



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	v2 (current)
This version publication date	27 December 2019
First version publication date	17 August 2017
Version creation reason	<ul style="list-style-type: none">• New data added to full data set New available data added to the full data set.

Trial information

Trial identification

Sponsor protocol code	113681
-----------------------	--------

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	Final
Date of interim/final analysis	26 April 2018
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	Ghana: 197
Country: Number of subjects enrolled	Burkina Faso: 508
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:	
<p>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.</p>	
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:	
<p>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.</p>	
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
------------------	---------------------------

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	131	128	123
Not completed	11	14	18
Adverse event, non-fatal	3	5	4
Lost to follow-up	8	9	14

Number of subjects in period 1	Engerix B Regimen A Group	Engerix B Regimen B Group
Started	141	139
Completed	132	129
Not completed	9	10
Adverse event, non-fatal	2	1
Lost to follow-up	7	9

Baseline characteristics

Reporting groups

Reporting group title	RTS,S Regimen A Group
-----------------------	-----------------------

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
-----------------------	-----------------------

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
-----------------------	-----------------------

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
-----------------------	---------------------------

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
-----------------------	---------------------------

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			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	142	142	141
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: weeks			
arithmetic mean	8.4	8.3	8.3
standard deviation	± 0.83	± 0.62	± 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			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	141	139	705
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: weeks			
arithmetic mean	8.3	8.3	-
standard deviation	± 0.74	± 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

Subject analysis sets

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, Engerix B and vaccines against yellow fever and against measles. 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.

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

Subject analysis set description:

Subjects in this group were subjects from the Engerix B Regimen A and Engerix B Regimen B groups who were administered Engerix 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. 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 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 regiment received, doses of Infanrix-Hib, Polio Sabin, Rotarix, Synflorix, Rotarix, Engerix B and vaccines against yellow fever and against measles. 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.

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 regiment received, doses of Infanrix-Hib, Polio Sabin, Rotarix, Synflorix, Rotarix, Engerix B and vaccines against yellow fever and against measles. 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.

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, Engerix B and vaccines against yellow fever and against measles. 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 values	RTS,S Group	Engerix B Group	RTS,S Lot 1 Group
Number of subjects	425	280	141
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	425	280	141
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: weeks			
arithmetic mean	0	0	0
standard deviation	± 0	± 0	± 0
Gender categorical			
Units: Subjects			
Female	195	144	59
Male	230	136	82
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage/African American	425	280	141

Reporting group values	RTS,S Lot 2 Group	RTS,S Lot 3 Group	
Number of subjects	142	142	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	142	142	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: weeks			
arithmetic mean	0	0	

standard deviation	± 0	± 0	
--------------------	-----	-----	--

Gender categorical			
Units: Subjects			
Female	66	70	
Male	76	72	
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage/African American	142	142	

End points

End points reporting groups

Reporting group title	RTS,S Regimen A Group
Reporting group description:	
<p>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.</p>	
Reporting group title	RTS,S Regimen B Group
Reporting group description:	
<p>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.</p>	
Reporting group title	RTS,S Regimen C Group
Reporting group description:	
<p>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.</p>	
Reporting group title	Engerix B Regimen A Group
Reporting group description:	
<p>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.</p>	
Reporting group title	Engerix B Regimen B Group
Reporting group description:	
<p>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.</p>	

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 who 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 RTS,S Group and Enderix B Group

End point title	Anti-Hepatitis B (HBs) antibody concentrations RTS,S Group and Enderix B Group ^[1]
-----------------	---

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
----------------	---------

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: This outcome was descriptive; hence no statistical analyses were required.

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 for all study Groups

End point title	Anti-Hepatitis B (HBs) antibody concentrations for all study Groups ^[2]
-----------------	--

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, for each RTS,S Regimen A, B, C and each Engerix B Regimen A and B study groups.

End point type	Primary
----------------	---------

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: This outcome was descriptive; hence no statistical analyses were required.

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

Primary: Percentage of seroprotected subjects against Anti-Hepatitis B (HBs) antigen

End point title	Percentage of seroprotected subjects against Anti-Hepatitis B (HBs) antigen
-----------------	---

End point description:

A seroprotected subject was defined as a subject with anti-HBs antibody titers greater than or equal to (\geq) the cutoff of 10 milli-international units per milliliter (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
----------------	---------

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 Group	Engerix B Group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	397	253		
Units: Percentage of subjects				
number (confidence interval 95%)	100 (99.1 to 100)	96 (92.9 to 98.1)		

Statistical analyses

Statistical analysis title	Anti-HBs: difference in seroprotection rate
Statistical analysis description: Non-inferiority of the immune response to the hepatitis B antigen induced by RTS,S/AS01E vaccine versus a licensed hepatitis B vaccine.	
Comparison groups	RTS,S Group v Engerix B Group
Number of subjects included in analysis	650
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
Method	ANOVA
Parameter estimate	Difference in percent seroprotection
Point estimate	-3.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.12
upper limit	-2.16

Notes:

[3] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the difference in percent seroprotection below 5% between recipients of licensed hepatitis B vaccine (Engerix-B) and recipients of RTS,S/AS01E vaccine.

Secondary: Anti-Hepatitis B (HBs) antibody concentrations at Month 3

End point title	Anti-Hepatitis B (HBs) antibody concentrations at Month 3
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)	
--------	---------------------------	---------------------------	---------------------------	--

Statistical analyses

Statistical analysis title	Anti-HBs: lot1-to-lot2 consistency
Statistical analysis description:	
To demonstrate the lot-to-lot consistency in terms of anti-HBs immunogenicity between three commercial lots of the RTS,S/AS01E candidate malaria vaccine.	
Comparison groups	RTS,S Lot 2 Group v RTS,S Lot 1 Group
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	equivalence ^[4]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.2

Notes:

[4] - Criteria for consistency: one month post Dose 3 of RTS,S/AS01E, the two-sided 95% confidence interval (CI) of the geometric mean concentration (GMC) ratio between all pairs of lots are within [0.5, 2].

Statistical analysis title	Anti-HBs: lot1-to-lot3 consistency
Statistical analysis description:	
To demonstrate the lot-to-lot consistency in terms of anti-HBs immunogenicity between three commercial lots of the RTS,S/AS01E candidate malaria vaccine.	
Comparison groups	RTS,S Lot 1 Group v RTS,S Lot 3 Group
Number of subjects included in analysis	263
Analysis specification	Pre-specified
Analysis type	equivalence ^[5]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.32

Notes:

[5] - Criteria for consistency: one month post Dose 3 of RTS,S/AS01E, the two-sided 95% confidence interval (CI) of the geometric mean concentration (GMC) ratio between all pairs of lots are within [0.5, 2].

Statistical analysis title	Anti-HBs: lot2-to-lot3 consistency
Statistical analysis description:	
To demonstrate the lot-to-lot consistency in terms of anti-HBs immunogenicity between three commercial lots of the RTS,S/AS01E candidate malaria vaccine.	

Comparison groups	RTS,S Lot 2 Group v RTS,S Lot 3 Group
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	equivalence ^[6]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.45

Notes:

[6] - Criteria for consistency: one month post Dose 3 of RTS,S/AS01E, the two-sided 95% confidence interval (CI) of the geometric mean concentration (GMC) ratio between all pairs of lots are within [0.5, 2].

Secondary: Anti-Hepatitis B (HBs) antibody concentrations at Month 14 and 26

End point title	Anti-Hepatitis B (HBs) antibody concentrations at Month 14 and 26
-----------------	---

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 each RTS,S Regimen A, B & C, and for each Engerix B Regimen A & B study groups.

End point type	Secondary
----------------	-----------

End point timeframe:

At Months 14 and 26, aka at 12 and 24 months 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	133	118	129	127
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs – At Month 14	1530.1 (1259.4 to 1859.1)	2430.9 (1975.7 to 2991.0)	2189.1 (1840.3 to 2603.9)	119.5 (91 to 157)
Anti-HBs – At Month 26	1092.6 (867.4 to 1376.3)	1896.0 (1487.2 to 2417.3)	1849.8 (1478.9 to 2313.6)	68.8 (50.7 to 93.3)

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	114			

Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs – At Month 14	137.5 (103.3 to 183.2)			
Anti-HBs – At Month 26	71 (51.6 to 97.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies to the Hepatitis B RF1 surface antigen (anti-HBs RF1) at Month 3

End point title	Concentrations of antibodies to the Hepatitis B RF1 surface antigen (anti-HBs RF1) at Month 3
-----------------	---

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. The table shows results for each RTS,S Regimen A, B & C, and for each Engerix B Regimen A & B study groups.

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 at Month 3

End point title	Anti-circumsporozoite protein (anti-CS) antibody concentrations at Month 3
-----------------	--

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 for each RTS,S Regimen A, B & C, and for each Engerix B Regimen A & B study groups.

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)	0.3 (0.3 to 0.3)

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 at Month 14

End point title	Anti-circumsporozoite protein (anti-CS) antibody concentrations at Month 14
-----------------	---

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 for each RTS,S Regimen A, B & C, and for each Engerix B Regimen A & B study groups. No anti-CS results are available for the time point 24 months post Dose 3 (Month 26) because the quantity of serum available for the anti-CS assay was insufficient for many samples.

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 14, aka at 12 months 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	91	82	96	85
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
EL.U/mL	5.7 (4.2 to 7.7)	6.8 (5.0 to 9.4)	7.5 (5.3 to 10.6)	0.3 (0.3 to 0.3)

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	76			
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: Pneumococcal antibody concentrations against Synflorix pneumococcal vaccine serotypes at Month 3

End point title	Pneumococcal antibody concentrations against Synflorix pneumococcal vaccine serotypes at Month 3 ^[7]
-----------------	---

End point description:

Antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), 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 the standard ELISA value of 0.35 µg/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
----------------	-----------

End point timeframe:

At Month 3, aka at one month 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 results in this study were tabulated by the study groups pooled by co-administration. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

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 (3.0 to 4.0)	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 (1.0 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 (5.0 to 6.7)	5.7 (4.7 to 7.0)		
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

Statistical analysis title	Antibody against pneumococcal serotype 1 response
----------------------------	---

Statistical analysis description:

To demonstrate the non-inferiority of antibody against serotype 1 responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.

Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[8]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.39

Notes:

[8] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Antibody against pneumococcal serotype 4 response
-----------------------------------	---

Statistical analysis description:

To demonstrate the non-inferiority of antibody against serotype 4 responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.

Comparison groups	Engerix B Regimen A Group v RTS,S Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[9]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.48

Notes:

[9] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Antibody against pneumococcal serotype 5 response
-----------------------------------	---

Statistical analysis description:

To demonstrate the non-inferiority of antibody against serotype 5 responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.

Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[10]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.52

Notes:

[10] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

	Antibody against pneumococcal serotype 6B response
--	--

Statistical analysis title	
Statistical analysis description:	
To demonstrate the non-inferiority of antibody against serotype 6B responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.	
Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[11]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.65

Notes:

[11] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for Nothing selected the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Antibody against pneumococcal serotype 7F response
Statistical analysis description:	
To demonstrate the non-inferiority of antibody against serotype 7F responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.	
Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[12]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.33

Notes:

[12] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Antibody against pneumococcal serotype 9V response
Statistical analysis description:	
To demonstrate the non-inferiority of antibody against serotype 9V responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.	
Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group

Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[13]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	1.63

Notes:

[13] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Antibody against pneumococcal serotype 14 response
Statistical analysis description:	
To demonstrate the non-inferiority of antibody against serotype 14 responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.	
Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[14]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.27

Notes:

[14] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Antibody against pneumococcal serotype18C response
Statistical analysis description:	
To demonstrate the non-inferiority of antibody against 18C responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.	
Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[15]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	2.38

Notes:

[15] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Antibody against pneumococcal serotype19F response
-----------------------------------	--

Statistical analysis description:

To demonstrate the non-inferiority of antibody against serotype 19F responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.

Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[16]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.65

Notes:

[16] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Antibody against pneumococcal serotype23F response
-----------------------------------	--

Statistical analysis description:

To demonstrate the non-inferiority of antibody against 23F responses to the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.

Comparison groups	RTS,S Regimen A Group v Engerix B Regimen A Group
Number of subjects included in analysis	276
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[17]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.55

Notes:

[17] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of 10 pneumococcal serotypes titers (measured with an ELISA test), is below a limit of 2 for the pneumococcal conjugate vaccine when co-administered with versus without RTS,S/AS01E.

Secondary: Pneumococcal antibody concentrations against Synflorix pneumococcal vaccine serotypes at Month 17

End point title	Pneumococcal antibody concentrations against Synflorix pneumococcal vaccine serotypes at Month 17 ^[18]
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 the standard ELISA value of 0.35 µg/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

End point timeframe:

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

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The results in this study were tabulated by the study groups pooled by co-administration. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

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 8.0)		
ANTI-5	6.5 (5.5 to 7.8)	7.6 (6.4 to 9.1)		
ANTI-6B	4.7 (4.0 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	6.0 (5.1 to 7.1)	5.7 (4.9 to 6.6)		
ANTI-14	9.0 (7.6 to 10.7)	9.0 (7.4 to 10.8)		
ANTI-18C	13.7 (11.5 to 16.3)	14.5 (12.3 to 17.2)		
ANTI-19F	6.0 (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 at Month 3

End point title	Titers for opsonophagocytic activity against Synflorix pneumococcal vaccine serotypes at Month 3 ^[19]
-----------------	--

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 coadministration, that is, for the RTS,S Regimen A and Engerix-B Regimen A groups.

End point type	Secondary
----------------	-----------

End point timeframe:

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

Notes:

[19] - 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 results in this study were tabulated by the study groups pooled by co-administration. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

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 at Month 17

End point title	Titers for opsonophagocytic activity against Synflorix pneumococcal vaccine serotypes at Month 17 ^[20]
-----------------	---

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 coadministration, that is, for the RTS,S Regimen A and Engerix -B Regimen A groups.

End point type	Secondary
----------------	-----------

End point timeframe:

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

Notes:

[20] - 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 results in this study were tabulated by the study groups pooled by co-administration. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

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 at Month 3

End point title	Anti-protein D (PD) antibody concentrations at Month 3 ^[21]
-----------------	--

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
----------------	-----------

End point timeframe:

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

Notes:

[21] - 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 results in this study were tabulated by the study groups pooled by co-administration. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

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 at Month 17

End point title	Anti-protein D (PD) antibody concentrations at Month 17 ^[22]
-----------------	---

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
----------------	-----------

End point timeframe:

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

Notes:

[22] - 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 results in this study were tabulated by the study groups pooled by co-administration. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

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) at Day 0 and at Month 3

End point title	Concentrations of antibodies against acellular B-pertussis (BPT) at Day 0 and at Month 3
-----------------	--

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. The table shows results for study groups pooled by primary vaccine administered (RTS,S vs Engerix -B).

End point type	Secondary
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

Statistical analysis title	Anti-PT response
Statistical analysis description: To demonstrate the non-inferiority of antibody response to the acellular B pertussis antigen, pertussis toxoid, (PT) of the DTPa/Hib vaccine when co-administered with RTS,S/AS01E as part of an EPI regimen.	
Comparison groups	RTS,S Group v Engerix B Group
Number of subjects included in analysis	654
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[23]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.2

Notes:

[23] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of anti-PT, anti-FHA, anti-PRN antibody concentrations, is below a limit of 2 for the DTPa/Hib vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Anti-FHA response
Statistical analysis description: To demonstrate the non-inferiority of antibody response to the acellular B pertussis antigen, filamentous haemagglutinin (FHA), of the DTPa/Hib vaccine when co-administered with RTS,S/AS01E as part of an EPI regimen.	
Comparison groups	Engerix B Group v RTS,S Group
Number of subjects included in analysis	654
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[24]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.21

Notes:

[24] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of anti-PT, anti-FHA, anti-PRN antibody concentrations, is below a limit of 2 for the DTPa/Hib vaccine when co-administered with versus without RTS,S/AS01E.

Statistical analysis title	Anti-PRN response
Statistical analysis description: To demonstrate the non-inferiority of antibody response to the acellular B pertussis antigen, pertactin (anti-PRN), of the DTPa/Hib vaccine when co-administered with RTS,S/AS01E as part of an EPI regimen.	
Comparison groups	RTS,S Group v Engerix B Group

Number of subjects included in analysis	654
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[25]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.22

Notes:

[25] - Criteria for non-inferiority: one month post Dose 3, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the GMC ratios of anti-PT, anti-FHA, anti-PRN antibody concentrations, is below a limit of 2 for the DTPa/Hib vaccine when co-administered with versus without RTS,S/AS01E.

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

End point title	Anti-Rotavirus (anti-RV) antibody concentrations ^[26]
-----------------	--

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
----------------	-----------

End point timeframe:

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

Notes:

[26] - 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 results in this study were tabulated by the study groups pooled by co-administration. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

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

Statistical analysis title	Anti-RV response
----------------------------	------------------

Statistical analysis description:

To demonstrate the non-inferiority of antibody response to the rotavirus vaccine when co-administered with versus without RTS,S/AS01E as part of an EPI regimen.

Comparison groups	Engerix B Regimen B Group v RTS,S Regimen B Group
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[27]
Method	ANOVA
Parameter estimate	GMC ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.61

Notes:

[27] - Criteria for non-inferiority: one month post Dose 2, upper limit (UL) of the 2-sided 95% confidence interval (CI) on the geometric mean concentrations (GMC) ratios of rotavirus antibodies (IgA) concentrations is below 2 for the rotavirus vaccine when coadministered with versus without RTS,S/AS01E.

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms
-----------------	--

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
-----------------	--

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
----------------	-----------

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) from Day 0 to Month 8

End point title	Number of subjects with potential immune mediated disorders (pIMDs) from Day 0 to Month 8
-----------------	---

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
----------------	-----------

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) from Day 0 to Month 26

End point title	Number of subjects with potential immune mediated disorders (pIMDs) from Day 0 to Month 26
-----------------	--

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
----------------	-----------

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)
-----------------	--

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
----------------	-----------

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)

within the 30-day follow-up periods (Days 0-29)

End point title	Number of subjects with any and fatal serious adverse events (SAEs) within the 30-day follow-up periods (Days 0-29)
-----------------	---

End point description:

A serious adverse event (SAE) was defined as any untoward medical occurrence that resulted in death, was lifethreatening, 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:

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) from Day 0 to Month 8

End point title	Number of subjects with any and fatal serious adverse events (SAEs) from Day 0 to Month 8
-----------------	---

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) from Day 0 to Month 26

End point title	Number of subjects with any and fatal serious adverse events (SAEs) from Day 0 to Month 26
-----------------	--

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 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

Secondary: Anti-Hepatitis B (HBs) antibody concentrations at Month 38, 50 and 51

End point title	Anti-Hepatitis B (HBs) antibody concentrations at Month 38, 50 and 51
-----------------	---

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 each RTS,S Regimen A, B & C, and for each Engerix B Regimen A & B study groups.

End point type	Secondary
----------------	-----------

End point timeframe:

At Months 38, 50 and 51, aka 36 and 48 months post Dose 3 of RTS,S vaccine or Engerix-B and one month post the Month 50 booster dose of 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	131	111	122	127
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Month 38	706.8 (548.0 to 911.6)	1081.7 (845.3 to 1384.2)	977.4 (786.7 to 1214.3)	39.0 (29.0 to 52.4)
Month 50	499.4 (382.2 to 652.6)	765.3 (590.5 to 992.0)	807.3 (649.6 to 1003.4)	29.2 (22.0 to 38.7)
Month 51	32345.9 (24758.5 to 42258.4)	54977.1 (43579.1 to 69356.4)	59630.0 (48606.1 to 73154.0)	8995.0 (5935.8 to 13631.0)

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Month 38	41.2 (29.8 to 57.0)			
Month 50	32.9 (23.9 to 45.4)			
Month 51	9578.9 (6374.2 to 14395.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies to the Hepatitis B RF1 surface antigen (anti- HBs RF1) at Month 51

End point title	Concentrations of antibodies to the Hepatitis B RF1 surface antigen (anti- HBs RF1) at Month 51
-----------------	---

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. The table shows results for each RTS,S Regimen A, B & C, and for each Engerix B Regimen A & B study groups.

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 51, aka one month post the Month 50 booster dose of 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	124	104	113	107
Units: EL.U/mL				
geometric mean (confidence interval 95%)	307.8 (239.0 to 396.4)	471.6 (372.5 to 597.1)	514.5 (415.3 to 637.5)	120.5 (86.6 to 167.6)

End point values	Engerix B Regimen B			
------------------	---------------------	--	--	--

	Group			
Subject group type	Reporting group			
Number of subjects analysed	95			
Units: EL.U/mL				
geometric mean (confidence interval 95%)	127.9 (94.5 to 173.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-circumsporozoite protein (anti-CS) antibody concentrations at Month 38 and 50

End point title	Anti-circumsporozoite protein (anti-CS) antibody concentrations at Month 38 and 50
-----------------	--

End point description:

Anti-CS antibody concentrations were determined by enzyme-linked immunosorbent assay (ELISA) and 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) 1.9 EL.U/mL. The table shows results for each RTS,S Regimen A, B & C, and for each Engerix B Regimen A & B study groups.

End point type	Secondary
----------------	-----------

End point timeframe:

At Months 38 and 50, aka 36 and 48 months 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	131	111	122	127
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Month 38	2.6 (2.2 to 3.1)	2.8 (2.3 to 3.4)	3.5 (2.9 to 4.2)	1.0 (1.0 to 1.1)
Month 50	2.3 (2.0 to 2.7)	2.4 (2.0 to 2.8)	2.7 (2.3 to 3.2)	1.1 (1.0 to 1.1)

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	107			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Month 38	1.0 (1.0 to 1.0)			
Month 50	1.1 (1.0 to 1.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with potential immune mediated disorders (pIMDs) from Day 0 up to Study End (Month 51)

End point title	Number of subjects with potential immune mediated disorders (pIMDs) from Day 0 up to Study End (Month 51)
-----------------	---

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
----------------	-----------

End point timeframe:

From Day 0 up to Study End (Month 51)

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	0	0	0	0

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, fatal and related serious adverse events (SAEs) from Day 0 up to Study End (Month 51)

End point title	Number of subjects with any, fatal and related serious adverse events (SAEs) from Day 0 up to Study End (Month 51)
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. A related SAE was defined as a SAE assessed by the investigator as being causally related to vaccination.	
End point type	Secondary
End point timeframe:	
From Day 0 up to Study End (Month 51)	

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	3	10	9	6
Fatal SAEs	3	5	4	2
Related SAEs	0	0	0	0

End point values	Engerix B Regimen B Group			
Subject group type	Reporting group			
Number of subjects analysed	139			
Units: Subject				
Any SAEs	6			
Fatal SAEs	1			
Related SAEs	0			

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 co-administration vaccination. SAEs: during the entire study period (Month 0 to Month 51).

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	20.1
--------------------	------

Reporting groups

Reporting group title	RTS,S Regimen A Group
-----------------------	-----------------------

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
-----------------------	-----------------------

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
-----------------------	-----------------------

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
-----------------------	---------------------------

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
-----------------------	---------------------------

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.

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	3 / 142 (2.11%)	10 / 142 (7.04%)	9 / 141 (6.38%)
number of deaths (all causes)	3	5	4
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
Glucose-6-phosphate dehydrogenase deficiency			
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
Cardiac disorders			
Cardiac failure congestive			
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
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	1 / 142 (0.70%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Intravascular haemolysis			
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
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
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
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
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	1 / 142 (0.70%)	2 / 142 (1.41%)	2 / 141 (1.42%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
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	1 / 142 (0.70%)	2 / 142 (1.41%)	2 / 141 (1.42%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	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
Bacterial sepsis			
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
Bronchiolitis			

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
Meningitis bacterial			
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
Meningitis streptococcal			
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
Salmonella sepsis			
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
Sepsis			
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 / 1
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 A Group	Engerix B Regimen B Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 141 (4.26%)	6 / 139 (4.32%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	0	0	

Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (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 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glucose-6-phosphate dehydrogenase deficiency			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (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 / 141 (0.71%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 141 (2.13%)	2 / 139 (1.44%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Intravascular haemolysis			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 141 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 141 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaria			
subjects affected / exposed	2 / 141 (1.42%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (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	0 / 141 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal infection			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (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	2 / 141 (1.42%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trichomoniasis intestinal			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (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 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 141 (0.00%)	1 / 139 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Meningitis bacterial			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis streptococcal			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonella sepsis			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (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 / 141 (0.00%)	0 / 139 (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: 0 %

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	135 / 142 (95.07%)	129 / 142 (90.85%)	132 / 141 (93.62%)
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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Allergic bronchitis subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	2 / 142 (1.41%) 2	2 / 141 (1.42%) 2
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	28 / 142 (19.72%) 33	18 / 142 (12.68%) 21	27 / 141 (19.15%) 33
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	1 / 142 (0.70%) 1	0 / 141 (0.00%) 0
Foreign body in eye subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	1 / 142 (0.70%) 1	0 / 141 (0.00%) 0
Wound subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	0 / 142 (0.00%) 0	1 / 141 (0.71%) 1
Congenital, familial and genetic disorders Respiratory tract malformation subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Nervous system disorders Somnolence subjects affected / exposed occurrences (all)	8 / 142 (5.63%) 10	2 / 142 (1.41%) 2	5 / 141 (3.55%) 6
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 2	0 / 142 (0.00%) 0	1 / 141 (0.71%) 1
Iron deficiency anaemia			

subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Ear and labyrinth disorders Excessive cerumen production subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	1 / 142 (0.70%) 1	1 / 141 (0.71%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	1 / 142 (0.70%) 1	1 / 141 (0.71%) 1
Anal fissure subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	1 / 142 (0.70%) 1	1 / 141 (0.71%) 1
Enteritis subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Skin and subcutaneous tissue disorders Erythema alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	19 / 142 (13.38%) 19	8 / 142 (5.63%) 8	20 / 141 (14.18%) 20
Dermatitis subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	1 / 142 (0.70%) 1	1 / 141 (0.71%) 1

Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Dermatitis atopic subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	3 / 142 (2.11%) 3	0 / 141 (0.00%) 0
Dermatitis diaper subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	1 / 142 (0.70%) 1	0 / 141 (0.00%) 0
Dermatosis subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	1 / 142 (0.70%) 1	3 / 141 (2.13%) 3
Eczema subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	0 / 142 (0.00%) 0	1 / 141 (0.71%) 1
Prurigo subjects affected / exposed occurrences (all)	1 / 142 (0.70%) 1	0 / 142 (0.00%) 0	4 / 141 (2.84%) 4
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	1 / 142 (0.70%) 1	0 / 141 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all)	0 / 142 (0.00%) 0	0 / 142 (0.00%) 0	0 / 141 (0.00%) 0
Infections and infestations Conjunctivitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	8 / 142 (5.63%) 8	10 / 142 (7.04%) 10	11 / 141 (7.80%) 12
Malaria alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	44 / 142 (30.99%) 50	44 / 142 (30.99%) 54	39 / 141 (27.66%) 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	16 / 142 (11.27%)	8 / 142 (5.63%)	12 / 141 (8.51%)
occurrences (all)	18	9	15
Respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 142 (7.04%)	14 / 142 (9.86%)	15 / 141 (10.64%)
occurrences (all)	10	16	18
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	8 / 142 (5.63%)	5 / 142 (3.52%)	5 / 141 (3.55%)
occurrences (all)	9	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
Abscess			
subjects affected / exposed	2 / 142 (1.41%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences (all)	2	0	1
Acarodermatitis			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	1	0	0
Anal fungal infection			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	0	0	0
Bullous impetigo			
subjects affected / exposed	3 / 142 (2.11%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	3	0	0
Candida infection			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences (all)	0	0	1
Conjunctivitis bacterial			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences (all)	1	0	1
Dysentery			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	1 / 141 (0.71%)
occurrences (all)	0	1	1
Ear infection			
subjects affected / exposed	2 / 142 (1.41%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	2	0	0
Folliculitis			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	1	0	0
Fungal infection			

subjects affected / exposed	3 / 142 (2.11%)	3 / 142 (2.11%)	5 / 141 (3.55%)
occurrences (all)	3	3	5
Furuncle			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal candidiasis			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences (all)	0	0	1
Impetigo			
subjects affected / exposed	3 / 142 (2.11%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences (all)	3	1	0
Laryngitis			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	2 / 141 (1.42%)
occurrences (all)	1	0	2
Oral candidiasis			
subjects affected / exposed	5 / 142 (3.52%)	3 / 142 (2.11%)	3 / 141 (2.13%)
occurrences (all)	5	3	3
Oral herpes			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	4 / 142 (2.82%)	3 / 142 (2.11%)	1 / 141 (0.71%)
occurrences (all)	4	3	1
Otitis media acute			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	1	0	0
Parasitic gastroenteritis			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences (all)	0	1	0
Pyoderma			
subjects affected / exposed	5 / 142 (3.52%)	7 / 142 (4.93%)	5 / 141 (3.55%)
occurrences (all)	7	7	5
Rash pustular			

subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	0	0	0
Skin bacterial infection			
subjects affected / exposed	1 / 142 (0.70%)	1 / 142 (0.70%)	1 / 141 (0.71%)
occurrences (all)	1	1	1
Staphylococcal infection			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	0	0	0
Staphylococcal skin infection			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	0 / 141 (0.00%)
occurrences (all)	1	0	0
Tinea infection			
subjects affected / exposed	0 / 142 (0.00%)	2 / 142 (1.41%)	2 / 141 (1.42%)
occurrences (all)	0	2	2
Urinary tract infection			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	3 / 141 (2.13%)
occurrences (all)	0	1	3
Viral infection			
subjects affected / exposed	1 / 142 (0.70%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences (all)	1	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 142 (0.70%)	1 / 142 (0.70%)	1 / 141 (0.71%)
occurrences (all)	1	1	1
Visceral larva migrans			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 141 (0.71%)
occurrences (all)	0	0	1
Wound infection			
subjects affected / exposed	1 / 142 (0.70%)	1 / 142 (0.70%)	0 / 141 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	7 / 142 (4.93%)	2 / 142 (1.41%)	4 / 141 (2.84%)
occurrences (all)	9	2	4

Non-serious adverse events	Engerix B Regimen A Group	Engerix B Regimen B Group	
Total subjects affected by non-serious adverse events			

subjects affected / exposed	135 / 141 (95.74%)	119 / 139 (85.61%)	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	48 / 141 (34.04%)	25 / 139 (17.99%)	
occurrences (all)	71	32	
Swelling			
subjects affected / exposed	23 / 141 (16.31%)	10 / 139 (7.19%)	
occurrences (all)	30	11	
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	55 / 141 (39.01%)	34 / 139 (24.46%)	
occurrences (all)	65	37	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 141 (0.00%)	2 / 139 (1.44%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis			
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Irritability			
subjects affected / exposed	19 / 141 (13.48%)	5 / 139 (3.60%)	
occurrences (all)	25	6	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 141 (0.00%)	1 / 139 (0.72%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences (all)	0	0	
Foreign body in eye			

subjects affected / exposed occurrences (all)	0 / 141 (0.00%) 0	0 / 139 (0.00%) 0	
Wound subjects affected / exposed occurrences (all)	0 / 141 (0.00%) 0	1 / 139 (0.72%) 1	
Congenital, familial and genetic disorders			
Respiratory tract malformation subjects affected / exposed occurrences (all)	0 / 141 (0.00%) 0	0 / 139 (0.00%) 0	
Nervous system disorders			
Somnolence subjects affected / exposed occurrences (all)	5 / 141 (3.55%) 7	0 / 139 (0.00%) 0	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	2 / 141 (1.42%) 2	2 / 139 (1.44%) 2	
Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 141 (0.00%) 0	0 / 139 (0.00%) 0	
Ear and labyrinth disorders			
Excessive cerumen production subjects affected / exposed occurrences (all)	1 / 141 (0.71%) 1	0 / 139 (0.00%) 0	
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	2 / 141 (1.42%) 2	2 / 139 (1.44%) 2	
Anal fissure subjects affected / exposed occurrences (all)	2 / 141 (1.42%) 2	1 / 139 (0.72%) 1	
Diarrhoea subjects affected / exposed occurrences (all)	2 / 141 (1.42%) 2	0 / 139 (0.00%) 0	
Enteritis			

subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	0 / 141 (0.00%)	1 / 139 (0.72%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Erythema			
alternative assessment type: Non-systematic			
subjects affected / exposed	12 / 141 (8.51%)	6 / 139 (4.32%)	
occurrences (all)	13	6	
Dermatitis			
subjects affected / exposed	1 / 141 (0.71%)	1 / 139 (0.72%)	
occurrences (all)	1	1	
Dermatitis allergic			
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences (all)	1	0	
Dermatitis atopic			
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)	
occurrences (all)	1	0	
Dermatitis diaper			
subjects affected / exposed	2 / 141 (1.42%)	1 / 139 (0.72%)	
occurrences (all)	2	1	
Dermatosis			
subjects affected / exposed	4 / 141 (2.84%)	1 / 139 (0.72%)	
occurrences (all)	4	1	
Eczema			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences (all)	0	0	
Prurigo			

subjects affected / exposed occurrences (all)	0 / 141 (0.00%) 0	1 / 139 (0.72%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 141 (0.00%) 0	0 / 139 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthritis subjects affected / exposed occurrences (all)	0 / 141 (0.00%) 0	1 / 139 (0.72%) 1	
Infections and infestations Conjunctivitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Malaria alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Gastroenteritis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Rhinitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Bronchitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Pharyngitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	9 / 141 (6.38%) 10 49 / 141 (34.75%) 52 43 / 141 (30.50%) 57 31 / 141 (21.99%) 36 28 / 141 (19.86%) 31 15 / 141 (10.64%) 18	7 / 139 (5.04%) 7 44 / 139 (31.65%) 53 38 / 139 (27.34%) 47 31 / 139 (22.30%) 36 29 / 139 (20.86%) 37 17 / 139 (12.23%) 18	

Otitis media		
alternative assessment type: Non-systematic		
subjects affected / exposed	15 / 141 (10.64%)	10 / 139 (7.19%)
occurrences (all)	19	11
Upper respiratory tract infection		
alternative assessment type: Non-systematic		
subjects affected / exposed	8 / 141 (5.67%)	7 / 139 (5.04%)
occurrences (all)	9	10
Respiratory tract infection		
alternative assessment type: Non-systematic		
subjects affected / exposed	12 / 141 (8.51%)	10 / 139 (7.19%)
occurrences (all)	13	11
Fungal skin infection		
alternative assessment type: Non-systematic		
subjects affected / exposed	12 / 141 (8.51%)	4 / 139 (2.88%)
occurrences (all)	12	4
Bronchiolitis		
alternative assessment type: Non-systematic		
subjects affected / exposed	4 / 141 (2.84%)	4 / 139 (2.88%)
occurrences (all)	4	4
Pneumonia		
alternative assessment type: Non-systematic		
subjects affected / exposed	11 / 141 (7.80%)	2 / 139 (1.44%)
occurrences (all)	11	2
Abscess		
subjects affected / exposed	2 / 141 (1.42%)	0 / 139 (0.00%)
occurrences (all)	2	0
Acarodermatitis		
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0
Anal fungal infection		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Bullous impetigo		

subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0
Candida infection		
subjects affected / exposed	2 / 141 (1.42%)	0 / 139 (0.00%)
occurrences (all)	2	0
Conjunctivitis bacterial		
subjects affected / exposed	2 / 141 (1.42%)	0 / 139 (0.00%)
occurrences (all)	2	0
Dysentery		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	2	0
Ear infection		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Folliculitis		
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0
Fungal infection		
subjects affected / exposed	3 / 141 (2.13%)	4 / 139 (2.88%)
occurrences (all)	3	4
Furuncle		
subjects affected / exposed	2 / 141 (1.42%)	2 / 139 (1.44%)
occurrences (all)	2	2
Gastrointestinal candidiasis		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Impetigo		
subjects affected / exposed	2 / 141 (1.42%)	4 / 139 (2.88%)
occurrences (all)	2	4
Laryngitis		
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0
Nasopharyngitis		
subjects affected / exposed	0 / 141 (0.00%)	3 / 139 (2.16%)
occurrences (all)	0	3
Oral candidiasis		

subjects affected / exposed	4 / 141 (2.84%)	1 / 139 (0.72%)
occurrences (all)	4	1
Oral herpes		
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0
Otitis externa		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Otitis media acute		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Parasitic gastroenteritis		
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0
Pyoderma		
subjects affected / exposed	6 / 141 (4.26%)	3 / 139 (2.16%)
occurrences (all)	7	3
Rash pustular		
subjects affected / exposed	0 / 141 (0.00%)	1 / 139 (0.72%)
occurrences (all)	0	1
Skin bacterial infection		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Staphylococcal infection		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Staphylococcal skin infection		
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)
occurrences (all)	0	0
Tinea infection		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Urinary tract infection		
subjects affected / exposed	1 / 141 (0.71%)	0 / 139 (0.00%)
occurrences (all)	1	0
Viral infection		

subjects affected / exposed	1 / 141 (0.71%)	1 / 139 (0.72%)	
occurrences (all)	1	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 141 (0.00%)	1 / 139 (0.72%)	
occurrences (all)	0	1	
Visceral larva migrans			
subjects affected / exposed	0 / 141 (0.00%)	0 / 139 (0.00%)	
occurrences (all)	0	0	
Wound infection			
subjects affected / exposed	0 / 141 (0.00%)	1 / 139 (0.72%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 141 (3.55%)	1 / 139 (0.72%)	
occurrences (all)	8	1	

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