



FOOD AND DRUG ADMINISTRATION
CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

MEMORANDUM

Minutes of Face-to-Face Meeting with Sponsor

Date/Time: September 1, 2009, 10:30 AM – 1:00 PM
Location: WOC, Conference Room 2
File: BLA 125324
Product: Prevnar 13™
Sponsor: Wyeth Pharmaceuticals Inc.

Purpose: To Discuss and Agree on a Path Forward for Outstanding CMC Issues

Sponsor Attendees:

Jack Love and Kathrin Jansen

CBER Attendees:

Office of Vaccines Research and Review (OVR) Management:

Marion Gruber and Theresa Finn

BLA 125324 Review Committee:

Milan Blake, Willie Vann, John Cipollo, Tina Roecklein, Julienne Vaillancourt and Mike Smith

Reference:

- 1) Letters issued to the sponsor by CBER:
 - Deficiencies Identified (June 12, 2009)
 - Major Amendment Acknowledgement (August 10, 2009)
- 2) Amendments to BLA 125324:
 - #19, Serotype 5 (b)(4) information requested by CBER during the June 15, 2009 telecon, submitted to the BLA on June 26, 2009
 - #22, Wyeth's response to CMC questions discussed during June 18, 2009 telecon regarding assay validation and -----(b)(4)-----stability data, submitted to the BLA on July 23, 2009
- 3) Meetings/Telecons with the sponsor:
 - June 28, 2008, Pre-BLA (CMC) Meeting Minutes
 - June 15, 2009, Telecon on CMC Issues, mainly serotype 5 issues
 - June 19, 2009, Telecon on CMC Issues, mainly questions about assay validation and conjugate in final product
 - July 28, 2009, Face-to-Face Meeting on CMC Issues, topics were: serotype 5,

- assay validation and conjugate in final product
- August 6, 2009; the Office of Vaccines Research and Review informed the sponsor about the Agency's decision to cancel the September 10, 2009, VRBPAC meeting to discuss Prevnar 13, because it considered this meeting to be premature, given outstanding CMC issues identified in the review of the Prevnar 13 BLA to date, in particular, information contained in the July 23rd submission.
- August 7, 2009, Telecon to inform Wyeth that the July 23rd submission would be deemed a major amendment. Thus, the review clock would be extended by 90 days. Additionally, VRBPAC will be rescheduled to November 18th or 19, 2009.

4) E-mails

- June 12, 2009, e-mail from Mike Smith to Jack Love and Carmel Devlin, titled "RE: Talking points for June 15 teleconference to discuss the(b)(4)of serotype 5."
- June 18, 2009, e-mail from Mike Smith to Jack Love and Carmel Devlin, titled "RE: Talking points for June 19 teleconference to discuss drug product and drug substance issues."
- August 5, 2009, e-mail from Jack Love to Julie Vaillancourt and Mike Smith with attachment, titled "Type 5 (b)(4) Expts 5Aug2009."

Attachments:

- 1) Hand-out, titled "CBER Talking Points," given to sponsor and CBER attendees at start of meeting.
- 2) Table, titled "Summary of Discussed Pathway Forward for Outstanding CMC Issues"

Background: This meeting was arranged as an action item in follow-up to the August 7, 2009, teleconference between CBER (Karen Midthun, Norman Baylor and Marion Gruber) and the sponsor (Jack Love, Carmel Devlin and Emilio Emini), during which CBER informed the sponsor that the July 23, 2009 amendment to the BLA was deemed a major amendment, which would thus extend the clock by 3 months to December 30, 2009.

Discussion:

Outstanding CMC Issues

CBER provided a hand-out, which summarized the outstanding CMC issues, considered to be critical by the Agency for moving forward toward eventual licensure (see attachment 1). In general, these issues pertain to two overarching concerns: 1) consistency of serotype 5 conjugate manufacture, and 2) current lack of a specification for conjugate in final drug product (FDP). In discussing these issues, CBER stated pre- and post-licensure requirements for each and the sponsor acknowledged and agreed to fulfill them accordingly. The attached table (see attachment 2) provides a summary of CBER's requirements concerning these outstanding issues and the agreements made between CBER and the sponsor for addressing them, as a path forward.

Tentative Closed VRBPAC Session

CBER stressed the importance of the sponsor submitting the required pre-licensure items concerning serotype 5, particularly the data demonstrating extent of (b)(4) with

------(b)(4)-----, by the end of September 2009, so that CBER would have adequate time to review the items in order to make a decision about whether it would be necessary to have a closed VRBPAC session. CBER clarified that the draft announcement for the VRBPAC meeting must be sent to the Federal Register by mid-October and at a minimum two weeks would be necessary to preliminarily review the data to make a decision about the actual need for a closed VRBPAC session.

[Follow-up Note: This information concerning the due dates for Federal Register notices has since been corroborated, and in fact the draft notice for a closed session would be due September 29, 2009. This would leave no time for CBER to review the expected serotype 5 conjugate -(b)(4)--data, unless the data are submitted to CBER in mid-September, which is unlikely, based on discussion with the sponsor during the September 1, 2009, meeting.]

Additional CMC Issues

At the end of the meeting CBER noted that there were a number of additional CMC issues pertaining to assay validation for lot release specifications, but agreed that these items could be addressed by the sponsor as post marketing commitments.

Conclusion

It was agreed that the minutes of this meeting would clearly reflect CBER's requirements for additional CMC information from the sponsor in order to move from this point forward toward eventual licensure of Prevnar 13, from a CMC perspective. It was agreed also, that no new pre-licensure requests for additional CMC information, beyond the requests discussed during the present meeting, would be made by CBER.

Drafted by: J. Vaillancourt, M. Smith
Reviewed by: J. Cipollo, W. Vann, R. Gupta, T. Finn, M. Gruber

Attachment 1:

CBER TALKING POINTS

CBER has identified the following outstanding CMC issues, with pending action:

1. With regard to serotype 5 --(b)(4)--:
 - a. Submission of a proposed scheme to assure consistency of the serotype 5 conjugation process for CBER review and concurrence. In this regard,
 - o The experimental plan is expected to be a long-term effort, extending beyond the pending action due date of December 30, 2009.
 - b. -----

----- (b)(4) -----

-----.]
 - c. -----

----- (b)(4) -----

-----.]
 - o ----- (b)(4) -----.
 - o ----- (b)(4) -----.
2. An agreed upon specification and related assay to confirm conjugate in final drug product is pending.
 - o The sponsor has proposed “----- (b)(4) -----” defined as the ----- (b)(4) -----.
 - o CBER requests an explanation of the sponsor’s rationale for this proposed specification and clarification of how the value is obtained, whether it is an appropriate measure of conjugate in final product and it’s relation to other product specifications, as the percentages seemingly do not add up.

Attachment 2: Summary of Discussed Pathway Forward for Outstanding CMC Issues

Issue #1: Serotype 5 Conjugate Manufacture

[(b)(4)]

Issue #1: Serotype 5 Conjugate Manufacture

[

(b)(4)

]

2 pages determined not to be releasable: (b)(4)