Information Request Email, July 31, 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: 31-Jul-2014 2:58 PM
Initiated by FDA? Yes
Telephone Number: N/A (email)
Communication Categories: Information Request
Author: Laura Montague

Telecon Summary: IR #16 – Data collection at (b)(3)(b)(4)(b)(7) clinical sites

FDA Participants: Laura Montague, Bharat Khurana
Non-FDA Participants: Alison Fisher
Trans-BLA Group: No
Related STNs: None
Related PMCs: None

Telecon Body:

From: Montague, Laura
Sent: Thursday, July 31, 2014 2:58 PM
To: alison_fisher@merck.com
Cc: Khurana, Bharat
Subject: STN 125506/0; IR #16

Dear Alison,

CBER has the following requests for information regarding clinical sites in (b)(3)(b)(4)(b)(7) participating in study V503-002.

1. We have recently become aware of ----------(b)(3)(b)(4)(b)(7)----------. Please

comment on whether your study V503-002 (including any of its (b)(3)(b)(4)(b)(7) study sites or study personnel as participants in this study) is a ---------- (b)(3)(b)(4)(b)(7)----------.

2. We have been informed that the ----------(b)(3)(b)(4)(b)(7)----------. Please comment on whether you were aware of this request and whether subjects enrolled at study site V503-002---------(b)(3)(b)(4)(b)(7) ------ received study vaccinations subsequent to the date of the request.

3. Please comment on whether any individuals other than the clinical investigator and sub-investigators for study site V503-002-(b)(3)(b)(4)(b)(7) participated in the recruitment, enrollment, treatment, or follow-up of subjects at this site and describe their training for the purposes of participation in the conduct of the study.

4. Please comment on whether all study documents provided to subjects enrolled at (b)(3)(b)(4)(b)(7) sites for study V503-002 (e.g., informed consent documents), clearly stated that Merck (MSD) was the sponsor of the study.

5. Please comment on whether recruitment efforts for study V503-002 in (b)(3)(b)(4)(b)(7) included communication of any of the following information to potential subjects or their families:

   a. That the investigational vaccine, V503, was known to be effective.
   b. That the usual cost of the study vaccine was (b)(3)(b)(4)(b)(7).
   c. That subjects who participated in the study would receive financial compensation.

6. Please describe the procedures for obtaining consent from guardians and assent from subjects in (b)(3)(b)(4)(b)(7) who were enrolled in study V503-002.

7. Please provide copies of the signed informed consent/assent forms for all subjects enrolled in study V503-002 at sites (b)(3)(b)(4)(b)(7). Please provide English

translations of each version used at these two sites if these documents were not written in English.

8. The study vaccinations at (b)(3)(b)(4)(b)(7) sites for study V503-002 appear to have been administered at very similar dates for all subjects, starting in March 2010 and ending in October 2010. Please comment on whether there was coordination among sites in (b)(3)(b)(4)(b)(7) so that all vaccinations would occur at approximately the same time.

9. The temperatures recorded post-vaccination at study site V503-002-(b)(3)(b)(4)(b)(7) all appear to be within the range of 36-37ºC (i.e., normal range). Please provide your assessment of this lack of variability compared with the temperatures recorded at other (b)(3)(b)(4)(b)(7) sites.

10. There appear to be substantially fewer injection site adverse events reported at study site V503- 002-(b)(3)(b)(4)(b)(7) compared with other (b)(3)(b)(4)(b)(7) sites and compared with the overall V503 safety population. Please provide your assessment for this difference.

11. Please comment on whether you have conducted monitoring visits of study sites V503-002-(b)(3)(b)(4)(b)(7) and V503-002-(b)(3)(b)(4)(b)(7) and submit the monitoring reports. Please also provide all medical monitor reports, assessments, and communications related to these two sites.

12. Please provide analyses of the primary endpoints of study V503-002 when excluding subjects from all (b)(3)(b)(4)(b)(7) sites (----------(b)(3)(b)(4)(b)(7)----------) and when excluding subjects from sites (b)(3)(b)(4)(b)(7).

Please respond by August 8.

Thank you,
Laura

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