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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: 29-Aug-2014 03:02 PM Initiated by FDA? Yes

Telephone Number:

Communication Categorie(s):
1. Information Request

Author: MICHAEL SMITH

Telecon Summary:
Six Epi IR's and one clinical IR

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: Friday, August 29, 2014 3:02 PM
To: Devlin, Carmel (Carmel.Devlin@pfizer.com)
Cc: Burns, Drusilla L.; Garnett, Theodore; Naik, Ramachandra
Subject: STN 125549: IR on Epidemiology/Pharmacovigilance and clinical issues

Carmel,

The review team has the attached information requests (IR's) on Epidemiology/Pharmacovigilance and Clinical issues. Please confirm receipt of these IR's and let us know if you can provide responses to the BLA by Friday, September 5th.

Regards,

Mike

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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: **August 29, 2014**

Pages: **4**

To:
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From:
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STN#: **125549/0**

Product: **Meningococcal Group B Vaccine**

Subject: **CBER information request regarding Epidemiology/Pharmacovigilance and Clinical issues**

Epidemiology/Pharmacovigilance:

The following comments pertain to the document located under eCTD section 5.3.5.2 entitled, "B1971012 – Study Body Report":

1. Regarding Table 11 on page 64 entitled, "Vaccine as Administered vs Vaccine Group as Randomized – All Subjects," please clarify why the distribution of subjects in each study group who received bivalent rLP2086 vaccine "as administered" for dose 1 (for Group 5, this would correspond to injection visit 3) differs from the distribution of subjects for whom demographic characteristics for the safety population are described for rLP2086 dose 1 as seen in Table 10 on page 62 entitled, "Demographic Characteristics –Safety Population."

   For each treatment group in study 1012, please provide the counts of subjects who received ≥1 dose of rLP2086, as well as the counts of subjects who received saline-only (no rLP2086) and the counts of subjects who were randomized, but who received NO injections throughout the study period. Also, please confirm that all subjects receiving ≥1 dose of rLP2086 or saline-only (even if not at injection visit 1) were included in the safety analyses.

2. Regarding Table 11 on page 64 entitled, "Vaccine as Administered vs Vaccine Group as Randomized – All Subjects," it appears the final number of subjects in Group 5 that received ≥1 dose of rLP2086 was 125 subjects and three subjects missed the rLP2086 dose at injection visit 3; however, we cannot tell if these three subjects received rLP2086 at the next visit. It appears the final number of subjects in Group 5 that received saline-only (no rLP2086), even if they eventually dropped out early, ranges from (144-125) to (144-128), or 16-19.

   Please provide the breakdown of what was received at each injection visit for the three subjects who received nothing at injection visit 2 and for the three subjects who received nothing at injection visit 3. Also, please confirm the exact number of subjects who received saline-only (no rLP2086) during the study.

3. Regarding Table 11 on page 64 entitled, "Vaccine as Administered vs Vaccine Group as Randomized – All Subjects," please clarify why the distribution of study 1012 subjects in each group who received bivalent rLP2086 vaccine doses 1-3 "as administered" at the designated visit or "as randomized" differs from the distribution of study 1012 subjects in each group included in Table 6 of the Summary of Clinical Safety [eCTD section 2.7.4, page 38].

The following comment pertains to the document located under eCTD section 5.2 entitled, "Tabular Listing of Clinical Studies":

4. Section 5.2 lists study 1012 as an uncontrolled study and its counts are included with the counts of subjects in uncontrolled studies. However, in Table 1 entitled, "Tabular Listing of Clinical Studies Included in the Biologic License Application," it is also described as a "Phase 2, randomized, placebo-controlled,

single-blind, multicenter study." In this study, all subjects are randomized to receive at least two doses of bivalent rLP2086 vaccine; however, not all subjects received rLP2086 during the course of the study (some subjects received saline-only). Please confirm that study 1012 is an uncontrolled study for the purposes of the safety analyses.

The following comment pertains to the document located under eCTD section 2.7.4 entitled, "Clinical Safety":

5. Page 7 states that 4,576 subjects received ≥1 dose of bivalent rLP2086 vaccine, while 1,012 subjects were randomized to a control group and 16 subjects from study 1012 received saline-only (control). We've noted subject count discrepancies in three of the seven BLA studies: study 1010, study 1011, and study 1012 (please see Table 1 in the appendix); Using Tables 2 and 6, we have counted 4,576 subjects who received ≥1 dose of bivalent rLP2086 vaccine, but 1,028 who received control-only injections (no rLP2086) during the study period. With regard to the safety analyses, please provide the final subject counts for each study arm in studies 1010, 1011, and 1012.

   For each of the seven BLA studies, please confirm the number of subjects in the categories below:

   - Subjects who received ≥1 dose of bivalent rLP2086 vaccine;
   - Subjects who received ≥1 dose of control injections-only (no rLP2086);
   - Subjects who were randomized, but received NO injections throughout the study (and were thus NOT included in the safety analyses)

   Please confirm the total number of subjects for the above mentioned categories in each category for all seven BLA studies combined.

6. After the subject count discrepancies have been clarified for each BLA study, please provide the cumulative person-time-at-risk for the following:

   a. All subjects in the four controlled BLA studies (studies 1004, 1005, 1010, 1011)

      i. who received ≥1 dose rLP2086 during the study period

      ii. who received control injection-only (no rLP2086) during the study period

   b. All subjects in the three uncontrolled BLA studies (Studies 1003, 1012, and 1042)

i. who received ≥1 dose rLP2086 during the study period

ii. who received control injection-only (no rLP2086) during the study period

c. All subjects in all seven BLA studies

i. who received ≥1 dose rLP2086 during the study period

ii. who received control injection-only (no rLP2086) during the study period

d. For cases with autoimmune or neuroinflammatory conditions (including subject 10541016 with Bell's palsy), please censor by symptom onset date or diagnosis date (if symptom onset date is not available), or estimate duration of time in study before onset if neither symptom date nor diagnosis date is available.

Clinical:

7. Regarding study B1971012, please provide a sensitivity analysis of hSBA GMTs using the left-censored maximum likelihood estimation for strain PMB80 [A22] using a LLOQ of 16 (mITT population).

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.