

MID-CYCLE MEETING MINUTES

FILE: STN 125363

SPONSOR: GlaxoSmithKline Biologicals

PRODUCT: Meningococcal Groups C and Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine (MenHibrix)

INDICATION: Active immunization of infants and toddlers 6 weeks through 15 months of age for the prevention of invasive diseases caused by Haemophilus influenzae type b and Neisseria meningitidis serogroups C and Y

MEETING DATE: July 11, 2011

MEETING LOCATION: CBER Conf. WOC2-2201

MEETING TIME: 1:00 PM

CALL IN INFO: -----b(4)-----

MEETING RECORDER: Kirk Prutzman

Review Assignment	Committee Member	Supervisor	Attended
Chair	Joseph Temenak	Elizabeth Sutkowski	✓
RPM	David Staten	Elizabeth Sutkowski	✓
RPM	Kirk Prutzman	Elizabeth Sutkowski	✓
Clinical Reviewer	Meghan Ferris	Lucia Lee	✓
Product CMC/Serology	Mustafa Akkoyunlu	Willie Vann	✓
Product CMC	Willie Vann	Jay Slater	✓
Product CMC	Daron Freedberg	Willie Vann	
Product CMC	Drusilla L Burns	Jay Slater	✓
Product CMC	Annisa Cheung		
Product CMC	James E Keller	Drusilla Burns	✓
Product CMC	Majid Laassri	Konstantin Chumakov	
Product CMC	Steven A Rubin	Konstantin Chumakov	
Product CMC	Michael Schmitt		✓
Product CMC	Shuang Tang	Philip Krause	✓
Product CMC	Iryna Zubkova		
Toxicology	Steven C Kunder	David Green	✓
Product CMC	Tina Roecklein	Jay Slater	✓
Facilities/DMPQ	Sean Byrd	Carolyn Renshaw	✓
Advertising/			
Promotional Labeling	Maryann Gallagher	Lisa Stockbridge	✓
Clinical Statistical Reviewer	Barbara Krasnicka	Dale Horne	✓
Assays Statistical Reviewer	Tsai-Lien Lin	Dale Horne	
Epidemiology	Manette Niu	Thomas Buttolph	On Leave
DPQ/Lot Testing Plan	Rajesh Gupta	Bill McCormick	On Leave
DPQ/Lot Testing Plan	Karen Campbell	Bill McCormick	✓

Review Assignment	Committee Member	Supervisor	Attended
Lot Release	Joe Quander	Jay Elterman	
BiMo	Soloman Yimam	Patricia Holobaugh	✓
Electronic Integrity Review	David Schwab	Laraine Henschel	

Other Attendees

Wellington Sun

Elizabeth Sutkowski

Jennifer Bridgewater (DBPAP Regulatory Coordinator)

Manju Joshi

MEETING AGENDA:

1. PDUFA MS Project Milestones (projected, pending final submissions)

- ~~Application Received~~ ~~April 15, 2011~~
- ~~Committee Assignment~~ ~~May 2, 2011~~
- ~~1st Committee Meeting~~ ~~May 9, 2011~~
- Mid-Cycle Review Meeting July 11, 2011
- **1st draft reviews** **July 14, 2011**
- **2nd draft reviews** **August 13, 2011**
- **Final Reviews (Signed/Uploaded)** **September 28, 2011 (Sunday)**
- Present to PeRC August 14, 2011
 - **PeRC Scheduled for August 31, 2011**
- PMC to FDAAA SWG August 31, 2011
- Labeling Target September 28, 2011 (Sunday)
- PMC Study Target September 28, 2011 (Sunday)
- **First Action Due** **October 15, 2011 (Saturday)**

2. Discussion Points:

A. CR Letter Assignments/Progress

The reviewer assignments for each item on the CR letter (maintained on an Excel Spreadsheet) were discussed and updated. The reviewers were told to update the RPMs as to their responses to their assigned items.

B. Review Reports/Issues

- Clinical

Meghan reported that her first draft review was complete and that all of the items in the CR letter (13-19) were addressed satisfactorily. It was discussed that the final clinical review and the final labeling was contingent on the serology assay review. The serology assays are the only measure of efficacy.

- Product / CMC

Mustafa Akkoyunlu reported that his first draft review was complete and submitted to his supervisor (Willie Vann). Mustafa discussed his preliminary review of the hSBA serology assays and indicated that there are serious problems. The CR issues 1 and 2 are about the significantly –b(4)- titers obtained with study 005 and 008 sera in the retest hSBA. CBER had asked for explanations for the –b(4)-- in titers in the retest results. In their response, GSK indicated that this could be the result of either -b(4)----- events of the serum between assays (GSK claims at least –b(4)----- events for 005 sera) or an out of date complement lot. However, GSK submitted –b(4)----- control test results from –b(4)----- cycles that indicated ---b(4)----- would not significantly –b(4)-- SBA titer levels in their hSBA assay. Additionally, the out of date complement lot was not used in all of the re-test data and could not account for all of the –b(4)--- SBA titer results. It was discussed that the hSBA serology assay may not be reliable and therefore this was a major issue that may result in a CR letter. It affects the clinical review as this is the only measure of efficacy. It was also discussed that this may be a fatal error in all of GSK's clinical studies. MenHibrix approval will be in doubt until GSK is able to produce a reliable, reproducible assay to accurately measure SBA titer.

Willie Vann reported that the MenHibrix free polysaccharide review was ongoing and there were no updates at the meeting. It was discussed that the free polysaccharide issue was still a potential CR issue unless GSK had sufficiently addressed it.

- Biostatistics

Barbara Krasnicka indicated that her first draft review was almost complete. There were also significant issues with the biostatistics review of the hSBA serology assay. Barbara was not ready to present her final analysis but indicated that the preliminary results showed inconsistent results. Barbara also indicated that GSK may not meet their endpoints for lot consistency. It was discussed that these issues are consistent with poor re-test data and strengthened a possible CR letter.

- DPMQ / Lot Testing

Sean Byrd updated the review team as to the issues involved in the diluent –b(4)--- (see June 30, 2011 tcon). He indicated that GSK should have enough time to manually inspect the –b(4)----but if they could not resolve this issue then it is a CR issue. It was discussed that these –b(4)-- did not need to be inspected under the IND.

Karen Campbell indicated that GSK's proposed lots and reagents being sent to CBER for testing (including the lots that were "under quarantine") were probably sufficient. She wanted to check with Rajesh Gupta (on leave during this meeting) before she could be certain.

- BiMo

No Report

- Pharmacovigilance

Manette Nui reported that Trish Rohan submitted a completed PVP review (for –b(4)--) in June, 2010. There are no significant additions with regard to the safety database. Therefore the original review still stands