative temperature increments as well as the occurrence of grade 3 fever (> 39.0°C axillary temperature) with causal relationship to vaccination.
- The verbatim reports of unsolicited AEs will be reviewed by a physician and the signs and symptoms will be coded according to MedDRA. Every verbatim term will be matched with the appropriate Preferred Term. The percentage of subjects with unsolicited AEs occurring within 31-day (Day 0- Day 30) follow-up period after any dose with its exact 95% CI [Clopper, 1934] will be tabulated by group, and by preferred term. Similar tabulation will be done for unsolicited AEs rated as grade 3, for unsolicited AEs with causal relationship to vaccination and AEs/SAEs leading to withdrawal from the study.
- The percentage of subjects who receive concomitant medication and antipyretic medication during the 4-day (Day 0- Day 3) follow-up period and the 31-day follow-up (Day 0 – Day 30) will be tabulated (with exact 95% CI [Clopper, 1934]) after each vaccine dose and overall.
- SAEs reported from first vaccination dose up to study end will be described in detail.
- Withdrawal due to AEs and SAEs following vaccinations will be described in detail.

Handling of missing data:

- For a given subject and the analysis of solicited AEs 4 days post-vaccination, missing or non-evaluable measurements will not be replaced. Therefore, the analysis of the solicited AEs based on the TVC will include only vaccinated subjects and doses with documented safety data (i.e. symptom screen completed).
- For analysis of unsolicited AEs, such as SAEs or AEs by primary Medical Dictionary for Regulatory Activities (MedDRA) term, and for the analysis of concomitant medications, all vaccinated subjects will be considered. Subjects, who do not report the event or the concomitant medication, will be considered as subjects without the event or the concomitant medication, respectively.
- For summaries reporting both solicited and unsolicited AEs, all vaccinated subjects will be considered. Subjects, who do not report the event or the concomitant medication, will be considered as subjects without the event or the concomitant medication, respectively.

6.4.2. Additional considerations

6.4.2.1. Combined Solicited and Unsolicited Adverse Events

For clintrial.gov and EudraCT posting purposes, a summary of combined solicited and unsolicited non-serious adverse events will be produced by System Organ Class and preferred terms and according to occurrence of each event.

A summary of subjects with all combined solicited (regardless of their duration) and unsolicited adverse events will be provided. Solicited adverse events will be coded by MedDRA as per the following codes.

Solicited symptom	Lower level term code	Corresponding Lower level term decode
PA	10022086	Injection site pain
RE	10022098	Redness at injection site
SW	10053425	Swelling at injection site
TE	10016558	Temperature/Fever
FU	10022998	Irritability/Fussiness
DR	10013649	Drowsiness
LO	10003028	Loss of appetite

7. ANALYSIS INTERPRETATION

All analyses will be conducted in a descriptive manner.

8. CONDUCT OF ANALYSES

Any deviation(s) or change(s) from the original statistical plan outlined in this protocol will be described and justified in the final study report.

8.1. Sequence of analyses

The final analyses of all data will be conducted when all data are available. This analysis will include the final analysis of immunogenicity and the final analysis of solicited and unsolicited symptoms and SAEs. A clinical study report containing all data will be written and made available to the investigators.

Description	Analysis ID	Disclosure Purpose (CTRS=public posting, SR=study report, internal, public posting)	Dry run review needed (Y/N)	Study Headline Summary (SHS)requiring expedited communication to upper management (Yes/No)	Reference for TFL
Final	E1_01	SR	Yes	Yes	TFL TOC

8.2. Statistical considerations for interim analyses

NA

9. CHANGES FROM PLANNED ANALYSES

- During the course of the study, the assays used to measure the anti-D, anti-T, anti-PT, anti-FHA and anti-PRN IgG concentrations were re-developed and re-validated and both assay units and assay cut-offs were adapted. The new ELISA's for PT, FHA and PRN were calibrated against the WHO International Standard (NIBSC 06/140). This allowed the expression of concentrations measured with the new ELISA's in international units per milliliter (IU/mL) instead of the formerly used ELISA units per milliliter (ELU/mL). The newly validated DTPa ELISA's used in the study have a lower assay cut-off as compared to the one described in the protocol. The current assay cut-off is 0.057 IU/mL for anti-D, 0.043 IU/mL for anti- T, 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA and 2.187 IU/mL for anti- PRN. An agreement between the old and new ELISAs was shown with regards to the two thresholds of clinical relevance for the DI/TE response (0.1 IU/mL and 1.0 IU/mL) and therefore the clinical endpoints and anti-D and anti-T are unchanged. In the absence of a correlate of protection for the B. pertussis antigens, the pertussis endpoints were redefined based on the assay cut-off (see section 5.7.5 of protocol).
- In addition, following CBER feedback on the anti-D re-validated assay, a calibration factor of 0.543 was applied in the analysis of anti-D in order to align the ELISA assay to the WHO 10/262 reference samples which are measured as 2 IU/mL by Di neutralization. Assay since 54 WHO 10/262 reference samples measured by GSK re-validated ELISA led to GMC was about two fold (1.841) higher than the expected value (2 IU/mL).

- Note: Due to re-validation of all assays, the cut-offs presented in Table 11 of the protocol of few antigens have changed. Below table has an updated threshold.

Antigen	**Threshold for positivity**
• Anti-PT	• 2.693 IU/mL
• Anti-FHA	• 2.046 IU/mL
• Anti-PRN	• 2.187 IU/mL
• Anti-D	• 0.057 IU/mL
• Anti-T	• 0.043 IU/mL
• Anti-polio	• 8 dilution
• Anti-PRP	• 0.066 µg/mL
• Anti-HBs	• 6.2 mIU/mL
• Anti-pneumococcal serotypes (1)	• 0.080 µg/mL
• Anti-pneumococcal serotypes (3)	• 0.075 µg/mL
• Anti-pneumococcal serotypes (4)	• 0.061 µg/mL
• Anti-pneumococcal serotypes (5)	• 0.198 µg/mL
• Anti-pneumococcal serotypes (6A)	• 0.111 µg/mL
• Anti-pneumococcal serotypes (6B)	• 0.102 µg/mL
• Anti-pneumococcal serotypes (7F)	• 0.063 µg/mL
• Anti-pneumococcal serotypes (9V)	• 0.066 µg/mL
• Anti-pneumococcal serotypes (14)	• 0.160 µg/mL
• Anti-pneumococcal serotypes (18C)	• 0.111 µg/mL
• Anti-pneumococcal serotypes (19A)	• 0.199 µg/mL
• Anti-pneumococcal serotypes (19F)	• 0.163 µg/mL
• Anti-pneumococcal serotypes (23F)	• 0.073 µg/mL

10. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC (Tables Figures and Listings Table Of Contents) provides the list of tables/listings and figures needed for the study report (synopsis, in-text, post-text) and for public disclosure (CTRS).

The following group names will be used in the TFLs:

Group order in tables	Group label in tables	Group definition for footnote	Pooled Groups label in tables	Pooled definition for footnote
1	dTpa Group	Infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047] where mothers received dTpa during pregnancy. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.	NA	NA
2	Control Group	Infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047] where mothers received placebo during pregnancy. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.	NA	NA

Tables will be generated on ATP cohort for immunogenicity with the following sub-group names inherited from the study 116945 [DTPA (BOOSTRIX)-047]

Sub-group order in tables	Sub-group label in tables	Sub-group definition for footnote
1	18-24Y	18-24 years old subjects
2	25-34Y	25-34 years old subjects
3	35-45Y	35-45 years old subjects
4	27-32W	27-32 weeks of gestation of foetus at dose 1
5	33-36W	33-36 weeks of gestation of foetus at dose 1

11. ANNEX 1 STANDARD DATA DERIVATION RULE AND STATISTICAL METHODS

11.1. Statistical Method References

- The exact two-sided 95% CIs for a proportion within a group will be the Clopper-Pearson exact CI [Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. Biometrika. 1934; 26:404-413].
- The 95% CI for geometric mean titers/concentrations (GMTs/GMCs) will be obtained within each group separately. The 95% CI for the mean of log-transformed titer/concentration will be first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs/GMCs will be then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titer/concentration.

11.2. Standard data derivation

11.2.1. Date derivation

- SAS date derived from a character date: In case day is missing, 15 is used. In case day & month are missing, 30 June is used.
- Onset day for an event for the infant (AE, medication, vaccination, …): The onset day is the number of days from date of last study dose & the onset/start date of the event. This is 0 for an event starting on the same day of last study dose. There could also be events reported in the infant before delivery (anomalies diagnosed during pregnancy at ultrasound investigation), for these cases onset day will be negative '-' days. See SAS date derived in case the start date of the event is incomplete.
- Duration: Duration of an event is expressed in days. It is the number of days between the start & the stop dates + 1. Therefore duration is 1 day for an event starting & ending on the same day.

11.2.2. Dose number

The study dose number is defined in reference to the number of study visits at which vaccination occurred. More specifically dose 1 refers to all vaccines administered at the first vaccination visit while dose 2 corresponds to all vaccinations administered at the second vaccination visit even if this is the first time a product is administered to the subject.

Relative dose: the relative dose for an event (AE, medication, vaccination) is the most recent study dose given before an event. In case the event takes place on the day a study dose is given, the related dose will be that of the study dose, even if the event actually took place before vaccination. For instance, if an adverse event begins on the day of the study vaccination but prior to administration of the vaccine, it will be assigned to this dose. In case a study dose is not administered and an event occurs after the subsequent study dose (e.g. 3rd study dose), the relative dose of the event will be study dose associated to the subsequent study dose (e.g. dose 3).

The number of doses for a product is the number of time the product was administered to a subject.

The incidence per dose is the number of vaccination visits at which an event (vaccination visit is a visit at which study vaccine was administered) was reported among all vaccination visits.

11.2.3. Demography

Age: Age at the reference activity, computed as the number of units between the date of birth and the reference activity.

Conversion of weight to kg

The following conversion rule is used:

Weight in Kilogram= weight in Pounds / 2.2

Weight in Kilogram =weight in oncs / 35.2

The result is rounded to 2 decimals.

Conversion of height to cm

The following conversion rule is used:

Height in Centimetres = Height in Feet * 30.48

Height in Centimetres = Height in Inch * 2.54

The result is rounded to the unit (i.e no decimal)

Conversion of temperature to °C

The following conversion rule is used:

Temperature in °Celsius = ((Temperature in °Fahrenheit -32) *5)/9

The result is rounded to 1 decimal.

11.2.4. Immunogenicity

For a given subject and given immunogenicity measurement, missing or non-evaluable measurements will not be replaced. Therefore, an analysis will exclude subjects with missing or non-evaluable measurements.

The Geometric Mean Concentrations/Titres (GMC/Ts) calculations are performed by taking the anti-log of the mean of the log titre transformations. Antibody titres below the cut-off of the assay will be given an arbitrary value of half the cut-off of the assay for the purpose of GMT calculation. The cut-off value is defined by the laboratory before the analysis and is described in the protocol.

A seronegative subject is a subject whose antibody titre is below the cut-off value of the assay. A seropositive subject is a subject whose antibody titre is greater than or equal to the cut-off value of the assay.

The assay cut-off is the value under which there is no quantifiable result available. For an assay with a specific 'cut_off', numerical immunogenicity result is derived from a character field (rawres):

If rawres is 'NEG' or '-' or '(-)', numeric result= cutt_off/2,

if rawres is 'POS' or '+' or '(+)', numeric result = cut_off,

if rawres is '< value' and value<=cut_off, numeric result =cut_off/2,

if rawres is '< value' and value>cut_off, numeric result =value,

if rawres is '> value' and value<cut_off, numeric result =cut_off/2,

if rawres is '> value' and value>=cut_off, numeric result =value,

if rawres is '<= value' or '>= value' and value<cut_off, numeric result =cut_off/2,

if rawres is '<= value' or '>= value' and value>=cut_off, numeric result =value,

if rawres is a value < cut_off, numeric result = cut_off/2,

if rawres is a value >= cut_off, numeric result = rawres,

if rawres is a value >= cut_off, numeric result = rawres,

else numeric result is left blank.

All CI computed will be two-sided 95% CI.

11.2.5. Safety

For analysis of solicited, unsolicited adverse events such as serious adverse events or adverse events by primary MedDRA term, and for the analysis of concomitant medications, all vaccinated subjects will be considered. Subjects who did not report the event or the concomitant medication will be considered as subjects without the event or the concomitant medication respectively.

For a given subject and the analysis of solicited adverse events within 4 days post-vaccination, missing or non-evaluable measurements will not be replaced. Therefore, the analysis of the solicited adverse events based on the Total Vaccinated Cohort will include only vaccinated subjects for doses with documented safety data (i.e., symptom screen completed). More specifically the following rules will be used:

- Subjects who documented the absence of a solicited adverse events after one dose will be considered not having that adverse events after that dose.
- Subjects who documented the presence of a solicited symptom and fully or partially recorded daily measurement over the solicited period will be included in the summaries at that dose and classified according to their maximum observed daily recording over the solicited period.
- Subjects who documented the presence of a solicited symptom after one dose without having recorded any daily measurement will be assigned to the lowest intensity category at that dose (i.e., 37.5°C for fever or grade 1 for other symptoms).
- Doses without symptom sheets documented will be excluded.
- The intensity of the following solicited adverse events will be assessed as described in the below table

Table 4 Intensity scales for solicited symptoms in infants less than 6 years of age

Adverse Event	Intensity grade	Parameter
Pain at injection site	0	None
	1	Mild: Minor reaction to touch
	2	Moderate: Cries/protests on touch
	3	Severe: Cries when limb is moved/spontaneously painful
Redness at injection site		Record greatest surface diameter in mm
Swelling at injection site		Record greatest surface diameter in mm
Fever*		Record temperature in °C/°F
Irritability/Fussiness	0	Behaviour as usual
	1	Mild: Crying more than usual/no effect on normal activity
	2	Moderate: Crying more than usual/interferes with normal activity
	3	Severe: Crying that cannot be comforted/prevents normal activity
Drowsiness	0	Behaviour as usual
	1	Mild: Drowsiness easily tolerated
	2	Moderate: Drowsiness that interferes with normal activity
	3	Severe: Drowsiness that prevents normal activity
Loss of appetite	0	Appetite as usual
	1	Mild: Eating less than usual/no effect on normal activity
	2	Moderate: Eating less than usual/interferes with normal activity
	3	Severe: Not eating at all

*Fever is defined as temperature ≥ 37.5°C / 99.5°F for oral, axillary or tympanic route, or ≥ 38.0°C / 100.4°F for rectal route. The preferred route for recording temperature in this study will be rectal/axillary.

The maximum intensity of local injection site redness/swelling will be scored at GSK Biologicals as follows:

0	Absent
1	≤ 5 mm
2	> 5 mm and ≤ 20 mm
3	> 20 mm

The maximum intensity of fever (oral, axillary or tympanic route) will be scored at GSK Biologicals as follows:

Grade	Temperature
0	<37.5°C
1	≥37.5°C to ≤38.0°C
2	>38.0°C to ≤39.0°C
3	> 39.0°C

The investigator will assess the maximum intensity that occurred over the duration of the event for all unsolicited AEs (including SAEs) recorded during the study. The assessment will be based on the investigator's clinical judgement.

The intensity should be assigned to one of the following categories:

1 (mild)	=	An AE which is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An AE which is sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An AE which prevents normal, everyday activities (in a young child, such an AE would, for example, prevent attendance at school/kindergarten/a day-care centre and would cause the parent(s)/LAR(s) to seek medical advice.

An AE that is assessed as Grade 3 (severe) should not be confused with a SAE. Grade 3 is a category used for rating the intensity of an event; and both AEs and SAEs can be assessed as Grade 3. An event is defined as 'serious' when it meets one of the pre-defined outcomes as described in Section 8.1.2 in the protocol.

The way the percentage of subjects will be derived will depend on the event analysed (see table below for details). As a result, the N value will differ from one table to another.

Event	N used for deriving % per subject	N used for deriving % per dose
Concomitant vaccination	All subjects with study vaccine administered	All study visits with study vaccine administered
Solicited general AEs	All subjects with at least one solicited general AE documented as either present or absent (i.e., symptom screen completed)	All study visits with study vaccine administered and with at least one solicited general AE documented as either present or absent (i.e., symptom screen completed)
Solicited local AEs	All subjects with at least one solicited local AE documented as either present or absent (i.e., symptom screen completed)	All study visits with study vaccine administered and with at least one solicited local AE documented as either present or absent (i.e., AE screen completed)
Unsolicited AEs	All subjects with study vaccine administered	All study visits with study vaccine administered
Concomitant medication	All subjects with study vaccine administered	All study visits with study vaccine administered

11.2.6. Number of decimals displayed:

The following decimal description from the decision rules will be used for the demography, immunogenicity and safety/reactogenicity.

Display Table	Parameters	Number of decimal digits
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	1
Immunogenicity	GMT/GMC	3 for anti-D, anti-T and anti-PRP 2 for Strepto antigens 1 for anti-PT, anti-FHA and anti-PRN, anti-HBs, anti-Polio 1, anti-Polio 2 and anti-Polio 3
Reactogenicity	Mean, Min, Q1, Median, Q3, Max for duration	1
All summaries	% of count, including LL & UL of CI	1

12. ANNEX 3: STUDY SPECIFIC MOCK TFL

The following drafted study specific mocks will be used.

The data display, title and footnote is for illustration purpose and will be adapted to the study specificity as indicated in the TFL TOC.

These templates were copied from recent studies. Note that there may be few changes between the study specific SAP mock TFL and the final TFLs as editorial/minor changes do not require a SAP amendment.

Template 1 Number of subjects enrolled by center (Total vaccinated cohort)

	dTpa Group	Control group	Total	
Center	**n**	**N**	**n**	**%**
PPD				
PPD				
PPD				
PPD				
PPD				
PPD				
PPD				
PPD				
PPD				
PPD				
PPD				
All				

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
n = number of subjects included in each group or in total for a given center or for all centers
All = sum of all subjects in each group or in total (sum of all groups)
% = n/All x 100

Template 2 Number of subjects enrolled by country (Total vaccinated cohort)

	dTpa Group	Control group	Total	
Country	**n**	**N**	**n**	**%**
Australia				
Belgium				
Canada				
Czechia				
Finland				
Italy				
Spain				
All				

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
n = number of subjects included in each group or in total for a given country or for all countries
All = sum of all subjects in each group or in total (sum of all groups)
% = n/All x 100

Template 3 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal (Total vaccinated cohort)

	dTpa Group	Control Group	Total
Number of subjects vaccinated			
Number of subjects completed			
Number of subjects withdrawn			
Reasons for withdrawal:			
Serious Adverse Event			
Non-serious adverse event			
Protocol violation			
Consent withdrawal (not due to an adverse event)			
Migrated/moved from study area			
Lost to follow-up (subjects with incomplete vaccination course)			
Lost to follow-up (subjects with complete vaccination course)			
Others			

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for last study visit

Template 4 Number of subjects at each visit and list of withdrawn subjects (Total Vaccinated Cohort)

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
dTpa Group	VISIT 1	508		
			no. PP	CONSENT WITHDRAWAL
			no. PP	CONSENT WITHDRAWAL
			no. PPD	CONSENT WITHDRAWAL
			no. PPD	CONSENT WITHDRAWAL
	VISIT 2	504		
			no. PPD	CONSENT WITHDRAWAL
			no. PPD	CONSENT WITHDRAWAL
			no. PPD	SERIOUS ADVERSE EXPERIENCE
	VISIT 3	501		
			no. P	MIGRATION FROM STUDY AREA
			no. PP	CONSENT WITHDRAWAL
			no. PP	MIGRATION FROM STUDY AREA
			no. PP	CONSENT WITHDRAWAL
			no. PP	MIGRATION FROM STUDY AREA
			no. PP	MIGRATION FROM STUDY AREA
			no. PPD	CONSENT WITHDRAWAL
			no. PPD	MIGRATION FROM STUDY AREA
			no. PPD	MIGRATION FROM STUDY AREA
Control Group	VISIT 1	257		
			no. PP	PROTOCOL VIOLATION
			no. PPD	CONSENT WITHDRAWAL
	VISIT 2	255		
			no. PPD	CONSENT WITHDRAWAL
	VISIT 3	254		
			no. PP	MIGRATION FROM STUDY AREA
			no. PP	LOST TO FOLLOW-UP
			no.PPD	LOST TO FOLLOW-UP
			no. PP	CONSENT WITHDRAWAL
			no. PP	MIGRATION FROM STUDY AREA
			no. PPD	LOST TO FOLLOW-UP
			no. PPD	ADVERSE EXPERIENCE

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
N = number of subjects who are still in the study up to the visit
Withdrawn = subject who did not return after the visit

Template 5 Number of subjects enrolled into the study as well as excluded from ATP analyses with reasons for exclusion

	Total				dTpa Group			Control Group		
Title	**N**	**n**	**s**	**%**	**N**	**n**	**s**	**N**	**n**	**s**
Total enrolled cohort	**1200**				**300**			**300**		
Invalid informed consent or fraud data (code 900)										
Study vaccine dose not administered AT ALL but subject number allocated (code 1030)										
TVC	**1200**			**100**	**300**			**300**		
Administration of vaccine(s) forbidden in the protocol (code 1040)		2	2			0	0		0	0
Randomisation code broken at the investigator site OR at GSK Safety department (1060)										
Study vaccine dose not administered according to protocol (code 1070)		73	73			23	23		16	16
Vaccine temperature deviation (code 1080)										
Expired vaccine administered (code 1090)		10	11			3	3		1	1
Protocol violation (inclusion/exclusion criteria) (code 2010)		1	1			1	1		0	0
Administration of any medication forbidden by the protocol (code 2040)		1	1			0	0		1	1
Underlying medical condition forbidden by the protocol (code 2050)		1	1			0	0		0	0
Concomitant infection related to the vaccine which may influence immune response (2060)										
Concomitant infection not related to the vaccine which may influence immune response (code 2070)		0	1			0	0		0	1
Noncompliance with vaccination schedule (including wrong and unknown dates) (code 2080)		14	16			6	7		3	4
Noncompliance with blood sampling schedule (including wrong and unknown dates) (code 2090)		12	16			3	5		4	5
Essential serological data missing (code 2100)		87	95			20	22		23	26
Obvious incoherence, abnormal serology evolution or error in data (code 2120)		1	1			0	0		0	0
ATP cohort for analysis of immunogenicity	**998**			**83.2**	**244**			**252**		

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Note: Subjects may have more than 1 elimination code assigned
n = number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
s = number of subjects with the elimination code assigned
% = percentage of subjects in the per protocol set (ATP) relative to the TVC(ES)

Template 6 Deviations from specifications for age and intervals between study visits for subjects vaccinated with Infanrix hexa(<2> dose schedule - 1 dose/visit) (Total Vaccinated Cohort)

		Age	VAC:1-VAC:2	VAC:2-SER:2
Group		**Protocol**	**Protocol**	**Protocol**
		from 6 to 14 weeks and 6 days	from 52 to 78 days	from 21 to 48 days
dTpa Group	N			
	n			
	%			
	range			
Control Group	N			
	n			
	%			
	range			

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
N = total number of subjects with available results
n(%) = number(percentage) of subjects with results outside of the interval
range = minimum-maximum for age and intervals
VAC:1 = vaccination at visit 1
VAC:2 = vaccination at visit 2
SER:2 = blood sample collected before the first dose and 1 month after the last dose of the primary vaccination course
2 dose schedule = subjects who received 2 dose of *Infanrix hexa* at 2,4 months of age or 3,5 months of age, co-administered with *Prevenar 13* (according to the routine national immunisation schedule of the country).

Template 7 Summary of demographic characteristics (Total vaccinated cohort)

		dTpa Group N =		Control Group N =		Total N =	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (week) at vaccination dose: 1	Mean						
	SD						
	Median						
	Q1						
	Q3						
Gender	Female						
	Male						
Geographic Ancestry	African Heritage / African American						
	American Indian or Alaskan Native						
	Asian - Central / South Asian Heritage						
	Asian - East Asian Heritage						
	Asian - Japanese Heritage						
	Asian - South East Asian Heritage						
	Native Hawaiian or Other Pacific Islander						
	White - Arabic / North African Heritage						
	White - Caucasian / European Heritage						
	Other (Hispanic)						
Dose schedule	2 dose schedule						
	3 dose schedule						
Maternal age group	18-24Y						
	25-34Y						
	35-45Y						
Gestational week of foetus at dose 1	27-32W						
	33-36W						

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
N = total number of subjects
n(%) = number(percentage) of subjects in a given category
Value = value of the considered parameter
SD = standard deviation
Q1 = Quartile 1
Q2 = Quartile 3
2 dose schedule = subjects who received 2 dose of Infanrix hexa at 2,4 months of age or 3,5 months of age, co-administered with Prevenar 13 (according to the routine national immunisation schedule of the country).
3 dose schedule = subjects who received 3 dose of Infanrix hexa at 2,3,4 months of age or 2,4,6 months of age, co-administered with Prevenar 13.Prevenar 13 could be administered as 2-doses or 3-doses primary vaccination schedule (according to the routine national immunisation schedule of the country).
18-24Y = 18-24 years old subjects
25-34Y = 25-34 years old subjects
35-45Y = 35-45 years old subjects
27-32W = 27-32 weeks of gestation of foetus at dose 1
33-36W = 33-36 weeks of gestation of foetus at dose 1

Template 8 Summary of vital signs characteristics (Total Vaccinated Cohort)

		dTpa Group (N = 335)	Control Group (N = 336)	Total (N = 671)
Characteristics	**Parameters**	**Value**	**Value**	**Value**
Height (cm)	Mean			
	SD			
	Median			
	Q1			
	Q3			
	Unknown			
Weight (kg)	Mean			
	SD			
	Median			
	Q1			
	Q3			
	Unknown			
Head circumference (cm)	Mean			
	SD			
	Median			
	Q1			
	Q3			
	Unknown			
Body mass index in [kg/m2]	Mean			
	SD			
	Median			
	Q1			
	Q3			
	Unknown			

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
N = total number of subjects
Value = value of the considered parameter
SD = standard deviation
Height (cm) = height expressed in centimeters
Weight (kg) = weight expressed in kilograms
Head circumference(cm) = head circumference expressed in centimeters.
Body mass index in [kg/m2] = body mass index expressed in kilograms per meter square
SD = standard deviation
Q1 = Quartile 1
Q2 = Quartile 3

Template 9 Study population (TVC)

Study population (Total vaccinated cohort)		
Number of subjects	**dTpa group**	**Control group**
Planned, N	225	225
Randomised, N (Total Vaccinated Cohort)	224	227
Completed, n (%)	224 (100)	227 (100)
Demographics	**dTpa group**	**Control group**
N (Total Vaccinated Cohort)	224	227
Females: Males	97:127	115:112
Mean Age, weeks (SD)	8.8 (1.1)	8.8 (1.1)
Median Age, weeks (minimum, maximum)	9 (7, 11)	9 (7, 11)
Most frequent race: Asian - East Asian Heritage, n (%)	224 (100)	226 (99.6)

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
N = total number of subjects enrolled in the study
n/% = number/percentage of subjects in a given category
SD = Standard Deviation
Mean Age = age calculated from Date of birth to first study vaccination

Template 10 Seropositivity rates and GMCs for anti-PT, anti-FHA and anti-PRN antibodies before the first dose and 1 month after the last dose of the primary vaccination (ATP cohort for immunogenicity)

				≥ assay cut-off*				**GMC**		
									95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
Anti-PT	dTpa Group	Pre-Pri								
		Post-Pri								
	Control Group	Pre-Pri								
		Post-Pri								
Anti-FHA	dTpa Group	Pre-Pri								
		Post-Pri								
	Control Group	Pre-Pri								
		Post-Pri								
Anti-PRN	dTpa Group	Pre-Pri								
		Post-Pri								
	Control Group	Pre-Pri								
		Post-Pri								

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
*Assay cut-off is 2.693 IU/mL for anti- PT, 2.046 IU/mL for anti-FHA and 2.187 IU/mL for anti-PRN
GMC = geometric mean antibody concentration calculated on all subjects
N = number of subjects with available results
n(%)=number(percentage) of subjects with antibody concentrations above the specified cut-off
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Pre-Pri = blood sample to be collected before the first dose of the primary vaccination course
Post-Pri = blood sample to be collected 1 month after the last dose of the primary vaccination course

Template 11 Seropositivity, seroprotection and GMC rates for <anti-tetanus> antibodies before the first dose and 1 month after the last dose of the primary vaccination (ATP cohort for immunogenicity)

				≥ assay cut-off*				≥ 0.1 IU/mL				≥ 1.0 IU/mL				GMC		
						95% CI				95% CI				95% CI			95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**n**	**%**	**UL**	**UL**	**value**	**LL**	**UL**
Anti-tetanus	dTpa Group	Pre-Pri																
		Post-Pri																
	Control Group	Pre-Pri																
		Post-Pri																
Anti-diphtheria	dTpa Group	Pre-Pri																
		Post-Pri																
	Control Group	Pre-Pri																
		Post-Pri																

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
*Assay cut-off is 0.043 IU/mL for anti-tetanus and 0.057 IU/mL for anti- diphtheria
GMC = geometric mean antibody concentration calculated on all subjects
N = number of subjects with available results
n(%)=number(percentage) of subjects with antibody concentrations above the specified cut-off
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Pre-Pri = blood sample to be collected before the first dose of the primary vaccination course
Post-Pri = blood sample to be collected 1 month after the last dose of the primary vaccination course

Template 12 Seroprotection rates for anti-poliovirus type 1,2,3 antibodies before the first dose and 1 month after the last dose of the primary vaccination (ATP cohort for immunogenicity)

				≥ 8				GMT		
						95% CI			95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**UL**	**UL**	**value**	**LL**	**UL**
anti-poliovirus type 1	dTpa Group	Pre-Pri								
		Post-Pri								
	Control Group	Pre-Pri								
		Post-Pri								
anti-poliovirus type 2	dTpa Group	Pre-Pri								
		Post-Pri								
	Control Group	Pre-Pri								
		Post-Pri								
anti-poliovirus type 3	dTpa Group	Pre-Pri								
		Post-Pri								
	Control Group	Pre-Pri								
		Post-Pri								

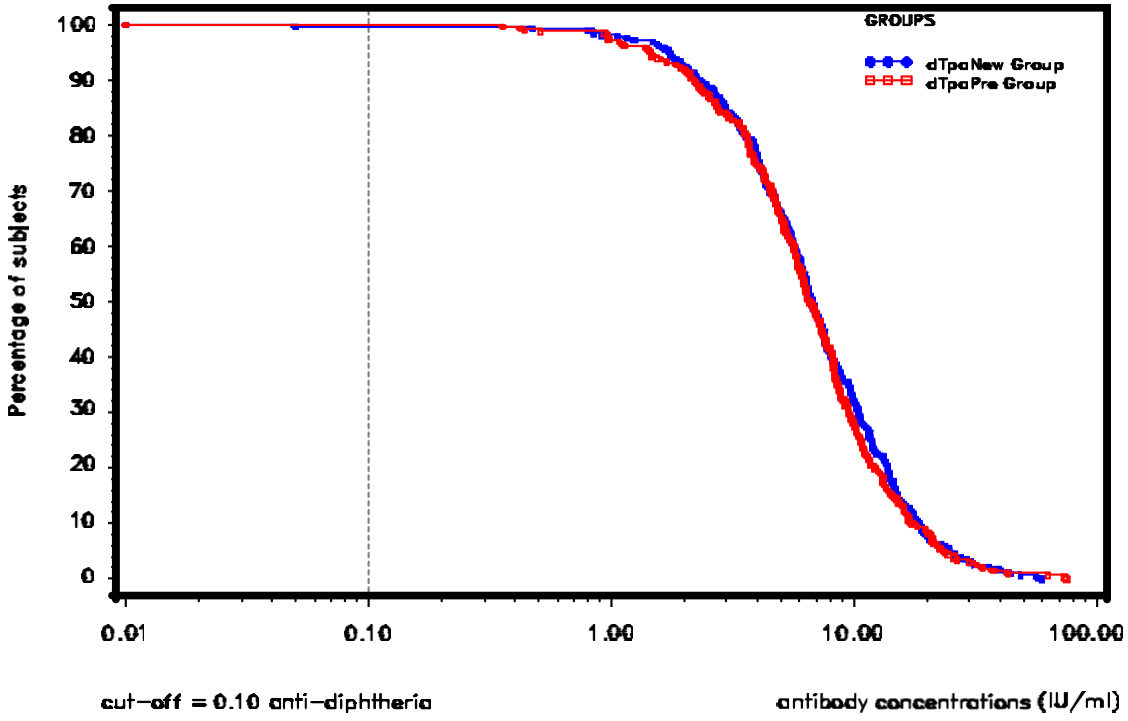
dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
GMT = geometric mean antibody concentration calculated on all subjects
N = number of subjects with available results
n(%)=number(percentage) of subjects with antibody concentrations above the specified cut-off
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Pre-Pri = blood sample to be collected before the first dose of the primary vaccination course
Post-Pri = blood sample to be collected 1 month after the last dose of the primary vaccination course

Template 13 Vaccine responses for anti-PT, anti-FHA and anti-PRN antibody concentration 1 month after the last dose of the primary vaccination course (ATP cohort for immunogenicity)

				Vaccine response			
						95% CI	
Antibody	**Group**	**Pre-Pri* status**	**N**	**n**	**%**	**LL**	**UL**
anti-PT	dTpa Group	S-					
		S+ (≥cut-off IU/mL)					
		Total					
	Control Group	S-					
		S+ (≥cut-off IU/mL)					
		Total					
anti-FHA	dTpa Group	S-					
		S+ (≥cut-off IU/mL)					
		Total					
	Control Group	S-					
		S+ (≥cut-off IU/mL)					
		Total					
anti-PRN	dTpa Group	S-					
		S+ (≥cut-off IU/mL)					
		Total					
	Control Group	S-					
		S+ (≥cut-off IU/mL)					
		Total					

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
S- = Initially seronegative subjects (antibody concentration below assay cut-off for anti-PT, anti-FHA, anti-PRN)
S+ = Initially seropositive (antibody concentration above assay cut-off for anti-PT, anti-FHA, anti-PRN)
Total = subjects either seropositive or ser1gative at pre-vaccination
Vaccine response to PT, FHA and PRN antigens is defined as:
For subjects with pre-vaccination antibody concentration below the assay cut-off, post-vaccination antibody concentration equal or above the assay cut-off,
For subjects with pre-vaccination antibody concentration equal or above the assay cut-off, post-vaccination antibody concentration equal or above the pre-vaccination antibody concentration
N = number of subjects with pre- and post-vaccination results available
n(%) = number(percentage) of subjects with booster response
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
*Pre-Pri = blood sample to be collected before the first dose of the primary vaccination course
Note: The assay cut-off is 2.693 IU/mL for anti-PT, 2.046 IU/mL for anti-FHA, and 2.187 IU/mL for anti-PRN.

Template 14 Reverse cumulative curve for anti-diphtheria antibody concentration before first dose and 1 month post last dose of the primary vaccination course (ATP cohort for immunogenicity)



dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Pre-Pri = blood sample to be collected before the first dose of the primary vaccination course
Post-Pri = blood sample to be collected 1 month after the last dose of the primary vaccination course
Note: The groups shown in figure are indicative only. Actual groups may differ.

Template 15 Number and percentage of subjects who received study vaccine doses by vaccination group (Total vaccinated cohort)

	dTpa group N =		Control group N =	
Total number of doses received	**n**	**%**	**n**	**%**
0				
1				
2				
3				
Any				

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
N = number of subjects in each group or in total included in the considered cohort
n(%) = number(percentage) of subjects receiving the specified total number of doses
Any = number and percentage of subjects receiving at least 1 dose

Template 16 Compliance in returning symptom sheets (Total vaccinated cohort)

Dose	Group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % general SS	Number of local SS	Compliance % local SS
1	dTpa group						
	Control group						
2	dTpa group						
	Control group						
3	dTpa group						
	Control group						
Total	dTpa group						
	Control group						

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
SS = Symptom sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom sheet return / number of administered doses) X 100

Template 17 Percentage and nature of <grade 3>symptoms (solicited and unsolicited) reported during the 4-day (Days 0-3) post-vaccination period following each dose and overall (Total vaccinated cohort)

		Any symptom					General symptoms					Local symptoms				
					95% CI					95% CI					95% CI	
	Group	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	dTpa group															
	Control group															
Dose 2	dTpa group															
	Control group															
Dose 3	dTpa group															
	Control group															
Overall/dose	dTpa group															
	Control group															
Overall/subject	dTpa group															
	Control group															

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
For each dose and overall/subject:
N= number of subjects with at least 1 administered dose
n(%) = number(percentage) of subjects presenting at least 1 type of symptom whatever the study vaccine administered
For overall/dose:
N= number of administered doses
n(%) = number(percentage) of doses followed by at least 1 type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 18 Percentage of solicited local symptoms reported during the 4-day (Day 0-3) post-vaccination period following each dose and overall (Total vaccinated cohort)

			each group									
			dTpa group					Control group				
						95 % CI					95 % CI	
Symptom	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Each dose											
Pain	Total	All										
		Grade 2 or 3										
		Grade 3										
		Medical advice										
	Infanrix hexa	All										
		Grade 2 or3										
		Grade 3										
		Medical advice										
	Prevenar 13	All										
		Grade 2 or 3										
		Grade 3										
		Medical advice										
Redness (mm)	Total	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Infanrix hexa	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Prevenar 13	All										
		> 5.0										
		> 20.0										
		Medical advice										
Swelling (mm)	Total	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Infanrix hexa	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Prevenar 13	All										
		> 5.0										
		> 20.0										
		Medical advice										
Overall/Dose												
Pain	Total	All										
		Grade 2 or 3										
		Grade 3										
		Medical advice										
	Infanrix hexa	All										
		Grade 2 or 3										
		Grade 3										
		Medical advice										

			each group									
			dTpa group					Control group				
						95 % CI					95 % CI	
Symptom	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Prevenar 13	All										
		Grade 2 or 3										
		Grade 3										
		Medical advice										
Redness (mm)	Total	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Infanrix hexa	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Prevenar 13	All										
		> 5.0										
		> 20.0										
		Medical advice										
Swelling (mm)	Total	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Infanrix hexa	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Prevenar 13	All										
		> 5.0										
		> 20.0										
		Medical advice										
Overall/Subject												
Pain	Total	All										
		Grade 2 or 3										
		Grade 3										
		Medical advice										
	Infanrix hexa	All										
		Grade 2 or 3										
		Grade 3										
		Medical advice										
	Prevenar 13	All										
		Grade 2 or 3										
		Grade 3										
		Medical advice										
Redness (mm)	Total	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Infanrix hexa	All										
		> 5.0										
		> 20.0										
		Medical advice										

			each group									
			dTpa group					Control group				
						95 % CI					95 % CI	
Symptom	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
	Prevenar 13	All										
		> 5.0										
		> 20.0										
		Medical advice										
Swelling (mm)	Total	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Infanrix hexa	All										
		> 5.0										
		> 20.0										
		Medical advice										
	Prevenar 13	All										
		> 5.0										
		> 20.0										
		Medical advice										

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
For each dose and overall/subject:
N= number of subjects with at least 1 documented dose
n(%) = number(percentage) of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n(%) = number(percentage) of doses followed by at least 1 type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 19 Percentage of solicited general symptoms reported during the 4-day (Days 0-3) post-vaccination period following each dose and overall (Total vaccinated cohort)

		dTpa group					Control group				
					95 % CI					95 % CI	
Symptom	Type	N	n	%	LL	UL	N	n	%	LL	UL
Each dose											
Drowsiness	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										
Irritability	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										
Loss of appetite	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										
Temperature/(Axillary) (°C)	All										
	>37.5										
	>38.0										
	>38.5										
	>39.0										
	>39.5										
	Related										
	>39*Related										
	Medical advice										
Overall/dose											
Drowsiness	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										
Irritability	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										
Loss of appetite	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										

		dTpa group					Control group				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Temperature/(Axillary) (°C)	All										
	>37.5										
	>38.0										
	>38.5										
	>39.0										
	>39.5										
	Related										
	>39*Related										
	Medical advice										
Overall/subject											
Drowsiness	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										
Irritability	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										
Loss of appetite	All										
	Grade 2 or 3										
	Grade 3										
	Related										
	Grade 3*Related										
	Medical advice										
Temperature/(Axillary) (°C)	All										
	>37.5										
	>38.0										
	>38.5										
	>39.0										
	>39.5										
	Related										
	>39*Related										
	Medical advice										

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule. For each dose and overall/subject:
N= number of subjects with at least 1 documented dose
n(%) = number(percentage) of subjects reporting the symptom at least once
For Overall/dose:
N= number of documented doses
n(%) = number(percentage) of doses followed by at least 1 type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Related: Symptoms which is assessed by the investigator as related to vaccination

Template 20 Percentage of Unsolicited symptoms experienced by subjects classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) after any dose (Total vaccinated cohort)

		dTpa Group N =			Control Group N =		
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**n***	**n**	**%**
At least 1 symptom							
<each SOC>	<each PT term>						

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule. For each dose and overall/subject:
At least 1 symptom = at least 1 symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with the administered dose
n* = number of events reported
n(%) = number(percentage) of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 21 Number (%) of subjects with serious adverse events from the Day 0 to end of the study (Total Vaccinated cohort)

Type of Event	**Primary System Organ Class**	**Preferred Term (CODE)**	**dTpa Group N =**			**Control Group N =**		
			n*	**n**	**%**	**n***	**n**	**%**
SAE	At least 1 symptom							
	<each SOC>	<each PT>						
Related SAE	At least 1 symptom							
	<each SOC>	<each PT>						
Fatal SAE	At least 1 symptom							
	<each SOC>	<each PT>						
Related Fatal SAE	At least 1 symptom							
	<each SOC>	<each PT>						

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule. For each dose and overall/subject:
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the symptom at least once

Template 22 Solicited and unsolicited adverse events experienced by subjects classified by MedDRA Primary System Organ Class and Preferred Term within the 31-day (Days 0-30) post-vaccination period - SAE excluded (Total vaccinated cohort)

		dTpa Group N =			Control Group N=		
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**n***	**n**	**%**
At least 1 symptom							
<each SOC>	<each PT term>						

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule. For each dose and overall/subject:
At least 1 symptom = at least 1 symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the symptom at least once

Template 23 Number and percentage of subjects taking a concomitant medication and antipyretic medication during the 4-day (Days 0-3) follow-up period post-vaccination by dose and overall (Total vaccinated cohort)

	dTpa group					Control group				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Each dose										
Any										
Any antipyretic										
Prophylactic antipyretic										
Overall/dose										
Any										
Any antipyretic										
Prophylactic antipyretic										
Overall/subject										
Any										
Any antipyretic										
Prophylactic antipyretic										

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule. For each dose and overall/subject:
For each dose and overall/subject:
N= number of subjects with at least 1 administered dose
n(%) = number(percentage) of subjects who started to take the specified concomitant medication at least once during the menti1d period
For overall/dose:
N= number of administered doses
n(%) = number(percentage) of doses after which the specified concomitant medication was started at least once during the menti1d period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 24 Minimum and maximum activity dates (Total vaccinated cohort)

Visit	Minimum date	Maximum date
1	19JUN2007	29DEC2007
2	24JUL2007	08FEB2008
3	24AUG2007	18MAR2008
4	25MAR2008	22NOV2008

Database Lock Date = 31MAR2009

Template 25 Number of enrolled subjects by age category at visit1

		dTpa group N =	Control group N =	Total N =
Characteristics	**Categories**	**n**	**n**	**n**
Age category	Infants (6 weeks – 14 weeks and 6 days)			
	Missing			

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule. For each dose and overall/subject:
N = Number of enrolled subjects
n = number of enrolled subjects included in each group or in total for a given age category or for all age categories
Missing = subjects who are enrolled in the study but not vaccinated and for which age is unknown

Template 26 Listing of SAEs from Day 0 up study (Total vaccinated cohort)

Group	Sub No.	Case Id	Age at onset (Week)	Sex	Verbatim	Preferred term	System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome
dTpa group														
Control group														

dTpa Group = This group will consist of infants born to mothers belonging to the dTpa Group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule.
Control Group: This group will consist of infants born to mothers belonging to the Control group in study 116945 [DTPA (BOOSTRIX)-047]. All subjects in this group will receive *Infanrix hexa* co-administered with *Prevenar 13* according to the routine national immunisation schedule. For each dose and overall/subject:
Med type = Type of medical advice; HO= Hospitalisation, ER = Emergency room

Template 27 Listing of dropouts due to AEs, SAEs and solicited symptoms (Total vaccinated cohort)

Group	Sub. No.	Country	Gender	AE Description	SAE	Causality	Outcome	Type of discontinuation
dTpa group	PP	Germany	F	SUBJECT DIED	Y		Fatal	Study at visit/contact: VISIT11 (Y5)
Control group	PP	Germany	F	SUBJECT DIED	Y		Fatal	Study at visit/contact: VISIT11 (Y5)