GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	A Phase IV, observer-blind, randomised, cross-over, placebo-controlled, multicentre study to assess the immunogenicity and safety of a single dose of Boostrix in pregnant women.
eTrack study number and Abbreviated Title	116945 [DTPA (BOOSTRIX)-047]
Scope:	All data pertaining to the above study.
Date of Statistical Analysis Plan	Final: 20-Feb-2018
Co-ordinating author:	PPD (Statistician)
Reviewed by:	PPD (Clinical and Epidemiology R&D Project Leader) PPD (Clinical Research and Development Lead) PPD (Lead statistician) PPD (Lead statistical analyst) PPD Scientific writer) PPD (Regulatory Affair) PPD (SERM physician) PPD (Public disclosure representative)
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APP 9000058193 Statistical Analysis Plan Template (Effective date: 14April 2017)

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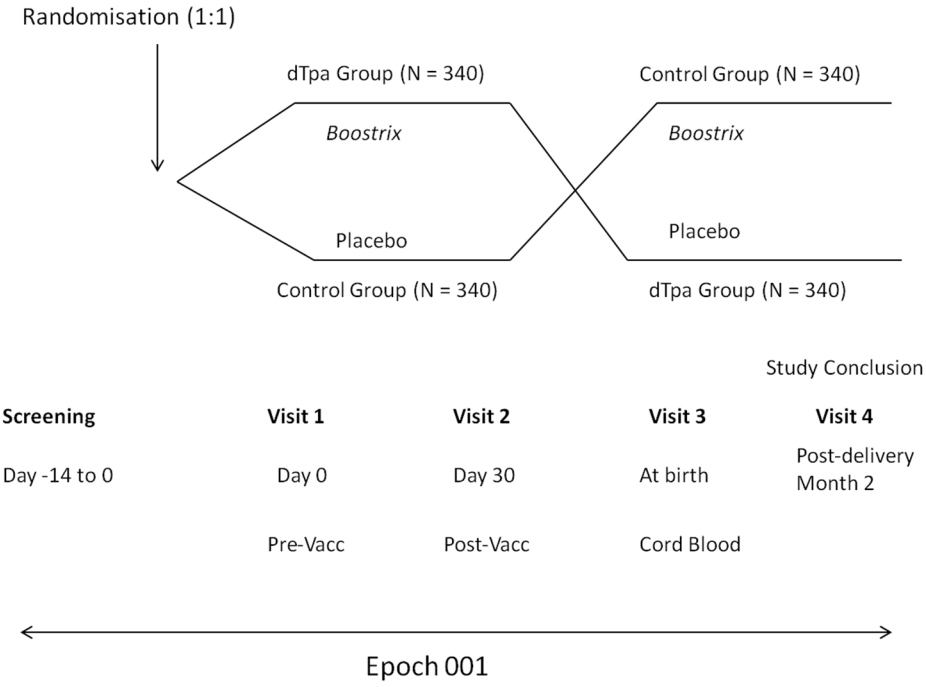
LIST OF ABBREVIATIONS

AE	Adverse event
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
CI	Confidence Interval
CRF	Case Report Form
CSR	Clinical Study Report
CTRS	Clinical Trial Registry Summary
EL.U/ml	ELISA unit per milliliter
Eli Type	Internal GSK database code for type of elimination code
ELISA	Enzyme-linked immunosorbent assay
ES	TVC
GMC	Geometric mean antibody concentration
GMT	Geometric mean antibody titer
GSK	GlaxoSmithKline
IU/ml	International units per milliliter
LL	Lower Limit of the confidence interval
MedDRA	Medical Dictionary for Regulatory Activities
N.A.	Not Applicable
PD	Protocol Deviation
PPS	Per Protocol Set
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBIR	GSK Biological's Internet Randomization System
SD	Standard Deviation
SR	Study Report
TFL	Tables Figures and Listings
TOC	Table of Content
UL	Upper Limit of the confidence interval

1. DOCUMENT HISTORY

Date	Description	Protocol Version
20-FEB-2018	first version	Administrative Change 1 Final: 06-SEP-2016

2. STUDY DESIGN



N: Number of subjects planned to be enrolled
Pre-vacc: Blood sample to be collected before the dose of the booster vaccination in pregnant women (Visit 1).
Post-vacc: Blood sample to be collected one month after the booster vaccination in pregnant women (Visit 2).

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 protocol), are essential and required for study conduct.

- Experimental design: Phase IV, observer-blind, randomised, placebo-controlled, multi-centric, multi-country study with two cross-over groups. All eligible household contacts of the infants born to pregnant women enrolled in Spain will be eligible to receive a single dose of *Boostrix* as part of an assessment of cocooning.
- Duration of the study: The intended duration of the study will be approximately 5 months for each subject.
  - Epoch 001: Booster vaccination starting at Screening visit (Day -14 to 0) and ending at Visit 4 (post-delivery Month 2).

- Study groups: The study groups are defined as follows:

  – dTpa Group: This group will consist of pregnant women who will receive a single dose of *Boostrix* at 27-36 weeks (i.e. completed 27 weeks until 36 weeks) of gestation (Visit 1) and will receive a dose of the placebo post-delivery (within 72 hours).

  – Control Group: This group will consist of pregnant women who will receive a single dose of placebo at 27-36 weeks (i.e. completed 27 weeks until 36 weeks) of gestation (Visit 1) and will receive a dose of *Boostrix* post-delivery (within 72 hours).

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	18 years - 45 years	x
Control Group	340	18 years - 45 years	x

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

Table 2 Study groups and treatment foreseen in the study

Treatment name	Vaccine name	Study Groups	
		dTpa Group	Control Group
Boostrix *	dTpa	x	x
Placebo for dTpa vaccine	Placebo	x	x

*All eligible household contacts of the infants born to pregnant women enrolled in Spain will be eligible to receive a single dose of *Boostrix* as part of an assessment of cocooning.

- Control: placebo control

- Vaccination schedule:

  – All subjects will receive a single dose of *Boostrix* or placebo at 27-36 weeks (i.e. completed 27 weeks until 36 weeks) of gestation (Visit 1). Subjects who receive *Boostrix* at Visit 1 will receive a dose of placebo post-delivery (Visit 3) while those who receive placebo at Visit 1 will receive *Boostrix* post-delivery (Visit 3).

  – All eligible household contacts of the infants born to pregnant women enrolled in Spain will be eligible to receive a single dose of *Boostrix* as part of an assessment of cocooning. Although the vaccine can be administered anytime during the study, it is recommended that the vaccine is administered preferably 2 weeks before birth of the infant.

- Treatment allocation: randomised.

- Blinding: Observer-blind. Refer to Section 5.3 of protocol for details of the of blinding procedure.

The blinding of study epoch is presented in Table 3

Table 3 Blinding of study epoch

Study Epoch	Blinding
Epoch 001	observer-blind

- Sampling schedule: Blood samples will be collected at the following time-points:
  - Pre-Vacc (Visit 1): Before the booster vaccination, approximately 5 mL of blood sample will be collected from all subjects.
  - Post-Vacc (Visit 2): One month after the booster vaccination, approximately 5 mL of blood sample will be collected from all subjects.
  - Cord blood (Visit 3): approximately 2.5 mL of blood sample from the umbilical cord will be collected from all subjects.
- Type of study: self-contained
- Data collection: Electronic Case Report Form (eCRF).
- Safety monitoring: An independent data monitoring committee (IDMC) (including obstetrician, paediatrician, statistician and a neonatologist) will be put in place to oversee the safety aspects of *Boostrix* in the clinical study i.e. each SAE/congenital anomaly/foetal malformation case/incidence of grade 3 local and general solicited adverse events (AEs) will be reviewed by this committee (See Section5.4.1 of protocol for details).

3. OBJECTIVES

Primary

- To demonstrate that the maternally transferred antibodies against pertussis in the dTpa Group is superior to that in the Control Group in terms of geometric mean concentrations (GMCs) for the pertussis antibodies, in the cord blood sample.

  Criterion:

  – The lower limit (LL) of the 95% confidence interval (CI) of the GMC ratio [dTpa Group divided by Control Group] for anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibodies is ≥ 1.5.

Secondary

- To assess the safety of a single dose of Boostrix in pregnant women, administered during 27-36 weeks of gestation, in terms of the outcomes of pregnancy and listed pregnancy-related adverse events of interest/neonate-related events of interest up to study end (Visit 4).
- To assess the immunogenicity of a single dose of Boostrix administered during pregnancy in terms of seropositivity status for antibodies against pertussis, in the cord blood sample.
- To assess the immunogenicity of a single dose of Boostrix administered during pregnancy in terms of seroprotection/seropositivity status, vaccine response and GMCs for antibodies against diphtheria, tetanus and pertussis, one month post-vaccination.
- To evaluate the reactogenicity of a single dose of Boostrix administered during pregnancy and post-delivery in terms of solicited symptoms during the 8-day (Day 0 – Day 7) follow-up period after vaccination.
- To assess the safety of a single dose of Boostrix administered during pregnancy and post-delivery in terms of unsolicited symptoms during the 31-day (Day 0 – Day 30) follow-up period after vaccination and serious adverse events (SAEs) during the period from Visit 1 up to Visit 4.
- To assess the acceptance rate of a single dose of Boostrix among eligible household contacts of the infants born to pregnant women enrolled in Spain, as part of an assessment of cocooning.
- To assess the safety of a single dose of Boostrix in terms of SAEs among the vaccinated household contacts of the infants born to pregnant women in Spain, as part of an assessment of cocooning, from the day of vaccination till 30 days after the vaccination.

4. ENDPOINTS

Primary

- Immunogenicity with respect to components of the study vaccine, at delivery (in cord blood sample):
  - Anti-PT, anti-FHA and anti-PRN antibody concentrations.

Secondary

- Outcome of pregnancy in terms of pregnancy outcomes up to study end (Visit 4).
  - Pregnancy outcomes will include live birth with no congenital anomalies, live birth with congenital anomalies, still birth with no congenital anomalies, still birth with congenital anomalies, elective termination with no congenital anomalies and elective termination with congenital anomalies.
- Outcome of pregnancy in terms of listed pregnancy-related adverse events of interest/ neonate-related events of interest up to study end (Visit 4).
  - Listed pregnancy-related adverse events of interest/ neonate-related events of interest will include gestational diabetes, pregnancy-related hypertension, premature rupture of membranes, preterm premature rupture of membranes, premature labour, premature uterine contractions, intrauterine growth restriction/poor foetal growth, pre-eclampsia, eclampsia, vaginal or intrauterine haemorrhage, maternal death, preterm birth, neonatal death, small for gestational age, neonatal hypoxic ischaemic encephalopathy and failure to thrive/growth deficiency.
- Immunogenicity with respect to components of the study vaccine received during pregnancy, one month post vaccination
  - Anti-D, anti-T, anti-PT, anti-FHA and anti-PRN seroprotection/seropositivity status and antibody concentrations.
  - Vaccine response to PT, FHA and PRN. Refer to section 11.2.4
  - Vaccine response to anti-D and anti-T. Refer to section 11.2.4
- Immunogenicity with respect to components of the study vaccine, in the cord blood sample.
  - Anti-PT, anti-FHA and anti-PRN seropositivity status.
- Solicited local and general symptoms (at Visit 1 and Visit 3).
  - Occurrence of each solicited local/general symptoms during the 8-day (Day 0-Day 7) follow-up period after the vaccination.
- Unsolicited adverse events (at Visit 1 and Visit 3).
  - Occurrence of unsolicited AEs within 31 days (Day 0 – Day 30) after any vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.
- Serious adverse events (SAEs).

  - Occurrence of serious adverse events from Dose 1 up to study end (Visit 4).

- Percentage of household contacts of the infants born to pregnant women vaccinated in Spain who accepted *Boostrix* vaccine as part of an assessment of cocooning among the eligible household contacts.
- Occurrence of SAEs among the vaccinated household contacts of the infants born to pregnant women in Spain, as part of an assessment of cocooning, from the day of vaccination till 30 days after vaccination.

5. ANALYSIS SETS

5.1. Definition

5.1.1. Total Vaccinated cohort

- The Total Vaccinated cohort (TVC) analysis will be performed per treatment actually administered. A safety analysis based on the TVC will include all subjects with the study vaccine administration documented.
- An immunogenicity analysis based on the TVC will include all subjects vaccinated during pregnancy (Visit 1) for whom data concerning at least one immunogenicity endpoint measure is available.

5.1.2. According-To-Protocol cohort for analysis of safety

The ATP cohort for safety will consist of all subjects from the TVC who complied with vaccine administration up to the end of the Epoch 001, namely:

- Who have received the dose of study vaccine (at Visit 1) according to their random assignment,
- For whom administration site of study vaccine is known, and is according to protocol,
- Who have not received a vaccine not specified or forbidden in the protocol,
- For whom the randomisation code is not broken.

5.1.3. ATP cohort for analysis of immunogenicity

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

- Who meet all eligibility criteria.
- Who comply with the procedures and intervals defined in the protocol.
- Who are within the maximum interval allowed as defined in the protocol.
- Who do not meet any of the criteria for elimination from an ATP analysis (refer to Section 6.7.2 from protocol) during the study.
- Who did not receive a product leading to exclusion from an ATP analysis as listed in Section 6.7.2 from protocol.
- Who did not present with a medical condition leading to exclusion from an ATP analysis as listed in Section 6.8 from protocol.
- Who have the cord blood collection at least 21 days post-vaccination.
- 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 vaccine antigen component one month after vaccination i.e. Visit 3 in the cord blood sample.

5.1.4. Total cohort for household contacts in Spain

Total cohort for household contacts will include all eligible household contacts of the infants born to pregnant women vaccinated in Spain. For the analysis of safety, all vaccinated household contacts will be considered.

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.

5.2.1.1. Elimination from ATP cohort for immunogenicity Excluded subjects

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

Code	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 administrated at all but subject number allocated => subjects enrolled but not vaccinated
1040	Administration of concomitant vaccine(s) forbidden in the protocol Previous vaccination containing diphtheria, tetanus or pertussis antigens or diphtheria and tetanus toxoids at any time during the current pregnancy.
1050	Randomisation failure (subject who received a vaccine not compatible with randomization)
1060	Randomisation code broken at the investigator site OR at GSK Safety department
1070	Site or route of study vaccine administration wrong or unknown.
1080	Vaccine has been administered (effective treatment number) despite a temperature deviation qualified by Status QA GMP NON Use.
1090	Vaccine has been administered (effective treatment number) out of the expiration date at the time of administration.
2010	Protocol violation linked to the inclusion/exclusion criteria including age and excluding codes mentioned below.
2040	Administration of any medication forbidden by the protocol
2050	Underlying medical condition forbidden by the protocol
2060	Concomitant infection related to the vaccine which may influence immune response
2070	Concomitant infection not related to the vaccine which may influence immune response
2090	Blood sample taken but non-compliance with blood sampling schedule for the cord blood sample (dates of BS not corresponding to adapted protocol intervals or unknown BS/vaccination dates))=> Cord blood should be at least 21 days after vaccination
2100	Serological results not available for all antigens from the cord blood sample
2120	Obvious incoherence, abnormal serology evolution or error in data in cord blood sample (incoherence between CRF and results, wrong sample labelling.

5.3. Important protocol deviation not leading to elimination from per-protocol analysis set

Refer to the protocol deviation management plan for important protocol deviation not leading to elimination from ATP cohort for immunogenicity.

6. STATISTICAL ANALYSES

Note that standard data derivation rule and stat methods are described in 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 at the booster dose in years, race, height [cm], weight [kg], 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 error will be provided for continuous data such as age.

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

Summary statistics by height [cm], weight [kg], head circumference [cm], body mass index [BMI in kg/m²] and Apgar score of the infant will be tabulated as a whole and per group.

6.1.1.1. Analysis of eligible household contacts

Analysis of eligible household contacts will be performed on the Total cohort for household contacts in Spain.

- Demographic characteristics (age, sex, and race) will be summarised for the eligible household contacts as a whole and per group using descriptive statistics.
- Reasons for refusal of the cocooning vaccination will be summarised for the eligible household contacts as a whole and per group.
- Percentage of household contacts of the infants born to pregnant women vaccinated in Spain who accepted *Boostrix* vaccine as part of an assessment of cocooning among the eligible household contacts will be tabulated as a whole and per group.

6.1.2. Additional considerations

Breast feeding status, gestational age at vaccination and the time between vaccination and delivery will be summarised as a whole and per group using descriptive statistics.

The total number of household contacts approached, summary statistics for the number of household contacts by vaccinated subject will be generated in the subset of subjects in Spain.

Note that for a few of the household contacts, since they were later on classified as eligible based on the reasons for refusal, their demographic information is missing.

Apgar score will be summarized at 1 minute and 5 minutes post vaccination. No summary will be provided at 10 minutes as the measurement is optional.

6.2. Exposure

The number of pregnant mother vaccinated will be provided by study group and refer to section 6.1.1.1 for exposure in household contacts.

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 vaccinated subjects with serological results excluded from this ATP cohort is 5% or more, a second analysis based on the TVC will be performed to complement the ATP analysis.

6.3.1.1. Within group assessment:

For each treatment group, before and one month after vaccination during pregnancy and if blood sample result is available:

- Seroprotection rates and their exact 95% CIs for antibodies against diphtheria and tetanus will be calculated.
- Seropositivity rates and their exact 95% CIs for antibodies against PT, FHA, PRN, will be tabulated.
- GMCs and their 95% CIs for antibodies against all vaccine antigens will be calculated.
- The distribution of antibody concentrations pre, one month after booster vaccination for each antigen will be displayed using reverse cumulative distribution curves.
- Vaccine response to diphtheria, tetanus and pertussis antigens and their exact 95% CI will be calculated.

In the cord blood sample, if the blood sample result is available:

- Seropositivity rates and their exact 95% CIs for antibodies against PT, FHA, PRN, will be tabulated.
- GMCs and their 95% CIs for antibodies against PT, FHA, PRN antigens will be calculated.

6.3.1.2. Between group assessment:

- The primary objective is to demonstrate that, the immune response in the dTpa Group is superior to that in the Control Group for the pertussis antigens, in the cord blood sample.
  - *The LL of the 95% CI of the GMC ratio [dTpa Group divided by Control Group] for anti-PT, anti-FHA and anti-PRN antibodies are ≥ 1.5.*

The CI of the group GMC ratios will be computed using a two-sample t test assuming heterogeneity of variance.

6.3.2. Additional considerations

Percentage of subjects with anti-D and anti-T antibody concentrations ≥ 1.0 IU/ml will be calculated along with its exact 95% CI by vaccine group at each visit.

For the distribution of antibody concentrations displayed using reverse cumulative distribution curves, the pre booster will also be included in the same graph as the one month after booster vaccination.

The distribution of antibody concentrations measured from the cordon blood will also be generated in separated graphs.

The following descriptive analysis will be performed by sub-group of gestational age (27-32, 33-36 weeks of gestation of foetus at dose 1) and age of mother (18-24, 25-34, 35-45).

For each treatment group, before and one month after vaccination during pregnancy, cord blood sample and if blood sample result is available:

- Seroprotection rates and percentage of subjects with anti-D and anti-T antibody concentrations ≥ 1.0 IU/ml will be calculated along with and their exact 95% CIs for antibodies against diphtheria and tetanus.
- Seropositivity rates and their exact 95% CIs for antibodies against PT, FHA, PRN, will be tabulated.
- GMCs and their 95% CIs for antibodies against all vaccine antigens will be calculated.

6.4. Analysis of safety

6.4.1. Analysis of safety planned in the protocol

The primary analysis will be performed on the TVC. If in any vaccine group, 5% or more of the vaccinated subjects are eliminated from the TVC, a second analysis will be performed on the ATP cohort for analysis of safety. Analysis of safety in household contacts will be performed on the Total cohort for household contacts in Spain.

- The percentage of subjects with each specific pregnancy outcomes and listed pregnancy-related adverse events of interest/neonate-related events of interest will be tabulated with its exact 95% CI.
- The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE during the 8-day (Day 0–Day 7) follow-up period after the vaccination will be tabulated after each dose with exact 95% CI. The same calculations will be performed for any Grade 3 (solicited or unsolicited) symptoms, any causal relationship to vaccination and for any symptoms requiring medical attention.
- The percentage of subjects reporting each individual solicited local and general AE during the 8-day (Day 0-Day 7) follow-up period after booster vaccination will be tabulated with its exact 95% CI for each group.
- 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), for Grade 3 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.
- Any large injection site reaction (defined as any local swelling with diameter > 100 mm and/or any noticeable diffuse injection site swelling (diameter not measurable) and/or any noticeable increased circumference of the injected limb) onset within 8 days (Day 0–Day 7) after each vaccination will be described in detail.
- The verbatim reports of unsolicited symptoms 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 symptoms occurring within 31 days (Day 0–Day 30) with its exact 95% CI will be tabulated by preferred term. Similar tabulation will be done for Grade 3 unsolicited symptoms and for unsolicited symptoms possibly related to vaccination.
- The percentage of subjects who started to receive at least one concomitant medication (i.e. any medication, antipyretic medication, prophylactic antipyretics) during the 4-day and 31-day follow-up period after vaccination will be tabulated after each dose with exact 95% CI.

- SAEs and withdrawal due to AEs and SAEs following booster dose up to Visit 4 will be described in detail.
- All SAEs assessed as being possibly related to study participation occurring throughout the study period will be described.
- All SAEs assessed as being possibly related to a concurrent GSK medication occurring throughout the study period will be described.
- For the vaccinated household contacts in Spain, SAEs following *Boostrix* vaccination up to 30 days will be described in detail.

6.4.2. Additional considerations

- The safety analysis will be performed for each vaccination dose separately ie pregnancy dose and post-delivery dose.
- The percentage of infants with unsolicited symptoms occurring from delivery until 2 months with its exact 95% CI will be tabulated by preferred term. Similar tabulation will be done for Grade 3 unsolicited symptoms and for unsolicited symptoms possibly related to vaccination.
- The summary on concomitant medication (i.e. any medication, antipyretic medication, prophylactic antipyretics) will be performed over the 8 day period instead of 4 days.
- All SAEs will be summarized without distinction of SAEs possibly related to GSK concurrent medication.
- The analysis of safety in the household contacts will be performed on the vaccinated household contacts instead of the Total cohort for household contacts in Spain.

7. ANALYSIS INTERPRETATION

For analysis on the primary objective with pre-defined success criteria and an appropriate type I error control, appropriate conclusion can be drawn.

The secondary objectives of the study are descriptive and should be interpreted as such.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

Description	Analysis ID	Disclosure Purpose (IN=internal, CTRS=public posting, SR=study report and 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

No statistical interim analysis will be performed.

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.
- Refer to section 6.1.2, 6.3.2 and 6.4.2 for other changes.

10. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC provides the list of tables/listings and figures needed for the study report. It also identifies the tables eligible for each analyses and their role (synopsis, in-text, post-text, SHS, CTRS,…). Note that all TFL aimed to be included as post-text are noted as post-text even if these are tabulation of individual data such as listing of SAE. The post-text material contains all source material for the study report and accordingly a post-text table may be redundant with an in-text table.

Add the text below as applicable

The mock tables referred under column named 'layout' can be found in legacy-NV/GSK SDD dedicated folder for standard tables and in section 12 for study specific mock table/figure/listing. The latter table/figure/listing are identified by the prefix SS_ in the TFL Toc.

The following group names will be used in the TFL TOC:

Group order in tables	Group label in tables	Group definition for footnote	Pooled Groups label in tables	Pooled definition for footnote
1	dTpa Group	Mothers received dTpa during pregnancy	NA	NA
2	Control Group	Mothers received placebo during pregnancy	NA	NA

If sub-groups are defined in the protocol, you can use the following example to describe these.

The following sub-group names will be used in the TFLs

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% CIs of the group GMC ratios will be computed using an ANOVA model on the logarithm10 transformation of the concentrations. The ANOVA model will include the vaccine group as fixed effects. The CI of the group GMC ratios will be computed using a two-sample Welch's t test assuming heterogeneity of variance.

The 95% CI for GMTs/GMCs will be obtained within each group separately. The 95% CI for the mean of log-transformed titre/concentration will be first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs/GMCs will then be obtained by exponential-transformation of the 95% CI for the mean of log-transformed titre/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 mother (AE, medication, vaccination, …): The onset day is the number of days between the last study vaccination & the onset/start date of the event. This is 0 for an event starting on the same day as a vaccination. See SAS date derived in case the start date of the event is incomplete.
- Onset day for an event for the infant (AE, medication, vaccination, …): The onset day is the number of days from date of birth of infant & the onset/start date of the event. This is 0 for an event starting on the same day of birth. 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 injection occurred. More specifically dose 1 refers to all injections administered at the first vaccination visit (Visit 1) while dose 2 corresponds to all injections administered at the second vaccination visit (Visit 3) 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.
- Relative dose for infant : Since the infants are not receiving any vaccine in this study, relative dose will be '0'.
- The number of doses for a product is the number of time the product is administered to a subject.
- The incidence per dose is the number of vaccination visits at which an event was reported among all vaccination visits.

11.2.3. Demography

- Age of mother: Age at the reference activity, computed as the number of units between the date of birth and the reference activity. Note that due to incomplete date, the derived age may be incorrect by 1 month when month is missing from the birthdate. This may lead to apparent inconsistency between the derived age and the eligibility criteria/the age category used for randomization. Gestational age at delivery : The gestational age at delivery is calculated by adding the number of weeks between screening and delivery to the gestational age recorded at the ultrasound screening.
- Gestational age at dose 1: The gestational age at dose 1 is calculated by adding the number of weeks between screening and dose1 to the gestational age recorded at the ultrasound screening.
- Age of infant: Age at the reference activity, computed as the number of complete weeks 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 ounces / 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 Inch * 2.54

  The result is rounded to the unit (ie 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.
- The Geometric Mean Concentrations (GMCs) calculations are performed by taking the anti-log of the mean of the log titre transformations. Antibody concentrations 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 GMC calculation.
- A seronegative subject is a subject whose antibody concentration is below the assay cut-off value. A seropositive subject is a subject whose antibody concentration is greater than or equal to the assay cut-off value.

Vaccine response definition:

- Vaccine response to D and T antigens was defined as:
  - for subjects with pre-vaccination concentration < 0.1 IU/mL antibody (ie below the seroprotection cut-off), antibody concentrations at least ≥ 0.4 IU/mL, one month after vaccination, and
  - for subjects with pre-vaccination concentration ≥ 0.1 IU/mL (ie equal or above the seroprotection cut-off), an increase in antibody concentrations of at least four times the pre-vaccination concentration, one month after vaccination.
- Vaccine response to PT, FHA and PRN antigens was defined as:
  - for subjects with pre-vaccination antibody concentration below the assay cut-off, post-vaccination antibody concentration ≥4 times the assay cut-off,
  - for subjects with pre-vaccination antibody concentration between the assay cut-off and below 4 times the assay cut-off, post-vaccination antibody concentration ≥4 times the pre-vaccination antibody concentration, and
  - for subjects with pre-vaccination antibody concentration ≥4 times the assay cut-off, post-vaccination antibody concentration ≥ 2 times the pre-vaccination antibody concentration.

The thresholds defining seropositivity are provided below as per new re-validated assay are the following.

Table 4 Humoral Immunity (Antibody determination)

System	Component	Method	Kit/Manufacturer	Unit	*Cut-off*†	Laboratory*
Serum	*Corynebacterium diphtheriae.Diphtheria Toxoid Ab.IgG*	ELI	NA	IU/ml	0.057	GSK Biologicals or designated laboratory
Serum	*Clostridium tetani.Tetanus Toxoid Ab.IgG*	ELI	NA	IU/ml	0.043	GSK Biologicals or designated laboratory
Serum	*Bordetella pertussis.Pertussis Toxin Ab.IgG*	ELI	NA	IU/ml	2.693	GSK Biologicals or designated laboratory
Serum	*Bordetella pertussis.Filamentous Hemaglutinin Ab.IgG*	ELI	NA	IU/ml	2.046	GSK Biologicals or designated laboratory
Serum	*Bordetella pertussis.Pertactin Ab.IgG*	ELI	NA	IU/ml	2.187	GSK Biologicals or designated laboratory

ELI: ELISA
NEU: Neutralisation assay
NA: Not Applicable
IU/ml: International Units per millilitre
†Assays for diphtheria, tetanus and pertussis were re-developed and re-validated as per most recent CBER recommendations (Guidance for Industry "Bioanalytical Method Validation" from September 2013). The new assay cut-off's that apply are listed in the table.
*GSK Biologicals laboratory refers to the Clinical Laboratory Sciences (CLS) in Rixensart, Belgium and Wavre, Belgium.

- In general, the assay cut-off is the value under which there is no quantifiable result available. For an assay with a specific 'assay cut_off' , numerical immuno result is derived from a character field (rawres):
  - If rawres is 'NEG' or '-' or '(-)', numeric result= assay cut_off/2,
  - if rawres is 'POS' or '+' or '(+)', numeric result = assay cut_off,
  - if rawres is '< value' and value<=assay cut_off, numeric result =assay cut_off/2,
  - if rawres is '< value' and value>assay cut_off, numeric result =value,
  - if rawres is '> value' and value<assay cut_off, numeric result =assay cut_off/2,
  - if rawres is '> value' and value>=assay cut_off, numeric result =value,
  - if rawres is '<= value' or '>= value' and value<assay cut_off, numeric result =assay cut_off/2,
  - if rawres is '<= value' or '>= value' and value>=assay cut_off, numeric result =value,
  - if rawres is a value < assay cut_off, numeric result = assay cut_off/2,
  - if rawres is a value >= assay cut_off, numeric result = rawres,
  - else numeric result is left blank.

11.2.5. Safety analysis

11.2.5.1. Solicited Adverse Events

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.

The following rules will be used for the analysis of solicited symptoms:

- Subject who didn't document the presence or absence of a solicited symptom after one dose will be considered not having that symptom after that dose in the analysis done on "administered dose"
- Subjects who documented the absence of a solicited symptom after one dose will be considered not having that symptom 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 considered as having that symptom after that dose (at the lowest intensity).
- Intensity of the following solicited AEs will be assessed as described below.

Table 5 Intensity scales for solicited symptoms in adults

Adverse Event	Intensity grade	Parameter
Pain at injection site	0	None
	1	Mild: Any pain neither interfering with nor preventing normal every day activities.
	2	Moderate: Painful when limb is moved and interferes with every day activities.
	3	Severe: Significant pain at rest. Prevents normal every day activities.
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
Headache	0	Normal
	1	Mild: Headache that is easily tolerated
	2	Moderate: Headache that interferes with normal activity
	3	Severe: Headache that prevents normal activity
Fatigue	0	Normal
	1	Mild: Fatigue that is easily tolerated
	2	Moderate: Fatigue that interferes with normal activity
	3	Severe: Fatigue that prevents normal activity
Gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain)	0	Normal
	1	Mild: Gastrointestinal symptoms that are easily tolerated
	2	Moderate: Gastrointestinal symptoms that interfere with normal activity
	3	Severe: Gastrointestinal symptoms that prevent normal activity

*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 oral/axillary.

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

0 : Absent
1 : ≤ 20 mm
2 : > 20 mm and ≤ 50 mm
3 : > 50 mm

Event	N used for deriving % per subject for Vaccination phase	N used for deriving % per dose for Vaccination phase
Concomitant vaccination	All subjects with study vaccine administered	All study visits with study vaccine administered
Solicited general symptom	Primary analysis: all subjects with study vaccine administered Sensitivity analysis: all subjects with at least one solicited general symptom documented as either present or absent (i.e., symptom screen completed)	Primary analysis: all study visits with study vaccine administered Sensitivity analysis: all study visits with study vaccine administered and with at least one solicited general symptom documented as either present or absent (i.e., symptom screen completed)
Unsolicited symptom	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

Body temperature will be broken down by route of measurement according to the recommendations of the Brighton collaboration and will be summarized according to the 2 schemes described below:

- by 0.5 °C increments:
  - >=37.5
  - >=38.0
  - >38.5
  - >39.0
  - >39.5
  - >40.0

Fever, defined as a body temperature of ≥37.5°C irrespective of route of measurement, will be integrated to the summaries as a systemic adverse event.

11.2.5.2. Combined Solicited and Unsolicited Adverse Events

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
Fever	10016558	Fever
Headache	10019211	Headache
Fatigue	10016256	Fatigue
Gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain)	10017944	Gastrointestinal disorder
Pain at injection site	10022086	Injection site pain
Redness at injection site	10022098	Redness at injection site
Swelling at injection site	10053425	Swelling at injection site

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.

11.2.6. Management of missing data

Demography:

- For a given subject and a given demographic variable, missing measurements will not be replaced.

Immunogenicity:

- For a given subject and a given immunogenicity measurement time point, missing or non-evaluable measurements will not be replaced.

Reactogenicity and safety:

- Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) will be treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

11.2.7. 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
All summaries	% of count, including LL & UL of CI	1
All summaries	% of difference, including LL & UL of CI	2
Demographic characteristics	Mean, median age, SD (age)	1
Reactogenicity	Mean, Min, Q1, Median, Q3, Max for duration	1
Immunogenicity	Ratio of GMT/GMC	2
Immunogenicity	GMC	2 (D and T) 1 (PT, FHA and PRN)

12. ANNEX 3: STUDY SPECIFIC MOCK TFL

The following draft study specific mock TFLs will be used.

The data display, title and footnote are for illustration purpose and will be adapted to the study specificity such as one group and one dose for the study.

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. These editorial/minor changes will not lead to a SAP amendment.

Template 1 Number of subjects enrolled by center (Total Vaccinated Cohort)

	Combo group		Control group	Total	
Center	n		n	n	%
PPD	20		21	41	9.1
PPD	27		28	55	12.2
PPD	7		7	14	3.1
PPD	16		16	32	7.1
PPD	27		26	53	11.8
PPD	26		26	52	11.5
PPD	25		25	50	11.1
PPD	23		24	47	10.4
PPD	22		22	44	9.8
PPD	24		25	49	10.9
PPD	7		7	14	3.1
All	224		227	451	100

<group description >
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 vaccinated, completed and withdrawn with reason for withdrawal at Visit 3 (Total Vaccinated Cohort)

	dTpa Group	Control Group
Number of subjects vaccinated	300	300
Number of subjects completed	298	297
Number of subjects withdrawn	2	3
Reasons for withdrawal :		
Serious Adverse Event	0	1
Non-serious adverse event	0	0
Protocol violation	0	0
Consent withdrawal (not due to an adverse event)	1	2
Migrated/moved from study area	1	0
Lost to follow-up (subjects with incomplete vaccination course)	0	0
Lost to follow-up (subjects with complete vaccination course)	0	0
Others	0	0

HRV LIQ = HRV vaccine liquid formulation
HRV LYO = HRV vaccine HRV Lyophilised formulation
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed study visit 3
Withdrawn = number of subjects who did not come for study visit 3

Template 3 Number of subjects at each visit and list of withdrawn subjects (Total Vaccinated Cohort)

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
HRV Liq	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
	VISIT 4	492		
HRV Lyo	VISIT 1	257		
			no. PP	PROTOCOL VIOLATION
			no. PPD	CONSENT WITHDRAWAL
	VISIT 2	255		
			no. PPD	CONSENT WITHDRAWAL
	VISIT 3	254		
			no. PPD	MIGRATION FROM STUDY AREA
			no. PPD	LOST TO FOLLOW-UP
			no. PP	LOST TO FOLLOW-UP
			no. PP	CONSENT WITHDRAWAL
			no. PP	MIGRATION FROM STUDY AREA
			no. PPD	LOST TO FOLLOW-UP
			no. PPD	ADVERSE EXPERIENCE
	VISIT 4	247		

Template 4 Number of subjects enrolled into the study as well as the number of subjects excluded from ATP analyses with reasons for exclusion

	Total				HRV LIQ			HRV LYO		
Title	**N**	**n**	**s**	**%**	**N**	**n**	**s**	**N**	**n**	**s**
Total enrolled cohort	**1200**				**300**			**300**		
TVC	**1200**			**100**	**300**			**300**		
Administration of vaccine(s) forbidden in the protocol (code 1040)		2	2			0	0		0	0
Study vaccine dose not administered according to protocol (code 1070)		73	73			23	23		16	16
Initially seropositive or unknown anti-rotavirus IgA antibody on day of dose 1 (code 1500)		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 not related to the vaccine which may influence immune response (code 2070)		0	1			0	0		0	1
Non compliance with vaccination schedule (including wrong and unknown dates) (code 2080)		14	16			6	7		3	4
Non compliance 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
Subjects with incomplete study vaccination schedule but with post serological result (code 2500)		1	1			0	0		0	0
ATP	**998**			**83.2**	**244**			**252**		

HRV LIQ = HRV vaccine liquid formulation Lot C HRV LYO = HRV vaccine HRV Lyophilised formulation
Note: Subjects may have more than one 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 5 Deviations from specifications for age and intervals between study visits (Total Vaccinated Cohort)

		Age	VAC_1-SER_2	
Group		**Protocol**	**Protocol**	**Adapted**
		from 10 to 15 year	from 30 to 48 days	from 21 to 48 days
dTpaNew Group	N	335	329	329
	n	0	11	8
	%	0.0	3.3	2.4
	range	10 to 15	28 to 74	28 to 74
dTpaPre Group	N	336	329	329
	n	0	10	8
	%	0.0	3.0	2.4
	range	10 to 15	29 to 95	29 to 95

HRV LIQ = HRV vaccine liquid formulation Lot A
HRV LIQ = HRV vaccine liquid formulation Lot B
HRV LIQ = HRV vaccine liquid formulation Lot C
HRV LYO = HRV vaccine HRV Lyophilised formulation
dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
Adapted = interval used for defining the ATP cohorts for immunogenicity
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 = vaccination
SER = Blood Sampling

Template 6 Summary of demography and baseline characteristics (ATP cohort for Immunogenicity)

		dTpaNew Group N = 335		dTpaPre Group N = 336		Total N = 671	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age (years) at vaccination dose: 1	Mean						
	SD						
	Median						
	Minimum						
	Maximum						
Gender	Female						
	Male						
Geographic Ancestry	African Heritage / African American						
	American Indian or Alaskan Native						
	White - Arabic / North African Heritage						
	White - Caucasian / European Heritage						
	Other (Hispanic)						
Height (km)	Mean						
	SD						
	Median						
	Minimum						
	Maximum						
Weight (kg)	Mean						
	SD						
	Median						
	Minimum						
	Maximum						
BMI (kg/m²)	Mean						
	SD						
	Median						
	Minimum						
	Maximum						
Gestational week at dose 1	Below 27						
	27 to 32						
	33 to 36						
	Above 36						
	Mean						
	SD						
	Median						
	Minimum						
	Maximum						
Gestational week at delivery	Mean						
	SD						
	Median						
	Minimum						
	Maximum						

		dTpaNew Group N = 335		dTpaPre Group N = 336		Total N = 671	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Number of days between vaccination (dose 1) and delivery	Mean						
	SD						
	Median						
	Minimum						
	Maximum						
Breast feeding	Yes						
	No						
	Never						
Breast feeding (number of times in a day)	Mean						
	SD						
	Median						
	1st Quartile						
	3rd Quartile						
Duration of breast feeding	Mean						
	SD						
	Median						
Formula feeding	Yes						
	No						
Apgar score (1min)	Mean						
	SD						
	Median						
	Minimum						
	Maximum						
	Unknown						
Apgar score (5min)	Mean						
	SD						
	Median						
	Minimum						
	Maximum						
	Unknown						

dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
N = total number of subjects
n(%) = Number(percentage) of subjects in a given category
Value = value of the considered parameter
SD = standard deviation
Height (cm) = Height expressed in centimeters
Weight (kg) = Weight expressed in kilograms
BMI (kg/m^2) = Body Mass Index expressed in kilograms per meter square

Template 7 Study population (TVC)

Study population (Total vaccinated cohort)		
Number of subjects	**Combo group**	**Control group**
Planned, N	225	225
Randomised, N (Total Vaccinated Cohort)	224	227
Completed, n (%)	224 (100)	227 (100)
Demographics	**Combo 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)

Combo group = Subjects received DTPa-IPV/Hib vaccine as a single injection at 2, 4 and 6 months of age
Control group = Subjects received DTPa-IPV and Hib vaccines at different injection sites at 2, 4 and 6 months of age
N = Total number of subjects enrolled in the study
n/% = Number/percentage of subjects in a given category
SD = Standard Deviation
MeaAge = Age calculated from Date of birth to first study vaccination

Template 8 Summary of household contacts in Spain (Total vaccinated cohort: (subset of subjects in Spain))

		Household group	
		N =	
Characteristics	**Parameters or categories**	**n or value**	**%**
Household contacts approached	Yes No		
Number of household contacts by vaccinated subject	Mean		
	SD		
	Median		
	1st Quartile		
	3rd Quartile		
Household contact approached	Total		
Eligible Household contact	Total		

N = Total number of subjects vaccinated in Spain
n(%) = Number(percentage) of subjects in a given category
value = value of the considered parameter

Template 9 Summary of vaccination of household contacts in Spain (Total cohort for household contacts in Spain)

		Household Group			
		N =			
				95% CI	
	Parameters or Categories	Value or n	Per	LL	UL
Household contacts who accepted vaccination					
Household contacts who refused vaccination					
Reasons for refusal					
Reason 1					
Reason 2					

dTpa group = Mothers received dTpa during pregnancy
Control group = Mothers received placebo during pregnancy
N = Total number of eligible household contacts
n/Per = number/percentage of subjects reporting
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 10 Seropositivity and seroprotection rates and GMCs for anti-diphtheria and anti-tetanus antibodies before and one month after the booster vaccination and cord blood sample (ATP cohort for immunogenicity)

				≥ assay cut-off*				≥ 0.1 IU/mL				GMC		
						95% CI				95% CI			95% CI	
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**
anti-diphtheria	dTpaNew Group	PRE	321	284	88.5	84.5	91.8	83	25.9	21.2	31.0	0.472	0.403	0.553
		POST	321	320	99.7	98.3	100	315	98.1	96.0	99.3	6.784	6.178	7.450
		CORD												
	dTpaPre Group	PRE	319	286	89.7	85.8	92.8	89	27.9	23.0	33.2	0.456	0.392	0.530
		POST	319	319	100	98.9	100	310	97.2	94.7	98.7	6.493	5.915	7.128
		CORD												
anti-tetanus	dTpaNew Group	PRE	321	311	96.9	94.3	98.5	151	47.0	41.5	52.7	0.956	0.835	1.095
		POST	321	321	100	98.9	100	321	100	98.9	100	18.937	17.313	20.713
		CORD												
	dTpaPre Group	PRE	319	314	98.4	96.4	99.5	143	44.8	39.3	50.5	0.899	0.789	1.026
		POST	319	319	100	98.9	100	319	100	98.9	100	18.515	16.851	20.342
		CORD												

dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
Seroprotection=anti-diphtheria and anti-tetanus antibody concentration ≥0.1 IU/mL
*Assay cut-off is 0.057 IU/mL and 0.043 IU/mL for anti-diphtheria and anti-tetanus respectively
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 = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE=Pre-booster blood sampling time point
POST=Post-booster blood sampling time point

Template 11 GMC ratio between groups [dTpa Group divided by Control Group] and their 95% CIs for anti-PT, anti-FHA and anti-PRN antigens in cord blood sample (ATP cohort for immunogenicity)

	dTpa group		Control group		GMC Ratio (dTpa / Control)		
Antibody	N	GMC	N	GMC	GMC ratio	95% CI	
						LL	UL
anti-PT							
anti-FHA							
anti-PRN							

Tdap = Subjects receiving a second dose of Tdap vaccine
N= Number of subjects with available results
95% CI = 95% confidence interval for the adjusted GMC ratio LL = lower limit, UL = upper limit. The associated CI was will be computed using a two-sample t test assuming heterogeneity of variance.
GMC = geometric mean antibody concentration calculated on all subjects

Template 12 Vaccine responses for anti-PT, anti-FHA and anti-PRN antibody concentration one month after the booster vaccination (ATP cohort for immunogenicity)

				Booster response			
						95% CI	
Antibody	Group	Pre-vaccination status	N	n	%	LL	UL
anti-PT	dTpaNew Group	S-	142	135	95.1	90.1	98.0
		S+ (< 4*assay cut-off)	104	103	99.0	94.8	100
		S+ (≥4*assay cut-off)	71	60	84.5	74.0	92.0
		Total	317	298	94.0	90.8	96.4
	dTpaPre Group	S-	143	131	91.6	85.8	95.6
		S+ (<4*assay cut-off)	114	112	98.2	93.8	99.8
		S+ (≥4*assay cut-off)	61	52	85.2	73.8	93.0
		Total	318	295	92.8	89.3	95.4
anti-FHA	dTpaNew Group	S-	6	6	100	54.1	100
		S+ (<4*assay cut-off)	57	57	100	93.7	100
		S+ (≥4*assay cut-off)	251	242	96.4	93.3	98.3
		Total	314	305	97.1	94.6	98.7
	dTpaPre Group	S-	5	5	100	47.8	100
		S+ (<4*assay cut-off)	55	55	100	93.5	100
		S+ (≥4*assay cut-off)	255	244	95.7	92.4	97.8
		Total	315	304	96.5	93.8	98.2
anti-PRN	dTpaNew Group	S-	52	50	96.2	86.8	99.5
		S+ (<4*assay cut-off)	152	151	99.3	96.4	100
		S+ (≥4*assay cut-off)	117	114	97.4	92.7	99.5
		Total	321	315	98.1	96.0	99.3
	dTpaPre Group	S-	47	47	100	92.5	100
		S+ (<4*assay cut-off)	159	159	100	97.7	100
		S+ (≥4*assay cut-off)	112	111	99.1	95.1	100
		Total	318	317	99.7	98.3	100

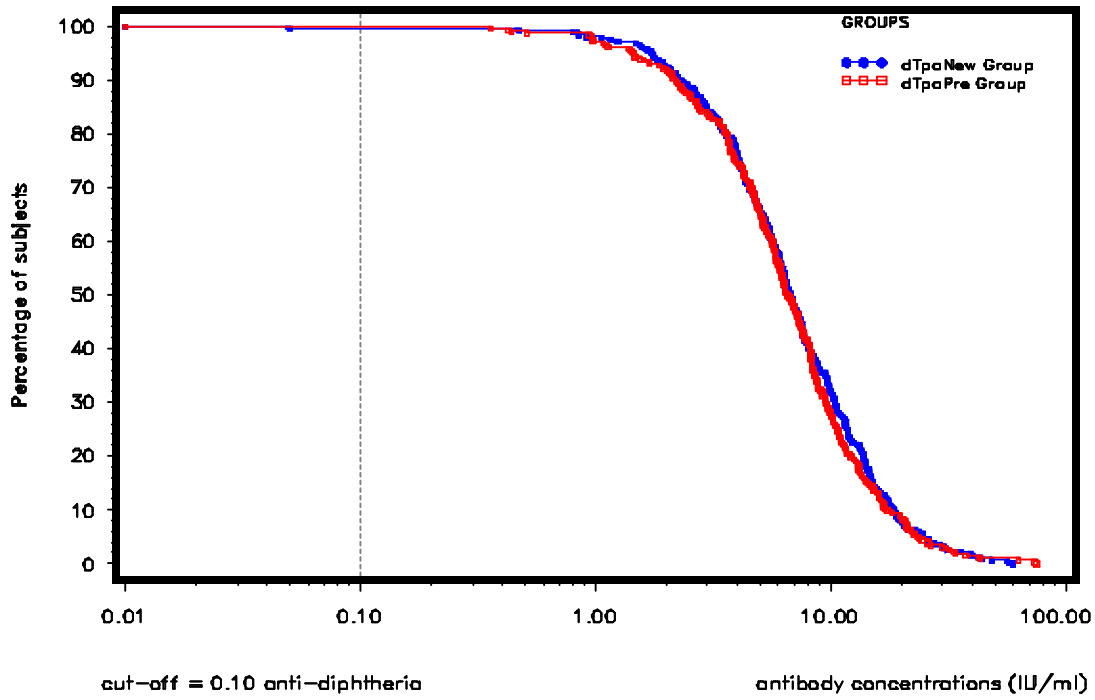
dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
S- = Initially seronegative subjects prior to vaccination
S+ = Initially seropositive subjects prior to vaccination
Total = subjects either seropositive or seronegative at pre-vaccination
S- = seronegative subjects (antibody concentration below assay cut off for anti-PT, anti-FHA, anti-PRN)
S+ = seropositive (antibody concentration below assay cut off for anti-PT, anti-FHA, anti-PRN)

Booster response to PT, FHA and PRN antigens is defined as:

- initially seronegative subjects (pre-booster antibody concentration below the assay cut-off) with an increase of at least four times the assay cut-off one month after vaccination,
- initially seropositive subjects with anti-body concentration < four times the assay cut-off with an increase of at least four times the pre-booster antibody concentration one month after vaccination
- initially seropositive subjects with anti-body concentration ≥ four times the assay cut-off with an increase of at least two times the pre-booster antibody concentration one month after vaccination

Assay cut-off is 2.693 IU/mL, 2.046 IU/mL and 2.187 IU/mL for anti-PT, FHA and PRN respectively
N = number of subjects with both pre- and post-vaccination results available
n(%) = number(percentage) of subjects with a booster response
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 13 Reverse cumulative curve for anti-diphtheria antibody concentration one month after the booster vaccination (ATP cohort for immunogenicity)



dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
PRE = Pre-vaccination at Day 0
POST = Post-vaccination 1 at Day 28 for primed subject or post-vaccination 2 at Day 56 for unprimed subjects

Template 14 Percentage of subjects by pregnancy outcome (Total vaccinated cohort-Mother)

	dTpa Group				Control Group			
	N =				N =			
			95% CI				95% CI	
Pregnancy outcome	**n**	**Per**	**LL**	**UL**	**n**	**Per**	**LL**	**UL**
Live infant NO apparent congenital anomaly								
Live infant congenital anomaly								
Elective termination NO apparent congenital anomaly								
Elective termination congenital anomaly								
Spontaneous abortion NO apparent congenital anomaly								
Spontaneous abortion congenital anomaly								
Stillbirth NO apparent congenital anomaly								
Stillbirth congenital anomaly								
Ectopic pregnancy								
Molar pregnancy								
Lost to follow-up								
Pregnancy ongoing								

dTpa group = Mothers received dTpa during pregnancy
Control group = Mothers received placebo during pregnancy
N = number of subjects with at least one administered dose
n/Per = number/percentage of subjects reporting a specific pregnancy outcome
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 15 Percentage of subjects with listed pregnancy/neonate related adverse events of interest (Total vaccinated cohort)

Pregnancy-related adverse events of interest/neonate-related events of interest	dTpa Group N =				Control Group N =			
	n	%	Exact 95%CI		n	%	Exact 95%CI	
			LL	UL			LL	UL
Gestational diabetes								
Pregnancy-related hypertension								
Premature rupture of membranes								
Preterm premature rupture of membranes								
Premature labour								
Premature uterine contractions								
Intrauterine growth restriction/poor foetal growth								
Pre-eclampsia								
Eclampsia								
Vaginal or intrauterine haemorrhage								
Maternal death								
Preterm birth								
Neonatal death								
Small for gestational age								
Neonatal hypoxic ischaemic encephalopathy								
Failure to thrive/growth deficiency								

dTpa group = Mothers received dTpa during pregnancy
Control group = Mothers received placebo during pregnancy
N = number of subjects with at least one administered dose
n/Per = number/percentage of pregnancies/neonate with a specific adverse event
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 16 Number and percentage of subjects who received study vaccine doses - TVC

		HRV LIQ N = 300		HRV LYO N = 300		Total N = 1200	
VACCINE	Total number of doses received	n	%	n	%	n	%
Pediarix	1	0	0.0	1	0.3	3	0.3
	2	300	100	299	99.7	1197	99.8
	3						
Any	Any	300	100	300	100	1200	100
Hiberix	1	0	0.0	1	0.3	3	0.3
	2	300	100	299	99.7	1197	99.8
	3						
Any	Any	300	100	300	100	1200	100
Prevnar	1	0	0.0	1	0.3	3	0.3
	2	300	100	299	99.7	1197	99.8
	3						
Any ON COAD	Any	300	100	300	100	1200	100

HRV LIQ = HRV vaccine Liquid formulation lot A HRV LIQ = HRV vaccine Liquid formulation lot B
HRV LIQ = HRV vaccine Liquid formulation lot C HRV LYO = HRV vaccine HRV Lyophilised formulation
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 one dose

Template 17 Compliance in returning symptom information (Total Vaccinated Cohort)

Group	Number of doses	Doses NOT according to protocol	Number of general SS	Compliance % general SS	Number of local SS	Compliance % local SS
dTpaNew Group	335	0	330	98.5	330	98.5
dTpaPre Group	336	1	329	97.9	329	97.9

dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
SS = Symptom screens/sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom screen/sheet return / number of administered doses) X 100

Template 18 Incidence and nature of grade 3 symptoms (solicited and unsolicited) reported during the 4-day (Days 0-3) period after vaccination 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
dTpaNew Group	335	264	78.8	74.0	83.1	335	134	40.0	34.7	45.5	335	250	74.6	69.6	79.2
dTpaPre Group	336	279	83.0	78.6	86.9	336	151	44.9	39.5	50.4	336	264	78.6	73.8	82.8

dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
N = number of subjects with the administered dose
n(%)= number(percentage) of subjects presenting at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 19 Incidence of solicited local symptoms reported during the 4-day (Days 0-3) period after vaccination following each dose and overall (Total Vaccinated Cohort)

		dTpaNew Group					dTpaPre Group				
					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Pain	All	330	237	71.8	66.6	76.6	329	248	75.4	70.4	79.9
	Grade 3	330	24	7.3	4.7	10.6	329	20	6.1	3.8	9.2
	Medical advice	330	0	0.0	0.0	1.1	329	0	0.0	0.0	1.1
Redness (mm)	All	330	113	34.2	29.1	39.6	329	94	28.6	23.8	33.8
	Grade 3	330	4	1.2	0.3	3.1	329	1	0.3	0.0	1.7
	Medical advice	330	0	0.0	0.0	1.1	329	0	0.0	0.0	1.1
Swelling (mm)	All	330	98	29.7	24.8	34.9	329	90	27.4	22.6	32.5
	Grade 3	330	6	1.8	0.7	3.9	329	5	1.5	0.5	3.5
	Medical advice	330	0	0.0	0.0	1.1	329	0	0.0	0.0	1.1

dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
N = number of subjects with the documented dose
n(%)= number(percentage) of subjects reporting the symptom at least once
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 20 Incidence of solicited general symptoms reported during the 4-day (Days 0-3) post-vaccination period (Total Vaccinated Cohort)

		Boostrix					Adacel					Control				
					95 % CI					95 % CI					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Fatigue	All	306	71	23.2	18.6	28.3	137	23	16.8	11.0	24.1	358	51	14.2	10.8	18.3
	Grade 2 or 3	306	23	7.5	4.8	11.1	137	10	7.3	3.6	13.0	358	9	2.5	1.2	4.7
	Grade 3	306	3	1.0	0.2	2.8	137	1	0.7	0.0	4.0	358	0	0.0	0.0	1.0
	Related	306	57	18.6	14.4	23.4	137	21	15.3	9.7	22.5	358	34	9.5	6.7	13.0
	Grade 3 Related	306	3	1.0	0.2	2.8	137	1	0.7	0.0	4.0	358	0	0.0	0.0	1.0
	Medical advice	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
Gastrointestinal symptoms	All	306	27	8.8	5.9	12.6	137	4	2.9	0.8	7.3	358	29	8.1	5.5	11.4
	Grade 2 or 3	306	6	2.0	0.7	4.2	137	0	0.0	0.0	2.7	358	9	2.5	1.2	4.7
	Grade 3	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
	Related	306	18	5.9	3.5	9.1	137	4	2.9	0.8	7.3	358	17	4.7	2.8	7.5
	Grade 3 Related	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
	Medical advice	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
Headache	All	306	52	17.0	13.0	21.7	137	25	18.2	12.2	25.7	358	53	14.8	11.3	18.9
	Grade 2 or 3	306	12	3.9	2.0	6.7	137	6	4.4	1.6	9.3	358	8	2.2	1.0	4.4
	Grade 3	306	0	0.0	0.0	1.2	137	1	0.7	0.0	4.0	358	1	0.3	0.0	1.5
	Related	306	37	12.1	8.7	16.3	137	19	13.9	8.6	20.8	358	28	7.8	5.3	11.1
	Grade 3 Related	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
	Medical advice	306	1	0.3	0.0	1.8	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
Temperature (°C)	All	306	2	0.7	0.1	2.3	137	0	0.0	0.0	2.7	358	2	0.6	0.1	2.0
	>38.5	306	1	0.3	0.0	1.8	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
	>39.0	306	1	0.3	0.0	1.8	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
	>39.5	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
	>40.0	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
	Related	306	2	0.7	0.1	2.3	137	0	0.0	0.0	2.7	358	2	0.6	0.1	2.0
	>40.0 Related	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0
	Medical advice	306	0	0.0	0.0	1.2	137	0	0.0	0.0	2.7	358	0	0.0	0.0	1.0

dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
N = number of subjects with the documented dose
n(%)= number(percentage) of subjects reporting the symptom at least once
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit
Related = Symptoms which is assessed by the investigator as related to vaccination
Grade3*Related = Grade 3 symptom which is assessed by the investigator as related to vaccination
Grade 3 For Headache: Headache that prevented normal activity
For Fatigue: Fatigue that prevented normal activity
For Gastrointestinal symptoms: Gastrointestinal symptoms that prevented normal activity
For Fever: >39.0 °C

Template 21 Incidence of any large injection site reaction (defined as a swelling with a diameter > 100 mm, noticeable diffuse swelling or noticeable increase in limb circumference) with onset within 4 days (Day 0–3) after booster vaccination (Total Vaccinated Cohort at Year 9)

Type of Swelling	(Each group) N=				Total N=			
	n	%	95%CI		n	%	95% CI	
			LL	UL			LL	UL
Any								
Local Swelling								
Diffuse Swelling								
Involving at least one adjacent joint								

Boostrix group= Subjects who had received GSK Biologicals' Tdap vaccine (Boostrix) in study 106316 and a second dose of Tdap vaccine (Boostrix) at Year 9 Visit 6
Adacel group= Subjects who had received Sanofi Pasteurs' Tdap vaccine (Adacel) in study 106316 and a second dose of Tdap vaccine (Boostrix) at Year 9 Visit 6
Control group= Subjects who will receive the first dose of Tdap vaccine (Boostrix) at Year 9 Visit 6
N = Number of subjects with documented dose
n/% = number/percentage of subjects reporting a specified symptom
95% CI = Exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 22 Percentage of doses with grade 3 unsolicited symptoms classified by MedDRA SOC and PT from Day 0 to Day 30 after vaccination in each HRV vaccine liquid formulation group - TVC

		HRV LIQ N = 603				HRV LIQ N = 600			
				95% CI				95% CI	
Primary System Organ Class (CODE)	Preferred Term (CODE)	n	%	LL	UL	n	%	LL	UL
At least one symptom		30	5.0	3.4	7.0	38	6.3	4.5	8.6
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	1	0.2	0.0	0.9	0	0.0	0.0	0.6
Eye disorders (10015919)	Conjunctivitis (10010741)	1	0.2	0.0	0.9	1	0.2	0.0	0.9
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	2	0.3	0.0	1.2	1	0.2	0.0	0.9
	Flatulence (10016766)	1	0.2	0.0	0.9	2	0.3	0.0	1.2
General disorders and administration site conditions (10018065)	Injection site erythema (10022061)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
	Injection site pain (10022086)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
	Injection site swelling (10053425)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
	Irritability (10022998)	1	0.2	0.0	0.9	1	0.2	0.0	0.9
	Pyrexia (10037660)	3	0.5	0.1	1.4	4	0.7	0.2	1.7
Immune system disorders (10021428)	Hypersensitivity (10020751)	1	0.2	0.0	0.9	0	0.0	0.0	0.6
Infections and infestations (10021881)	Bronchitis (10006451)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
	Ear infection (10014011)	3	0.5	0.1	1.4	2	0.3	0.0	1.2
	Exanthema subitum (10015586)	1	0.2	0.0	0.9	0	0.0	0.0	0.6
	Eye infection (10015929)	0	0.0	0.0	0.6	0	0.0	0.0	0.6
	Gastroenteritis (10017888)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
	Impetigo (10021531)	0	0.0	0.0	0.6	0	0.0	0.0	0.6
	Influenza (10022000)	1	0.2	0.0	0.9	0	0.0	0.0	0.6
	Laryngitis (10023874)	0	0.0	0.0	0.6	0	0.0	0.0	0.6
	Otitis media (10033078)	7	1.2	0.5	2.4	12	2.0	1.0	3.5
	Perianal abscess (10034447)	0	0.0	0.0	0.6	0	0.0	0.0	0.6
	Pneumonia (10035664)	1	0.2	0.0	0.9	0	0.0	0.0	0.6
	Respiratory tract infection (10062352)	2	0.3	0.0	1.2	0	0.0	0.0	0.6
	Respiratory tract infection viral (10062106)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
	Rhinitis (10039083)	1	0.2	0.0	0.9	3	0.5	0.1	1.5
	Upper respiratory tract infection (10046306)	6	1.0	0.4	2.2	8	1.3	0.6	2.6
	Varicella (10046980)	1	0.2	0.0	0.9	2	0.3	0.0	1.2
Psychiatric disorders (10037175)	Crying (10011469)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.2	0.0	0.9	6	1.0	0.4	2.2
	Nasal congestion (10028735)	0	0.0	0.0	0.6	0	0.0	0.0	0.6
	Rales (10037833)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
Skin and subcutaneous tissue disorders	Dermatitis allergic (10012434)	1	0.2	0.0	0.9	0	0.0	0.0	0.6

		HRV LIQ N = 603				HRV LIQ N = 600			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
(10040785)	Eczema (10014184)	0	0.0	0.0	0.6	1	0.2	0.0	0.9
	Rash (10037844)	0	0.0	0.0	0.6	0	0.0	0.0	0.6

HRV LIQ = HRV vaccine liquid formulation Lot A
HRV LIQ = HRV vaccine liquid formulation Lot B
HRV LIQ = HRV vaccine liquid formulation Lot C
N = Total number of doses administered
n/% = number/percentage of doses followed by at least one report of the specified unsolicited symptom
At least one symptom = number of doses followed by at least one report of an unsolicited symptom whatever the MedDRA PT
95% CI = Exact 95% Confidence Interval; LL = Lower Limit, UL = Upper Limit

Template 23 Number (%) of subjects with serious adverse events from first study vaccination up to Visit 3 including number of events reported (TVC)

			Gr 1 N =			Gr2 N =		
Type of Event	**Primary System Organ Class**	**Preferred Term (CODE)**	**n***	**n**	**%**	**n***	**n**	**%**
SAE	At least one symptom							
	<each SOC>	<each PT term>						
Related SAE	At least one symptom							
	<each SOC>	<each PT term>						
Fatal SAE	At least one symptom							
	<each SOC>	<each PT term>						
Related fatal SAE	At least one symptom							
	<each SOC>	<each PT term>						

Gr 1 = Group 1 description
Gr 2 = Group 2 description
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 24 Subjects with Serious Adverse Events reported up to Visit 3 - TVC

Sub. No.	Case Id	Age at onset (Week)	Sex	Verbatim	Preferred term	System Organ Class	MA type	Dose	Day of onset	Duration	Causality	Outcome
P P	PPD	12	M	Kawasaki's disease	Kawasaki's disease	Infections and infestations	HO	1	12	29	N	Recovered/resolved
PP D	PPD	18	M	Influenza-b	Influenza	Infections and infestations	HO	2	2	5	N	Recovered/resolved
PP D	PPD	17	M	Acute gastroenteritis	Gastroenteritis	Infections and infestations	HO	2	9	5	N	Recovered/resolved
PP D	PPD	17	F	Infantile spasms	Infantile spasms	Nervous system disorders	HO	2	2	51	N	Recovered/resolved with sequelae
PP D	PPD	21	M	Rs-virus bronchiolitis	Respiratory syncytial virus bronchiolitis	Infections and infestations	HO	2	30	16	N	Recovered/resolved
PP D	PPD	13	M	Gastroenteritis	Gastroenteritis	Infections and infestations	HO	1	25	6	N	Recovered/resolved
PP D	PPD	22	M	Pneumonia	Pneumonia	Infections and infestations	HO	2	32	13	N	Recovered/resolved
		23		Middle ear infection	Otitis media	Infections and infestations	HO	2	37	8	N	Recovered/resolved
PP D	PPD	14	F	Secretory otitis media	Otitis media	Infections and infestations	HO	1	7	25	N	Recovered/resolved
PPD	PPD	20	M	Viral pneumonia	Pneumonia viral	Infections and infestations	HO	2	13	23	N	Recovered/resolved
PPD	PPD	14	M	Middle ear infection, left	Otitis media	Infections and infestations	HO	1	19	8	N	Recovered/resolved
		14		Pneumonia	Pneumonia	Infections and infestations	HO	1	19	8	N	Recovered/resolved
PPD	PPD	13	M	Acute lymphadenitis	Lymphadenitis	Blood and lymphatic system disorders	HO	1	13	22	N	Recovered/resolved
PPD	PPD	10	F	Pyelonephritis acute	Pyelonephritis acute	Infections and infestations	HO	1	6	12	N	Recovered/resolved
PPD	PPD	19	M	Laryngitis	Laryngitis	Infections and infestations	HO	2	11	7	N	Recovered/resolved

Sub. No.	Case Id	Age at onset (Week)	Sex	Verbatim	Preferred term	System Organ Class	MA type	Dose	Day of onset	Duration	Causality	Outcome
PPD	PPD	14	M	Bronchitis acuta	Bronchitis	Infections and infestations	HO	1	23	12	N	Recovered/resolved
PPD	PPD	19	M	Bronchiolitis acuta	Bronchiolitis	Infections and infestations	HO	2	26	7	N	Recovered/resolved
PPD	PPD	19	F	Laryngitis acuta	Laryngitis	Infections and infestations	HO	2	7	4	N	Recovered/resolved
PPD	PPD	18	F	Laryngitis	Laryngitis	Infections and infestations	HO	2	7	4	N	Recovered/resolved
PPD	PPD	14	F	Gastroenteritis	Gastroenteritis	Infections and infestations	HO	1	22	7	N	Recovered/resolved

MA = medical attention
HO = hospitalisation
Dose = dose given prior to the start of the SAE
Day of onset = number of days since last study vaccine dose

Template 25 Number and percentage of doses and of subjects who took at least one concomitant medication from Day 0 to Day 7 after vaccination by type in each HRV vaccine liquid formulation group - TVC

	HRV LIQ					HRV LIQ					HRV LIQ				
				95% CI					95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1															
Any	298	173	58.1	52.2	63.7	302	175	57.9	52.2	63.6	300	157	52.3	46.5	58.1
Any antipyretic	298	97	32.6	27.3	38.2	302	94	31.1	25.9	36.7	300	71	23.7	19.0	28.9
Prophylactic antipyretic	298	8	2.7	1.2	5.2	302	6	2.0	0.7	4.3	300	9	3.0	1.4	5.6
Dose 2															
Any	297	105	35.4	29.9	41.1	301	117	38.9	33.3	44.6	300	89	29.7	24.6	35.2
Any antipyretic	297	98	33.0	27.7	38.7	301	109	36.2	30.8	41.9	300	86	28.7	23.6	34.1
Prophylactic antipyretic	297	7	2.4	1.0	4.8	301	8	2.7	1.2	5.2	300	6	2.0	0.7	4.3
Overall/dose															
Any	595	278	46.7	42.7	50.8	603	292	48.4	44.4	52.5	600	246	41.0	37.0	45.1
Any antipyretic	595	195	32.8	29.0	36.7	603	203	33.7	29.9	37.6	600	157	26.2	22.7	29.9
Prophylactic antipyretic	595	15	2.5	1.4	4.1	603	14	2.3	1.3	3.9	600	15	2.5	1.4	4.1
Overall/subject															
Any	298	194	65.1	59.4	70.5	302	205	67.9	62.3	73.1	300	182	60.7	54.9	66.2
Any antipyretic	298	130	43.6	37.9	49.5	302	141	46.7	41.0	52.5	300	111	37.0	31.5	42.7
Prophylactic antipyretic	298	11	3.7	1.9	6.5	302	12	4.0	2.1	6.8	300	13	4.3	2.3	7.3

HRV LIQ = HRV vaccine liquid formulation Lot A
HRV LIQ = HRV vaccine liquid formulation Lot B
HRV LIQ = HRV vaccine liquid formulation Lot C
For each dose and overall/subject:
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned 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 mentioned period
95% CI = exact 95% Confidence Interval, LL = Lower Limit, UL = Upper Limit

Template 26 Solicited and Unsolicited symptoms 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)

		HPV_2D N =			MMR_DTPa N =		
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**n***	**n**	**%**
At least one symptom							
<each SOC>	<each PT term>						

HPV_2D = females aged 4-6 years who received two doses of HPV-16/18 L1 VLP AS04 vaccine at Day 0 and Month 6
MMR_DTPa = females aged 4-6 years who received MMR vaccine at Day 0 and DTPa vaccine at Month 6
At least one symptom = at least one 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 27 Minimum and maximum activity dates (TVC)

Visit	Minimum date	Maximum date
1	19JUN2007	29DEC2007
2	24JUL2007	08FEB2008
3	24AUG2007	18MAR2008
4	25MAR2008	22NOV2008
5	24MAR2009	31MAR2009*

*Database Lock Date = 31MAR2009

Template 28 Number of enrolled subjects by age category (TVC)

		dTpa group-Mother N =	Control group - Mother	dTpa group-Infant N =	Control group - Infant	Household group
Characteristics	**Categories**	**n**	**n**	**n**	**n**	**n**
Age category	In utero					
	Preterm newborn infants (gestational age < 37 wks)					
	Newborns (0-27 days)					
	Infants and toddlers (28 days-23 months)					
	Children (2-11 years)					
	Adolescents (12-17 years)					
	Adults (18-64 years)					
	From 65-84 years					
	85 years and over					
	Missing					

Gr 1 = Group 1 description
Gr 2 = Group 2 description
Gr 3 = Group 3 description
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 = <describe missing>

Template 29 Number of subjects by country

	ACWY-TT N = 259	ACWYHPV N = 259	HPV N = 261	Co-ad N = 260	Tdap N = 261	Total N = 1300
Country	**n**	**n**	**N**	**n**	**n**	**n**
Dominican Republic	86	87	88	87	87	435
Estonia	87	86	87	87	88	435
Thailand	86	86	86	86	86	430

ACWY-TT = Subjects who received MenACWY-TT at Month 0 and Cervarix at Month 1, 2 and 7
ACWYHPV = Subjects who received MenACWY-TT and Cervarix at Month 0 and Cervarix at Month 1 and 6
HPV = Subjects who received Cervarix at Month 0, 1 and 6
Co-ad = Subjects who received MenACWY-TT, Cervarix and Boostrix at Month 0 and Cervarix at Month 1 and 6
Tdap = Subjects who received Boostrix and Cervarix at Month 0 and Cervarix at Month 1 and 6
N = number of subjects
n= number of enrolled subjects included in each group or in total for a given age category or for all age categories

Template 30 Listing of dropouts due to AEs, SAEs and solicited symptoms (Total cohort)

Study-Subject No.	Country	Gender	AE Description	SAE	Causality	Outcome	Type of discontinuation
PPD	Germany	F	SUBJECT DIED	Y		Fatal	Study at visit/contact: VISIT11 (Y5)
PPD	Germany	F	SUBJECT DIED	Y		Fatal	Study at visit/contact: VISIT11 (Y5)

Template 31 Summary of demographic characteristics of household contacts in Spain (Total cohort for household contacts in Spain)

		Household Group			
		N =			
				95% CI	
	Parameters or Categories	Value or n	Per	LL	UL
Age at vaccination	Mean				
	SD				
	Median				
	Minimum				
	Maximum				
Gender	Female				
	Male				
Geographic ancestry	African Heritage / African American				
	American Indian or Alaskan Native				
	White - Arabic / North African Heritage				
	White - Caucasian / European Heritage				
	Other (Hispanic)				

dTpa group = Mothers received dTpa during pregnancy
Control group = Mothers received placebo during pregnancy
N = Total number of eligible household contacts
n/Per = number/percentage of subjects reporting
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Table 6 Percentage of subjects with grade 3 unsolicited symptoms classified by MedDRA SOC and PT from Day 0 to Day 30 after any vaccination (Total Vaccinated Cohort)

Primary System Organ Class (CODE)	Preferred Term (CODE)	HRV LIQ N = 298				HRV LIQ N = 302				HRV LIQ N = 300			
				95% CI				95% CI				95% CI	
		n	%	LL	UL	n	%	LL	UL	n	%	LL	UL
At least one symptom		24	8.1	5.2	11.7	26	8.6	5.7	12.4	33	11.0	7.7	15.1
Ear and labyrinth disorders (10013993)	Ear pain (10014020)	0	0.0	0.0	1.2	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Eye disorders (10015919)	Conjunctivitis (10010741)	1	0.3	0.0	1.9	1	0.3	0.0	1.8	1	0.3	0.0	1.8
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)	0	0.0	0.0	1.2	2	0.7	0.1	2.4	1	0.3	0.0	1.8
	Flatulence (10016766)	1	0.3	0.0	1.9	1	0.3	0.0	1.8	2	0.7	0.1	2.4
General disorders and administration site conditions (10018065)	Injection site erythema (10022061)	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Injection site pain (10022086)	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Injection site swelling (10053425)	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Irritability (10022998)	0	0.0	0.0	1.2	1	0.3	0.0	1.8	1	0.3	0.0	1.8
	Pyrexia (10037660)	4	1.3	0.4	3.4	3	1.0	0.2	2.9	4	1.3	0.4	3.4
Immune system disorders (10021428)	Hypersensitivity (10020751)	0	0.0	0.0	1.2	1	0.3	0.0	1.8	0	0.0	0.0	1.2
Infections and infestations (10021881)	Bronchitis (10006451)	2	0.7	0.1	2.4	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Ear infection (10014011)	1	0.3	0.0	1.9	3	1.0	0.2	2.9	2	0.7	0.1	2.4
	Exanthema subitum (10015586)	1	0.3	0.0	1.9	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Eye infection (10015929)	1	0.3	0.0	1.9	0	0.0	0.0	1.2	0	0.0	0.0	1.2
	Gastroenteritis (10017888)	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Impetigo (10021531)	1	0.3	0.0	1.9	0	0.0	0.0	1.2	0	0.0	0.0	1.2
	Influenza (10022000)	0	0.0	0.0	1.2	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Laryngitis (10023874)	1	0.3	0.0	1.9	0	0.0	0.0	1.2	0	0.0	0.0	1.2
	Otitis media (10033078)	5	1.7	0.5	3.9	6	2.0	0.7	4.3	11	3.7	1.8	6.5
	Perianal abscess (10034447)	1	0.3	0.0	1.9	0	0.0	0.0	1.2	0	0.0	0.0	1.2

Primary System Organ Class (CODE)	Preferred Term (CODE)	HRV LIQ N = 298				HRV LIQ N = 302				HRV LIQ N = 300			
		n	%	95% CI LL	95% CI UL	n	%	95% CI LL	95% CI UL	n	%	95% CI LL	95% CI UL
	Pneumonia (10035664)	0	0.0	0.0	1.2	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Respiratory tract infection (10062352)	3	1.0	0.2	2.9	2	0.7	0.1	2.4	0	0.0	0.0	1.2
	Respiratory tract infection viral (10062106)	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Rhinitis (10039083)	2	0.7	0.1	2.4	1	0.3	0.0	1.8	3	1.0	0.2	2.9
	Upper respiratory tract infection (10046306)	2	0.7	0.1	2.4	5	1.7	0.5	3.8	7	2.3	0.9	4.7
	Varicella (10046980)	0	0.0	0.0	1.2	1	0.3	0.0	1.8	2	0.7	0.1	2.4
Psychiatric disorders (10037175)	Crying (10011469)	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Respiratory, thoracic and mediastinal disorders (10038738)	Cough (10011224)	1	0.3	0.0	1.9	1	0.3	0.0	1.8	6	2.0	0.7	4.3
	Nasal congestion (10028735)	1	0.3	0.0	1.9	0	0.0	0.0	1.2	0	0.0	0.0	1.2
	Rales (10037833)	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
Skin and subcutaneous tissue disorders (10040785)	Dermatitis allergic (10012434)	1	0.3	0.0	1.9	1	0.3	0.0	1.8	0	0.0	0.0	1.2
	Eczema (10014184)	0	0.0	0.0	1.2	0	0.0	0.0	1.2	1	0.3	0.0	1.8
	Rash (10037844)	2	0.7	0.1	2.4	0	0.0	0.0	1.2	0	0.0	0.0	1.2

HRV LIQ = HRV vaccine liquid formulation Lot A
HRV LIQ = HRV vaccine liquid formulation Lot B
HRV LIQ = HRV vaccine liquid formulation Lot C
N = number of subjects with at least one administered dose
n/% = number/percentage of subjects reporting at least once a specified unsolicited symptom
At least one symptom = number of subjects reporting at least one unsolicited symptom, whatever the MedDRA PT
95% CI = exact 95% Confidence Interval, LL = Lower Limit, UL = Upper Limit

Table 7 Number (%) of subjects with serious adverse events from first study vaccination up to Visit 3 including number of events reported (Total Vaccinated Cohort)

			Gr 1 N =			Gr2 N =		
Type of Event	**Primary System Organ Class**	**Preferred Term (CODE)**	**n***	**n**	**%**	**n***	**n**	**%**
SAE	At least one symptom							
	<each SOC>	<each PT term>						
Related SAE	At least one symptom							
	<each SOC>	<each PT term>						
Fatal SAE	At least one symptom							
	<each SOC>	<each PT term>						
Related fatal SAE	At least one symptom							
	<each SOC>	<each PT term>						

Gr 1 = Group 1 description
Gr 2 = Group 2 description
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the symptom at least once

Table 8 Subjects with Serious Adverse Events reported up to Visit 2 (Total Vaccinated Cohort)

Sub. No.	Case Id	Age at onset (Week)	Sex	Verbatim	Preferred term	System Organ Class	MA type	Dose	Day of onset	Duration	Causality	Outcome
PPD	PPD	12	M	Kawasaki's disease	Kawasaki's disease	Infections and infestations	HO	1	12	29	N	Recovered/resolved
PPD	PPD	18	M	Influenza-b	Influenza	Infections and infestations	HO	2	2	5	N	Recovered/resolved
PPD	PPD	17	M	Acute gastroenteritis	Gastroenteritis	Infections and infestations	HO	2	9	5	N	Recovered/resolved
PPD	PPD	17	F	Infantile spasms	Infantile spasms	Nervous system disorders	HO	2	2	51	N	Recovered/resolved with sequelae
PPD	PPD	21	M	Rs-virus bronchiolitis	Respiratory syncytial virus bronchiolitis	Infections and infestations	HO	2	30	16	N	Recovered/resolved
PPD	PPD	13	M	Gastroenteritis	Gastroenteritis	Infections and infestations	HO	1	25	6	N	Recovered/resolved
PPD	PPD	22	M	Pneumonia	Pneumonia	Infections and infestations	HO	2	32	13	N	Recovered/resolved
		23		Middle ear infection	Otitis media	Infections and infestations	HO	2	37	8	N	Recovered/resolved
PPD	PPD	14	F	Secretory otitis media	Otitis media	Infections and infestations	HO	1	7	25	N	Recovered/resolved
PPD	PPD	20	M	Viral pneumonia	Pneumonia viral	Infections and infestations	HO	2	13	23	N	Recovered/resolved
PPD	PPD	14	M	Middle ear infection, left	Otitis media	Infections and infestations	HO	1	19	8	N	Recovered/resolved
		14		Pneumonia	Pneumonia	Infections and infestations	HO	1	19	8	N	Recovered/resolved
PPD	PPD	13	M	Acute lymphadenitis	Lymphadenitis	Blood and lymphatic system disorders	HO	1	13	22	N	Recovered/resolved
PPD	PPD	10	F	Pyelonephritis acute	Pyelonephritis acute	Infections and infestations	HO	1	6	12	N	Recovered/resolved
PPD	PPD	19	M	Laryngitis	Laryngitis	Infections and infestations	HO	2	11	7	N	Recovered/resolved

Sub. No.	Case Id	Age at onset (Week)	Sex	Verbatim	Preferred term	System Organ Class	MA type	Dose	Day of onset	Duration	Causality	Outcome
PPD	PPD	14	M	Bronchitis acuta	Bronchitis	Infections and infestations	HO	1	23	12	N	Recovered/resolved
PPD	PPD	19	M	Bronchiolitis acuta	Bronchiolitis	Infections and infestations	HO	2	26	7	N	Recovered/resolved
PPD	PPD	19	F	Laryngitis acuta	Laryngitis	Infections and infestations	HO	2	7	4	N	Recovered/resolved
PPD	PPD	18	F	Laryngitis	Laryngitis	Infections and infestations	HO	2	7	4	N	Recovered/resolved
PPD	PPD	14	F	Gastroenteritis	Gastroenteritis	Infections and infestations	HO	1	22	7	N	Recovered/resolved

MA = medical attention
HO = hospitalisation
Dose = dose given prior to the start of the SAE
Day of onset = number of days since last study vaccine dose

Table 9 Number and percentage of subjects who started at least one concomitant medication from Day 0 to Day 7 (Total Vaccinated Cohort)

	dTpaNew Group					dTpaPre Group				
				95% CI					95% CI	
	N	n	%	LL	UL	N	n	%	LL	UL
Any	335	41	12.2	8.9	16.2	336	43	12.8	9.4	16.8
Any antipyretic	335	37	11.0	7.9	14.9	336	41	12.2	8.9	16.2
Prophylactic antipyretic	335	2	0.6	0.1	2.1	336	2	0.6	0.1	2.1

dTpaNew Group = Subjects who received *Boostrix* in new syringe presentation
dTpaPre Group = Subjects who received *Boostrix* in previous syringe presentation
N = number of subjects with the administered dose
n(%)= number(percentage) of subjects who started to take the specified concomitant medication at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Table 10 Solicited and Unsolicited symptoms 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)

		HPV_2D N =			MMR_DTPa N =		
Primary System Organ Class (CODE)	Preferred Term (CODE)	n*	n	%	n*	n	%
At least one symptom							
<each SOC>	<each PT term>						

HPV_2D = females aged 4-6 years who received two doses of HPV-16/18 L1 VLP AS04 vaccine at Day 0 and Month 6
MMR_DTPa = females aged 4-6 years who received MMR vaccine at Day 0 and DTPa vaccine at Month 6
At least one symptom = at least one 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

Table 11 Minimum and maximum activity dates (TVC)

Visit	Minimum date	Maximum date
1	19JUN2007	29DEC2007
2	24JUL2007	08FEB2008
3	24AUG2007	18MAR2008
4	25MAR2008	22NOV2008
5	24MAR2009	31MAR2009*

*Database Lock Date = 31MAR2009

Table 12 Number of enrolled subjects by age category (TVC)

		Gr 1 N =	Gr 2 N =	Gr 3 N =	Total N =
Characteristics	**Categories**	**n**	**n**	**n**	**n**
Age category	In utero				
	Preterm newborn infants (gestational age < 37 wks)				
	Newborns (0-27 days)				
	Infants and toddlers (28 days-23 months)				
	Children (2-11 years)				
	Adolescents (12-17 years)				
	Adults (18-64 years)				
	From 65-84 years				
	85 years and over				
	Missing				

Gr 1 = Group 1 description
Gr 2 = Group 2 description
Gr 3 = Group 3 description
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 = <describe missing>

Table 13 Number of subjects by country

	ACWY-TT N = 259	ACWYHPV N = 259	HPV N = 261	Co-ad N = 260	Tdap N = 261	Total N = 1300
Country	**n**	**n**	**N**	**n**	**n**	**n**
Dominican Republic	86	87	88	87	87	435
Estonia	87	86	87	87	88	435
Thailand	86	86	86	86	86	430

ACWY-TT = Subjects who received MenACWY-TT at Month 0 and Cervarix at Month 1, 2 and 7
ACWYHPV = Subjects who received MenACWY-TT and Cervarix at Month 0 and Cervarix at Month 1 and 6
HPV = Subjects who received Cervarix at Month 0, 1 and 6
Co-ad = Subjects who received MenACWY-TT, Cervarix and Boostrix at Month 0 and Cervarix at Month 1 and 6
Tdap = Subjects who received Boostrix and Cervarix at Month 0 and Cervarix at Month 1 and 6
N = number of subjects
n= number of enrolled subjects included in each group or in total for a given age category or for all age categories

Table 14 Listing of dropouts due to AEs, SAEs and solicited symptoms (Total cohort)

Study-Subject No.	Country	Gender	AE Description	SAE	Causality	Outcome	Type of discontinuation
PPD	Germany	F	SUBJECT DIED	Y		Fatal	Study at visit/contact: VISIT11 (Y5)
PPD	Germany	F	SUBJECT DIED	Y		Fatal	Study at visit/contact: VISIT11 (Y5)