Bioresearch Monitoring Final Review memo - KINRIX

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

DATE: December 11, 2007

FROM:
Joseph P. Manik, Bioresearch Monitoring Branch, HFM-664
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH:
Patricia A. Holobaugh
Bioresearch Monitoring Branch Chief, HFM-664

TO:
Michael Schmitt., HFM-437, Chair, BLA Committee
Joseph Temenak, HFM-481, Regulatory Project Manager

SUBJECT:
Bioresearch Monitoring Final Review memo
STN: BLA 125260/0
Sponsor: GlaxoSmithKline Biologicals
Product: Diptheria and Tetanus Toxoids, Acellular Pertussis Vaccine Adsorbed and Inactivated Poliovirus Vaccine Combined *KINRIXT*

FINAL SUMMARY STATEMENT

Results of three bioresearch monitoring inspections of three clinical sites did not reveal problems that impact the data submitted in the application.

BACKGROUND

Inspections of three clinical investigators were performed in support of this Biologics License Application (BLA). Information from the BLA was compared to source documents during the inspections. The inspections focused on specific questions concerning the study.

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B. The investigator will inquire about the occurrence of AEs/SAEs at every visit/contact during the study
C. All AEs occurring within 31 days following administration of each dose of vaccine/comparator must be recorded on the Adverse Event form in the subject's electronic Case Report Form (eCRF), irrespective of severity or whether or not they are considered vaccination-related

Dr. Long: Our inspection noted that adverse events were not documented in the eCRF for 4 study subjects (106527, 106529, 106535, and 106546). In response to this inspectional finding the corrective actions implemented include re-educating the staff on the importance of recording all adverse events as specified in the protocol and also asking the sponsor to provide clear written instructions for adverse event reporting during follow-up periods.

No findings were observed at Dr. Herz's/Dr. Klein's site (#10452) or Dr. Sander's site (#22818).

The Establishment Inspection Report is pending for Site # 22818, Arkansas Pediatric Clinic, Scott Mitchell Sanders, M.D.

BIMO ADMINISTRATIVE FOLLOW-UP

Correspondence addressing concerns raised by the inspection was issued to Dr. William W. Long. A close out letter was issued to Dr. Klein. Correspondence will be issued to Dr. Sanders after complete review of the establishment inspection reports and final classification.

Should you have any questions or comments about the contents of this memorandum or any aspect of Bioresearch Monitoring, please contact me at (301) 827-6335.

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Joseph P. Manik
Consumer Safety Officer

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Consumer Safety Officer

STUDY TITLE:
A phase III, open (double-blind for consistency lots), randomized, multicenter, clinical trial of the safety, immunogenicity and consistency of three manufacturing lots of GSK Biologicals' DTaP-IPV candidate vaccine compared to that of separate injections of GSK Biologicals' DTaP vaccine *(Infanrix)* and Aventis Pasteur's IPV vaccine (IPOL) administered as booster doses to healthy children 4 to 6 years of age, each co-administered with Merck and Company's MMR vaccine (M-M-R_{II})

Inspection of clinical sites and outcome

Clinical Investigator	**Study Site Site Number**	**Location**	**Number of Subjects**	**Form FDA 483 Issued**	**Final Classification**
Arnd Herz, M.D. (subinvestigator) Nicola P. Klein, M.D., Ph.D. (principal investigator)	Kaiser Permanente - Hayward Site # 10542	Hayward , California	394	No	NAI
William W. Long, M.D.	Children's Hospital Site # 22942	Columbus , Ohio	44	Yes	VAI
Scott Mitchell Sanders, M.D.	Arkansas Pediatric Clinic Site # 22818	Little Rock , Arkansas	89	No	EIR Pending

NAI - No Action Indicated, VAI - Voluntary Action INdicated

SPONSOR ISSUES

No sponsor or monitoring issues were noted.

INSPECTIONAL FINDINGS

Clinical Investigator (CI) issues:

Failure to report to the sponsor adverse effects that may reasonably be regarded as caused by, or probably caused by, an investigational drug.

Section 8 of Protocol 213503/048 (DTaP-IPV 048) states:

A. The investigator is responsible for the detection and documentation of events meeting the criteria and definition of an Adverse Event (AE) or Serious Adverse Event (SAE)