

Serology Review Memo, Additional comments, March 27, 2012 - MenHibrix

Date March 27, 2012
To File for 125363/0
From Freyja Lynn, Consumer Safety Officer, DBPAP/OVRR
Through Jay E. Slater, M.D., Director, DBPAP/OVRR
Subject Serology Review Memo for BLA Supplement 125363/0/21 (MenHibrix)
 Response to CBER CR letter of September 21, 2011
 Additional comments
Sponsor GlaxoSmithKline (GSK)
Documents Reviewed: BLA supplement 125363/0/21, file name: "efficacy1-3.pdf."

Summary/Background:

Due to ongoing concerns regarding the quality of the meningococcal serum bactericidal assays (SBA) used to assess the efficacy of the Group Y component of the vaccine, CBER issued a second CR letter on 21 September 2011, with three questions related to the serology. GSK submitted a partial response (125363/0/19) on 26 October, 2011 and this partial submission was discussed in a telecon between GSK and CBER on 8 November, 2011. Based on the questions posed in the CR letter and the additional feedback from the telecon, GSK submitted a full response to the CR letter on 1 December, 2011. On January 19, 2012, I sent a memo to the file to request additional information and analyses from GSK to address ongoing concerns regarding the performance of the hSBA.

CBER held internal discussion and CBER statisticians performed additional analyses that showed that the study endpoints for Hib-MenCY-TT-009/010 were still met when higher cutoff values were used (see Table 1 below).

Table 1: Percentage of subjects with hSBA-MenC and hSBA-MenY antibody titers greater than or equal to 1:8, 1:16 and 1:32; results for the post-fourth dose and According-To-Protocol (ATP) fourth dose cohort for immunogenicity

Antibody	≥ 1:8				≥ 1:16				≥ 1:32	
	Estimated				Estimated				Estimtaed	
	N	n	Endpoint (%)	95% CI	n	Endpoint (%)	95% CI	n	Endpoint (%)	95% CI
MenC	335	330	98.5	(97, 99)	330	98.5	(97, 99)	327	97.6	(95, 99)
MenY	346	342	98.8	(97, 99)	342	98.8	(97, 99)	342	98.8	(97, 99)

The most critical concern, that of the variability of the assays, is addressed by this analysis demonstrating that the clinical outcome, and therefore the assessment of

efficacy, do not change when conservative endpoints are used to compensate for the variability of the assay.

Issues identified during review of this BLA will be addressed in the context of ongoing IND studies of studies with meningococcal C and Y components. Therefore the questions for the sponsor included in my memo of January 19, 2012 do not need to be sent to the sponsor under this BLA.