RECORD OF TELEPHONE CONVERSATION

Submission Type: BLA Submission ID: 125549/0 Office: OVRR

Product:
Meningococcal Group B Vaccine

Applicant:
Wyeth Pharmaceuticals Inc.

Telecon Date/Time: 30-Sep-2014 04:12 PM Initiated by FDA? Yes

Telephone Number:

Communication Categorie(s):
1. Information Request

Author: MICHAEL SMITH

Telecon Summary:
Six additional IR's reagrding Pfizer's 9/24/14 responses to CBER's 8/29/14

FDA Participants: Mike Smith, Drusilla Burns, Ted Garnett and Ram Naik

Non-FDA Participants: Carmel Devlin

Trans-BLA Group: No

Related STNs: None

Related PMCs: None

Telecon Body:

See e-mail below:

From: Smith, Michael (CBER)
Sent: Tuesday, September 30, 2014 4:12 PM
To: Devlin, Carmel (Carmel.Devlin@pfizer.com)
Cc: Burns, Drusilla L.; Garnett, Theodore; Naik, Ramachandra
Subject: STN 125549: Additional comments regarding Pfizer's September 24th responses to CBER's August 29th CMC IR's

Carmel,

I attached additional comments from the review team regarding Pfizer's September 24th responses to CBER's August 29th CMC Information Requests (IR's). If needed, the review team is available for a teleconference to discuss these comments.

Regards,

Mike

- Please confirm receipt of these comments

Mike Smith, Ph.D.
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See contents of attached PDF below:

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH
OFFICE OF VACCINES RESEARCH AND REVIEW
DIVISION OF VACCINES AND RELATED PRODUCT APPLICATIONS

Date: **September 30, 2014**

Pages: **5**

To:
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From:
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Office of Vaccines Research and Review
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STN#: **125549/0**

Product: **Meningococcal Group B Vaccine**

Subject: **CBER additional comments regarding your 24 September 2014 response to our 29 August 29 2014 information request (IR) on Chemistry, Manufacturing and Control (CMC) issues.**

We find the responses provided to CBER's IR letter of 29 August 2014 to be adequate with the exception of the following issues.

1. The following comments concern your hold time validations.

   a. We acknowledge your response to Question 7 of the 29 August 2014 IR. You propose to ----------(b)(4)----------. You have provided commercial scale data to support a maximum hold time of ----------(b)(4)-. Please revise your hold time to reflect the data that you have supporting this hold time. Alternatively, please commit to performing a hold time validation study on three commercial scale lots to support a maximum hold time of (b)(4) post approval.

   b. We do not concur with your response to Questions 8A-C of the 29 August 2014 IR. You propose the following hold times for ----------(b)(4)----------. You propose the following hold times for ----------(b)(4)----------. We do not concur with your hold time validation studies supporting the above hold times used in the manufacture of ----------(b)(4)----------. Please revise your hold time to reflect only what you define as routine manufacturing. Alternatively, please commit to performing a hold time validation study post approval on three commercial scale lots to support the cumulative hold time.

   c. We do not concur with your response to Question 9 of the 29 August 2014 IR. You propose a hold time for ----------(b)(4)----------. You have provided data supporting this hold time on (b)(4) small scale validation batches using ----------(b)(4)---------- between the small scale studies and the manufacturing scale. In addition, ----------(b)(4)---------- were not evaluated at the end of hold time for these studies. Please note that we concur with your proposal to not include ---------(b)(4)----------. You have provided commercial scale data to support a hold time of ----------(b)(4)---------- under routine manufacturing conditions. Please revise your hold time to reflect what you define as

routine manufacturing. Alternatively, please commit to performing a hold time validation study post approval on three commercial scale lots to support a hold time of ----------(b)(4)----------.

2. We do not concur with your response to Question 11 of the 29 August 2014 IR concerning ----(b)(4)---- reuse.

   a. You have provided both small scale and commercial scale data to support -----(b)(4)------ reuse. You are requesting approval for the maximum number of commercial scale cycles as outlined in Table 5 of your response. This request is supported by small scale data only. We do not concur with the use of small scale data to support commercial scale reuse. Please revise your request for the maximum number of commercial cycles that are supported by commercial scale data.

   b. We concur with your proposal to use a Comparability Protocol (CP) to allow for future increases in the maximum number of -(b)(4)- reuses to be submitted in your Annual Report. As part of your proposed CP, please clarify the acceptance criterion for Subfamily B "----------(b)(4)----------" as the performance criteria differ between Tables 5 and 12 of the CP.

3. The following comments concern your proposed testing and specifications.

   a. We note in your response to Question 17A of the 29 August 2014 IR that you have agreed to continue to test commercial batches of ------(b)(4)------ for -----(b)(4)-----. You have proposed a release specification of ----------(b)(4)--. This proposed specification is wider than the calculated tolerance interval. Please provide your justification for the proposed release specification.

   b. We note in your response to Question 17B of the 29 August 2014 IR that you propose to not test for ----------(b)(4)---------- as a release test for -----(b)(4)-----. You propose to use this test only as an in-process test for control on commercial batches. We still do not concur with this proposal. ----------(b)(4)---------- should be tested at release until enough data have been collected to support removal of the testing. Please continue to test commercial batches of ----------(b)(4)---------. We would concur on adding ----------(b)(4)---------- as a ------(b)(4)------- release test post approval through a written commitment if this testing could not be performed on your launch lots. Also, to remove redundant testing, we would concur with the removal of the in-process test for control testing of ---------(b)(4)--------- on the --------(b)(4)--------.

c. We note in your response to Question 17C of the 29 August 2014 IR that you propose to not test for ----------(b)(4)---------- as a release test for -------(b)(4)------. We have reviewed the additional data presented in your response. We still do not concur with this proposal. The level of all ---------(b)(4)--------- should be tested at release until enough data have been collected to support removal of the testing. Please continue to test commercial batches of -----(b)(4)----- for ----------(b)(4)---------. We would concur on adding ----------(b)(4)---------- as a -----(b)(4)------ release test post approval through a written commitment if this testing could not be performed on your launch lots. .

d. We note in your response to Questions 17F and 29C of the 29 August 2014 IR that you propose to submit a commitment to address these comments. You propose that the commitment will provide a proposal for either incorporating ----------(b)(4)---------- as a stability test for ----------(b)(4)------- drug product or providing data to show than any significant trend in ----------(b)(4)---------- is reflected in a similar trend in ----------(b)(4)----------. We do not concur with this commitment. Please revise your commitment to add ----------(b)(4)---------- as a stability test for ----------(b)(4)--------- drug product. You may submit a Prior Approval Supplement to request removal of this testing at a future time, if supportive data become available.

4. The following comments relate to the control of $AlPO_4$. We do not concur with your responses to Questions 25 A-B of the 29 August 2014 IR.

a. $AlPO_4$ ----------(b)(4)---------- facility for both MnB rLP2086 and --(b)(4)---------- facility with the limits based on (b)(4) sigma limits. We do not concur with this approach. Please revise your release specification limits for ----------(b)(4)---------- based on data obtained from batches ----------(b)(4)----------. As stated in the 7 February 2014 meeting, we request that the methodology used for setting specifications be to calculate tolerance intervals with 95% confidence and 99% coverage, which is the level of coverage usually accepted when tolerance interval is used to set product specifications. Please provide your justification if you propose limits outside of the tolerance interval. Alternatively, this revision in specification could be agreed to in the form of a post-approval commitment.

b. We note that you request to not add ---(b)(4)--- as a stability specification for (B)(4). We have reviewed the stability data presented on three process

validation batches of (b)(4). We also note that -----(b)(4)----- has been documented for your --(b)(4)-- product that uses the same (b)(4). We do not occur with your proposal at this time. Please add ----(b)(4)----- as a stability specification for (b)(4). You may submit a Prior Approval Supplement to request removal of this testing at a future time, if enough data are collected to demonstrate that -----(b)(4)------ does not change over time.

5. We do not concur with the Comparability Protocol (CP) that you submitted in your response to Question 36 of the 29 August 2014 IR. The CP provided in your response does not provide enough details on the preparation, testing, and qualification of the new reference materials. In addition, CPs should be assay specific. Please withdraw your CP for future reference materials. We note that you had stated in the 1 May 2014 meeting that you are experiencing ----(b)(4)----------. Please indicate ----------(b)(4)---------- and for which assays these reference materials are used. Please submit the qualification data for the new reference materials in lieu of a CP. If the qualification data are not available at this time, please submit this request as a supplement post approval. We will commit to do an expedited review of the supplement post approval.

6. The following commitments were noted during review of the file. Please provide a complete list of all commitments made for the BLA. This list should include the commitments listed below as well as any made in response to an IR comment.

   a. The proposed ----------(b)(4)---------- specification for ----------(b)(4)---------- is ---(b)(4)---. Consideration is given to the assay variability and limited experience at commercial scale as the ----------(b)(4)---------- represents a calculated value derived from the results of (b)(4) analytical procedures, potentially resulting in higher variability. The variability will be assessed as additional data are accumulated and subject to statistical analysis to determine true process and method variability. (Section 3.2.S.4.5.10).

   b. The proposed purity specification for ----------(b)(4)---------- is (b)(4). This specification will be redefined as additional commercial process experience is obtained. (Section 3.2.S.4.5.12).

   c. The proposed *(b)(4)* potency test for drug product has not been validated in the final testing laboratory. The validation report will be submitted when validation is complete.

   d. The proposed *(b)(4)* potency for drug product is ---(b)(4)--- for ----------(b)(4)----------. The specification for ---*(b)(4)*--- potency will be re-evaluated and appropriately adjusted following the testing of an additional (b)(4) commercial lots at release. (Section 3.2.P.5.6.9).

e. The proposed ----------(b)(4)---------- specification for drug product is (b)(4). Consideration is given to the assay variability and limited experience at commercial scale as the ----------(b)(4)---------- represents a calculated value derived from the results of (b)(4) analytical procedures, potentially resulting in higher variability. The variability will be assessed as additional data are accumulated and subject to statistical analysis to determine true process and method variability. (Section 3.2.P.5.6.12).

In your reply to this information request, we recommend that you restate the item and follow it with your explanation or clarification. Use of this format helps organize the relevant information and provides a self-contained document that facilitates future reference. If you have any questions, please contact CDR Mike Smith, Ph.D. at 301-796-2640.