The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: 112076

Title: A study to evaluate GlaxoSmithKline (GSK) Biologicals' investigational vaccination regimen in healthy young adults

Rationale: This study was designed to assess the safety and immunogenicity of a GSK Biologicals' investigational vaccination regimen in a healthy young adult population. *Engerix*™-B was used as a comparator.
Engerix™-B (HBV): GSK Biologicals' hepatitis B vaccine (HBV)

Phase: I

Study Period: 08 January 2009 to 10 June 2010

Study Design: Observer-blind through 30 days post-dose 2, then partially blind until study conclusion, single centre, randomized (2:2:1), controlled study with 3 study groups.

Data from the group receiving the currently registered GSK Biologicals' vaccine are presented. Data from the groups receiving an investigational vaccination regimen that is not yet approved or marketed are not reported at this time.

Centers: One center in Sweden.

Indication: Vaccination against hepatitis B virus in healthy young adult subjects aged between 18 years old and 40 years old, inclusive.

Treatment: The treatment groups were as follows:

- 2 groups received an investigational vaccination regimen.
- HBV Group: subjects received 3 doses of HBV vaccine at Month 0, 2 and 6.

HBV vaccine was administered intramuscularly into the deltoid region of the non-dominant arm.

Objectives:
Only objectives related to GSK Biologicals' licensed vaccine are presented.
To evaluate the safety profile of HBV vaccine when administered intramuscularly in healthy young adults. as single doses, administered at Month 0, 2 and 6.

Primary Outcome/Efficacy Variable:
Only outcome variables related to GSK Biologicals' licensed vaccine are presented.

- Occurrence of any solicited local and general symptoms during a 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after vaccine doses 1 and 2.
- Occurrence of any unsolicited adverse events (AEs) during a 30-day follow-up period (i.e. day of vaccination and 29 subsequent days) after vaccine doses 1 and 2.
- Occurrence of hematological (red blood cells [RBC] complete count, white blood cells [WBC] complete count, WBC differential count, platelets count, and hemoglobin level) or biochemical (alanine aminotransferase [ALT], aspartate aminotransferase [AST], urea, and creatinine) laboratory abnormalities during 7 days (i.e. day of vaccination and 6 subsequent days) after vaccine doses 1 and 2.
- Occurrence of hematological (complete blood count [RBC, WBC], WBC differential count, platelets count and hemoglobin level) or biochemical (ALT, AST, urea and creatinine) laboratory abnormalities at Day 180, Day 300 and Day 420.
- Occurrence of any serious adverse events (SAE) occurring from first vaccine dose to study conclusion.

Secondary Outcome/Efficacy Variable(s):
Only outcome variables related to GSK Biologicals' licensed vaccine are presented.
Not applicable.

Statistical Methods:
The analyses were performed on the Total Vaccinated cohort, which included all subjects with at least one study vaccine administration documented.

Analysis of safety
The safety analysis was performed on the Total Vaccinated cohort.
The percentage of subjects with each individual solicited local and general symptom reported during the 7-day (Day 0-6) solicited follow-up period after Dose 1 and Dose 2 was tabulated with exact 95% confidence interval (CI). The same tabulation was performed for Grade 3 solicited local and general symptoms and for solicited general symptoms assessed by the investigator as causally related to vaccination.
The occurrence of unsolicited AEs within 30 days (Day 0-29) after Dose 1 and Dose 2 was tabulated according to the

Medical Dictionary for Regulatory Activities (MedDRA) preferred terms.
The occurrence of SAEs during the entire study was tabulated according to the MedDRA preferred terms.
For routine hematology and biochemistry results, Grade 3 or greater (per the local laboratory normative ranges with grading adapted from Food and Drug Administration [FDA] guidance "Toxicity Grading Scale for Healthy Adults and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials", AND judged clinically significant by the Investigator) abnormalities were presented, during the 7 days after doses 1 and 2 and at Days 180, 300 and 420.

Study Population: Healthy male and female adults aged 18 - 40 years at the time of first vaccination, free of obvious health problems as established by medical history and clinical examination before entering the study were included. If female, the subject was of non-childbearing potential or if of childbearing potential, she had to practice adequate contraception for 30 days prior to vaccination and continue such precautions for 2 months after completion of the vaccination series. Written informed consent was obtained from the subject prior to any study procedure.

Number of Subjects:	**HBV Group**
Planned, N	8
Randomized, N (Total Vaccinated cohort)	8
Completed (Day 480), n (%)	7 (87.5)
Total Number Subjects Withdrawn, n (%)	1 (12.5)
Withdrawn due to Adverse Events, n (%)	0 (0.0)
Withdrawn due to Lack of Efficacy, n (%)	Not applicable
Withdrawn for other reasons, n (%)	1 (12.5)
Demographics	**HBV Group**
N (Total Vaccinated cohort)	8
Females: Males	5:3
Mean Age, years (SD)	26.6 (5.50)
White - Caucasian / European heritage, n (%)	8 (100)

Primary Efficacy Results: Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and across doses (Total Vaccinated cohort)

		HBV Group				
					95 % CI	
Symptom	**Intensity**	**N**	**N**	**%**	**LL**	**UL**
Dose 1						
Pain	Any	8	2	25.0	3.2	65.1
	Grade 3	8	0	0.0	0.0	36.9
Redness (mm)	Any	8	1	12.5	0.3	52.7
	>50.0	8	0	0.0	0.0	36.9
Swelling (mm)	Any	8	0	0.0	0.0	36.9
	>50.0	8	0	0.0	0.0	36.9
Dose 2						
Pain	Any	7	3	42.9	9.9	81.6
	Grade 3	7	0	0.0	0.0	41.0
Redness (mm)	Any	7	0	0.0	0.0	41.0
	>50.0	7	0	0.0	0.0	41.0
Swelling (mm)	Any	7	0	0.0	0.0	41.0
	>50.0	7	0	0.0	0.0	41.0
Across doses						
Pain	Any	8	4	50.0	15.7	84.3
	Grade 3	8	0	0.0	0.0	36.9
Redness (mm)	Any	8	1	12.5	0.3	52.7
	>50.0	8	0	0.0	0.0	36.9
Swelling (mm)	Any	8	0	0.0	0.0	36.9
	>50.0	8	0	0.0	0.0	36.9

N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting at least once the symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any= occurrence of any local symptom regardless of intensity grade
Grade 3 pain= pain that prevented normal activity

Primary Efficacy Results: Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and across doses (Total Vaccinated cohort)						
		HBV Group				
					95 % CI	
Symptom	**Intensity/ Relationship**	**N**	**N**	**%**	**LL**	**UL**
Dose 1						
Fatigue	Any	8	4	50.0	15.7	84.3
	Grade 3	8	0	0.0	0.0	36.9
	Related	8	1	12.5	0.3	52.7
Gastrointestinal	Any	8	1	12.5	0.3	52.7
	Grade 3	8	0	0.0	0.0	36.9
	Related	8	0	0.0	0.0	36.9
Headache	Any	8	4	50.0	15.7	84.3
	Grade 3	8	0	0.0	0.0	36.9
	Related	8	2	25.0	3.2	65.1
Malaise	Any	8	2	25.0	3.2	65.1
	Grade 3	8	0	0.0	0.0	36.9
	Related	8	0	0.0	0.0	36.9
Myalgia	Any	8	3	37.5	8.5	75.5
	Grade 3	8	1	12.5	0.3	52.7
	Related	8	0	0.0	0.0	36.9
Temperature/ (Orally) (°C)	≥ 37.5	8	2	25.0	3.2	65.1
	> 39.5	8	0	0.0	0.0	36.9
	Related	8	0	0.0	0.0	36.9
Dose 2						
Fatigue	Any	7	1	14.3	0.4	57.9
	Grade 3	7	0	0.0	0.0	41.0
	Related	7	1	14.3	0.4	57.9
Gastrointestinal	Any	7	0	0.0	0.0	41.0
	Grade 3	7	0	0.0	0.0	41.0
	Related	7	0	0.0	0.0	41.0
Headache	Any	7	2	28.6	3.7	71.0
	Grade 3	7	1	14.3	0.4	57.9
	Related	7	2	28.6	3.7	71.0
Malaise	Any	7	0	0.0	0.0	41.0
	Grade 3	7	0	0.0	0.0	41.0
	Related	7	0	0.0	0.0	41.0
Myalgia	Any	7	0	0.0	0.0	41.0
	Grade 3	7	0	0.0	0.0	41.0
	Related	7	0	0.0	0.0	41.0
Temperature/ (Orally) (°C)	≥ 37.5	7	0	0.0	0.0	41.0
	> 39.5	7	0	0.0	0.0	41.0
	Related	7	0	0.0	0.0	41.0
Across doses						
Fatigue	Any	8	5	62.5	24.5	91.5
	Grade 3	8	0	0.0	0.0	36.9
	Related	8	2	25.0	3.2	65.1
Gastrointestinal	Any	8	1	12.5	0.3	52.7
	Grade 3	8	0	0.0	0.0	36.9
	Related	8	0	0.0	0.0	36.9
Headache	Any	8	5	62.5	24.5	91.5
	Grade 3	8	1	12.5	0.3	52.7
	Related	8	3	37.5	8.5	75.5
Malaise	Any	8	2	25.0	3.2	65.1

	Grade 3	8	0	0.0	0.0	36.9
	Related	8	0	0.0	0.0	36.9
Myalgia	Any	8	3	37.5	8.5	75.5
	Grade 3	8	1	12.5	0.3	52.7
	Related	8	0	0.0	0.0	36.9
Temperature/ (Orally) (°C)	≥ 37.5	8	2	25.0	3.2	65.1
	> 39.5	8	0	0.0	0.0	36.9
	Related	8	0	0.0	0.0	36.9

N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting at least once the symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Any= occurrence of any general symptom regardless of intensity grade and relationship to vaccination
Grade 3= general symptom that prevented normal activities
Related= general symptom assessed by the investigator as causally related to the study vaccination

Primary Efficacy Results: Number (%) of subjects with unsolicited AEs reported during the 30-day (Days 0-29) post-vaccination period (Total Vaccinated cohort): Please refer to the safety section at the end of this summary.

Primary Efficacy Results: Incidence of hematology and biochemistry abnormalities over time (Total Vaccinated cohort)

				Any		**Grade ≥ 3**	
Laboratory test	**Group**	**Timing**	**N**	**n**	**%**	**n**	**%**
ALT	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	6	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
AST	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	6	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
BASOPHILS	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
CREATININE	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	5	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
EOSINOPHILS	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0

		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
HEMOGLOBIN	HBV	Screening	8	1	12.5	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	1	14.3	0	0.0
		PII (D67)	7	1	14.3	0	0.0
		PI (D7) or PII (D67)	8	1	12.5	0	0.0
		PII (D180)	7	1	14.3	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
LYMPHOCYTES	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
MONOCYTES	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
NEUTROPHILS	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
PLATELETS	HBV	Screening	8	0	0.0	0	0.0
		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
RED BLOOD	HBV	Screening	8	1	12.5	0	0.0
CELLS		PI (D7)	8	1	12.5	0	0.0
		PI (D60)	7	2	28.6	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	1	12.5	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	1	14.3	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
UREA	HBV	Screening	8	0	0.0	0	0.0

		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	5	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
WHITE BLOOD	HBV	Screening	8	0	0.0	0	0.0
CELLS (HIGH)		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
WHITE BLOOD	HBV	Screening	8	0	0.0	0	0.0
CELLS (LOW)		PI (D7)	8	0	0.0	0	0.0
		PI (D60)	7	0	0.0	0	0.0
		PII (D67)	7	0	0.0	0	0.0
		PI (D7) or PII (D67)	8	0	0.0	0	0.0
		PII (D180)	7	0	0.0	0	0.0
		PIII (D300)	7	0	0.0	0	0.0
		PIII (D420)	7	0	0.0	0	0.0
ALL	HBV	PI (D7)	8	1	12.5	0	0.0
		PII (D67)	7	1	14.3	0	0.0
		PI (D7) or PII (D67)	8	2	25.0	0	0.0

n/%= number/percentage of subjects in the category
N= number of subjects with blood sample for hematological / biochemical testing at the specified visit
Screening: pre-Day 0
PRE: pre dose 1 (a repeat screening measure performed at D0 if initial screening measure was greater than 96 hours prior to D0)
PI (D7): post dose 1- Day 7
PI (D60): post dose 1- Day 60
PII (D67): post dose 2- Day 67
PII (D180): post dose 2- Day 180
PIII (D300): post dose 3- Day 300
PIII (D420): post dose 3- Day 420

Primary Efficacy Results: Occurrence of any serious adverse events occurring from first vaccine dose to study conclusion (Total Vaccinated cohort): Please refer to the safety section at the end of this summary.

Secondary Outcome Variable(s): Not applicable

Safety results: Number (%) of subjects with unsolicited AEs reported during the 30-day (Days 0-29) post-vaccination period (Total Vaccinated cohort)

Most frequent adverse events - On-Therapy (occurring within Day 0-29 following vaccination)	**HBV Group N = 8**
Subjects with any AE(s), n (%)	6 (75.0)
Abdominal pain upper	1 (12.5)
Nasopharyngitis	1 (12.5)
Tonsillitis	1 (12.5)
Viral infection	1 (12.5)
Myalgia	2 (25.0)
Headache	2 (25.0)
Paraesthesia	1 (12.5)
Oropharyngeal pain	1 (12.5)

Safety results: Number (%) of subjects with serious adverse events occurring from first vaccine dose to study conclusion (Total Vaccinated cohort)

Serious adverse event, n (%) [n considered by the investigator to be related to study medication]	
All SAEs	**HBV Group N = 8**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
Fatal SAEs	**HBV Group N = 8**
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]

Conclusion:
The most frequent solicited local symptom reported was pain, reported in 4 (50%) subjects of the HBV Group.
The most frequent solicited general symptoms reported in the HBV Group were fatigue and headache (each in 5 subjects [62.5%]).
No Grade 3 or greater biochemical and hematological abnormalities were reported in the HBV Group.
Six (75.0%) subjects of the HBV Group reported at least one unsolicited AE.
No SAEs were reported in the HBV Group during the study.

Publications: None

Date updated: 09-Jun-2011