Clinical trial results:
A Phase III, open, multicentre study to assess the long-term persistence of a booster dose of GlaxoSmithKline (GSK) Biologicals' Haemophilus influenzae type b-meningococcal serogroup C conjugate vaccine (Hib-MenC) compared to a booster dose of Infanrix™ hexa (combined diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated polio-Hib vaccine) when given to 14-month-old subjects who were primed in study 217744/097 (DTPa-HBV-IPV-097) and boosted in study Hib-MenC-TT-010
BST: DTPa-HBV-IPV-097

Summary

EudraCT number	2006-000518-19
Trial protocol	ES
Global end of trial date	08 September 2010

Results information

Result version number	v1
This version publication date	20 June 2016
First version publication date	22 May 2015

Trial information

Trial identification

Sponsor protocol code	106672;106673;106675;106679;-80

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00322335
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 September 2010
Global end of trial reached?	Yes
Global end of trial date	08 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the persistence of Meningococcal C antibodies on a yearly basis for a period of 5.5 years after booster vaccination.
To evaluate the persistence of Haemophilus influenzae type b antibodies on a yearly basis for a period of 5.5 years after booster vaccination

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the day of vaccination and the subsequent 30 days after the last vaccination administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 May 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 184
Worldwide total number of subjects	184
EEA total number of subjects	184

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	184
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Pre-assignment period milestones

Number of subjects started	184
Number of subjects completed	184

Period 1

Period 1 title	Month 18
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Menitorix/Pediarix Group Month 18

Arm description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Experimental
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Arm title	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with

Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Engerix-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as a birth dose

Investigational medicinal product name	NeisVac-C™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.

Investigational medicinal product name	Infanrix™ IPV/HIB
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 4 months of age.

Arm title	Infanrix hexa/Meningitec Group Month 18

Arm description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Meningitec™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Number of subjects in period 1	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Infanrix hexa/Meningitec Group Month 18
Started	58	123	3
Completed	58	123	3

Period 2

Period 2 title	Month 30
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Menitorix/Pediarix Group Month 30

Arm description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Experimental
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection

Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Arm title	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Engerix-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as a birth dose

Investigational medicinal product name	NeisVac-C™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.

Investigational medicinal product name	Infanrix™ IPV/HIB
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 4 months of age

Arm title	Infanrix hexa/Meningitec Group Month 30

Arm description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Meningitec™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Number of subjects in period 2[1]	Menitorix/Pediarix Group Month 30	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30	Infanrix hexa/Meningitec Group Month 30
Started	54	119	3
Completed	54	119	57
Joined	0	0	54
Late return to study visit	-	-	54

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all subjects completing one period came to the next study visit; however, a subject missing a previous visit was allowed to return to a subsequent one. Thus, the number of subjects starting every study period is based on the actual rate of return.

Period 3

Period 3 title	Month 42
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Menitorix/Pediarix Group Month 42

Arm description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Experimental
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Arm title	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Engerix-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details: Intramuscular injection into the thigh as a birth dose	
Investigational medicinal product name	NeisVac-C™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.	
Investigational medicinal product name	Infanrix™ IPV/HIB
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: Intramuscular injection into the thigh as primary vaccination at 4 months of age.	
Arm title	Infanrix hexa/Meningitec Group Month 42
Arm description: Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.	
Arm type	Active comparator
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).	
Investigational medicinal product name	Meningitec™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details: Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age	

Number of subjects in period 3[2]	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42	Infanrix hexa/Meningitec Group Month 42
Started	51	113	56
Completed	51	113	56

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all subjects completing one period came to the next study visit; however, a subject missing a previous visit was allowed to return to a subsequent one. Thus, the number of subjects starting every study period is based on the actual rate of return.

Period 4

Period 4 title	Month 54
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Menitorix/Pediarix Group Month 54

Arm description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Experimental
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Arm title	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group

HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Engerix-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as a birth dose

Investigational medicinal product name	NeisVac-C™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.

Investigational medicinal product name	Infanrix™ IPV/HIB
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 4 months of age.

Arm title	Infanrix hexa/Meningitec Group Month 54

Arm description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Meningitec™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Number of subjects in period 4[3]	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54
Started	50	108	56
Completed	50	108	56

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all subjects completing one period came to the next study visit; however, a subject missing a previous visit was allowed to return to a subsequent one. Thus, the number of subjects starting every study period is based on the actual rate of return.

Period 5

Period 5 title	Month 66
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Menitorix/Pediarix Group Month 66

Arm description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Experimental
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ penta
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Arm title	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66

Arm description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of

age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator
Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	Haemophilus influenzae type b- and meningococcal (vaccine)
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age (group HibMenC) and as booster dose at 14 months of age (groups HibMenC and group NeisPoo).

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Engerix-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as a birth dose

Investigational medicinal product name	NeisVac-C™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2 and 4 months of age.

Investigational medicinal product name	Infanrix™ IPV/HIB
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 4 months of age.

Arm title	Infanrix hexa/Meningitec Group Month 66

Arm description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Arm type	Active comparator

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and/or 6 months of age (groups NeisPoo and MenCCRM) and/or as booster dose at 14 months of age (group MenCCRM).

Investigational medicinal product name	Meningitec™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection into the thigh as primary vaccination at 2, 4 and 6 months of age

Number of subjects in period 5[4]	Menitorix/Pediarix Group Month 66	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66
Started	48	104	53
Completed	48	104	53

Notes:

[4] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all subjects completing one period came to the next study visit; however, a subject missing a previous visit was allowed to return to a subsequent one. Thus, the number of subjects starting every study period is based on the actual rate of return.

Baseline characteristics

Reporting groups	
Reporting group title	Menitorix/Pediarix Group Month 18

Reporting group description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Meningitec Group Month 18

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Reporting group values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Infanrix hexa/Meningitec Group Month 18
Number of subjects	58	123	3
Age categorical Units: Subjects			
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			
Age continuous Units: months			
arithmetic mean	31.3	31.4	31.3
standard deviation	± 0.54	± 0.64	± 0.58
Gender categorical Units: Subjects			
Female	27	55	1
Male	31	68	2

Reporting group values	Total		
Number of subjects	184		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	83		
Male	101		

End points

End points reporting groups

Reporting group title	Menitorix/Pediarix Group Month 18

Reporting group description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Meningitec Group Month 18

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Menitorix/Pediarix Group Month 30

Reporting group description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Meningitec Group Month 30

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Menitorix/Pediarix Group Month 42

Reporting group description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Meningitec Group Month 42

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Menitorix/Pediarix Group Month 54

Reporting group description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Meningitec Group Month 54

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Menitorix/Pediarix Group Month 66

Reporting group description:

Subjects were primed with 3 doses of Pediarix™ co-administered intramuscularly with Menitorix™ in the right and left thigh respectively in the primary study (NCT00352963) at 2, 4 and 6 months of age. This was followed by a booster dose of Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66

Reporting group description:

Subjects were either primed in the primary study (NCT00352963) with 3 doses of Infanrix™ hexa administered intramuscularly in the right thigh at 2, 4 and 6 months of age and 2 doses of NeisVac-C™ administered intramuscularly in the left thigh at 2 and 4 months of age or with Engerix-B at birth intramuscularly in the right thigh, Infanrix™ hexa intramusculary in the right thigh at 2 and 6 months of age and NeisVac-C™ intramuscularly in the left thigh at 2 and 4 months of age, Infanrix™ IPV/Hib was administered intramuscularly in the right thigh at 4 months of age. All subjects were boosted with Menitorix™ administered intramuscularly in the left thigh between 13 and 14 months of age in study NCT00323050. No vaccines were administered during this long-term persistence phase of the study.

Reporting group title	Infanrix hexa/Meningitec Group Month 66

Reporting group description:

Subjects were primed with Infanrix™ hexa co-administered intramuscularly with Meningitec™ in the right and left thigh respectively at 2, 4 and 6 months of age during the primary study (NCT00352963), followed by a booster dose of Infanrix™ hexa intramuscularly in the right thigh between 13 and 14 months of age in study (NCT00323050). No vaccines were administered during this long-term

persistence phase of the study.

Primary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:8

End point title	Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:8[1][2]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after booster dose (Day 0)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Menitorix/Pediarix Group Month 30	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	96	48	101
Units: Subjects	44	93	39	96

End point values	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42	Infanrix hexa/Meningitec Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	50	110	52
Units: Subjects	31	39	106	33

End point values	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54	Menitorix/Pediarix Group Month 66
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	106	51	46
Units: Subjects	38	103	33	38

End point values	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	46		
Units: Subjects	95	28		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:32

End point title	Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:32[3][4]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after booster dose (Day 0)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Menitorix/Pediarix Group Month 30	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	96	48	101
Units: Subjects	40	93	36	94

End point values	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42	Infanrix hexa/Meningitec Group Month 42

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	50	110	52
Units: Subjects	25	38	100	30

End point values	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54	Menitorix/Pediarix Group Month 66
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	106	51	46
Units: Subjects	37	100	29	37

End point values	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	46		
Units: Subjects	88	25		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:128

End point title	Number of subjects with meningococcal serogroup C serum bactericidal assay using rabbit complement (rSBA-MenC) titers equal to or above cut-off value of 1:128[5][6]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after booster dose (Day 0)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Menitorix/Pediarix Group Month 30	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	96	48	101
Units: Subjects	27	82	27	80

End point values	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42	Infanrix hexa/Meningitec Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	50	110	52
Units: Subjects	12	30	89	13

End point values	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54	Menitorix/Pediarix Group Month 66
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	106	51	46
Units: Subjects	27	86	15	28

End point values	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	46		
Units: Subjects	69	18		

Statistical analyses

No statistical analyses for this end point

Primary: rSBA-MenC titers

End point title	rSBA-MenC titers[7][8]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after booster dose (Day 0)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Menitorix/Pediarix Group Month 30	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	96	48	101
Units: Titers				
geometric mean (confidence interval 95%)	221.5 (137.2 to 357.7)	801.1 (570.3 to 1125.3)	109.1 (61.9 to 192.3)	441.7 (309.4 to 630.6)

End point values	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42	Infanrix hexa/Meningitec Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	50	110	52
Units: Titers				
geometric mean (confidence interval 95%)	40.3 (21.9 to 74.1)	98.9 (56.7 to 172.5)	409.8 (297.7 to 564.2)	36.1 (20.4 to 63.8)

End point values	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54	Menitorix/Pediarix Group Month 66
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	106	51	46
Units: Titers				
geometric mean (confidence interval 95%)	90.4 (52.8 to 154.8)	344.6 (255.9 to 463.9)	36.7 (21.1 to 64)	121.5 (71 to 207.9)

End point values	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	46		
Units: Titers				
geometric mean (confidence interval 95%)	227.6 (160.2 to 323.3)	42.7 (22.3 to 81.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 0.15 µg/mL

End point title	Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 0.15 µg/mL[9]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Infanrix hexa/Meningitec Group Month 18	Menitorix/Pediarix Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	122	3	53
Units: Subjects	56	121	3	53

End point values	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	53	50	110
Units: Subjects	112	53	50	109

End point values	Infanrix hexa/Meningitec Group Month 42	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	49	106	52
Units: Subjects	51	49	105	52

End point values	Menitorix/Pediarix Group Month 66	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	101	47	
Units: Subjects	47	101	46	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 1.0 µg/mL

End point title	Number of subjects with anti-polyribosylribitol phosphate (Anti-PRP) concentrations equal to or above cut-off value of 1.0 µg/mL[10]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Infanrix hexa/Meningitec Group Month 18	Menitorix/Pediarix Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	122	3	53
Units: Subjects	44	112	3	36

End point values	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	53	50	110

Units: Subjects	98	40	33	91

End point values	Infanrix hexa/Meningitec Group Month 42	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	49	106	52
Units: Subjects	34	27	86	35

End point values	Menitorix/Pediarix Group Month 66	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	101	47	
Units: Subjects	26	84	26	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-PRP concentrations

End point title	Anti-PRP concentrations[11]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Infanrix hexa/Meningitec Group Month 18	Menitorix/Pediarix Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	122	3	53
Units: µg/mL				
geometric mean (confidence interval 95%)	2.921 (2.15 to 3.968)	5.45 (4.39 to 6.766)	2.547 (0.39 to 16.651)	1.914 (1.383 to 2.648)

End point values	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	53	50	110
Units: µg/mL				
geometric mean (confidence interval 95%)	3.524 (2.813 to 4.415)	2.224 (1.578 to 3.133)	1.735 (1.243 to 2.423)	2.986 (2.395 to 3.722)

End point values	Infanrix hexa/Meningitec Group Month 42	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	49	106	52
Units: µg/mL				
geometric mean (confidence interval 95%)	2.005 (1.365 to 2.946)	1.552 (1.154 to 2.087)	2.688 (2.149 to 3.361)	1.799 (1.267 to 2.555)

End point values	Menitorix/Pediarix Group Month 66	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	47	101	47	
Units: µg/mL				
geometric mean (confidence interval 95%)	1.602 (1.107 to 2.32)	2.625 (2.113 to 3.261)	1.763 (1.17 to 2.657)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-polysaccharide C (Anti-PSC) concentrations equal to or above cut-off value of 0.3 µg/mL

End point title	Number of subjects with anti-polysaccharide C (Anti-PSC) concentrations equal to or above cut-off value of 0.3 µg/mL[12][13]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Menitorix/Pediarix Group Month 30	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	122	52	108
Units: Subjects	38	100	19	58

End point values	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42	Infanrix hexa/Meningitec Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	49	107	52
Units: Subjects	19	17	52	17

End point values	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54	Menitorix/Pediarix Group Month 66
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	105	52	45
Units: Subjects	14	52	17	12

End point values	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	45		
Units: Subjects	34	11		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-polysaccharide C (Anti-PSC) concentrations equal to or above cut-off value of 2.0 µg/mL

End point title	Number of subjects with anti-polysaccharide C (Anti-PSC) concentrations equal to or above cut-off value of 2.0 µg/mL[14][15]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Menitorix/Pediarix Group Month 30	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	122	52	108
Units: Subjects	1	31	1	18

End point values	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42	Infanrix hexa/Meningitec Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	49	107	52
Units: Subjects	3	0	14	2

End point values	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54	Menitorix/Pediarix Group Month 66
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	105	52	45
Units: Subjects	1	10	1	0

End point values	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	45		
Units: Subjects	8	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with serious adverse events

End point title	Number of subjects with serious adverse events[16]

End point description:

End point type	Primary

End point timeframe:

From last study contact of the booster study (NCT00323050) to Month 66 after booster dose (Day 0)

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Infanrix hexa/Meningitec Group Month 18	Menitorix/Pediarix Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	123	3	54
Units: Subjects	0	0	0	0

End point values	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	119	57	51	113
Units: Subjects	0	0	0	0

End point values	Infanrix hexa/Meningitec Group Month 42	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	50	108	56
Units: Subjects	0	0	0	0

End point values	Menitorix/Pediarix Group Month 66	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	104	53	
Units: Subjects	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Anti-PSC concentrations

End point title	Anti-PSC concentrations[17][18]

End point description:

End point type	Primary

End point timeframe:

18, 30, 42, 54 and 66 months after the booster dose (Day 0)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The analysis was only performed on groups with more than 0 subjects with available blood samples for the respective timepoint.

End point values	Menitorix/Pediarix Group Month 18	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 18	Menitorix/Pediarix Group Month 30	Infanrix hexa/Infanrix IPV-Hib co-ad Group Month 30
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	122	52	108
Units: µg/mL				
geometric mean (confidence interval 95%)	0.5 (0.39 to 0.64)	1.01 (0.8 to 1.29)	0.26 (0.21 to 0.33)	0.47 (0.37 to 0.61)

End point values	Infanrix hexa/Meningitec Group Month 30	Menitorix/Pediarix Group Month 42	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 42	Infanrix hexa/Meningitec Group Month 42
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	49	107	52
Units: µg/mL				
geometric mean (confidence interval 95%)	0.3 (0.23 to 0.39)	0.25 (0.2 to 0.31)	0.4 (0.32 to 0.51)	0.28 (0.21 to 0.37)

End point values	Menitorix/Pediarix Group Month 54	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 54	Infanrix hexa/Meningitec Group Month 54	Menitorix/Pediarix Group Month 66
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	105	52	45
Units: µg/mL				
geometric mean (confidence interval 95%)	0.24 (0.19 to 0.3)	0.36 (0.29 to 0.45)	0.26 (0.2 to 0.32)	0.22 (0.18 to 0.27)

End point values	Infanrix hexa/Infanrix IPV/Hib co-ad Group Month 66	Infanrix hexa/Meningitec Group Month 66		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	45		
Units: µg/mL				
geometric mean (confidence interval 95%)	0.29 (0.23 to 0.36)	0.22 (0.18 to 0.28)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From last study contact of the booster study (NCT00323050) to Month 66 after booster dose (Day 0)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Menitorix/Pediarix Group
Reporting group description: -	
Reporting group title	Infanrix hexa (or IPV/Hib)/NeisVac-C/Engerix-B/Menitorix Group
Reporting group description: -	
Reporting group title	Infanrix hexa/Meningitec Group
Reporting group description: -	

Serious adverse events	Menitorix/Pediarix Group	Infanrix hexa (or IPV/Hib)/NeisVac-C/Engerix-B/Menitorix Group	Infanrix hexa/Meningitec Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 58 (0.00%)	0 / 123 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Menitorix/Pediarix Group	Infanrix hexa (or IPV/Hib)/NeisVac-C/Engerix-B/Menitorix Group	Infanrix hexa/Meningitec Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 58 (0.00%)	0 / 123 (0.00%)	0 / 3 (0.00%)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious adverse events were collected in this study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported