



Clinical trial results:

A phase IV, non-randomised, open-label, multicentre study with two parallel groups to assess the immunogenicity and safety of GlaxoSmithKline (GSK) Biologicals' combined DTPa-HBV-IPV/Hib vaccine administered as a three-dose primary vaccination course at 2, 4 and 6 months of age in healthy infants in Canada.

Summary

EudraCT number	2013-003428-34
Trial protocol	Outside EU/EEA
Global end of trial date	12 March 2013

Results information

Result version number	v2 (current)
This version publication date	21 August 2022
First version publication date	30 May 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set• Minor corrections of the full study results.

Trial information

Trial identification

Sponsor protocol code	103506
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00753649
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 November 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2013
Global end of trial reached?	Yes
Global end of trial date	12 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immune response to the Hib component of GSK Biologicals' combined DTPa-HBV-IPV/Hib preservative-free vaccine in terms of seroprotection rates one month after the three-dose primary vaccination course in "Aboriginal infants" and "Other Non-Aboriginal infants".

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 September 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 224
Worldwide total number of subjects	224
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)	224
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:

Study started on 23-Sep-2008 and enrolled 224 subjects from Canada.

Pre-assignment

Screening details:

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

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	Infanrix Hexa Aboriginal Group

Arm description:

Subjects of aboriginal origins who received 3 doses of Infanrix Hexa vaccine at 2, 4, and 6 months of age, administered as an intramuscular injection into the right side of the thigh. Subjects also received two doses of Rotarix vaccine at 2 and 4 months of age (administered orally), a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine according to the recommended provincial infant immunisation schedules.

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

Dosage and administration details:

Three doses of Infanrix Hexa vaccine were administered by injection, intramuscularly in the right side of the thigh, at 2, 4 and 6 months of age. All subjects were offered co-administered vaccines: a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine.

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

Dosage and administration details:

Two doses of Rotarix vaccine were administered concomitantly with the first two doses of Infanrix Hexa vaccine. Rotarix was given orally at 2 and 4 months of age, according to the immunization schedule.

Arm title	Infanrix Hexa Non-Aboriginal Group
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Arm description:

Subjects of non-aboriginal origins who received 3 doses of Infanrix Hexa vaccine at 2, 4, and 6 months of age, administered as an intramuscular injection into the right side of the thigh. Subjects also received two doses of Rotarix vaccine at 2 and 4 months of age (administered orally), a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine according to the recommended provincial infant immunisation schedules.

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

Dosage and administration details:

Three doses of Infanrix Hexa vaccine were administered by injection, intramuscularly in the right side of the thigh, at 2, 4 and 6 months of age. All subjects were offered co-administered vaccines: a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine.

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

Dosage and administration details:

Two doses of Rotarix vaccine were administered concomitantly with the first two doses of Infanrix Hexa vaccine. Rotarix was given orally at 2 and 4 months of age, according to the immunization schedule.

Number of subjects in period 1	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group
Started	112	112
Completed	105	112
Not completed	7	0
Lost to follow-up (subjects with complete vaccinat	1	-
Protocol Violation	2	-
Lost to follow-up (subjects with incomplete vaccin	3	-
Migrated/moved from study area	1	-

Baseline characteristics

Reporting groups

Reporting group title	Infanrix Hexa Aboriginal Group
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Reporting group description:

Subjects of aboriginal origins who received 3 doses of Infanrix Hexa vaccine at 2, 4, and 6 months of age, administered as an intramuscular injection into the right side of the thigh. Subjects also received two doses of Rotarix vaccine at 2 and 4 months of age (administered orally), a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine according to the recommended provincial infant immunisation schedules.

Reporting group title	Infanrix Hexa Non-Aboriginal Group
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Reporting group description:

Subjects of non-aboriginal origins who received 3 doses of Infanrix Hexa vaccine at 2, 4, and 6 months of age, administered as an intramuscular injection into the right side of the thigh. Subjects also received two doses of Rotarix vaccine at 2 and 4 months of age (administered orally), a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine according to the recommended provincial infant immunisation schedules.

Reporting group values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group	Total
Number of subjects	112	112	224
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	9.3	9.2	
standard deviation	± 1.38	± 1.3	-
Gender categorical			
Units: Subjects			
Female	62	52	114
Male	50	60	110

End points

End points reporting groups

Reporting group title	Infanrix Hexa Aboriginal Group
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Reporting group description:

Subjects of aboriginal origins who received 3 doses of Infanrix Hexa vaccine at 2, 4, and 6 months of age, administered as an intramuscular injection into the right side of the thigh. Subjects also received two doses of Rotarix vaccine at 2 and 4 months of age (administered orally), a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine according to the recommended provincial infant immunisation schedules.

Reporting group title	Infanrix Hexa Non-Aboriginal Group
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Reporting group description:

Subjects of non-aboriginal origins who received 3 doses of Infanrix Hexa vaccine at 2, 4, and 6 months of age, administered as an intramuscular injection into the right side of the thigh. Subjects also received two doses of Rotarix vaccine at 2 and 4 months of age (administered orally), a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine according to the recommended provincial infant immunisation schedules.

Primary: Number of seroprotected subjects against Polyribosyl-ribitol phosphate (anti-PRP)

End point title	Number of seroprotected subjects against Polyribosyl-ribitol phosphate (anti-PRP) ^[1]
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End point description:

A seroprotected subject was a subject whose anti-PRP antibody concentration was greater or equal to (\geq) 0.15 microgram per milliliter ($\mu\text{g}/\text{mL}$). The analysis was performed on the According-to-protocol (ATP) cohort for immunogenicity, which included all evaluable subjects who had received 3 doses of Infanrix Hexa vaccine and for whom data concerning immunogenicity outcome measures were available.

End point type	Primary
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End point timeframe:

One month after (POST) Dose 3.

Notes:

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

Justification: The analysis of the primary endpoint was descriptive, hence no statistical hypothesis test was performed.

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	107		
Units: Subjects				
Anti-PRP, POST-M1 [N=94,107]	92	106		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-Polyribosyl-ribitol phosphate (anti-PRP) antibodies with concentrations $\geq 1\mu\text{g}/\text{mL}$

End point title	Number of subjects with anti-Polyribosyl-ribitol phosphate
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End point description:

For this assay, 1 $\mu\text{g/mL}$ was considered as the seropositivity cut-off. The analysis was performed on the According-to-protocol (ATP) cohort for immunogenicity, which included all evaluable subjects who had received 3 doses of Infanrix Hexa vaccine and for whom data concerning immunogenicity outcome measures were available.

End point type Secondary

End point timeframe:

One month after (POST) Dose 3

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	107		
Units: Subjects				
Anti-PRP, POST-M1 [N=94,107]	83	91		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title Anti-PRP antibody concentrations

End point description:

Anti-PRP antibody concentrations were presented as Geometric mean Concentrations (GMC), expressed as micrograms per milliliter ($\mu\text{g/mL}$). The analysis was performed on the According-to-protocol (ATP) cohort for immunogenicity, which included all evaluable subjects who had received 3 doses of Infanrix Hexa vaccine and for whom data concerning immunogenicity outcome measures were available.

End point type Secondary

End point timeframe:

One month after (POST) Dose 3

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	107		
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP, POST-M1 [N=94,107]	6.123 (4.498 to 8.334)	3.51 (2.745 to 4.488)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against Hepatitis B (anti-HBs)

End point title	Number of seroprotected subjects against Hepatitis B (anti-HBs)
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End point description:

A seroprotected subject was a subject with anti-HBs antibody concentrations ≥ 10 milli-International Units per milliliter (mIU/mL). A decrease in the specificity of the anti-HB 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. Some of the available blood samples initially tested with ELISA were re-tested using the new assay, CLIA. The analysis was performed on the According-to-protocol (ATP) cohort for immunogenicity, which included all evaluable subjects who had received 3 doses of Infanrix Hexa vaccine and for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary
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End point timeframe:

One month after (POST) Dose 3.

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	103		
Units: Subjects				
Anti-HBs, POST-M1 [N=91,103]	91	103		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-HBs antibody concentrations ≥ 100 mIU/mL

End point title	Number of subjects with Anti-HBs antibody concentrations ≥ 100 mIU/mL
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End point description:

The testing was done using the Enzyme-Linked Immunosorbent assay (ELISA) assay. The analysis was performed on the According-to-protocol (ATP) cohort for immunogenicity, which included all evaluable subjects who had received 3 doses of Infanrix Hexa vaccine and for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary
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End point timeframe:

One month after (POST) Dose 3

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	103		
Units: Subjects				
Anti-HBs, POST-M1 [N=91,103]	89	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations
End point description:	
Anti-HBs antibody concentrations were assessed by Enzyme-Linked Immunosorbent assay (ELISA) and expressed as geometric mean concentrations (GMCs). The analysis was performed on the According-to-protocol (ATP) cohort for immunogenicity, which included all evaluable subjects who had received 3 doses of Infanrix Hexa vaccine and for whom data concerning immunogenicity outcome measures were available.	
End point type	Secondary
End point timeframe:	
One month after (POST) Dose 3	

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	103		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, POST-M1 [N=91,103]	1797.9 (1375.1 to 2350.7)	1544.4 (1210.4 to 1970.5)		

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 covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and 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. The analysis was based on the Total Vaccinated cohort, which included all subjects with at least one dose of Infanrix hexa	

administration documented.

End point type	Secondary
End point timeframe:	
During the 31 day (Days 0-30) post vaccination	

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Any AEs, [N=112,112]	26	19		

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:	
Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. The analysis was based on the Total Vaccinated cohort, which included all subjects with at least one dose of Infanrix hexa administration documented.	
End point type	Secondary
End point timeframe:	
During the entire study period up to Last subject last visit on 03/12/2013	

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Any SAEs, [N=112,112]	6	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited AEs during the 31-day post-vaccination period, SAEs during the entire period up to Last subject last visit on 03/12/2013.

Adverse event reporting additional description:

During this study, no solicited adverse events were collected, therefore none are reported.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Infanrix Hexa Aboriginal Group
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Reporting group description:

Subjects of aboriginal origins who received 3 doses of Infanrix Hexa vaccine at 2, 4, and 6 months of age, administered as an intramuscular injection into the right side of the thigh. Subjects also received two doses of Rotarix vaccine at 2 and 4 months of age (administered orally), a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine according to the recommended provincial infant immunisation schedules.

Reporting group title	Infanrix Hexa Non-Aboriginal Group
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Reporting group description:

Subjects of non-aboriginal origins who received 3 doses of Infanrix Hexa vaccine at 2, 4, and 6 months of age, administered as an intramuscular injection into the right side of the thigh. Subjects also received two doses of Rotarix vaccine at 2 and 4 months of age (administered orally), a pneumococcal conjugate vaccine, meningococcal serogroup C conjugate vaccine and an influenza vaccine according to the recommended provincial infant immunisation schedules.

Serious adverse events	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 112 (5.36%)	0 / 112 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 112 (1.79%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 112 (5.36%)	0 / 112 (0.00%)	
General disorders and administration site conditions			

Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 112 (5.36%)	0 / 112 (0.00%)	
occurrences (all)	6	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2010	Amendment 2 The protocol was originally designed for sites in British Columbia (BC) and therefore the vaccines that the subject may receive outside of the study were recommended according to the BC vaccination schedule. New sites were selected in provinces where the recommended schedule for vaccine co-administration is different from BC, therefore the protocol is being amended to allow vaccine coadministration according to the provincial schedule rather than the BC schedules. <ul style="list-style-type: none">• Some formatting errors have been corrected in the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported