Information Request Email, April 25, 2014 - GARDASIL 9

RECORD OF TELEPHONE CONVERSATION

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

Product: Human Papillomavirus 9-valent Vaccine, Recombinant

Applicant: Merck Sharp & Dohme Corp.

Telecon Date/Time: 25-Apr-2014 03:22 PM Initiated by FDA? Yes

Telephone Number: Email

Communication Categorie(s): 1. Information Request

Author: BHARAT KHURANA

Telecon Summary: Information Request #7: Follow-up on sponsor's response to IR #4 regarding validation of assays

FDA Participants: Bharat Khurana

Non-FDA Participants: Alison Fisher, Merck

Trans-BLA Group: No
Related STNs: None
Related PMCs: None
Telecon Body:
The following email was forwarded to the sponsor:

From: Khurana, Bharat
Sent: Friday, April 25, 2014 3:22 PM
To: alison_fisher@merck.com
Cc: Montague, Laura
Subject: STN 125508/0; Information Request #7 (Follow-up on your response to IR #4)

Dear Alison,

We acknowledge the receipt of your responses to our Information Request #4, dated April 7, 2014, regarding validation of assays to quantitate antibody to the diphtheria, tetanus, pertussis and meningococcal antigens, which you had submitted via gateway as amendments #09 and #10, dated April 21, 2014 and April 24, 2014, respectively. As we review these amendments, we have the following requests for information:

1. In order to sufficiently support the use of the diphtheria, tetanus, pertussis, and meningococcal assays for their intended purposes we are requesting you provide additional information for the IgG ELISAs for tetanus toxin, pertussis toxin, filamentous hemagglutinin, pertactin and fimbriae, toxin ---(b)(4)---- assay for diphtheria toxin, and for the serum bactericidal assays for the meningococcal groups A, C, W-135 and Y. Please provide for each assay in a readable file format a listing of the assays performed to generate the data for samples from Protocol

005. Please include assay dates, operators and run numbers. For each assay please provide the values for all parameters used to assess system suitability (assay acceptance) including quality control samples, reference curve parameters, bacterial cell counts and any other measure used to assess assay performance. Please include the assays that were rejected due to quality control issues.

2. For the tetanus assay: Please provide the dates that samples for protocol 005 were tested and the version(s) of the SOP that were used during validation and during testing of samples for P005. If updates to the SOPs have occurred since validation, please summarize differences that have occurred with each version. This should include the procedure(s) for the calculation of results that were in use during these times. Please specifically address the following inconsistencies that were identified in your response to IR#4 (Amendment 10) with respect to the assay protocol that was used during validation as well as the calculation method used to generate reportable values.

   a) The report for standardization of (b)(4) Tetanus Standard -(b)(4)- (Doc No REP-8558) states that the reference was tested using SOP PDL-9539; this is different than the SOP that was used during validation (QA8510).

   b) The calculation method described in the validation report (Test No. QA8510), based on a -----(b)(4)-----, differs from the method described in supporting document REP-8419 (PQ report for the use of ----------(b)(4)---------- Assay), which uses a ----------(b)(4)---------- model. REP-8419 also mentions that the plate layout, sample dilution, and number of calibrator points used in the current version of the test method differs substantially from the previous version SOP.

Please respond to this information request within two weeks. If that is not possible, please provide a timeline as to when you expect to submit the data.

Thanks,
Bharat

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