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

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DATE December 2, 2014

FROM Dennis T. Cato, Bioresearch Monitoring Branch, HFM-664
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality
Telephone: 240-402-8906 Fax: 301-595-1304

THROUGH Patricia Holobaugh, Chief, Bioresearch Monitoring Branch

THROUGH Gilliam Conley, Director, Division of Inspections and Surveillance

TO

| | |
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| Matthew Steele | Chair, Review Committee |
| Juan Lacayo | RPM |
| Scott Norris | RPM |
| Sarah Browne | Clinical Reviewer |

SUBJECT Bioresearch Monitoring Discipline Review Memo

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|---|---|
| BLA/STN: | 125525/0 |
| IND: | 14668 |
| Sponsor: | Sanofi Pasteur Inc. |
| Product: | Diphtheria-Tetanus-Pertussis-Polio Vaccine (QUADRACEL) |

REVIEW SUMMARY

Bioresearch Monitoring (BIMO) inspections assignments were issued for 3 clinical investigators and 4 domestic clinical investigator study sites. Inspections at 3 of the clinical sites have been completed and the inspection reports were reviewed, and the inspections classified. An inspection at the 4th clinical study site is currently in-progress.

The Establishment Inspection Reports (EIRs) for the completed inspections did not reveal problems that impact the data submitted in this biologics licensing application (BLA).

BACKGROUND

Clinical Investigator Inspection Assignments were issued for 3 clinical investigators and 4 domestic clinical study sites in support of this BLA. The 4 selected sites represent 5.7 percent of all the clinical study sites that enrolled subjects. The 4 sites enrolled a total of 426 subjects combined and the number of subjects enrolled at the 4 sites inspected represents 12.6 percent of subjects enrolled in the study.

Bioresearch monitoring inspections are conducted in accordance with the FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. The inspection

assignments included specific questions related to the study protocol, and verification of the study data on efficacy endpoints submitted by the sponsor in the BLA.

PROTOCOL AUDITED

*A Controlled, Multi-Center, Randomized, Open Label Phase III Study Designed to Compare the Safety and Immunogenicity of DTaP-IPV to DAPTACEL® + IPOL® as the 5th Dose Booster in Children 4 to 6 Years of Age Who Have Been Previously Vaccinated with DAPTACEL and/or Pentacel Vaccines.* M5I02 Version 6.0

The table below summarizes the inspection results:

| Site Number | Study Site | Location | Enrolled Subjects | 483 Issued | Classification |
|---|---|---|---|---|---|
| 03 | Pediatrics and Adolescent Medicine, P.A. | Marietta, Georgia | 39 | No | NAI |
| 04 | Pediatrics and Adolescent Medicine, P.A. | Woodstock, Georgia | 20 | No | NAI |
| 10 | Cyn3rgy | Gresham, Oregon | 20 | Yes | NAI |
| 39 | Utah Valley Pediatrics, Timpanogos Office | Orem, Utah | 347 | Inspection in-progress | |

NAI = No Action Indicated

FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if and when s/he disclosed information about her/his financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children including if and when the information was updated. Each inspected study site had a copy of the financial disclosure forms on hand for the clinical investigators and sub-investigators.

INSPECTIONAL FINDINGS

Sponsor/Monitor Issues

There were no sponsor/monitor issued identified at any of the study sites audited.

Clinical Investigator (CI) Study Site Issues

A review was conducted of testing records, regulatory binders, study specific standard operating procedures, and general study conduct. In addition, source documents, including records of adverse events, protocol deviations, and subject dispositions were reviewed and the information contained was compared to the data tables submitted by the sponsor in the application. Individual site observations are listed below:

Study Site 03: A Form FDA 483 was not issued at close of this inspection and the inspection was classified as NAI.

Study Site 04: A Form FDA 483 was not issued at close of this inspection and the inspection was classified as NAI.

Study Site 10: A Form FDA 483 was issued at close of this inspection. A review of the EIR revealed no significant issues impacting the study conduct and/or the data submitted by the sponsor in support of the application. The inspection received a final classification of NAI.

Study Site 39: This inspection is currently in-progress. We will update the review committee as soon as new information becomes available.

BIMO ADMINISTRATIVE FOLLOW-UP

Information letters were issued for 3 study sites. We are awaiting receipt and review of the final EIR and will update the review committee as new information becomes available. Please contact me should you have any questions about this memo or any aspect of Bioresearch Monitoring.

Dennis T. Cato
Consumer Safety Officer

CC:

Access/Chron
STN 125525/0

Draft: Cato: 12/1/2014
Reviewed: Holobaugh: