

MEMORANDUM

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

DATE May 2, 2016

FROM Christine Drabick, Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Bioresearch Monitoring Branch Chief

THROUGH Gilliam Conley, Director, Division of Inspections and Surveillance

TO Goutam Sen, Chair, STN 125597/0
Tina Mongeau, Clinical Reviewer
Kelsy Hoffman, RPM
Christina Houck, RPM

SUBJECT Bioresearch Monitoring Final Discipline Review Memo
SPONSOR: PaxVax, Inc.
PRODUCT: PXVX0200 (*V. cholerae*, O1 Inaba Vaccine Strain CVD
103-HgR), Vaxchora
BLA: 125597/0

FINAL SUMMARY STATEMENT:

The Bioresearch Monitoring inspection of four clinical investigators did not reveal substantive problems that impact the data submitted in the application.

BACKGROUND:

Four clinical investigator assignments were issued in support of this Biologics License Application. The conduct of three protocols was reviewed during the BIMO inspections.

Protocol PXVX-VC-200-003 was conducted at three sites in the United States and enrolled 197 subjects. Study vaccine was received by 102 subjects and 95 received placebo. Two of the inspected sites conducted this protocol. The two inspected sites reviewed the records of 40 vaccine and 20 placebo subjects or 39% and 21% of the total enrollment for this protocol.

Protocol PXVX-VC-004 was conducted at 19 United States sites and six sites in Australia. Study vaccine was received by 2789 subjects and placebo by 351. Two of the inspected sites conducted this protocol. The two inspected sites reviewed the records of 60 vaccine and 20 placebo subjects or 2% and 6% of the total enrollment for this protocol.

Protocol PXVX-VC-200-005 was conducted at 16 United States locations. Study vaccine was received by 296 subjects and 99 received placebo. Three of the inspected sites conducted this protocol. The three inspected sites reviewed the records of 30 vaccine and 15 placebo subjects or 10% and 15% of the total enrollment for this protocol.

The four clinical sites were selected based on subject enrollment for each protocol, previous inspectional history, and geographic location.

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 this site. The inspection assignment included specific questions concerning the clinical study.

PROTOCOL TITLES:

The conduct of three protocols was reviewed during the BIMO inspections:

A Phase 3 Randomized, Double-Blind, Placebo-Controlled, Efficacy Trial of a Single Dose of Live Oral Cholera Vaccine Candidate, PXVX0200 CVD 103-HgR Strain, in Preventing Cholera Following Challenge with *Vibrio cholera* 01 E1 Tor Inaba 10 Days or 3 Months after Vaccination (PXVX-VC-200-003)

A Phase III Randomized, Double-Blind, Placebo-Controlled, Three Lot Consistency Study in Healthy Adult Volunteers to Assess Immunogenicity and Clinical Acceptability of a Single-dose of the Live Oral Cholera Vaccine Candidate PXVX0200 *Vibrio cholera* 01 Serotype Inaba Vaccine Strain CVD 103-HgR (PXVX-VC-200-004)

A Phase III Randomized, Double-Blind, Placebo-controlled Study in Older Adults to Assess Immunogenicity and Clinical Acceptability of a Single-dose of the Live Oral Cholera Vaccine Candidate PXVX0200 *Vibrio cholera* 01 Serotype Inaba Vaccine Strain CVD 103-HgR (PXVX-VC-200-005)

INSPECTION SITES:

Bioresearch Monitoring inspections were conducted at the following clinical sites:

Site Number	Location	Protocols	Form FDA 483 Issued	Final Classification or Status
03	Cincinnati, OH	PXVX-VC-200-003	No	NAI
04	Burlington, VT	PXVX-VC-200-003	Yes	VAI
04	Burlington, VT	PXVX-VC-200-005	No	NAI
13	Lenexa, KS	PXVX-VC-200-004 PXVX-VC-200-005	No	NAI
15	Salt Lake City, UT	PXVX-VC-200-004 PXVX-VC-200-005	Yes	VAI

NAI = No Action Indicated, VAI = Voluntary Action Indicated

SIGNIFICANT INSPECTIONAL FINDINGS

No significant inspectional findings were identified.

SPONSOR FINDINGS

No sponsor findings were identified.

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 the clinical investigators at all sites.

Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at 240-402-8928.

Christine J. Drabick
Consumer Safety Officer

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History

Draft: Drabick: May 2, 2016
Reviewed: Holobaugh: