

From: Sharon.W.Shapowal@gsk.com  
To: Sullivan, Helen M.  
Subject: Note re: site 4923  
Date: Thursday, May 03, 2007 9:17:46 AM

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Ref: BLA125259 (CERVARIX)

Dear Helen: As discussed during my conversation on April 30th with you and Gopa Raychaudhuri, the following information will give you added details regarding the types of violations that an audit by GSK revealed at the site of (b)(6). These findings (supplied by my colleagues in clinical compliance) support the reasons why we closed (b)(6) site, and why GSK proactively excluded the data from the efficacy & safety analyses of study HPV-008, even while the investigation of the site was underway.

Also, I have confirmed that the all data for this site (n=21 subjects) were included in the unblinded SAS data sets for study HPV-008, submitted under BLA 125259 and provided by the external statistician. In the dataset "ELIM" all subjects for this site have received an elimination code 1010 which have eliminated the data from those subjects on all analyses performed.

Safety information from this site was also included in Section 1.2 of the report, Ethical Conduct of the Study [See text: *"One serious adverse event was reported (i.e. spontaneous abortion) and four subjects reported medically significant conditions (i.e. nausea, streptococcal pharyngitis, joint sprain, spontaneous abortion, endodontic procedure, wisdom teeth removal)..."*]. Because the spontaneous abortion was an SAE, there is a narrative of the event, of course.

Please refer below for the additional details/site findings. I hope the information meets with your needs. We will amend the BLA with this information.

Kind regards, Sharon

S.W.Shapowal  
Director, Adult Vaccines  
(610) 787-3763  
(internal: 8-275-3763)

**Additional details of findings at site 4923 (Salt Lake City, USA):**

The audit revealed there was persistent non-compliance with Good Clinical Practice. Examples of this include, but are not limited to:

**1. Lack of adequate principal Investigator oversight**

- (b)(6) failed to ensure that all persons assisting in conducting the study were adequately trained and knowledgeable of the protocol;
- (b)(6) did not demonstrate control over the study management aspects of the study that were delegated to Wasatch Clinical Research, Site Management Organization (SMO);
- (b)(6) never accessed the remote data management system, consequently the data had not been verified by the PI as being accurate and correct;
- Review of a select number of clinic charts, and study specific source documents (498, 499, 501, 502, 505, 506, 515) revealed 2 instances where the validity of the data was suspect.

**2. Failing to conduct the study in compliance with the protocol**

- (b)(6) failed to comply with the protocol requirements for managing pregnancies that occurred throughout the study. Two pregnancies were not reported to GSK (subjects 501 and 515). Two pregnancies were reported late to GSK (502 and 505). Three of the 5 pregnant subjects (501, 502, 515) had cervical specimens obtained which is in violation of section 8.11 of the protocol which states 'Pelvic exams for collection of cervical specimens will be suspended in women known to be pregnant and will resume 3 months after resolution.'

"EMF <fda.hhs.gov>" made the following annotations.

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