



Clinical trial results:

A phase III, open, controlled study in South Africa to assess the immunogenicity, safety and reactogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine administered as a 3-dose (6, 10, 14 weeks) primary immunization course in HIV infected infants, HIV exposed uninfected infants and HIV unexposed uninfected infants followed by a booster vaccination at 9-10 months of age.

Summary

EudraCT number	2011-002077-35
Trial protocol	Outside EU/EEA
Global end of trial date	27 June 2012

Results information

Result version number	v1
This version publication date	16 February 2016
First version publication date	11 June 2015

Trial information

Trial identification

Sponsor protocol code	111634
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00829010
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)	Yes
EMA paediatric investigation plan number(s)	EMA-000673-PIP01-09
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	02 April 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 June 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate and characterize the immune response to the Synflorix™ vaccine one month following a 3-dose (6, 10 and 14 weeks of age) primary vaccination course in HIV infected infants, HIV exposed uninfected infants and HIV unexposed uninfected infants.

Protection of trial subjects:

All subjects were supervised after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Only eligible subjects that had no contraindications to any components of the vaccines were vaccinated. Subjects were followed-up after each vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	South Africa: 489
Worldwide total number of subjects	489
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)	489
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:

The oral poliovirus vaccine could be given at any time during the study (routinely given concurrently with Tritanrix™-HepB/Hib vaccine) but was not considered as study vaccine. Out of the 489 subjects enrolled in the study, only 484 subjects were assigned to a study group and received vaccination.

Pre-assignment

Screening details:

The study included 3 populations defined based on the human immunodeficiency virus status of the mother and the infant. Infant born from: •a HIV positive mother and HIV infected at Month 0 = HIV+/+. •a HIV positive mother and HIV exposed uninfected at screening = HIV+/- . •a HIV negative mother and HIV unexposed uninfected at Month 0 = HIV-

Pre-assignment period milestones

Number of subjects started	489
Number of subjects completed	484

Pre-assignment subject non-completion reasons

Reason: Number of subjects	subjects non-assigned to a study group: 5
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Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	HIV+/+ Group

Arm description:

Infants born from a HIV positive mother and confirmed as HIV infected. Subjects received 3 primary doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 and 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age and 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered intramuscularly in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ given orally.

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	GSK1024850A
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8).

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPW-HBV/Hib
Pharmaceutical forms	Solution for injection

Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).	
Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	HRV
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details:	
Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).	
Investigational medicinal product name	Measles
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received 2 doses at 9-10 months and 15-18 months of age.	
Arm title	HIV+/- Group
Arm description:	
<p>Infants born from a HIV positive mother and confirmed as HIV exposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.</p>	
Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	GSK1024850A
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8).	
Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPW-HBV/Hib
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).	
Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	HRV
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details:	
Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).	

Investigational medicinal product name	Measles
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects received 2 doses at 9-10 months and 15-18 months of age.	
Arm title	HIV-(3+1) Group

Arm description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	GSK1024850A
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8).

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPW-HBV/Hib
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).

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

Dosage and administration details:

Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).

Investigational medicinal product name	Measles
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses at 9-10 months and 15-18 months of age.

Arm title	HIV-(EPI) Group
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Arm description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses of Synflorix™ vaccine (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study

Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	GSK1024850A
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2).

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPW-HBV/Hib
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).

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

Dosage and administration details:

Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).

Investigational medicinal product name	Measles
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses at 9-10 months and 15-18 months of age.

Arm title	HIV-(2+1) Group
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Arm description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 2 primary doses (at 6 & 14 weeks of age at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	GSK1024850A
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 primary doses (at 6 & 14 weeks of age, at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8).

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPW-HBV/Hib
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14).

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

Dosage and administration details:

Subjects received 2 vaccine doses (at 10 & 14 weeks of age, at study Months 1 and 2).

Investigational medicinal product name	Measles
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses at 9-10 months and 15-18 months of age.

Number of subjects in period 1^[1]	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group
Started	87	97	100
Completed up to Month 9	81	92	98
Completed	81	92	98
Not completed	6	5	2
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	6	3	-
Migrated /moved from study area	-	1	-
Lost to follow-up	-	-	1

Number of subjects in period 1^[1]	HIV-(EPI) Group	HIV-(2+1) Group
Started	100	100
Completed up to Month 9	94	98
Completed	94	98
Not completed	6	2
Consent withdrawn by subject	-	2
Adverse event, non-fatal	3	-
Migrated /moved from study area	3	-

Lost to follow-up	-	-
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Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 5 subjects enrolled, but not allocated to a group and did not receive a vaccine

Baseline characteristics

Reporting groups

Reporting group title	HIV+/+ Group
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Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV infected. Subjects received 3 primary doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 and 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age and 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered intramuscularly in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ given orally.

Reporting group title	HIV+/- Group
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Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV exposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV-(3+1) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV-(EPI) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses of Synflorix™ vaccine (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV-(2+1) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 2 primary doses (at 6 & 14 weeks of age at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group
Number of subjects	87	97	100
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: weeks			
arithmetic mean	6.6	6.3	6.1
standard deviation	± 0.92	± 0.64	± 0.41
Gender categorical Units: Subjects			
Female	50	46	58
Male	37	51	42

Reporting group values	HIV-(EPI) Group	HIV-(2+1) Group	Total
Number of subjects	100	100	484
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: weeks			
arithmetic mean	6.1	6.1	-
standard deviation	± 0.35	± 0.29	-
Gender categorical Units: Subjects			
Female	50	47	251
Male	50	53	233

End points

End points reporting groups

Reporting group title	HIV+/+ Group
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Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV infected. Subjects received 3 primary doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 and 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 and 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age and 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered intramuscularly in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ given orally.

Reporting group title	HIV+/- Group
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Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV exposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV-(3+1) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV-(EPI) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses of Synflorix™ vaccine (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV-(2+1) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 2 primary doses (at 6 & 14 weeks of age at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Primary: Number of Subjects With Anti-pneumococcal Vaccine Serotype Antibody Concentrations Equal to or Above 0.20 Microgram Per Millilitre (µg/mL).

End point title	Number of Subjects With Anti-pneumococcal Vaccine Serotype Antibody Concentrations Equal to or Above 0.20 Microgram Per Millilitre (µg/mL). ^[1]
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End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. Results were not available at the time of the posting and are entered as equal to "9"

End point type	Primary
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End point timeframe:

1 month following primary immunization (post-Dose 3 at Month 3 for the HIV+/+ Group, HIV+/- Group, HIV- (3+1) Group, HIV- (EPI) Group and post-Dose 2 at Month 3 for the HIV- (2+1) Group)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The intent of this endpoint was descriptive, no comparison of groups was performed.

End point values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group	HIV-(EPI) Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	100	100
Units: Subject				
ANTI-1	9	9	9	9

End point values	HIV-(2+1) Group			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Subject				
ANTI-1	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any and Severe (Grade 3) Solicited Local Adverse Events (AEs).

End point title	Number of Subjects With Any and Severe (Grade 3) Solicited Local Adverse Events (AEs).
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End point description:

Solicited local AEs assessed were pain, redness and swelling. Any = incidence of any local symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling above 30 millimeter.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-primary vaccination period across doses.

End point values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group	HIV-(EPI) Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	98	98
Units: Subjects				
Any pain	76	90	92	95
Grade 3 pain	19	17	28	42
Any redness	66	76	83	83
Redness > 30 mm	14	10	17	20
Any swelling	71	79	84	91
Swelling > 30 mm	25	30	41	44

End point values	HIV-(2+1) Group			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: Subjects				
Any pain	97			
Grade 3 pain	34			
Any redness	84			
Redness > 30 mm	14			
Any swelling	84			
Swelling > 30 mm	31			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Any, Severe (Grade 3) and Related Solicited General Adverse Events (AEs).

End point title	Number of Subjects with Any, Severe (Grade 3) and Related Solicited General Adverse Events (AEs).
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End point description:

General AEs = diarrhoea, drowsiness, irritability, loss of appetite, vomiting and fever (axillary ≥ 37.5 degrees Celsius). Any= Incidence of any symptom regardless of intensity grade or relationship to vaccination. Grade 3: drowsiness = prevented normal activity. irritability = crying that could not be comforted/ prevented normal activity. loss of appetite = not eating at all. diarrhoea: ≥ 6 looser than normal stools/day. vomiting: ≥ 3 episodes of vomiting/day. Fever = $> 39.5^{\circ}\text{C}$ Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-primary vaccination period across doses.

End point values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group	HIV-(EPI) Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	98	98
Units: Subjects				
Any diarrhoea	8	5	12	10
Grade 3 diarrhoea	2	0	3	3
Related diarrhoea	8	5	11	9
Any drowsiness	50	61	70	70
Grade 3 drowsiness	1	6	5	7
Related drowsiness	48	57	67	66
Fever (axillary) $\geq 37.5^{\circ}\text{C}$	40	34	41	28
Fever (axillary) $> 39.5^{\circ}\text{C}$	0	0	2	0
Related fever	34	29	38	27
Any irritability	66	81	89	89
Grade 3 irritability	6	10	19	13
Related irritability	65	77	86	83
Any loss of appetite	37	52	56	57
Grade 3 loss of appetite	0	1	2	2
Related loss of appetite	36	46	53	53
Any vomiting	17	19	15	18
Grade 3 vomiting	3	3	4	5
Related vomiting	16	16	14	13

End point values	HIV-(2+1) Group			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: Subjects				
Any diarrhoea	5			
Grade 3 diarrhoea	2			
Related diarrhoea	5			
Any drowsiness	68			
Grade 3 drowsiness	8			
Related drowsiness	63			
Fever (axillary) $\geq 37.5^{\circ}\text{C}$	28			
Fever (axillary) $> 39.5^{\circ}\text{C}$	0			
Related fever	25			
Any irritability	91			
Grade 3 irritability	15			
Related irritability	85			
Any loss of appetite	62			
Grade 3 loss of appetite	5			
Related loss of appetite	58			
Any vomiting	23			
Grade 3 vomiting	2			

Related vomiting	17			
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Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any and Severe (Grade 3) Solicited Local Adverse Events (AEs).

End point title	Number of Subjects With Any and Severe (Grade 3) Solicited Local Adverse Events (AEs). ^[2]
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End point description:

Solicited local AEs assessed were pain, redness and swelling. Any = incidence of any local symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling above 30 millimeter.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) period following booster vaccination with Synflorix vaccine

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Since HIV - (EPI) Group didn't receive booster vaccination, there are no results to be analyzed for that timeframe.

End point values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group	HIV-(2+1) Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	91	96	96
Units: Subjects				
Any pain	42	56	62	60
Grade 3 pain	2	1	2	6
Any redness	27	29	39	45
Redness > 30 mm	5	1	3	0
Any swelling	30	37	38	53
Swelling > 30 mm	5	4	8	10

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any, Severe (Grade 3) and Related Solicited General Adverse Events (AEs).

End point title	Number of Subjects With Any, Severe (Grade 3) and Related Solicited General Adverse Events (AEs). ^[3]
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End point description:

Solicited general AEs = drowsiness, irritability, loss of appetite and fever (axillary ≥ 37.5 degrees Celsius). Any= Incidence of any symptom regardless of intensity grade or relationship to vaccination. Grade 3: drowsiness = prevented normal activity. irritability = crying that could not be comforted/prevented normal activity. loss of appetite = not eating at all. Fever = temperature > 39.5°C Related =

symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) period following booster vaccination with Synflorix vaccine.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Since HIV - (EPI) Group didn't receive booster vaccination, there are no results to be analyzed for that timeframe.

End point values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group	HIV-(2+1) Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	91	96	96
Units: Subjects				
Any drowsiness	19	26	34	33
Grade 3 drowsiness	2	0	1	1
Related drowsiness	18	25	31	32
Fever $\geq 37.5^{\circ}\text{C}$	9	11	7	11
Fever $> 39.5^{\circ}\text{C}$	0	0	0	0
Related fever	8	10	7	10
Any irritability	27	33	31	43
Grade 3 irritability	4	1	1	1
Related irritability	26	33	31	42
Any loss of appetite	17	23	29	37
Grade 3 loss of appetite	0	0	1	2
Related loss of appetite	16	23	29	33

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Unsolicited AEs.

End point title	Number of Subjects With Unsolicited AEs.
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End point description:

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

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) post-primary vaccination period.

End point values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group	HIV-(EPI) Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	100	100
Units: Subjects				
Any AE	76	89	93	90

End point values	HIV-(2+1) Group			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Subjects				
Any AE	97			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Unsolicited AEs.

End point title	Number of Subjects With Unsolicited AEs. ^[4]
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End point description:

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

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) post Synflorix booster vaccination period.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Since HIV - (EPI) Group didn't receive booster vaccination, there are no results to be analyzed for that timeframe.

End point values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group	HIV-(2+1) Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	92	98	98
Units: Subjects				
Any AEs	38	44	50	44

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events (SAEs).

End point title	Number of Subjects With Serious Adverse Events (SAEs).
End point description:	
SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects.	
End point type	Secondary
End point timeframe:	
From study start at Month 0 (6 weeks of age and above) up to 1 month after Sinflorix booster vaccination (up to Month 9).	

End point values	HIV+/+ Group	HIV+/- Group	HIV-(3+1) Group	HIV-(EPI) Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	97	100	100
Units: Subjects				
Any SAEs	27	14	9	8

End point values	HIV-(2+1) Group			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Subjects				
Any SAEs	8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: from Month 0 up to Month 9. Unsolicited AEs: within the 31-day post-primary and post booster Synflorix vaccination period. Solicited AEs: During the 4-day period following the primary and booster Synflorix vaccination.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	HIV+/+ Group
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Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV infected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered intramuscularly in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV+/- Group
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Reporting group description:

Infants born from a HIV positive mother and confirmed as HIV exposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV- (3+1) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV- (EPI) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 3 primary doses of Synflorix™ vaccine (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered

IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Reporting group title	HIV- (2+1) Group
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Reporting group description:

Infants born from a HIV negative mother and confirmed as HIV unexposed uninfected. Subjects received 2 primary doses (at 6 & 14 weeks of age at study Months 0 and 2) and 1 booster dose of Synflorix™ vaccine (at 9 months of age, at study Month 8). Subjects in the group also received 3 primary vaccine doses (at 6, 10 & 14 weeks of age, at study Months 0, 1 and 2) and 1 booster vaccine dose (at 15-18 months of age, at study Month 14) of Tritanrix™-HepB/Hib, 2 vaccine doses of Rotarix™ (at 10 & 14 weeks of age, at study Months 1 and 2), and 2 doses of measles vaccine (9-10 months of age & 15-18 months of age, at study Months 8 and 14). Measles vaccine was not considered as a study vaccine. The Synflorix™ vaccine was administered IM in the right thigh, the Tritanrix™-HepB/Hib vaccine was administered IM in the left anterolateral thigh during the primary vaccination and in the left anterolateral thigh or left deltoid region during booster vaccination. Rotarix™ was given orally.

Serious adverse events	HIV+/+ Group	HIV+/- Group	HIV- (3+1) Group
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 87 (31.03%)	14 / 97 (14.43%)	9 / 100 (9.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Herbal toxicity			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 100 (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
Near drowning			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 100 (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
Thermal burn			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 100 (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
Congenital, familial and genetic disorders			
Cerebral palsy			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 100 (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
Trisomy 21			

subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 100 (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
Ventricular septal defect			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 100 (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
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (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
Febrile convulsion			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 100 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (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
Sudden death			
subjects affected / exposed	2 / 87 (2.30%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0

Sudden infant death syndrome subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Vomiting			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis neonatal			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 100 (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
Renal and urinary disorders			
Renal impairment			

subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Aids encephalopathy			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 87 (1.15%)	1 / 97 (1.03%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	12 / 87 (13.79%)	3 / 97 (3.09%)	3 / 100 (3.00%)
occurrences causally related to treatment / all	0 / 12	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Croup infectious			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 100 (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
Cytomegalovirus infection			
subjects affected / exposed	2 / 87 (2.30%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	7 / 87 (8.05%)	3 / 97 (3.09%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	1 / 7	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
H1n1 influenza			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 100 (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
Measles			
subjects affected / exposed	1 / 87 (1.15%)	2 / 97 (2.06%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Meningitis meningococcal			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis tuberculous			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	4 / 87 (4.60%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 87 (1.15%)	1 / 97 (1.03%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			

subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	10 / 87 (11.49%)	1 / 97 (1.03%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 10	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	0 / 100 (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
Tuberculosis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 97 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 87 (2.30%)	2 / 97 (2.06%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	2 / 87 (2.30%)	1 / 97 (1.03%)	2 / 100 (2.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			

subjects affected / exposed	0 / 87 (0.00%)	1 / 97 (1.03%)	0 / 100 (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
Metabolism and nutrition disorders			
Kwashiorkor			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Marasmus			
subjects affected / exposed	1 / 87 (1.15%)	0 / 97 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	HIV- (EPI) Group	HIV- (2+1) Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 100 (8.00%)	8 / 100 (8.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Herbal toxicity			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Near drowning			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cerebral palsy			

subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trisomy 21			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular septal defect			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	2 / 100 (2.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Febrile convulsion			
subjects affected / exposed	0 / 100 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (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			
Death			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Sudden death			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sudden infant death syndrome			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis neonatal			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			

subjects affected / exposed	0 / 100 (0.00%)	2 / 100 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Aids encephalopathy			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 100 (0.00%)	2 / 100 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 100 (2.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1n1 influenza			

subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Measles			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis meningococcal			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis tuberculous			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (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	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			

subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Kwashiorkor			
subjects affected / exposed	1 / 100 (1.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Marasmus			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	HIV+/+ Group	HIV+/- Group	HIV- (3+1) Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 87 (87.36%)	90 / 97 (92.78%)	93 / 100 (93.00%)
General disorders and administration site conditions			
Diarrhoea (solicited post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[1]	8 / 87 (9.20%)	5 / 97 (5.15%)	12 / 98 (12.24%)
occurrences (all)	8	5	12
Drowsiness (solicited post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[2]	50 / 87 (57.47%)	61 / 97 (62.89%)	70 / 98 (71.43%)
occurrences (all)	50	61	70
Drowsiness (solicited post-booster)			
alternative assessment type: Systematic			

subjects affected / exposed ^[3]	19 / 78 (24.36%)	26 / 91 (28.57%)	34 / 96 (35.42%)
occurrences (all)	19	26	34
Fever (post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[4]	40 / 87 (45.98%)	34 / 97 (35.05%)	41 / 98 (41.84%)
occurrences (all)	40	34	41
Fever (post-booster)			
alternative assessment type: Systematic			
subjects affected / exposed ^[5]	9 / 78 (11.54%)	11 / 91 (12.09%)	7 / 96 (7.29%)
occurrences (all)	9	11	7
Irritability (post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[6]	66 / 87 (75.86%)	81 / 97 (83.51%)	89 / 98 (90.82%)
occurrences (all)	66	81	89
Irritability (post-booster)			
alternative assessment type: Systematic			
subjects affected / exposed ^[7]	27 / 78 (34.62%)	33 / 91 (36.26%)	31 / 96 (32.29%)
occurrences (all)	27	33	31
Loss of appetite (post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[8]	37 / 87 (42.53%)	52 / 97 (53.61%)	56 / 98 (57.14%)
occurrences (all)	37	52	56
Loss of appetite (post-booster)			
alternative assessment type: Systematic			
subjects affected / exposed ^[9]	17 / 78 (21.79%)	23 / 91 (25.27%)	29 / 96 (30.21%)
occurrences (all)	17	23	29
Pain (post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[10]	76 / 87 (87.36%)	90 / 97 (92.78%)	92 / 98 (93.88%)
occurrences (all)	76	90	92
Pain (post-booster)			
alternative assessment type: Systematic			
subjects affected / exposed ^[11]	42 / 78 (53.85%)	56 / 91 (61.54%)	62 / 96 (64.58%)
occurrences (all)	42	56	62

Redness (post-primary) alternative assessment type: Systematic subjects affected / exposed ^[12] occurrences (all)	66 / 87 (75.86%) 66	76 / 97 (78.35%) 76	83 / 98 (84.69%) 83
Redness (post-booster) alternative assessment type: Systematic subjects affected / exposed ^[13] occurrences (all)	27 / 78 (34.62%) 27	29 / 91 (31.87%) 29	39 / 96 (40.63%) 39
Swelling (post-primary) alternative assessment type: Systematic subjects affected / exposed ^[14] occurrences (all)	71 / 87 (81.61%) 71	79 / 97 (81.44%) 79	84 / 98 (85.71%) 84
Swelling (post-booster) alternative assessment type: Systematic subjects affected / exposed ^[15] occurrences (all)	30 / 78 (38.46%) 30	37 / 91 (40.66%) 37	38 / 96 (39.58%) 38
Vomiting (solicited post-primary) alternative assessment type: Systematic subjects affected / exposed ^[16] occurrences (all)	17 / 87 (19.54%) 17	19 / 97 (19.59%) 19	15 / 98 (15.31%) 15
Gastrointestinal disorders Diarrhoea (unsol. primary) subjects affected / exposed occurrences (all)	13 / 87 (14.94%) 13	16 / 97 (16.49%) 16	18 / 100 (18.00%) 18
Diarrhoea (unsol. post-booster) subjects affected / exposed ^[17] occurrences (all)	5 / 80 (6.25%) 5	10 / 92 (10.87%) 10	10 / 98 (10.20%) 10
Vomiting (unsolicited post-primary) subjects affected / exposed occurrences (all)	18 / 87 (20.69%) 18	16 / 97 (16.49%) 16	11 / 100 (11.00%) 11
Vomiting (unsolicited post-booster) subjects affected / exposed ^[18] occurrences (all)	1 / 80 (1.25%) 1	8 / 92 (8.70%) 8	7 / 98 (7.14%) 7
Respiratory, thoracic and mediastinal disorders			

Cough (post-primary) subjects affected / exposed occurrences (all)	38 / 87 (43.68%) 38	69 / 97 (71.13%) 69	67 / 100 (67.00%) 67
Cough (post-booster) subjects affected / exposed ^[19] occurrences (all)	19 / 80 (23.75%) 19	21 / 92 (22.83%) 21	24 / 98 (24.49%) 24
Nasal Obstruction (post-primary) subjects affected / exposed occurrences (all)	29 / 87 (33.33%) 29	40 / 97 (41.24%) 40	50 / 100 (50.00%) 50
Nasal Obstruction (post-booster) subjects affected / exposed ^[20] occurrences (all)	7 / 80 (8.75%) 7	4 / 92 (4.35%) 4	6 / 98 (6.12%) 6
Rhinorrhoea subjects affected / exposed ^[21] occurrences (all)	1 / 80 (1.25%) 1	5 / 92 (5.43%) 5	7 / 98 (7.14%) 7
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	9 / 87 (10.34%) 9	12 / 97 (12.37%) 12	11 / 100 (11.00%) 11
Rash (post-primary) subjects affected / exposed occurrences (all)	27 / 87 (31.03%) 27	24 / 97 (24.74%) 24	16 / 100 (16.00%) 16
Rash (post-booster) subjects affected / exposed ^[22] occurrences (all)	4 / 80 (5.00%) 4	4 / 92 (4.35%) 4	3 / 98 (3.06%) 3
Infections and infestations Upper respiratory tract infection (post-primary) subjects affected / exposed occurrences (all)	4 / 87 (4.60%) 4	13 / 97 (13.40%) 13	13 / 100 (13.00%) 13
Upper respiratory tract infection (post-booster) subjects affected / exposed ^[23] occurrences (all)	3 / 80 (3.75%) 3	4 / 92 (4.35%) 4	6 / 98 (6.12%) 6
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed ^[24] occurrences (all)	4 / 80 (5.00%) 4	6 / 92 (6.52%) 6	4 / 98 (4.08%) 4

Non-serious adverse events	HIV- (EPI) Group	HIV- (2+1) Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	95 / 100 (95.00%)	97 / 100 (97.00%)	
General disorders and administration site conditions			
Diarrhoea (solicited post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[1]	10 / 98 (10.20%)	5 / 98 (5.10%)	
occurrences (all)	10	5	
Drowsiness (solicited post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[2]	70 / 98 (71.43%)	68 / 98 (69.39%)	
occurrences (all)	70	68	
Drowsiness (solicited post-booster)			
alternative assessment type: Systematic			
subjects affected / exposed ^[3]	0 / 100 (0.00%)	33 / 96 (34.38%)	
occurrences (all)	0	33	
Fever (post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[4]	28 / 98 (28.57%)	28 / 98 (28.57%)	
occurrences (all)	28	28	
Fever (post-booster)			
alternative assessment type: Systematic			
subjects affected / exposed ^[5]	0 / 100 (0.00%)	11 / 96 (11.46%)	
occurrences (all)	0	11	
Irritability (post-primary)			
alternative assessment type: Systematic			
subjects affected / exposed ^[6]	89 / 98 (90.82%)	91 / 98 (92.86%)	
occurrences (all)	89	91	
Irritability (post-booster)			
alternative assessment type: Systematic			
subjects affected / exposed ^[7]	0 / 100 (0.00%)	43 / 96 (44.79%)	
occurrences (all)	0	43	
Loss of appetite (post-primary)			
alternative assessment type: Systematic			

subjects affected / exposed ^[8]	57 / 98 (58.16%)	62 / 98 (63.27%)
occurrences (all)	57	62
Loss of appetite (post-booster)		
alternative assessment type: Systematic		
subjects affected / exposed ^[9]	0 / 100 (0.00%)	37 / 96 (38.54%)
occurrences (all)	0	37
Pain (post-primary)		
alternative assessment type: Systematic		
subjects affected / exposed ^[10]	95 / 98 (96.94%)	97 / 98 (98.98%)
occurrences (all)	95	97
Pain (post-booster)		
alternative assessment type: Systematic		
subjects affected / exposed ^[11]	0 / 100 (0.00%)	60 / 96 (62.50%)
occurrences (all)	0	60
Redness (post-primary)		
alternative assessment type: Systematic		
subjects affected / exposed ^[12]	83 / 98 (84.69%)	84 / 98 (85.71%)
occurrences (all)	83	84
Redness (post-booster)		
alternative assessment type: Systematic		
subjects affected / exposed ^[13]	0 / 100 (0.00%)	45 / 96 (46.88%)
occurrences (all)	0	45
Swelling (post-primary)		
alternative assessment type: Systematic		
subjects affected / exposed ^[14]	91 / 98 (92.86%)	84 / 98 (85.71%)
occurrences (all)	91	84
Swelling (post-booster)		
alternative assessment type: Systematic		
subjects affected / exposed ^[15]	0 / 100 (0.00%)	53 / 96 (55.21%)
occurrences (all)	0	53
Vomiting (solicited post-primary)		
alternative assessment type: Systematic		
subjects affected / exposed ^[16]	18 / 98 (18.37%)	23 / 98 (23.47%)
occurrences (all)	18	23

Gastrointestinal disorders			
Diarrhoea (unsol. primary) subjects affected / exposed occurrences (all)	13 / 100 (13.00%) 13	7 / 100 (7.00%) 7	
Diarrhoea (unsol. post-booster) subjects affected / exposed ^[17] occurrences (all)	0 / 100 (0.00%) 0	8 / 98 (8.16%) 8	
Vomiting (unsolicited post-primary) subjects affected / exposed occurrences (all)	15 / 100 (15.00%) 15	12 / 100 (12.00%) 12	
Vomiting (unsolicited post-booster) subjects affected / exposed ^[18] occurrences (all)	0 / 100 (0.00%) 0	5 / 98 (5.10%) 5	
Respiratory, thoracic and mediastinal disorders			
Cough (post-primary) subjects affected / exposed occurrences (all)	58 / 100 (58.00%) 58	66 / 100 (66.00%) 66	
Cough (post-booster) subjects affected / exposed ^[19] occurrences (all)	0 / 100 (0.00%) 0	13 / 98 (13.27%) 13	
Nasal Obstruction (post-primary) subjects affected / exposed occurrences (all)	49 / 100 (49.00%) 49	51 / 100 (51.00%) 51	
Nasal Obstruction (post-booster) subjects affected / exposed ^[20] occurrences (all)	0 / 100 (0.00%) 0	6 / 98 (6.12%) 6	
Rhinorrhoea subjects affected / exposed ^[21] occurrences (all)	0 / 100 (0.00%) 0	5 / 98 (5.10%) 5	
Skin and subcutaneous tissue disorders			
Eczema subjects affected / exposed occurrences (all)	12 / 100 (12.00%) 12	14 / 100 (14.00%) 14	
Rash (post-primary) subjects affected / exposed occurrences (all)	28 / 100 (28.00%) 28	21 / 100 (21.00%) 21	

Rash (post-booster) subjects affected / exposed ^[22] occurrences (all)	0 / 100 (0.00%) 0	5 / 98 (5.10%) 5	
Infections and infestations Upper respiratory tract infection (post-primary) subjects affected / exposed occurrences (all)	11 / 100 (11.00%) 11	12 / 100 (12.00%) 12	
Upper respiratory tract infection (post-booster) subjects affected / exposed ^[23] occurrences (all)	0 / 100 (0.00%) 0	5 / 98 (5.10%) 5	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed ^[24] occurrences (all)	0 / 100 (0.00%) 0	4 / 98 (4.08%) 4	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the solicited symptom included only subjects with documented data.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the solicited symptom included only subjects with documented data.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

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[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

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[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

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[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

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[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

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[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the unsolicited symptom included only subjects with documented data.

[18] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

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[23] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

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[24] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the unsolicited symptom included only subjects with documented data.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 December 2008	<ul style="list-style-type: none">• Introduction of Prevenar in the national recommended vaccination program of South Africa as from April 2009.• Decision to consider rotavirus vaccine as study vaccine due to its anticipated introduction into the national vaccination program during 2009.• Addition of a rationale for including HIV exposed uninfected children in the study.
29 June 2009	<ul style="list-style-type: none">• Decision to test immunogenicity of the oral poliovirus vaccine (OPV) on request of local authorities.• Permission for inclusion of HIV infected infants with weight for age < 3rd percentile at Visit 1, using standard growth charts, at the discretion of the investigator.
24 February 2010	As a slow enrolment rate of HIV+/+ subjects was observed, it was decided to extend the recruitment time by approximately 6 months in Amendment 3 in order to increase the chance to reach target enrolment in the HIV+/+ study group.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported