



Clinical trial results:

Phase III randomized, open, controlled study to evaluate the immune response to the hepatitis B antigen of the RTS,S/AS01E candidate vaccine, when administered as primary vaccination integrated into an EPI regimen to infants living in sub-Saharan Africa.

Summary

EudraCT number	2011-001508-37
Trial protocol	Outside EU/EEA
Global end of trial date	09 February 2017

Results information

Result version number	v1
This version publication date	17 August 2017
First version publication date	17 August 2017

Trial information

Trial identification

Sponsor protocol code	113681
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01345240
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 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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	Interim
Date of interim/final analysis	09 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate in terms of antibody (ab) response to the HBs antigen, the non-inferiority (noninf) of RTS,S/AS01E (RTSS) to a primary vaccination regimen of a licensed hepatitis B vaccine (Engerix-B) integrated into an expanded program on immunization (EPI) regimen.

Protection of trial subjects:

The vaccinees were observed closely for at least 60 minutes following the administration of all vaccines used in the study, with appropriate medical treatment readily available in case of an anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	51 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Burkina Faso: 508
Country: Number of subjects enrolled	Ghana: 197
Worldwide total number of subjects	705
EEA total number of subjects	0

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)	705
Children (2-11 years)	0
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:

The study was conducted in 4 phases, a Primary Vaccination Phase (up to Month (M) 3), a Safety Follow-Up Phase (M3-8), a First Immunogenicity Follow-Up (FU) Phase (M8-26), and a Second Immunogenicity FU Phase (M26 to study end at M51).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	RTS,S Regimen A Group

Arm description:

This group results from the pooling of the RTS,S Regimen A Lot 1, RTS,S Regimen A Lot 2 and RTS,S Regimen A Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™, at Weeks 0, 4 and 8, and 2 doses of Rotarix™ vaccine, at Weeks 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Arm type	Experimental
Investigational medicinal product name	Candidate Plasmodium falciparum malaria vaccine
Investigational medicinal product code	RTS,S/AS02D
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the thigh

Investigational medicinal product name	Engerix-B Junior
Investigational medicinal product code	HBV Paediatric 10
Other name	Engerix-B
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the thigh.

Investigational medicinal product name	Infanrix-Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the deltoid.

Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
3-dose orally	
Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose intramuscular injection in the thigh.	
Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
2-dose orally	
Investigational medicinal product name	Measles and yellow fever vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1-dose intramuscular injection in the deltoid	
Arm title	RTS,S Regimen B Group
Arm description:	
This group results from the pooling of the RTS,S Regimen B Lot 1, RTS,S Regimen B Lot 2 and RTS,S Regimen B Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.	
Arm type	Experimental
Investigational medicinal product name	Candidate Plasmodium falciparum malaria vaccine
Investigational medicinal product code	RTS,S/AS02D
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose intramuscular injection in the thigh	
Investigational medicinal product name	Engerix-B Junior
Investigational medicinal product code	HBV Paediatric 10
Other name	Engerix-B
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
3-dose intramuscular injection in the thigh.	
Investigational medicinal product name	Infanrix-Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose intramuscular injection in the deltoid.	
Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
3-dose orally	
Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose intramuscular injection in the thigh.	
Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
2-dose orally	
Investigational medicinal product name	Measles and yellow fever vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1-dose intramuscular injection in the deltoid	
Arm title	RTS,S Regimen C Group
Arm description:	
This group results from the pooling of the RTS,S Regimen C Lot 1, RTS,S Regimen C Lot 2 and RTS,S Regimen C Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 6 and 10, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.	
Arm type	Experimental

Investigational medicinal product name	Candidate Plasmodium falciparum malaria vaccine
Investigational medicinal product code	RTS,S/AS02D
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose intramuscular injection in the thigh	
Investigational medicinal product name	Engerix-B Junior
Investigational medicinal product code	HBV Paediatric 10
Other name	Engerix-B
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose intramuscular injection in the thigh.	
Investigational medicinal product name	Infanrix-Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose intramuscular injection in the deltoid.	
Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
3-dose orally	
Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3-dose intramuscular injection in the thigh.	
Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
2-dose orally	
Investigational medicinal product name	Measles and yellow fever vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1-dose intramuscular injection in the deltoid	
Arm title	Engerix B Regimen A Group

Arm description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen A. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™ at Weeks 0, 4 and 8, and 2 doses of Rotarix™, at Weeks 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Arm type	Active comparator
Investigational medicinal product name	Engerix-B Junior
Investigational medicinal product code	HBV Paediatric 10
Other name	Engerix-B
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the thigh.

Investigational medicinal product name	Infanrix-Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the deltoid.

Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

3-dose orally

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the thigh.

Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2-dose orally

Investigational medicinal product name	Measles and yellow fever vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1-dose intramuscular injection in the deltoid

Arm title	Engerix B Regimen B Group
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Arm description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen B. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™ vaccine, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Arm type	Active comparator
Investigational medicinal product name	Engerix-B Junior
Investigational medicinal product code	HBV Paediatric 10
Other name	Engerix-B
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the thigh.

Investigational medicinal product name	Infanrix-Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the deltoid.

Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

3-dose orally

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3-dose intramuscular injection in the thigh.

Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2-dose orally

Investigational medicinal product name	Measles and yellow fever vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1-dose intramuscular injection in the deltoid

Number of subjects in period 1	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group
Started	142	142	141
Completed	140	128	131
Not completed	2	14	10
Lost to follow-up	1	12	8
Serious Adverse Event	1	2	2

Number of subjects in period 1	Engerix B Regimen A Group	Engerix B Regimen B Group
Started	141	139
Completed	131	132
Not completed	10	7
Lost to follow-up	8	6
Serious Adverse Event	2	1

Baseline characteristics

Reporting groups

Reporting group title	RTS,S Regimen A Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen A Lot 1, RTS,S Regimen A Lot 2 and RTS,S Regimen A Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™, at Weeks 0, 4 and 8, and 2 doses of Rotarix™ vaccine, at Weeks 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	RTS,S Regimen B Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen B Lot 1, RTS,S Regimen B Lot 2 and RTS,S Regimen B Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	RTS,S Regimen C Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen C Lot 1, RTS,S Regimen C Lot 2 and RTS,S Regimen C Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 6 and 10, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	Engerix B Regimen A Group
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Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen A. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™ at Weeks 0, 4 and 8, and 2 doses of Rotarix™, at Weeks 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	Engerix B Regimen B Group
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Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen B. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™ vaccine, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group
Number of subjects	142	142	141
Age categorical Units: Subjects			

Age continuous Units: weeks arithmetic mean standard deviation	8.4 ± 0.83	8.3 ± 0.62	8.3 ± 0.69
Gender categorical Units: Subjects			
Female	59	69	67
Male	83	73	74
Race/Ethnicity, Customized Units: Subjects			
African Heritage/African American	142	142	141

Reporting group values	Engerix B Regimen A Group	Engerix B Regimen B Group	Total
Number of subjects	141	139	705
Age categorical Units: Subjects			

Age continuous Units: weeks arithmetic mean standard deviation	8.3 ± 0.74	8.3 ± 0.74	-
Gender categorical Units: Subjects			
Female	81	63	339
Male	60	76	366
Race/Ethnicity, Customized Units: Subjects			
African Heritage/African American	141	139	705

End points

End points reporting groups

Reporting group title	RTS,S Regimen A Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen A Lot 1, RTS,S Regimen A Lot 2 and RTS,S Regimen A Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™, at Weeks 0, 4 and 8, and 2 doses of Rotarix™ vaccine, at Weeks 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	RTS,S Regimen B Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen B Lot 1, RTS,S Regimen B Lot 2 and RTS,S Regimen B Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	RTS,S Regimen C Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen C Lot 1, RTS,S Regimen C Lot 2 and RTS,S Regimen C Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 6 and 10, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	Engerix B Regimen A Group
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Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen A. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™ at Weeks 0, 4 and 8, and 2 doses of Rotarix™, at Weeks 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	Engerix B Regimen B Group
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Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen B. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™ vaccine, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Subject analysis set title	RTS,S Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects in this group were subjects from the RTS,S Regimen A, RTS,S Regimen B, and RTS,S Regimen C groups who were administered a 3-dose primary vaccination course of the RTS,S vaccine in any of its formulations, Lot 1, 2 or 3, at Weeks 0, 4 and 8. Subjects in this group were also administered, according to varied schedules depending on the RTS,S vaccination regimen received, doses of Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™, Enderix B™ and vaccines against yellow fever and against measles. The RTS,S vaccine and Enderix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Subject analysis set title	Enderix B Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects in this group were subjects from the Enderix B Regimen A and Enderix B Regimen B groups were administered Enderix B™ as a 3-dose primary vaccination course, at Weeks 0, 4 and 8, followed by a booster dose, at Month 50. Subjects in this group were also administered, according to varied schedules, depending on the vaccination regimen they were allocated too in their respective group, doses Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™ and of vaccines against yellow fever and against measles. Enderix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Subject analysis set title	RTS,S Lot 1 Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects in this group were subjects from the RTS,S Regimen A, RTS,S Regimen B, and RTS,S Regimen C groups who were administered a 3-dose primary vaccination course of the RTS,S vaccine in its Lot 1 formulation only, at Weeks 0, 4 and 8. Subjects in this group were also administered, according to varied schedules depending on the RTS,S vaccination regimen received, doses of Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™, Enderix B™ and vaccines against yellow fever and against measles. The RTS,S vaccine and Enderix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Subject analysis set title	RTS,S Lot 2 Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects in this group were subjects from the RTS,S Regimen A, RTS,S Regimen B, and RTS,S Regimen C groups who were administered a 3-dose primary vaccination course of the RTS,S vaccine in its Lot 2 formulation only, at Weeks 0, 4 and 8. Subjects in this group were also administered, according to varied schedules depending on the RTS,S vaccination regimen received, doses of Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™, Enderix B™ and vaccines against yellow fever and against measles. The RTS,S vaccine and Enderix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Subject analysis set title	RTS,S Lot 3 Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects in this group were subjects from the RTS,S Regimen A, RTS,S Regimen B, and RTS,S Regimen C groups who were administered a 3-dose primary vaccination course of the RTS,S vaccine in its Lot 3 formulation only, at Weeks 0, 4 and 8. Subjects in this group were also administered, according to varied schedules depending on the RTS,S vaccination regimen received, doses of Infanrix™-Hib, Polio Sabin™, Rotarix™, Synflorix™, Rotarix™, Enderix B™ and vaccines against yellow fever and against measles. The RTS,S vaccine and Enderix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Primary: Anti-Hepatitis B (HBs) antibody concentrations

End point title	Anti-Hepatitis B (HBs) antibody concentrations ^[1]
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End point description:

Concentrations, by enzyme-linked immunosorbent assay (ELISA), were presented as geometric mean concentrations (GMCs), and expressed in milli-international units per milliliter (mIU/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to ($\geq$) 10 mIU/mL. A decrease in the specificity of the anti-HBs ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The table shows updated results following partial or complete retesting/reanalysis, with study groups pooled by primary vaccine administered (RTS,S vs Engerix-B™).

End point type	Primary
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End point timeframe:

At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™

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.

End point values	RTS,S Group	Engerix B Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	397	253		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	6412.7 (5732.9 to 7173)	377.4 (310.6 to 458.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-Hepatitis B (HBs) antibody concentrations.

End point title	Anti-Hepatitis B (HBs) antibody concentrations. ^[2]
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End point description:

Concentrations, by enzyme-linked immunosorbent assay (ELISA), were presented as geometric mean concentrations (GMCs), and expressed in milli-international units per milliliter (mIU/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to ($\geq$) 10 mIU/mL. A decrease in the specificity of the anti-HBs ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The table shows updated results following partial or complete retesting/reanalysis, with study groups pooled by RTS,S or Engerix-B™ vaccination regimen received.

End point type	Primary
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End point timeframe:

At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™

Notes:

[2] - 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	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	123	134	135
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	5467.6 (4493.8 to 6652.5)	6989.9 (5747.5 to 8501)	6998.7 (5779.1 to 8475.7)	334.4 (253.4 to 441.4)

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
mIU/mL	433.4 (329.5 to 570.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Hepatitis B (HBs) antibody concentrations

End point title	Anti-Hepatitis B (HBs) antibody concentrations
End point description:	
Concentrations, by enzyme-linked immunosorbent assay (ELISA), were presented as geometric mean concentrations (GMCs), and expressed in milli-international units per milliliter (mIU/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to ($\geq$) 10 mIU/mL. A decrease in the specificity of the anti-HBs ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The table shows updated results following partial or complete retesting/reanalysis. Results presented are for the study groups receiving the RTS,S vaccine, pooled by vaccine lot, that is, for the RTS,S Lot 1, RTS,S Lot 2, and RTS,S Lot 3 groups, as defined below.	
End point type	Secondary
End point timeframe:	
At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™	

End point values	RTS,S Lot 1 Group	RTS,S Lot 2 Group	RTS,S Lot 3 Group	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	132	134	131	
Units: mIU/mL				
geometric mean (confidence interval 95%)				

mIU/mL	6214.3 (5115.6 to 7548.9)	6826.1 (5569.4 to 8366.3)	6209.2 (5144.2 to 7494.8)	
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Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Hepatitis B (HBs) antibody concentrations.

End point title	Anti-Hepatitis B (HBs) antibody concentrations. ^[3]
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End point description:

Concentrations, by enzyme-linked immunosorbent assay (ELISA), were presented as geometric mean concentrations (GMCs), and expressed in milli-international units per milliliter (mIU/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to ($\geq$) 10 mIU/mL.

End point type	Secondary
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End point timeframe:

At Months 14 and 26, aka at 12 and 24 months post Dose 3 of RTS,S vaccine or Engerix-B™

Notes:

[3] - 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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Engerix B Regimen A Group	Engerix B Regimen B Group	RTS,S Lot 1 Group	RTS,S Lot 2 Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	127	114	133	118
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs – At Month 14	119.5 (91 to 157)	137.5 (103.3 to 183.2)	1530.1 (1259.4 to 1859.1)	2430.9 (1975.7 to 2991)
Anti-HBs – At Month 26	68.8 (50.7 to 93.3)	71 (51.6 to 97.8)	1092.6 (867.4 to 1376.3)	1896 (1487.2 to 2417.3)

End point values	RTS,S Lot 3 Group			
Subject group type	Subject analysis set			
Number of subjects analysed	129			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs – At Month 14	2189.1 (1840.3 to 2603.9)			
Anti-HBs – At Month 26	1849.8 (1478.9 to 2313.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies to the Hepatitis B RF1 surface antigen (anti-HBs RF1).

End point title	Concentrations of antibodies to the Hepatitis B RF1 surface antigen (anti-HBs RF1).
End point description: Anti-HBs RF1 antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and presented as geometric mean concentrations (GMCs) expressed in ELISA units per milliliter (EL.U/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to ($\geq$) 33 EL.U/mL.	
End point type	Secondary
End point timeframe: At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™	

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	123	135	135
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	268.7 (226.8 to 318.3)	327.1 (272.2 to 393.1)	335.5 (283.2 to 397.5)	25.5 (22.8 to 28.7)

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	28.7 (24.6 to 33.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-circumsporozoite protein (anti-CS) antibody concentrations

End point title	Anti-circumsporozoite protein (anti-CS) antibody concentrations
End point description: Anti-CS antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and presented as geometric mean concentrations (GMCs) expressed in ELISA units per milliliter (EL.U/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to ($\geq$) 0.5 EL.U/mL. The table shows results with study groups pooled by vaccination regimen received.	
End point type	Secondary
End point timeframe: At Month 3, aka at one month post Dose 3 of RTS,S vaccine or Engerix-B™	

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	123	136	135
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	142.2 (116.4 to 173.7)	188.5 (156.5 to 227)	205.5 (167.3 to 252.5)	99999 (99999 to 99999)

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	118			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	0.3 (0.3 to 0.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-circumsporozoite protein (anti-CS) antibody concentrations .

End point title	Anti-circumsporozoite protein (anti-CS) antibody concentrations . ^[4]
End point description: Anti-CS antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and presented as geometric mean concentrations (GMCs) expressed in ELISA units per milliliter (EL.U/mL). The assay cut-off was the seropositivity cut-off value of greater than or equal to ($\geq$) 0.5 EL.U/mL.	
End point type	Secondary

End point timeframe:

At Month 14, aka at 12 months post Dose 3 of RTS,S vaccine or Engerix-B™.

Notes:

[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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Engerix B Regimen A Group	Engerix B Regimen B Group	RTS,S Lot 1 Group	RTS,S Lot 2 Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	85	76	91	82
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	0.3 (0.3 to 0.3)	0.3 (0.3 to 0.4)	5.7 (4.2 to 7.7)	6.8 (5 to 9.4)

End point values	RTS,S Lot 3 Group			
Subject group type	Subject analysis set			
Number of subjects analysed	96			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	7.5 (5.3 to 10.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pneumococcal antibody concentrations against Synflorix™ pneumococcal vaccine serotypes.

End point title	Pneumococcal antibody concentrations against Synflorix™ pneumococcal vaccine serotypes. ^[5]
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End point description:

Antibody concentrations were measured by GSK assay, and expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The pneumococcal vaccine serotypes assessed were the serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The cut-off of the assay, by GSK assay, was greater than or equal to ($\geq$) 0.2 µg/mL. This corresponds to a cut-off value of 0.35µg/mL by enzyme-linked immunosorbent assay (ELISA). This outcome concerns the subjects who received the RTS,S or Engerix-B™ vaccine co-administered with Synflorix™. Results presented are for the study groups pooled by co-administration, that is, for the RTS,S Regimen A and Engerix-B Regimen A groups.

End point type	Secondary
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End point timeframe:

At Month 3, aka at one month post Dose 3 of Synflorix™

Notes:

[5] - 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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RTS,S Regimen A Group	Engerix B Regimen A Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	135		
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-1	3.1 (2.8 to 3.6)	3.6 (3.1 to 4.2)		
ANTI-4	3.5 (3 to 4)	4.2 (3.5 to 4.9)		
ANTI-5	5.1 (4.5 to 5.8)	6.5 (5.6 to 7.4)		
ANTI-6B	1.1 (0.8 to 1.3)	1.2 (1 to 1.6)		
ANTI-7F	4.4 (3.9 to 4.9)	4.9 (4.3 to 5.7)		
ANTI-9V	2.8 (2.4 to 3.3)	3.7 (3.3 to 4.2)		
ANTI-14	5.8 (5 to 6.7)	5.7 (4.7 to 7)		
ANTI-18C	3.4 (2.8 to 4.1)	6.2 (5.1 to 7.5)		
ANTI-19F	4.2 (3.4 to 5.2)	5.1 (4.1 to 6.4)		
ANTI-23F	1.3 (1.1 to 1.6)	1.5 (1.1 to 1.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pneumococcal antibody concentrations against Synflorix™ pneumococcal vaccine serotypes.

End point title	Pneumococcal antibody concentrations against Synflorix™ pneumococcal vaccine serotypes. ^[6]
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End point description:

Antibody concentrations were measured by GSK assay, and expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The pneumococcal vaccine serotypes assessed were the serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The cut-off of the assay, by GSK assay, was greater than or equal to ($\geq$) 0.2 µg/mL. This corresponds to a cut-off value of 0.35µg/mL by enzyme-linked immunosorbent assay (ELISA).

End point type	Secondary
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End point timeframe:

At Month 17, aka one month post the Month 16 booster dose of Synflorix™

Notes:

[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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RTS,S Regimen A Group	Engerix B Regimen A Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	126		
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-1	4.5 (3.8 to 5.4)	5.4 (4.5 to 6.4)		
ANTI-4	6.1 (5.1 to 7.2)	6.8 (5.7 to 8)		
ANTI-5	6.5 (5.5 to 7.8)	7.6 (6.4 to 9.1)		

ANTI-6B	4.7 (4 to 5.5)	4.1 (3.5 to 4.9)		
ANTI-7F	7.1 (6.2 to 8.2)	7.2 (6.3 to 8.2)		
ANTI-9V	6 (5.1 to 7.1)	5.7 (4.9 to 6.6)		
ANTI-14	9 (7.6 to 10.7)	9 (7.4 to 10.8)		
ANTI-18C	13.7 (11.5 to 16.3)	14.5 (12.3 to 17.2)		
ANTI-19F	6 (4.9 to 7.4)	7.2 (5.8 to 8.8)		
ANTI-23F	4.1 (3.4 to 5.1)	3.9 (3.2 to 4.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against Synflorix™ pneumococcal vaccine serotypes.

End point title	Titers for opsonophagocytic activity against Synflorix™ pneumococcal vaccine serotypes. ^[7]
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End point description:

The pneumococcal vaccine serotypes assessed were the serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Streptococcus pneumoniae opsonophagocytic activity was presented as the dilution of serum (opsonic titer) able to sustain 50 % killing of live pneumococci under the assay conditions, expressed as geometric mean titers (GMTs). The cut-off of the assay was an opsonic dilution ≥ 8 . This outcome concerns the subjects who received the RTS,S or Engerix-B™ vaccine co-administered with Synflorix™. Results presented are for the study groups pooled by co-administration, that is, for the RTS,S Regimen A and Engerix-B Regimen A groups.

End point type	Secondary
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End point timeframe:

At Month 3, aka at one month (1M) post Dose 3 of Synflorix™

Notes:

[7] - 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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RTS,S Regimen A Group	Engerix B Regimen A Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	124		
Units: Titer				
geometric mean (confidence interval 95%)				
ANTI-1	48.9 (34.6 to 68.9)	65 (45 to 93.7)		
ANTI-4	768.3 (617.6 to 955.8)	810.9 (676.5 to 972)		
ANTI-5	77.6 (61.9 to 97.3)	93.8 (73.6 to 119.6)		
ANTI-6B	444.4 (295 to 669.5)	389.3 (250.1 to 606.1)		
ANTI-7F	3774 (3232.7 to 4405.8)	3947.4 (3338.3 to 4667.7)		
ANTI-9V	1257.7 (977.3 to 1618.7)	1469.3 (1180.4 to 1828.8)		

ANTI-14	1426.3 (1136 to 1790.9)	1269 (965.1 to 1668.6)		
ANTI-18C	192.6 (139.2 to 266.4)	249.7 (185 to 337)		
ANTI-19F	159.3 (109.9 to 231)	228.8 (160.4 to 326.3)		
ANTI-23F	760.9 (476.3 to 1215.5)	735.6 (456.3 to 1185.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against Synflorix™ pneumococcal vaccine serotypes.

End point title	Titers for opsonophagocytic activity against Synflorix™ pneumococcal vaccine serotypes. ^[8]
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End point description:

The pneumococcal vaccine serotypes assessed were the serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Streptococcus pneumoniae opsonophagocytic activity was presented as the dilution of serum (opsonic titer) able to sustain 50 % killing of live pneumococci under the assay conditions, expressed as geometric mean titers (GMTs). The cut-off of the assay was an opsonic dilution ≥ 8 .

End point type	Secondary
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End point timeframe:

At Month 17, aka one month post the Month 16 booster dose of Synflorix™

Notes:

[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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RTS,S Regimen A Group	Engerix B Regimen A Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130	121		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1	649.9 (464.7 to 908.9)	840.1 (603.4 to 1169.7)		
Opsono-4	2347.1 (1847.4 to 2982)	2527.8 (2064.1 to 3095.7)		
Opsono-5	324.2 (244.1 to 430.5)	392.8 (291.3 to 529.6)		
Opsono-6B	955.3 (761.4 to 1198.6)	828.2 (652.7 to 1050.9)		
Opsono-7F	9167.3 (7979.2 to 10532.3)	7794.6 (6577.6 to 9236.8)		
Opsono-9V	3035.3 (2523.3 to 3651.3)	3164.6 (2669.8 to 3751.1)		
Opsono-14	1975.7 (1565.8 to 2493)	1865 (1463.9 to 2375.9)		

Opsono-18C	1694.1 (1188.6 to 2414.7)	1548.7 (1096.3 to 2188)		
Opsono-19F	344.5 (223 to 532.3)	469.7 (320 to 689.4)		
Opsono-23F	3199.8 (2543.7 to 4025.1)	3198.1 (2526.5 to 4048.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-protein D (PD) antibody concentrations

End point title	Anti-protein D (PD) antibody concentrations ^[9]
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End point description:

Anti-PD antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs), in ELISA units per milliliter (EL.U/mL). The cut-off of the assay was the seropositivity cut-off value of greater than or equal to 100 EL.U/mL. This outcome concerns the subjects who received the RTS,S or Engerix-B™ vaccine co-administered with Synflorix™. Results presented are for the study groups pooled by co-administration, that is, for the RTS,S Regimen A and Engerix-B Regimen A groups.

End point type	Secondary
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End point timeframe:

At Month 3, aka at one month post Dose 3 of Synflorix™

Notes:

[9] - 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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RTS,S Regimen A Group	Engerix B Regimen A Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	141	134		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	2435.3 (2204.3 to 2690.6)	2956.7 (2647.5 to 3302.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-protein D (PD) antibody concentrations

End point title	Anti-protein D (PD) antibody concentrations ^[10]
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End point description:

Anti-PD antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs), in ELISA units per milliliter (EL.U/mL). The cut-off

of the assay was the seropositivity cut-off value of greater than or equal to 100 EL.U/mL.

End point type	Secondary
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End point timeframe:

At Month 17, aka one month post the Month 16 booster dose of Synflorix™

Notes:

[10] - 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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RTS,S Regimen A Group	Engerix B Regimen A Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	126		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	2648.3 (2194.2 to 3196.4)	2819.1 (2391.1 to 3323.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against acellular B-pertussis (BPT)

End point title	Concentrations of antibodies against acellular B-pertussis (BPT)
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End point description:

The antibodies against BPT assessed were against pertussis toxoid (anti-PT), against filamentous haemagglutinin (anti-FHA), and against pertactin (anti-PRN). Concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs), in ELISA units per milliliter (EL.U/mL). The cut-off of the assay was the seropositivity cut-off value of greater than or equal to ($\geq$) 5 EL.U/mL.

End point type	Secondary
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End point timeframe:

At Day 0 and at Month 3 (one month post Dose 3 of Infanrix™-Hib)

End point values	RTS,S Group	Engerix B Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	401	253		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT – At Day 0	3.8 (3.6 to 4.1)	4.3 (3.9 to 4.8)		
Anti-PT – At Month 3	105.9 (99.2 to 113.1)	114.2 (104.8 to 124.5)		
Anti-FHA – At Day 0	13.9 (12.7 to 15.2)	15.7 (14.1 to 17.5)		

Anti-FHA – At Month 3	271.1 (252.8 to 290.8)	292.9 (268.9 to 319.1)		
Anti-PRN – At Day 0	3.2 (3 to 3.4)	3.2 (3 to 3.5)		
Anti-PRN – At Month 3	164.1 (153.6 to 175.3)	179.7 (164.4 to 196.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Rotavirus (anti-RV) antibody concentrations

End point title	Anti-Rotavirus (anti-RV) antibody concentrations ^[11]
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End point description:

Anti-Rotavirus (anti-RV) antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs). The cut-off of the assay was the seropositive cut-off value of greater than or equal to ($\geq$) 20 units per milliliter (U/mL). This outcome measure was assessed in subjects who were administered Rotarix™ as part of an EPI regimen, with and without RTS,S vaccine co-administration. This outcome concerns the subjects who received the RTS,S or Engerix-B™ vaccine co-administered with Rotarix™. Results presented are for the study groups pooled by RTS,S or Engerix-B™ vaccine co-administration, that is, for the RTS,S Regimen B and Engerix-B Regimen B groups.

End point type	Secondary
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End point timeframe:

At Month 3, aka one month post Dose 2 of Rotarix™

Notes:

[11] - 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 of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	RTS,S Regimen B Group	Engerix B Regimen B Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	116		
Units: U/mL				
geometric mean (confidence interval 95%)				
U/mL	24.9 (19.3 to 32)	27.6 (20.8 to 36.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms
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End point description:

Assessed solicited local symptoms were pain, redness and swelling at the site of injection. All solicited local symptoms assessed were considered by the investigator as causally related to the study vaccination. Analysis for this outcome was performed solely for the 7-days follow-up periods following

the primary vaccination with RTS,S vaccine or Engerix-B™ (at Day 0, and Months 1 and 2). Data presented are those for any occurrence of the assessed solicited local symptoms, that is, the occurrences of these symptoms regardless of their intensity grade.

End point type	Secondary
End point timeframe:	
Within the 7-day follow-up period (Days 0-6) after administration of Dose (D) 1, 2 and 3, respectively, with RTS,S or Engerix-B™ vaccine	

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	142	142	141	141
Units: Subject				
Pain - Post D1	41	28	31	29
Pain - Post D2	30	14	21	24
Pain - Post D3	14	10	14	18
Redness - Post D1	1	0	2	5
Redness - Post D2	5	1	2	3
Redness - Post D3	3	0	1	3
Swelling - Post D1	5	2	6	10
Swelling - Post D2	8	3	4	9
Swelling - Post D3	7	2	6	11

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Pain - Post D1	15			
Pain - Post D2	9			
Pain - Post D3	7			
Redness - Post D1	1			
Redness - Post D2	0			
Redness - Post D3	0			
Swelling - Post D1	4			
Swelling - Post D2	4			
Swelling - Post D3	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms
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End point description:

Assessed solicited general symptoms were fever, irritability/fussiness, drowsiness, and loss of appetite. Fever was defined as axillary temperature higher than (>) 37.5 degrees Celsius (°C). Analysis for this outcome was performed solely for the 7-days follow-up periods following the primary vaccination with RTS,S vaccine or Engerix-B™ (at Day 0, and Months 1 and 2). Data presented are those for any occurrence of the assessed solicited general symptoms, that is, the occurrences of these symptoms regardless of their intensity grade or relationship to vaccination.

End point type	Secondary
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End point timeframe:

Within the 7-day follow-up period (Days 0-6) after administration of Dose (D) 1, 2 and 3, respectively, with RTS,S or Engerix-B™ vaccine

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	142	142	141	141
Units: Subject				
Fever – D1	44	20	16	23
Fever – D2	30	14	18	20
Fever – D3	38	20	26	16
Irritability – D1	15	11	11	9
Irritability – D2	13	7	12	10
Irritability – D3	5	3	10	6
Drowsiness – D1	2	1	3	3
Drowsiness – D2	5	1	1	3
Drowsiness – D3	3	0	2	1
Loss of appetite – D1	4	1	2	4
Loss of appetite – D2	3	1	1	3
Loss of appetite – D3	2	0	1	1

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Fever – D1	13			
Fever – D2	5			
Fever – D3	12			
Irritability – D1	5			
Irritability – D2	0			
Irritability – D3	1			
Drowsiness – D1	0			
Drowsiness – D2	0			
Drowsiness – D3	0			
Loss of appetite – D1	0			
Loss of appetite – D2	0			
Loss of appetite – D3	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential immune mediated disorders (pIMDs)

End point title	Number of subjects with potential immune mediated disorders (pIMDs)
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End point description:

A potential immune mediated disorder (pIMD) was defined as an event about which concerns arose that vaccination may have interfered with immunological self-tolerance of the subjects. IMDs assessed included among others neuroinflammatory disorders (such as optic neuritis, multiple sclerosis, or encephalitis), musculoskeletal disorders (such as cutaneous lupus, rheumatoid arthritis, juvenile arthritis, or psoriatic arthropathy), gastrointestinal disorders (ulcerative colitis and ulcerative proctitis, celiac disease), metabolic diseases (such as autoimmune thyroiditis, or diabetes Mellitus Type 1, Addison's disease), skin disorders (such as psoriasis or vitiligo), and other disorders such as vasculitis, pernicious anemia, or, sarcoidosis.

End point type	Secondary
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End point timeframe:

From Day 0 to Month 8.

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	142	142	141	141
Units: Subject				
Subject	0	0	0	0

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Subject	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential immune mediated disorders (pIMDs)

End point title	Number of subjects with potential immune mediated disorders (pIMDs)
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End point description:

A potential immune mediated disorder (pIMD) was defined as an event about which concerns arose that vaccination may have interfered with immunological self-tolerance of the subjects. IMDs assessed included among others neuroinflammatory disorders (such as optic neuritis, multiple sclerosis, or encephalitis), musculoskeletal disorders (such as cutaneous lupus, rheumatoid arthritis, juvenile arthritis, or psoriatic arthropathy), gastrointestinal disorders (ulcerative colitis and ulcerative proctitis, celiac disease), metabolic diseases (such as autoimmune thyroiditis, or diabetes Mellitus Type 1, Addison's disease), skin disorders (such as psoriasis or vitiligo), and other disorders such as vasculitis, pernicious anemia, or, sarcoidosis.

End point type	Secondary
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End point timeframe:

From study start at Day 0 to Month 26

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	142	142	141	141
Units: Subject				
Subject	0	0	0	0

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Subject	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)
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End point description:

An unsolicited AE was defined as an untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

End point type	Secondary
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End point timeframe:

Within the 30-day follow-up periods (Days 0-29) after vaccination with RTS,S vaccine or Engerix-B™

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	142	142	141	141
Units: Subject				
Subject	121	115	120	120

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Subject	105			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and fatal serious adverse events (SAEs)

End point title	Number of subjects with any and fatal serious adverse events (SAEs)
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End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or a reported adverse event of specific interest such as seizures occurring within a 30-day period of vaccination, immune-mediated disorders, and specific autoimmune diseases. A fatal SAE was defined as a SAE resulting in the death of the study subject.

End point type	Secondary
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End point timeframe:

Within the 30-day follow-up periods (Days 0-29) after vaccination with RTS,S vaccine or Engerix-B™

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	142	142	141	141
Units: Subject				
Subject with SAE(s)	1	3	3	1
Subjects with fatal SAE(s)	1	0	1	0

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Subject with SAE(s)	3			
Subjects with fatal SAE(s)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and fatal serious adverse events (SAEs)

End point title	Number of subjects with any and fatal serious adverse events (SAEs)
End point description:	
A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or a reported adverse event of specific interest such as seizures occurring within a 30-day period of vaccination, immune-mediated disorders, and specific autoimmune diseases. A fatal SAE was defined as a SAE resulting in the death of the study subject.	
End point type	Secondary
End point timeframe:	
From Day 0 to Month 8	

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	142	142	141	141
Units: Subject				
Subjects with SAE(s)	1	7	7	3
Subjects with fatal SAE(s)	1	2	2	0

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Subjects with SAE(s)	5			
Subjects with fatal SAE(s)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and fatal serious adverse events (SAEs)

End point title	Number of subjects with any and fatal serious adverse events (SAEs)
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End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or a reported adverse event of specific interest such as seizures occurring within a 30-day period of vaccination, immune-mediated disorders, and specific autoimmune diseases. A fatal SAE was defined as a SAE resulting in the death of the study subject.

End point type	Secondary
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End point timeframe:

From Day 0 to Month 26

End point values	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group	Engerix B Regimen A Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	142	142	141	141
Units: Subject				
Any SAEs - At Month 26	1	8	7	6
Fatal SAEs - At Month 26	1	3	2	2

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Any SAEs - At Month 26	6			
Fatal SAEs - At Month 26	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local, general symptoms and Unsolicited AEs: Within the 30-day periods after primary vaccination. SAEs: Within the 30-day periods after primary vaccination and from Day 0 to Month 26.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	RTS,S Regimen A Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen A Lot 1, RTS,S Regimen A Lot 2 and RTS,S Regimen A Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™, at Weeks 0, 4 and 8, and 2 doses of Rotarix™ vaccine, at Weeks 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	RTS,S Regimen B Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen B Lot 1, RTS,S Regimen B Lot 2 and RTS,S Regimen B Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	RTS,S Regimen C Group
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Reporting group description:

This group results from the pooling of the RTS,S Regimen C Lot 1, RTS,S Regimen C Lot 2 and RTS,S Regimen C Lot 3 groups. Subjects, healthy male and female infants aged between 8 and 12 weeks inclusive at the time of first vaccination, received 3 doses of RTS,S vaccine, Lot 1, 2 or 3, co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™, at Weeks 6 and 10, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. In addition, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. The RTS,S vaccine and Engerix B™ were administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	Engerix B Regimen B Group
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Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen B. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib and Polio Sabin™, at Weeks 0, 4 and 8, 2 doses of Rotarix™ vaccine, at Weeks 4 and 8, and 3 doses of Synflorix™ at Weeks 2, 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Reporting group title	Engerix B Regimen A Group
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Reporting group description:

Subjects, healthy male and female infants between 8 and 12 weeks of age inclusive at the time of first vaccination, received the Engerix-B Vaccination Regimen A. This regimen included 3 doses of Engerix B™ co-administered with Infanrix™-Hib, Polio Sabin™ and Synflorix™ at Weeks 0, 4 and 8, and 2 doses of Rotarix™, at Weeks 6 and 10. Additionally, subjects also received one dose of vaccine against yellow fever and against measles, at Week 32, and one booster dose of Infanrix™-Hib and Synflorix™, at Month 16, and one booster dose of Engerix B™ vaccine, at Month 50. Engerix B™ was administered intramuscularly (IM) in the left anterolateral thigh, Infanrix™-Hib IM in the right deltoid, Synflorix™ IM in the right anterolateral thigh, and Rotarix™ and Polio Sabin™ orally. The measles and yellow fever vaccines were administered IM in the deltoid.

Serious adverse events	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 142 (0.70%)	7 / 142 (4.93%)	7 / 141 (4.96%)
number of deaths (all causes)	1	3	2
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 142 (0.70%)	1 / 142 (0.70%)	2 / 141 (1.42%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Malaria			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 142 (0.00%)	2 / 142 (1.41%)	2 / 141 (1.42%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Trichomoniasis intestinal			

subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Serious adverse events	Engerix B Regimen B Group	Engerix B Regimen A Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 139 (3.60%)	3 / 141 (2.13%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			

subjects affected / exposed	1 / 139 (0.72%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 139 (0.72%)	1 / 141 (0.71%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 139 (0.72%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 139 (0.72%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaria			
subjects affected / exposed	1 / 139 (0.72%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 139 (0.72%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fungal infection			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 139 (0.72%)	2 / 141 (1.42%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trichomoniasis intestinal			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 139 (0.00%)	0 / 141 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	RTS,S Regimen A Group	RTS,S Regimen B Group	RTS,S Regimen C Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	129 / 142 (90.85%)	123 / 142 (86.62%)	128 / 141 (90.78%)
Nervous system disorders			
Somnolence			

subjects affected / exposed occurrences (all)	8 / 142 (5.63%) 10	2 / 142 (1.41%) 2	6 / 141 (4.26%) 5
General disorders and administration site conditions			
Pain			
subjects affected / exposed	55 / 142 (38.73%)	40 / 142 (28.17%)	47 / 141 (33.33%)
occurrences (all)	85	52	66
Swelling			
subjects affected / exposed	17 / 142 (11.97%)	7 / 142 (4.93%)	14 / 141 (9.93%)
occurrences (all)	20	7	16
Pyrexia			
alternative assessment type: Non- systematic			
subjects affected / exposed	81 / 142 (57.04%)	49 / 142 (34.51%)	50 / 141 (35.46%)
occurrences (all)	116	56	66
Eye disorders			
Conjunctivitis			
alternative assessment type: Non- systematic			
subjects affected / exposed	8 / 142 (5.63%)	10 / 142 (7.04%)	11 / 141 (7.80%)
occurrences (all)	8	10	12
Skin and subcutaneous tissue disorders			
Erythema			
alternative assessment type: Non- systematic			
subjects affected / exposed	19 / 142 (13.38%)	8 / 142 (5.63%)	20 / 141 (14.18%)
occurrences (all)	19	8	20
Psychiatric disorders			
Irritability / fussiness			
subjects affected / exposed	28 / 142 (19.72%)	18 / 142 (12.68%)	27 / 141 (19.15%)
occurrences (all)	33	21	33
Infections and infestations			
Malaria			
alternative assessment type: Non- systematic			
subjects affected / exposed	44 / 142 (30.99%)	44 / 142 (30.99%)	39 / 141 (27.66%)
occurrences (all)	50	54	46
Gastroenteritis			
alternative assessment type: Non- systematic			
subjects affected / exposed	42 / 142 (29.58%)	47 / 142 (33.10%)	51 / 141 (36.17%)
occurrences (all)	55	58	71

Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	32 / 142 (22.54%)	35 / 142 (24.65%)	33 / 141 (23.40%)
occurrences (all)	37	41	41
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	36 / 142 (25.35%)	33 / 142 (23.24%)	28 / 141 (19.86%)
occurrences (all)	47	35	35
Pharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	23 / 142 (16.20%)	13 / 142 (9.15%)	15 / 141 (10.64%)
occurrences (all)	24	15	19
Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	11 / 142 (7.75%)	12 / 142 (8.45%)	6 / 141 (4.26%)
occurrences (all)	11	13	6
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	15 / 142 (10.56%)	8 / 142 (5.63%)	12 / 141 (8.51%)
occurrences (all)	17	9	15
Respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 142 (4.23%)	8 / 142 (5.63%)	14 / 141 (9.93%)
occurrences (all)	6	8	17
Fungal skin infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 142 (0.70%)	7 / 142 (4.93%)	6 / 141 (4.26%)
occurrences (all)	1	7	6
Bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 142 (6.34%)	5 / 142 (3.52%)	5 / 141 (3.55%)
occurrences (all)	8	5	5
Pneumonia			
alternative assessment type: Non-systematic			

subjects affected / exposed	5 / 142 (3.52%)	14 / 142 (9.86%)	4 / 141 (2.84%)
occurrences (all)	5	15	4

Non-serious adverse events	Engerix B Regimen B Group	Engerix B Regimen A Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	114 / 139 (82.01%)	132 / 141 (93.62%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 139 (0.00%)	7 / 141 (4.96%)	
occurrences (all)	0	5	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	25 / 139 (17.99%)	48 / 141 (34.04%)	
occurrences (all)	32	71	
Swelling			
subjects affected / exposed	10 / 139 (7.19%)	23 / 141 (16.31%)	
occurrences (all)	11	30	
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	34 / 139 (24.46%)	55 / 141 (39.01%)	
occurrences (all)	37	65	
Eye disorders			
Conjunctivitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 139 (5.04%)	9 / 141 (6.38%)	
occurrences (all)	7	10	
Skin and subcutaneous tissue disorders			
Erythema			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 139 (4.32%)	12 / 141 (8.51%)	
occurrences (all)	6	13	
Psychiatric disorders			
Irritability / fussiness			
subjects affected / exposed	5 / 139 (3.60%)	19 / 141 (13.48%)	
occurrences (all)	6	25	
Infections and infestations			

Malaria		
alternative assessment type: Non-systematic		
subjects affected / exposed	44 / 139 (31.65%)	48 / 141 (34.04%)
occurrences (all)	53	51
Gastroenteritis		
alternative assessment type: Non-systematic		
subjects affected / exposed	38 / 139 (27.34%)	43 / 141 (30.50%)
occurrences (all)	47	57
Rhinitis		
alternative assessment type: Non-systematic		
subjects affected / exposed	31 / 139 (22.30%)	31 / 141 (21.99%)
occurrences (all)	36	36
Bronchitis		
alternative assessment type: Non-systematic		
subjects affected / exposed	29 / 139 (20.86%)	28 / 141 (19.86%)
occurrences (all)	37	31
Pharyngitis		
alternative assessment type: Non-systematic		
subjects affected / exposed	17 / 139 (12.23%)	14 / 141 (9.93%)
occurrences (all)	18	17
Otitis media		
alternative assessment type: Non-systematic		
subjects affected / exposed	10 / 139 (7.19%)	15 / 141 (10.64%)
occurrences (all)	11	19
Upper respiratory tract infection		
alternative assessment type: Non-systematic		
subjects affected / exposed	7 / 139 (5.04%)	8 / 141 (5.67%)
occurrences (all)	10	9
Respiratory tract infection		
alternative assessment type: Non-systematic		
subjects affected / exposed	6 / 139 (4.32%)	8 / 141 (5.67%)
occurrences (all)	7	9
Fungal skin infection		
alternative assessment type: Non-systematic		

subjects affected / exposed	4 / 139 (2.88%)	12 / 141 (8.51%)	
occurrences (all)	4	12	
Bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 139 (2.88%)	4 / 141 (2.84%)	
occurrences (all)	4	4	
Pneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 139 (1.44%)	11 / 141 (7.80%)	
occurrences (all)	2	11	

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