APPENDICES

BACKGROUND PAPER ON THE

RTS,S/AS01 MALARIA VACCINE

SEPTEMBER 2015

PREPARED BY THE JOINT TECHNICAL EXPERT GROUP ON MALARIA VACCINES (JTEG) AND WHO SECRETARIAT

Appendix 1. Clinical studies conducted with RTS,S/AS01 in subjects older than 17 months at first dose or with RTS,S/AS02

Provided by PATH-MVI on request.

Study *Status*	Objective(s)	Study Design *Schedule*	Study population Age *Country*	Study groups	TVC N	Publication(s)
Malaria-005 *Completed*	1°: Efficacy against blood stage infection 2°: Safety and immunogenicity	Phase IIb, double-blind, randomised (1:1), controlled, single-centre study with two groups. *0-28-150 days, 19 months*	Healthy, semi-immune male adults 18 - 45 years *The Gambia*	**Primary schedule** RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	153 153 **306**	Bojang 2001 Alloueche 2003 Reece 2004
				Booster schedule RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	84 88 **172**	
Malaria-015 *Completed*	1°: Safety and reactogenicity of three different formulations of RTS,S/AS02$_A$ 2°: Immunogenicity	Phase I, double-blind, randomized (2:1), controlled, staggered, single-centre study with six parallel groups. *0-1-3 months*	Healthy male and female children 6 - 11 years *The Gambia*	RTS,S/AS02$_A$, 10µg/0.1ml Rabies vaccine RTS,S/AS02$_A$, 25µg/0.25ml Rabies vaccine RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	20 10 20 10 20 10 **90**	Bojang 2005
Malaria-016 *Completed*	Long-term safety and immunogenicity	Continuation safety follow-up studies of Malaria-005 *N/A*	Subjects previously enrolled in Malaria-005 *The Gambia*	RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	88 81 **169**	Bojang 2009
Malaria-017 *Completed*				RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	91 91 **182**	
Malaria-018 *Completed*				RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	90 98 **188**	
Malaria-020 *Completed*	1°: Safety and reactogenicity of three different formulations of RTS,S/AS02$_A$ 2°: Immunogenicity	Phase I, double-blind, randomized (2:1), controlled, staggered, single-centre study with six parallel groups. *0-1-3 months*	Healthy male and female children 1 - 5 years *The Gambia*	RTS,S/AS02$_A$, 10µg/0.1ml Rabies vaccine RTS,S/AS02$_A$, 25µg/0.25ml Rabies vaccine RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	30 15 30 15 30 15 **135**	Bojang 2005

Study *Status*	Objective(s)	Study Design *Schedule*	Study population Age *Country*	Study groups	TVC N	Publication(s)
Malaria-022 *Completed*	Long-term safety and immunogenicity	Continuation safety follow-up study of Malaria-015 *N/A*	Subjects previously enrolled in Malaria-015 *The Gambia*	RTS,S/AS02$_A$, 10µg/0.1ml Rabies vaccine RTS,S/AS02$_A$, 25µg/0.25ml Rabies vaccine RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	17 10 17 10 19 9 **82**	Bojang 2005
Malaria-023 *Completed*	Long-term safety and immunogenicity	Continuation safety follow-up study of Malaria-020 *N/A*	Subjects previously enrolled in Malaria-020 *The Gambia*	RTS,S/AS02$_A$, 10µg/0.1ml Rabies vaccine RTS,S/AS02$_A$, 25µg/0.25ml Rabies vaccine RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	29 15 29 15 28 13 **129**	Bojang 2005
Malaria-025 *Completed*	1°: Safety and reactogenicity 2°: Immunogenicity	Phase I, double-blind, randomised (1:1), controlled, single-centre study with two groups *0-1-2 months*	Healthy male and female children 1 - 4 years *Mozambique*	RTS,S/AS02A, 25µg/0.25ml Engerix-B™	30 30 **60**	Macete 2007a
Malaria-026 *Completed*	1°: Efficacy against clinical disease (Cohort 1) 2°: Safety and immunogenicity; Efficacy against blood stage infection (Cohort 2)	Phase IIb, double-blind, randomized (1:1), single-centre study with four groups in two cohorts *0-1-2 months*	Healthy male and female children 1 - 4 years *Mozambique*	RTS,S/AS02$_A$, 25µg/0.25ml Control: ≥24mo of age: *Engerix-B* or <24mo: 2 doses *Prevnar*™ + 1 dose *Hiberix*™	**2022**	Alonso 2004 Alonso 2005 Enosse 2006 Sacarlal 2008 Guinovart 2009 Aide 2011
				<u>Cohort 1:</u> RTS,S/AS02$_A$, 25µg/0.25ml Control	803 802 **1605**	
				<u>Cohort 2:</u> RTS,S/AS02$_A$, 25µg/0.25ml Control	209 208 **417**	
Malaria-027 *Completed*	1°: Safety and reactogenicity 2°: Immunogenicity; Efficacy against blood stage infection; CMI	Phase I/IIa, double-blind, randomized (1:1), single-centre, controlled (human challenge) study with four groups in two cohorts. After vaccination, subjects were challenged 14-28 days post dose 3. Non-infected (protected) individuals were re-challenged 6 months post dose 3 *0-1-2 months*	Healthy male and female (of non-childbearing potential) malaria-naïve adults 18 - 45 years *USA*	RTS,S/AS01$_B$, 50µg/0.5ml RTS,S/AS02$_A$, 50µg/0.5ml Unvaccinated (challenge) Unvaccinated (re-challenge)	52 50 24 12 **138**	Kester 2009 Vahey 2010 Lumsden 2011

Study ***Status***	**Objective(s)**	**Study Design** ***Schedule***	**Study population Age** ***Country***	**Study groups**	**TVC N**	**Publicatio n(s)**
Malaria -034 *Comple ted*	1°: Safety; Non-inferiority of anti-CS immune response of two vaccine formulations 2°: Non-inferiority of anti-HBs immune response	Phase I/II, double-blind, randomized (1:1), single-centre bridging study with two groups *0-1-2 months*	Healthy male and female children 3 - 5 years *Mozambique*	RTS,S/AS02$_D$, 25µg/0.5ml RTS,S/AS02$_A$, 25µg/0.25ml	100 100 **200**	Macete 2007
Malaria -038 *Comple ted*	1°: Safety 2°: Non-inferiority of anti-CS and anti-HBs immune responses induced by RTS,S/AS02$_D$ compared to *Engerix-B*; Efficacy against blood stage infection	Phase I/IIb, double-blind, randomized (1:1), controlled, single-centre study with two groups *0-1-2 months*	Healthy male and female infants 6 - 12 weeks *Mozambique*	RTS,S/AS02$_D$, 25µg/0.5ml *Engerix-B* given at 10, 14, 18 weeks of age Both groups: *TETRActHib*™ (DTPw/Hib) staggered at 8, 12, 16 weeks of age	107 107 **214**	Aponte 2007a Barbosa 2009 Aide 2010
Malaria -039 *Comple ted*	1°: Long-term safety 2°: Persistence of immuno; Persistence of efficacy against clinical disease (Cohort 1)	Continuation safety follow-up study of Malaria-026 *N/A*	Subjects previously enrolled in Malaria-026 *Mozambique*	<u>Cohort 1:</u> RTS,S/AS02$_A$, 25µg/0.25ml Control	691 687 **1378**	Sacarlal 2009 Aide 2011
				<u>Cohort 2:</u> RTS,S/AS02$_A$, 25µg/0.25ml Control	176 183 **359**	
Malaria -040 *Comple ted*	1°: Safety; Non-inf. of EPI antibody responses when co-administered with RTS,S/AS02$_D$ 2°: Anti-CS antibody responses; Efficacy against blood stage infection	Phase IIb, double-blind, randomized (1:1), controlled, single-centre study with two groups *0-1-2 months*	Healthy male and female infants 6 - 10 weeks *Tanzania*	RTS,S/AS02$_D$, 25µg/0.5ml *Engerix-B* given at 8, 12, 16 weeks of age Both groups: *TETRActHib*™ (DTPw/Hib) co-administered at 8, 12, 16 weeks of age	170 170 **340**	Abdulla 2008
Malaria -044 *Comple ted*	1°: Safety 2°: Immunogenicity; Efficacy against blood stage infection	Phase IIb, double-blind, randomized (1:1:1), controlled, single-centre study with three groups *0-1-2 months*	Healthy male and female (of non-childbearing potential) semi-immune adults 18 - 35 years *Kenya*	RTS,S/AS01$_B$, 50µg/0.5ml RTS,S/AS02$_A$, 50µg/0.5ml Rabies vaccine	85 85 85 **255**	Polhemus 2009 Waitumbi 2009

Study ***Status***	**Objective(s)**	**Study Design** ***Schedule***	**Study population Age** ***Country***	**Study groups**	**TVC N**	**Publication(s)**
Malaria-046 *Completed*	1°: Safety; Non-inferiority of anti-CS immune response of RTS,S/AS01$_E$ compared to RTS,S/AS02$_D$ 2°: Non-inferiority of anti-HBs immune response	Phase II, double-blind, randomized (1:1), single-centre bridging study with two groups *0-1-2 months*	Healthy male and female children 18 months - 4 years *Gabon*	RTS,S/AS01$_E$, 25µg/0.5ml RTS,S/AS02$_D$, 25µg/0.5ml	90 90 **180**	Lell 2009 Agnandji 2011
Malaria-048 *Completed*	1°: Superiority of anti-CS immune response induced by the adjuvanted vaccine formulations compared to RTS,S/Saline 2°: Safety and immunogenicity	Phase II, double-blind, randomized (1:1:1), controlled, single-centre adjuvant justification study with three groups *0-1-2 months*	Healthy male and female (of non-childbearing potential) malaria-naïve adults 18 - 45 years *Belgium*	RTS,S/AS01$_B$, 50µg/0.5ml RTS,S/AS02$_A$, 50µg/0.5ml RTS,S/Saline, 50µg/0.5ml	12 12 12 **36**	Leroux-Roels 2014

N= number of subjects

Appendix 2. Representative ITT Vaccine Efficacy Analyses

Vaccine efficacy (95% CIs) against all episodes of clinical and severe malaria. Intention-to-treat analyses. Provided by GSK on request.

Study period*	6-12 weeks		5-17 months	
	VE against clinical malaria	VE against severe malaria	VE against clinical malaria	VE against severe malaria
0M-20M	27.0 (21.1-32.5)	12.0 (-20.6-35.7)	45.1 (41.4-48.7)	35.7 (17.7-49.8)
0M-SE (3 doses)	18.3 (11.7-24.4)	12.7 (-16.2-34.4)	28.3 (23.3-32.9)	-0.3 (-25.9-20.0)
0M-SE (4 doses)	25.9 (19.9-31.5)	15.4 (-13.8-37.1)	36.3 (31.8-40.5)	32.1 (12.9-47.1)

*20M is approximately 18 months after the third dose. SE (Study end) 6-12 weeks group: median 38 months after dose 1. SE (Study end) 5-17 months group: median 48 months after dose 1.

Appendix 3. Case counts and vaccine efficacy against clinical and severe malaria for Phase III trial (Mal-055)

Provided by GSK on request.

Table S1 VE against all episodes of clinical for [5-17] months (ATP population for efficacy)

Clinical Malaria 5-17 months (ATP efficacy)													VE of a 3-dose schedule				VE of a 4-dose schedule			
	N	n	T (year)	n/T	N	n	T (year)	n/T	N	n	T (year)	n/T	(%)	95% CI		P-value	(%)	95% CI		P-value
TIME PERIOD					R3R+R3C				C3C				R3R+R3C vs C3C							
2.5-8	-	-	-	-	4582	818	2188.6	0.374	2336	1137	1086.1	1.047	67.6	63.8	71.0	<.0001				
9-14	-	-	-	-	4475	1847	2097.1	0.881	2280	1445	1048.0	1.379	38.9	33.2	44.0	<.0001				
15-20	-	-	-	-	4366	1621	1937.3	0.837	2220	1096	973.54	1.126	27.9	20.2	34.9	<.0001				
	R3R				R3C				C3C				R3C vs C3C				R3R vs C3C			
21-32	2017	1384	1933.4	0.716	2057	1872	1956.1	0.957	2050	2135	1945.5	1.097	13.5	5.4	20.9	0.0015	38.4	32.2	44.1	<.0001
33-SE	1784	2254	2231.3	1.010	1838	2493	2266.4	1.100	1864	2539	2303.2	1.102	0.1	-9.9	9.1	0.9844	14.6	5.8	22.6	0.0017
2.5-SE	2276	5691	7247.4	0.785	2306	6597	7355.8	0.897	2336	8352	7352.4	1.136	26.2	20.8	31.2	<.0001	39.0	34.3	43.3	<.0001

VE (%) = Vaccine efficacy (Negative binomial random-effects model) LL, UL = 95% Lower and Upper confidence limits P-value from Negative binomial random-effects model adjusted for site

Table S2 VE against all episodes of severe for [5-17] months (ATP population for efficacy)

Severe Malaria 5-17 months (ATP efficacy)													VE of a 3-dose schedule				VE of a 4-dose schedule			
	N	n	T (year)	n/T	N	n	T (year)	n/T	N	N	T (year)	n/T	(%)	95% CI		P-value	(%)	95% CI		P-value
TIME PERIOD					R3R+R3C				C3C				R3R+R3C vs C3C							
2.5-8	-	-	-	-	4582	23	2217.5	0.010	2336	39	1127.1	0.035	70.1	49.0	82.5	<.0001				
9-14	-	-	-	-	4476	64	2165.3	0.030	2281	41	1102.7	0.037	20.5	-17.8	46.4	0.2527				
15-20	-	-	-	-	4366	42	1996.2	0.021	2221	25	1013.7	0.025	14.6	-41.0	48.2	0.5378				
	R3R				R3C				C3C				R3C vs C3C				R3R vs C3C			
21-32	2017	36	1986.0	0.018	2057	51	2026.5	0.025	2051	35	2026.4	0.017	-47.9	-134.6	6.8	0.0965	-6.0	-75.2	35.9	0.8206
33-SE	1784	20	2316.2	0.009	1838	29	2359.5	0.012	1864	17	2398.9	0.007	-74.2	-220.0	5.2	0.0737	-22.7	-137.9	36.8	0.5454
2.5-SE	2276	106	7459.6	0.014	2306	159	7600.5	0.021	2336	157	7664.8	0.020	-2.2	-31.3	20.4	0.8637	31.5	9.3	48.3	0.0082

VE (%) = Vaccine efficacy (Negative binomial random-effects model) LL, UL = 95% Lower and Upper confidence limits P-value from Negative binomial random-effects model non adjusted

Table S3 VE against all episodes of clinical for [6-12] weeks (ATP population for efficacy)

Clinical Malaria 6-12 weeks (ATP efficacy)													VE of a 3-dose schedule				VE of a 4-dose schedule			
	N	n	T (year)	n/T	N	n	T (year)	n/T	N	n	T (year)	n/T	(%)	95% CI		P-value	(%)	95% CI		P-value
TIME PERIOD					R3R+R3C				C3C				R3R+R3C vs C3C							
2.5-8	-	-	-	-	3990	792	1901.0	0.417	2007	679	946.05	0.718	45.6	37.3	52.8	<.0001				
9-14	-	-	-	-	3895	1566	1825.5	0.858	1950	974	904.38	1.077	23.8	14.6	31.9	<.0001				
15-20	-	-	-	-	3797	1502	1660.7	0.904	1894	814	822.46	0.990	11.8	0.3	22.0	0.0443				
	R3R				R3C				C3C				R3C vs C3C				R3R vs C3C			
21-32	1743	1520	1662.3	0.914	1788	1942	1687.0	1.151	1762	2012	1671.0	1.204	8.5	-0.6	16.7	0.0652	30.3	23.0	37.0	<.0001
33-SE	1516	1069	907.38	1.178	1548	1216	926.43	1.313	1546	1187	921.89	1.288	3.9	-7.5	14.1	0.4905	12.4	1.9	21.7	0.0217
2.5-SE	1985	4532	5245.2	0.864	2005	5072	5322.9	0.953	2007	5666	5264.6	1.076	18.2	11.4	24.5	<.0001	26.7	20.5	32.4	<.0001

VE (%) = Vaccine efficacy (Negative binomial random-effects model) LL, UL = 95% Lower and Upper confidence limits P-value from Negative binomial random-effects model adjusted for site

Table S4 VE against all episodes of severe for [6-12] weeks (ATP population for efficacy)

Severe Malaria 6-12 weeks (ATP efficacy)													VE of a 3-dose schedule				VE of a 4-dose schedule			
	N	n	T (year)	n/T	N	n	T (year)	n/T	N	n	T (year)	n/T	(%)	95% CI		P-value	(%)	95% CI		P-value
TIME PERIOD					R3R+R3C				C3C				R3R+R3C vs C3C							
2.5-8	-	-	-	-	3990	28	1929.5	0.015	2007	29	970.20	0.030	53.7	18.7	73.6	0.0074				
9-14	-	-	-	-	3895	34	1883.7	0.018	1950	21	940.81	0.022	18.2	-43.8	53.5	0.4849				
15-20	-	-	-	-	3797	50	1716.5	0.029	1894	18	853.23	0.021	-38.9	-143.2	20.6	0.2496				
	R3R				R3C				C3C				R3C vs C3C				R3R vs C3C			
21-32	1743	24	1719.1	0.014	1788	38	1759.4	0.022	1762	39	1746.1	0.022	4.7	-52.8	40.6	0.8402	37.7	-4.8	63.0	0.0747
33-SE	1516	12	947.49	0.013	1548	13	971.90	0.013	1546	14	966.54	0.014	7.7	-96.5	56.6	0.8362	13.8	-91.6	61.2	0.7162
2.5-SE	1985	96	5413.5	0.018	2005	103	5512.0	0.019	2007	121	5475.7	0.022	16.0	-14.5	38.4	0.2698	20.5	-9.8	42.5	0.1634

VE (%) = Vaccine efficacy (Negative binomial random-effects model) LL, UL = 95% Lower and Upper confidence limits P-value from Negative binomial random-effects model non adjusted

Appendix 4. Results from long-term follow-up of Phase 2b trials of RTS,S/AS02 and RTS,S/AS01

Data on long-term efficacy against clinical malaria are available from two additional Phase 2 studies, one in Mozambique of the RTS,S/AS02 vaccine, and one in Kenya of the RTS,S/AS01 vaccine. Both used the same 0/1/2 schedule as the Phase 3 study without the fourth dose.

In the Mozambican trial (n=1605), children were vaccinated at 1-4 years of age with RTS,S/AS02. Six months after the third dose, vaccine efficacy against all episodes of clinical malaria was 27.4% (95%CI 6.2, 43.8). Vaccine efficacy against severe malaria was estimated to be 57.7% (95%CI 16.2, 80.6) (Alonso 2004). From six months post-dose 3 to study month 21 (about 18 months post-dose 3), vaccine efficacy was estimated at 28.8% (95%CI 6.2, 45.9) (Alonso 2005). The overall efficacy up to month 21 was similar: 29.8% (95%CI 13.8, 42.8). Thus in this trial with AS02, up to month 21 there did not appear to be waning efficacy as measured against clinical malaria.

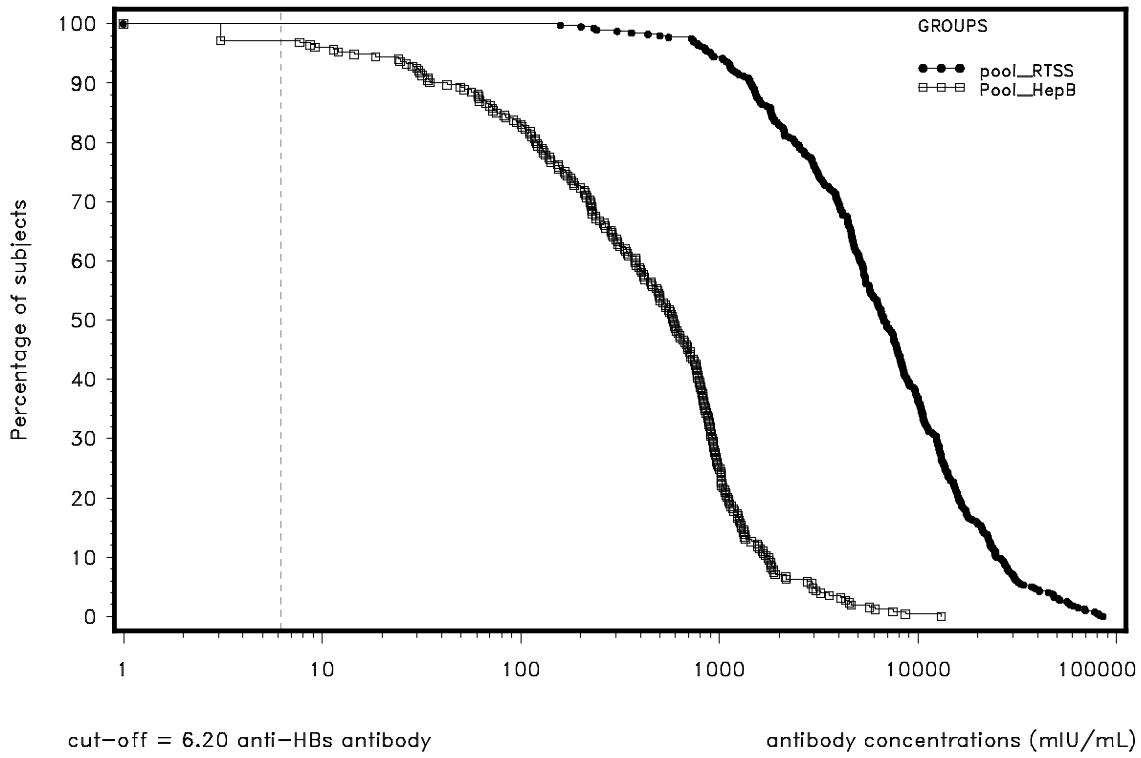
By study month 45, based on 1465 subjects (72.5% of the original trial population), vaccine efficacy against all episodes of clinical malaria was 25.6% (95%CI 11.9, 37.1)(Sacarlal 2009). VE against first episode of clinical malaria between months 21-33 was 16.8% (95%CI -2.5, 32.4) and for months 33-45, 11.8% (95%CI -20.1, 35.2). The vaccine efficacy against severe malaria during the 2.5- 45 months of follow up was 38.3% (95%CI 3.4, 61.3). This confidence intervals overlaps with the confidence interval for VE against severe malaria over the full study period in the Phase 3 trial.

In the Kenyan trial, children aged 5-17 months were vaccinated with RTS,S/AS01. Follow up during the first phase of the trial (median follow up 7.9 months) included sites in Tanzania as well (total n=894). The unadjusted vaccine efficacy against all clinical episodes during this time period was 58% (95%CI 34, 73) (Bejon 2008). When follow up was extended to 12 months, vaccine efficacy was estimated to be 44% (23, 59), and at 15 months (one site only), vaccine efficacy was estimated at 47% (22, 63) (Olutu 2011). At four years, 320 children (72% of the original 447 study population from Kenya) were still under follow up, with an estimated adjusted vaccine efficacy of 24.3% (95%CI 1.9, 41.6; Andersen-Gill Cox regression; similar results found with negative binomial regression). Analyses suggested a lower vaccine efficacy among participants with a higher malaria exposure index (compared to a low malaria exposure index). When stratified by year of follow up, vaccine efficacy against clinical malaria in year one was 46.2% (95%CI 21.2, 63.4), in year two was 24.7% (95%CI -19.1, 52.3), in year three was 22.0% (95%CI -17.0, 48.0), and in year four was -1.2% (95%CI -46.8, 31.2).

One trial has evaluated long-term protection after a booster dose of RTS,S/AS02 in a RCT of 306 semi-immune adult males (aged 18-45 years) in the Gambia. Vaccine efficacy against infection after three doses given at 0/1/5 months was 34% (95%CI 8.0, 53.0) (Bojang 2001). A booster dose was administered one year later (Month 19), and vaccine efficacy was estimated to be 47% (95%CI 4, 71) post-boost. The prevalence of parasitemia determined by cross-sectional surveys in the RTS,S/AS02 group at months 35, 46, and 58 were 5.4% (95%CI 1.1, 14.9), 0% (95%CI 0, 5.9), and 13.3% (95%CI 5.1, 26.8), compared to 12.1% (95%CI 5.0, 23.9), 0% (95%CI 0, 5.9), and 27.6% (95%CI 16.7, 40.9) at the same time points in the control group (Bojang 2009). By the last study visit, just over 50% of trial participants were available for follow up.

Appendix 5. Hepatitis B immunogenicity and indication

In a Phase III trial in Ghana (N=705), infants were randomized to receive RTS,S/AS01 or hepatitis B vaccine (co-administered with EPI antigens). Non-inferiority was demonstrated for anti-HBs seroprotection rates (Figure 8.1). By one month post dose 3, 100% of participants in the RTS,S group were seroprotected (anti-HB s≥10mIU/ml) compared to 96.0% in the HepB group. The anti-HBs GMTs were 6412.7 mIU/ml in the RTS,S group and 377.4 mIU/ml in the HepB group. These results are consistent with marked superiority of immunogenicity of RTS,S/AS01 over Hepatitis B vaccine for Hepatitis B IgG induction.



pool_RTSS = All study groups with RTS,S/AS01$_E$ vaccine (REP[Ro]_1 + REP[Ro]_2 + REP[Ro]_3 + RERo[P]_1 + RERo[P]_2 + RERo[P]_3 + RE[RoP]_1 + RE[RoP]_2 + RE[RoP]_3)
Pool_HepB = All study groups with *Engerix*-B vaccine (HEP[Ro]+ HERo[P])

Reverse Cumulative Curve at 1 month post Dose 3 for anti-HBs antibody titers (ATP cohort for immunogenicity) MAL-063. Provided by GSK on request.

Given the proposed recommendation by JTEG for administration in children at 5 months of age, JTEG assessed that there was limited public health relevance of the EMA-supported hepatitis B indication given three factors: 1) the need to vaccinate for hepatitis B as early in life as possible, at birth and through 6/10/14 week vaccination schedule; 2) very high efficacy and strong safety profile of licensed hepatitis B vaccines, as well as the lack of demonstrated superiority of RTS,S with respect to public health benefit for hepatitis B; 3) lack of any safety signal with co-administration or sequential administration of licensed hepatitis B vaccines and RTS,S/AS01.

Appendix 6. Incidence of malaria in the control group by site

Provided by GSK on request.

Overview of malaria incidence in controls ([5-17] months)

	Clinical malaria Incidence C3C	Severe malaria Incidence C3C	Parasite prevalence Month 20 C3C	Parasite prevalence Month 32 C3C	Parasite prevalence Month 44 C3C	Parasite prevalence Study end (early) C3C	Parasite prevalence Study end (late) C3C
Kilifi	0.08	0.003	0.01	0.02	0	0	0
Korogwe	0.1	0.006	0	0	-	0	-
Lambarene	0.23	0.019	0.03	0.1	0.13	0.12	0.15
Bagamoyo	0.27	0.006	0.01	0.02	0	0	0
Lilongwe	0.23	0.006	0.04	0.02	0.03	0	0.03
Agogo	1.01	0.021	0.14	0.16	0.12	0	0.09
Kombewa	1.64	0.031	0.17	0.15	0.24	0.28	0.22
Kintampo	1.71	0.035	0.2	0.25	0.28	0.38	0.31
Nanoro	2.69	0.016	0.22	0.28	0.32	0.67	0.55
Siaya	3.15	0.048	0.19	0.31	0.45	0.5	0.36

Clinical and severe malaria: all episodes, primary case definition, ATP [M2.5-SE]; Incidence: n/pyar; Parasite prevalence: n/N; Note: Manhica not in ATP 5-17 and Korogwe started enrolling later

Overview of malaria incidence in controls ([6-12] weeks)

	Clinical malaria Incidence C3C	Severe malaria Incidence C3C	Parasite prevalence Month 20 C3C	Parasite prevalence Month 32 C3C	Parasite prevalence Study end (early) C3C
Kilifi	0.04	0.003	0.04	0.01	0
Korogwe	0.09	0.002	0.01	0.01	0
Manhica	0.2	0.002	0.02	0	0.06
Lambarene	0.17	0.013	0.04	0.04	0.03
Bagamoyo	0.15	0.011	0.01	0.02	0
Lilongwe	0.42	0.012	0.06	0.02	0.01
Agogo	0.84	0.009	0.1	0.12	0.08
Kombewa	1.62	0.054	0.11	0.22	0.21
Kintampo	1.69	0.061	0.15	0.12	0.23
Nanoro	3.14	0.019	0.11	0.19	0.37
Siaya	3.12	0.063	0.21	0.3	0.31

Clinical and severe malaria: all episodes, primary case definition, ATP [M2.5-SE]; Incidence: n/pyar; Parasite prevalence: n/N

Appendix 7. 2014 Estimated Vaccine Coverage for Select Vaccines, by Country in AFR

Country in AFR	DTP3	MCV1	MCV2
Algeria	95	95	99
Angola	80	85	
Benin	90	87	
Botswana	94	90	85
Burkina Faso	91	88	17
Burundi	95	94	60
Cabo Verde	95	93	79
Cameroon	87	80	
Central African Republic (the)	45	59	
Chad	83	79	
Comoros (the)	80	80	
Congo (the)	90	80	
Côte d'Ivoire	87	72	
Democratic Republic of the Congo (the)	93	89	
Equatorial Guinea	45	43	
Eritrea	94	90	
Ethiopia	87	84	
Gabon	70	61	
Gambia (the)	96	96	73
Ghana	98	92	67
Guinea	60	62	
Guinea-Bissau	83	81	
Kenya	81	79	
Lesotho	69	58	54
Liberia	63	58	
Madagascar	89	87	
Malawi	91	85	
Mali	81	72	
Mauritania	84	84	
Mauritius	97	98	85
Mozambique	88	87	
Namibia	88	83	
Niger (the)	93	88	3
Nigeria	70	73	
Rwanda	98	97	77
Sao Tome and Principe	95	92	71
Senegal	89	80	13
Seychelles	99	99	98
Sierra Leone	83	80	
South Africa	95	91	81
South Sudan	58	52	
Swaziland	98	97	89
Togo	87	82	
Uganda	99	96	
United Republic of Tanzania	97	99	44
Zambia	86	85	33
Zimbabwe	91	92	

Source: WHO/UNICEF JRF