Information Request Email, May 9, 2014 - GARDASIL 9

RECORD OF EMAIL COMMUNICATION

Submission Type: BLA Submission ID: 125508/0 Office: OVRR

Product: Human Papillomavirus 9-valent Vaccine, Recombinant
Applicant: Merck Sharp & Dohme Corp.

Telecon Date/Time: 09-May-2014 10:37 AM
Initiated by FDA? Yes
Telephone Number: N/A (email)
Communication Category: Information Request
Author: LAURA MONTAGUE

Telecon Summary: IR #8 - regarding assays, and follow-up to IRs #4 and 7
FDA Participants: Laura Montague
Non-FDA Participants: Bharat Khurana
Trans-BLA Group: No
Related STNs: None
Related PMCs: None

Telecon Body:

From: Montague, Laura
Sent: Friday, May 09, 2014 10:37 AM
To: alison_fisher@merck.com
Cc: Khurana, Bharat
Subject: STN 125508/0; Information Request #8 (related to IRs 4 and 7)

Dear Alison,

We have reviewed the validations and stability data submitted for the assays to assess immune responses to Adacel and Menactra, including the amendment received 8 May 2014. We find these data to be insufficient to demonstrate the performance of the assays to support concomitant administration in study Protocol 005. We acknowledge that the assays were reviewed during the approval of Gardasil, however in some cases changes made to the assays since that review are not sufficiently supported, or new validation reports not adequate to demonstrate suitable performance of the assays. In order to verify that the assays performed adequately during the testing of samples for

Protocol 005, we are requesting additional information. The information to respond to comments 1 and 2 should be available from the laboratories as part of their routine assay monitoring and standard operating procedures. Comments 1 and 2 supersede CBER comment 1 in Information Request #7.

1. Please provide the algorithm for batching samples for analysis to prevent bias. Please also describe the means by which assay operators are blinded as to the subject, study group and time point for each sample.

2. Please provide the following information to demonstrate that the assays were adequately controlled during sample testing for Protocol 005.

   a. A description of the system suitability criteria used to accept or reject assay runs including the limits for each criterion and the basis for each criterion.
   b. The trending or tracking data for control samples run in each assay as part of the system suitability. Please include all data, including those from assays that were rejected.

3. Please provide the reverse cumulative distribution curves for pre and post immunization for both groups for the diphtheria, tetanus, pertussis and meningococcal antigens. Please plot all curves for a given antigen on the same figure for ease of comparison between pre and post and between study groups.

4. If you intend to use these assays to assess responses to diphtheria, tetanus, pertussis and meningococcal antigens in future Phase 3 studies, we recommend you address the gaps in the validations. Our detailed review of the validations submitted to the BLA will be provided to you in response to your submission of Protocol 005 in your IND 13447. Please acknowledge.

Thank you,

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