

**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 May 18, 2014

FROM Erin McDowell, Bioresearch Monitoring Branch  
Division of Inspections and Surveillance  
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Chief, Bioresearch Monitoring Branch

THROUGH Gilliam Conley, Director, Division of Inspections and Surveillance

TO Rana Chattopadhyay, BLA Committee Chair  
Ann Schwartz, Clinical Reviewer  
Kelsy Hoffman and Katie Rivers, RPMs

SUBJECT Bioresearch Monitoring Discipline Review Memo Addendum  
BLA: STN 125563/0  
IND: 14496  
PRODUCT: (b) (4) ® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP), Inactivated Poliovirus (IPV), Haemophilus b Conjugate (Hib) and Recombinant Hepatitis B Vaccine (HepB)]  
SPONSOR: MCM Vaccine Co.

**REVIEW SUMMARY**

Bioresearch Monitoring inspections of six clinical investigators were conducted in support of this Biologics Licensing Application (BLA). Inspections of these clinical investigators did not reveal significant problems that impact the data submitted in this BLA.

**BACKGROUND**

MCM Vaccine Co. (a partnership between Sanofi Pasteur, and Merck Sharp and Dohme Corporation, a subsidiary of Merck & Co., Inc.) submitted a Biologics License Application (BLA) for “Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed, Inactivated Poliovirus, Haemophilus b Conjugate [Meningococcal Protein Conjugate] and Hepatitis B [Recombinant] Vaccine (DTaP-IPV-Hib- HepB),” referred to as PR5I under IND 14496. The proposed trade name of this product is (b) (4) BIMO reviewed information submitted in the original BLA 125563/0 and amendments 1-4 in Modules 1, 2, and 5. Six clinical

investigator sites covering two pivotal studies were proposed for inspection by the Bioresearch Monitoring Branch member of the review committee. The review committee concurred with the proposed sites. The clinical sites were selected based on the number of subjects enrolled, site inspectional history, noteworthy subject noncompliance, and geographic location.

**STUDY TITLES**

A Phase III Randomized, Open-Label, Active-Comparator Controlled Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V419 in Infants When Given at 2, 4, and 6 Months Concomitantly with Pneumococcal Conjugate Vaccine (PCV) and RotaTeq™ (**Protocol No. V419-005**; NCT01337167)

A Phase III Randomized, Partially Double-Blind, Active-Comparator-Controlled, Lot-to-Lot Consistency Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V419 in Healthy Infants When Given at 2, 4, and 6 Months Concomitantly with PREVNAR 13™ and RotaTeq™ (**Protocol No. V419-006**; NCT01340937)

For study V419-005, 1473 subjects were enrolled at 39 United States sites. Two sites located in the United States were selected for inspection. The two selected sites inspected for study V419-005 represent ~9% of the enrolled subjects. For study V419-006, 2808 subjects were enrolled at 73 study centers within the United States. Four sites were selected for BIMO inspection, representing ~10% of the enrolled subjects.

**INSPECTION SITES:**

Bioresearch Monitoring inspections were conducted at the following clinical sites:

Study	#Subjects	Site#	Study Site	Location	Form FDA 483 Issued	Final Classification
V419-005	66	0010	Pediatrics Associates	Crestview Hills, Kentucky	No	No Action Indicated
V419-005	66	0029	Rockwood Research Center	Spokane, Washington	No	No Action Indicated
V419-006	38	0069				
V419-006	46	0007	West Houston Clinical Research Service	Houston, Texas	No	No Action Indicated
V419-006	52	0044	Wee Care Pediatrics	Layton, Utah	Yes	Voluntary Action Indicated
V419-006	81	0029	LSUHSC-Shreveport Pediatrics	Shreveport, Louisiana	No	No Action Indicated
V419-006	72, 99, and 88	0038, 0039, and 0040	Midwest Children’s Health Research	Lincoln, Nebraska	No	No Action Indicated

The inspections were conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. Information submitted in the BLA was compared to source documents at each clinical site. The inspection assignment included specific questions concerning the clinical study.

No Form FDA 483s were issued to the sites in Lincoln, Houston, Crestview Hills, Spokane, and Shreveport. The final inspection classification for these clinic sites was NAI (No Action Indicated).

The Layton, Utah site was issued a Form FDA 483. The FDA Form 483 listed at least 14 subjects' adverse event data from the diaries were missing or incorrectly transcribed into the case report forms. This inspection was classified as VAI (Voluntary Action Indicated).

#### SPONSOR ISSUES

No sponsor or monitoring issues were noted at the sites that were inspected.

#### FINANCIAL DISCLOSURE:

The Clinical Investigator Compliance Program directs the FDA investigator to ask the clinical investigator if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children, and if and when the information was updated. The information submitted to the BLA was verified for each of the inspected clinical sites.

#### ADMINISTRATIVE FOLLOW-UP:

Information letters were issued to six clinical investigators. Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at (240) 402-9140.

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Erin McDowell  
Consumer Safety Officer

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Draft: McDowell 3/5/2015  
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