

## Mid-Cycle Communication Telecon

**Application type and number:** Original Application, STN125597/0

**Product name:** Vaxchora®, Cholera Vaccine, Live, Oral

**Proposed Indication:** Active immunization against disease caused by *V. cholera* serogroup O1 in adults 18 years of age and older

**Applicant:** Pax Vax Bermuda Limited

**Meeting date & time:** February 03, 2016 11:00AM

**Committee Chair:** Goutam Sen, Ph.D.

**RPM:** LCDR Kelsy Hoffman, Ph.D./Christina Houck

### CBER Attendees:

Goutam Sen, Ph.D., Chair

LCDR Kelsy Hoffman, Ph.D., RPM

Christina Houck, RPM

Jennifer Bridgewater, M.P.H., Regulatory Coordinator

Scott Norris, B.S., Regulatory Coordinator

CAPT Jon Daugherty, Ph.D., Branch Chief

Wellington Sun, M.D., Division Director

Loris McVittie, Ph.D., Deputy Director

Scott Stibitz, Ph.D., Laboratory Chief

Roger Plaut, Ph.D., CMC Reviewer

Douglas Pratt, M.D., M.P.H., Associate Director of Medical Affairs

Manuel Osorio, Ph.D., CMC Reviewer

Freyja Williams, B.S., CMC Reviewer

Jay Slater, M.D., Division Director

Matthew Steele, Ph.D., Branch Team Leader

Christopher Sese, Contractor, Eastern Research Group

### Sponsor Attendees:

#### PaxVax:

Kevin Smyth, Vice President, Regulatory Affairs and Pharmacovigilance

Paul Shabram, Vice President, Technical Development

Jonathan Smith, Executive Vice President and Chief Scientific Officer

Lisa Danzig, Vice President, Clinical Development and Medical Affairs

Grace Benedict, Associate Director, Regulatory Affairs

Violet Carvalho, Associate Director, Quality Assurance

Lawrence Chew, Director, Fermentation

Amish Patel, Director, Product Development

Fiona Cameron, Regulatory Consultant

Erlinda Quijano, Associate Director, Quality Control

Volker Niedan, Head of Quality Control

Martin Dearden, Vice President, Quality Assurance and Quality Control

Nancy Waddell, Manager, Quality Control

### Discussion Summary:

CBER provided the Mid-Cycle Communication (plain and bold text below) agenda to the Applicant on February 1, 2016. Discussion between CBER and the Applicant during the February 3, 2016, Mid-cycle Communication is included below in italics.

**1. Any significant issues/major deficiencies identified by the review committee to date.**

The following issues have been identified during the review process:

- 1) In Section 2.3.S.2.1, you indicate that (b) (4) has replaced (b) (4) as the Working Seed Lot (WSL) manufacturer for PXVX0200. Use of the WSL manufactured by (b) (4), for PXVX0200, will require a post-approval supplement that includes a complete description and validation of the (b) (4) facilities and manufacturing process, validation of the new WSL (b) (4), and manufacturing information and testing data from three lots of final Drug Product (DP) manufactured using the (b) (4) WSL. Please submit stability data in support of the intermediate bulk drug substance (IBDS), bulk drug substance (BDS) and DP manufactured with the change.
- 2) In Section 3.2.P.2.3.1, you describe a proposed change to the manufacturing process in which the BDS is held at (b) (4) rather than (b) (4). Your clinical studies were conducted using material manufactured using the (b) (4) BDS hold time. The effect of the proposed manufacturing change on the vaccine is not clear and we do not agree with the proposed change. Please consider submitting a post-approval supplement to your Biologics License Application to implement the change.

*The applicant stated that all data requested for the change in working seed lot manufacturer is available with the exception of the (b) (4) analysis. The applicant stated their intention to submit all data to support this change during the original BLA application, and requested CBER's input. CBER responded that the information will be reviewed when it is submitted, and the applicant will receive CBER comment subsequently. The applicant then questioned the requirement for three lots of product, and if that is a requirement for new and old products alike. CBER indicated that a minimum of three lots is the general expectation for products. The applicant informed CBER that they would submit the required information for the (b) (4) hold time within the BLA review timeframe and asked if this was sufficient. CBER indicated we would review responses once submitted.*

**2. Information regarding major safety concerns.**

There are no major safety concerns identified at this time.

**3. Preliminary review committee thinking regarding risk management.**

We do not anticipate the necessity for a Risk Evaluation Mitigation Strategy (REMS) at this time. However, we anticipate the necessity for one or more Post-marketing Requirements (PMRs).

*The applicant informed CBER that a more detailed Pediatric Protocol Synopsis would be submitted by March 15, 2016, followed by the Pediatric Study Protocol to be submitted by the end of 2016.*

**4. Any information requests sent and not received**

We have not received responses for information requests sent on January 13, 2016 and January 19, 2016.

*The applicant informed CBER that the response to the information request dated January 13, 2016 would be submitted by February 12, 2016 and the response to the January 19, 2016 information request would be submitted the week of February 8, 2016. The applicant also mentioned that they will meet the timelines to address the February 2, 2016 information request.*

**5. Any new information requests to be communicated**

We anticipate requests for additional chemistry, manufacturing, and control information and a request for samples (drug product and buffer). We will also have additional comments regarding the Lot Release Protocol Templates.

**6. Proposed date(s) for the late-cycle meeting (LCM)**

The LCM between you and the review committee is currently scheduled for March 31, 2016. We intend to send the meeting materials to you no later than 12 business days in advance of the LCM. If these timelines change, we will communicate updates to you during the course of the review.

*CBER informed the applicant the LCM will be held as a telecon from 11:30AM-1:30PM on March 31, 2016 and PaxVax agreed.*

**7. Updates regarding plans for the Advisory Committee (AC) meeting**

We do not anticipate the need for an AC meeting at this time.

**8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates**

Late Cycle Meeting: To be held on March 31, 2016

Labeling Comments: To be submitted to you no later than May 16, 2016

Action Due: We will take action on this application no later than June 15, 2016