Information Request Email, January 9, 2014 - GARDASIL 9

(System Info - 260176 MONTAGUE LAURA 01/10/2014 12:52:15 MONTAGUEL)

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-Jan-2014 04:21 PM
Initiated by FDA? No
Telephone Number: N/A (email)
Communication Categories: Advice
Information Request
Author: LAURA MONTAGUE

Telecon Summary: Continued discussion regarding submission of samples, draft LRP template, and assay information

FDA Participants: Laura Montague
Non-FDA Participants: William Rankin
Trans-BLA Group: No
Related STNs: None
Related PMCs: None

Background:
On December 11, 2013, Merck initiated an email discussion regarding the submission of samples and assay information. CBER replied with advice on 12-30-2013. On 1-9-2014, Merck responded to CBER's 12-30-2013 email. The email discussion between CBER and Merck on 1-9-2013 is included below.

Telecon Body:

From: Rankin, _William M. (RAS-B) [mailto:william_rankin@merck.com]
Sent: Thursday, January 09, 2014 4:21 PM
To: Montague, Laura; Fisher, Alison L
Cc: Khurana, Bharat; Gutsch, David; Dodge, William H
Subject: RE: CBER Communication: V503 samples and (b)(4) Method Regional Attachment

Dear Laura,

Thank you very much for your timely feedback, it is most appreciated.

Regarding item #2, we acknowledge your request and will provide the draft protocols by Feb 21st , but we will make every effort to provide the documents sooner.

Regarding item #3, we are in a position to provide the updated version of the (b)(4) SOP asap. The initial proposed date of the end of January was conservative, as we are managing many other activities for the V503 program. Given your feedback on the level of importance below, we will prioritize this activity per your request.

Kind regards, Bill

William M. Rankin Associate Director, GRA Vaccines-CMC • ----------(b)(4)----------

From: Montague, Laura [mailto:Laura.Montague@fda.hhs.gov]
Sent: Thursday, January 09, 2014 3:47 PM
To: Rankin, _William M. (RAS-B); Fisher, Alison L
Cc: Khurana, Bharat; Gutsch, David; Dodge, William H
Subject: RE: CBER Communication: V503 samples and (b)(4) Method Regional Attachment

Dear Bill,

Thanks very much for your response. As requested, we have feedback regarding your response to item #1 of CBER's 12-30 email, as well as an additional request.

1) Please proceed with shipment of samples intended to support assay development as described in your response earlier today. We understand that the samples listed in the WORD document "HPV Sample Shipment.docx" will be sent to Karen Campbell on January 15.

2) Please submit a draft lot release protocol template to the BLA as an amendment prior to submitting draft lot release protocols for specific lots. We will review this template and get back to you on its acceptability for use. Please submit by February 21.

3) Please send us your current 9-valent (b)(4) assay SOP to facilitate assay establishment at CBER. It should be submitted as an amendment to your BLA. We understand that you are revising the procedure and have stated that you can submit the revised SOP by the end of this month. However, it is important that we receive the current SOP sooner, and request that you submit it as soon as possible.

Many thanks, Laura Montague

From: Rankin, _William M. (RAS-B) [mailto:william_rankin@merck.com]
Sent: Thursday, January 09, 2014 11:04 AM
To: Fisher, Alison L; Montague, Laura
Cc: Khurana, Bharat; Gutsch, David; Dodge, William H
Subject: RE: CBER Communication: V503 samples and (b)(4) Method Regional Attachment

Dear Laura,

Thank you very much for your feedback below. Please find our responses to your comments, questions, and concerns. Kindly note the request for further feedback within our response to item #1.

Regards, Bill

William M. Rankin Associate Director, GRA Vaccines-CMC • ----------(b)(4)----------

1) Please proceed to ship ---------(b)(4)-------- lots for the new HPV types listed in your spreadsheet "Proposal for CBER.xlsx." We acknowledge that some of the (b)(4) lots are beyond the proposed (b)(4) expiry.

- For lots that are beyond their expiration date, and therefore not intended for lot release at licensure: We request that samples of these expired lots along with any supporting data be shipped directly to Ms. Karen Campbell, DBSQC/OCBQ/CBER/FDA, Building B Room 2410, 5516 Nicholson Lane, Kensington, MD 20895. These lots will assist CBER with assay development. Please notify Ms. Campbell at 301-594-6255 when samples are shipped.

- For lots intended to be used for lot release in support of licensure: Samples of these lots and protocols should be shipped to Sample Custodian (ATTN: HFM-672), Center for Biologics Evaluation and Research, Bldg: NLRC-B, Room: 113, 5516 Nicholson Lane, Kensington, MD 20895

Response: Merck acknowledges and understands your instructions. Moving forward, the applicant will ship samples to the appropriate addressee based on sample as defined above. Based on the feedback below from CBER, the applicant proposes to break out sample shipments into two distinct categories. The first shipment category is proposed to consist purely of samples to support assay development (*and thus not to be tested for batch release*), which will be sent to Ms. Campbell on Wednesday January 15th. The sample information can be found in the attached WORD document. Note that this shipment consists of samples from new HPV Type -(b)(4)- lots and the 9-valent HPV vaccine. The applicant has made Ms. Campbell aware of the pending sample shipment as of this e-mail, and the timing is in alignment with Ms. Campbell's expectations. Shipping logistics require the applicant to provide a final invoice list on Monday January 13, so having your feedback by COB Friday January 10th would be most appreciated.

The second shipment category will consist of samples from lots to be tested for batch release in support of licensure. A schedule for shipment of these samples will be developed per the timing below in response to comment #2. Since samples for batch release will not be sent at this time, the applicant welcomes feedback regarding timing for the provision of DRAFT lot release protocols to CBER such that interactive dialogue can take place.

2) Regarding your proposed schedule of providing samples for lot release requirements in support of the license by 3Q2014, CBER is concerned that unanticipated problems with lots submitted late in the review cycle have the potential to delay regulatory action. Therefore, at your earliest convenience, please provide CBER with as specific information as possible regarding dates of submission of (b)(4) lots that are not immediately available for submission, and update the projected schedule as new information becomes available. It is critical that CBER have reliable submission dates by May 1, 2014. Please note that earlier receipt of samples would provide a greater assurance that testing and release can be completed before the likely action due date.

Response: Merck commits to providing reliable (b)(4) sample submission dates by May 1, 2014. Merck also recognizes the importance of providing the sample submission schedule and the samples themselves ASAP in order to ensure testing and release by the action due date. As such, Merck will seek every opportunity to provide the schedule and samples earlier than the stated dates.

3) CBER acknowledges that the SOP for the ---(b)(4)--- method (potency) is being revised to specify appropriate extravariability rules and will be submitted by the time Merck submits samples for lot release testing. Please provide your best estimate for when the extravariability evaluation method will be submitted. We request that you submit the final SOP as soon as possible, but no later than May 1, 2014

Response: Merck will provide the updated (b)(4) method by the end of January 2014.

Attachment titled “HPV Sample Shipment.doc.x” included in Merck’s 1-9-14, 11:04 email:

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