



MEMORANDUM

Date: April 22, 2016

From: Marie J. Anderson
Division of Biological Standards and Quality Control (DBSQC)
Office of Compliance and Biologics Quality (OCBQ)
Center for Biologics Evaluation and Research (CBER)
Food and Drug Administration (FDA)

To: Biologics License Application Submission Tracking Numbers 125597/0

Subject: Review of Lot Release Protocol (LRP) Template for Cholera Vaccine, Live, Oral

Through: William M. McCormick, Ph.D., Director, DBSQC/OCBQ/CBER/FDA

Cc: Goutam Sen, Ph.D., Chair, BLA Review Committee, DVRPA/OVRR/CBER/FDA
Kelsy Hoffman, Ph.D., RPM, BLA Review Committee, DVRPA/OVRR/CBER/FDA
Christina Houck, M.S., RPM, BLA Review Committee, DVRPA/OVRR/CBER/FDA

Applicant: Pax Vax Bermuda Limited

Products: Cholera Vaccine, Live, Oral
Trade Name - Vaxchora®

1 General Information

1.1 CMC Review Identifiers and Dates

1.1.1 Biologics License Application (BLA) Submission Tracking Number (STN): 125597/0

1.1.2 Submission received by CBER: October 16, 2015

1.1.3 Review completed: April 21, 2016

1.1.4 Material Reviewed:

LRP template submitted in BLA 125597/0

LRP template – Buffer submitted in sBLA 125597/0.4

Revised LRP template – Combined – Vaccine and Buffer submitted in BLA 125597/0.14

Revised LRP template – Combined – Vaccine and Buffer submitted in BLA 125597/0.29

Revised LRP template – Combined – Vaccine and Buffer submitted in BLA 125597/0.31

1.1.5 Related Master File, INDs and BLAs:

BLA 125597 Module 3, Quality

2 Executive Summary: The LRP template for Cholera Vaccine, Live, Oral (Vaxchora®) submitted in BLA 125597/0.31 on April 20, 2016 is acceptable for use.

3 Review

3.1 Documents Reviewed

1. LRP template for Cholera Vaccine, Live, Oral (Vaxchora®) submitted on October 16, 2015 in BLA 125597/0.
2. LRP template for Cholera Vaccine, Live, Oral - Buffer (Vaxchora®) submitted on January 8, 2016 in BLA 125597/0.4.
3. Revised LRP template for Cholera Vaccine, Live, Oral – Combined Vaccine and Buffer (Vaxchora®) submitted on March 4, 2016 in BLA 125597/0.14.
4. Revised LRP template for Cholera Vaccine, Live, Oral – Combined Vaccine and Buffer (Vaxchora®) submitted on April 6, 2016 in BLA 125597/0.29.
5. Revised LRP template for Cholera Vaccine, Live, Oral – Combined Vaccine and Buffer (Vaxchora®) submitted on April 20, 2016 in BLA 125597/0.31.

3.2 Review

On December 17, 2015 CBER submitted an IR to Pax Vax Bermuda Limited (Pax Vax) requesting the submission of a LRP template for the buffer component of the vaccine. On January 8, 2016 Pax Vax submitted an LRP template for the buffer in BLA 125597/0.4. The LRP templates for vaccine and buffer were reviewed by representatives of DBSQC and DMPQ LRB. On February 24, 2016 an IR was submitted to Pax Vax requesting changes to the LRP templates.

On March 4, 2016 Pax Vax submitted responses to the February 24, 2016 IR and a revised LRP in BLA 125597/0.14.

Note: CBER comments are in plain text; Pax Vax responses are italicized.

CBER Comment

1. Please submit one lot release protocol (LRP) template for the vaccine and buffer.

Throughout document

2. Please ensure each test clearly states the result.

3. Please add the specification for each test.

Page 6 of 7 (Vaccine LRP); Page 10 of 14 (Buffer)

4. (b) (4)

Please use the attached template – Bioburden Tests

Page 7 of 7 (Vaccine LRP); Pages 11 of 14 – 14/14 (Buffer)

5. Absence of Specified Organisms

Please use the attached template - Specified Microbiology Tests

Bioburden Tests on xxxx

(Test Sample description: e.g. (b) (4)

	Test Dates (start-end)	Media	Incubation Temp.	Result CFU/mL	Specification (Limit Acceptance)
Total Aerobe Count					
Yeast and Mold Count					

Specified Microbiology Tests (b) (4) In-house

(Test Sample description: e.g. (b) (4)

(b) (4)

Pax Vax Response

For the response to the items 1 through 5 as requested, PaxVax has consolidated the lot release protocols for the vaccine and buffer (3.2.R Regional Lot Release Protocol). The protocol clearly provides the results and the specification for each test. The (b) (4) and specified organism tests have been updated for both the vaccine and buffer to reflect the template provided by the Agency. The general safety test and (b) (4) have been removed based on the response submitted on February 19, 2016 (BLA 122597/SN 0011). The alert limits for the (b) (4) for the vaccine and buffer have also been added (BLA 122597/SN0007).

The LRP template – Combined Vaccine and Buffer was reviewed by representatives of DBSQC and DMPQ LRB. On April 1, 2016 an IR was submitted to Pax Vax requesting changes to the LRP template.

On April 6, 2016 Pax Vax submitted responses to the April 1, 2016 IR and a revised LRP in BLA 125597/0.29.

CBER comments

Page 1 of 10

1. Please change "Proper Name of Product" to "Trade Name".
Vaxchora is the trade name.

Page 5 of 10

2. Please remove the following (this information is only needed on page 1):

Reason for Submission: _____ For Release
_____ For Surveillance
_____ For Licensing Action
_____ Corrected Protocol

Manufacturer Name: PaxVax, Inc.

Manufacturer Address: (b) (4)

Proper Name of Product: Vaxchora

Label Strength:

Source Material:

Processing Method:

Manufacturer's Certification

All tests conducted on this lot are reported and pass specifications as required.

Signature: _____ Date: _____

Title: _____ Authorized Official

Page 7 of 10

4. Sachet Integrity

Please correct the specification – Inspection level II with AQL of (b) (4) Failures have defect (b) (4) opening.

The (b) (4) opening does not match the specification submitted in 125597/0.9 submitted to CBER on 2/19/2016; which states (b) (4) opening.

Pax Vax Response

- 1. The requested change has been made. The revised Lot Release Protocol is located in Section 3.2.R, Regional Information.*
- 2. The requested change has been made.*
- 3. The requested change has been made.*

The LRP template – Combined Vaccine and Buffer was reviewed by representatives of DBSQC, DVRPA and DBPAP. On April 18, 2016 an IR was submitted to Pax Vax for the correction of changes to the LRP template that were not requested.

On April 20, 2016 Pax Vax submitted responses to the April 18, 2016 IR and a revised LRP in BLA 125597/0.31.

CBER comments

Throughout document

1. Please revise the header throughout your Lot Release Protocol (LRP), so it is same as the LRP header you submitted in Amendment 14, which is as follows:

cc BLA Number: 125597

Lot Numbers Vaccine/Buffer:

Licensed Name of Product: Cholera Vaccine, Live, Oral

Pages 5 of 11, 11 of 11

2. In the tables titled “Absence of Specified Organisms”, please revise (b) (4) to the test name (b) (4).

Pax Vax Response

- 1. The lot release protocol has been edited as requested and is provided in Section 3.2.R, Regional Information.*
- 2. The lot release protocol has been edited as requested.*

3.3 Conclusions

Pax Vax Bermuda Limited responses and requested revisions to the LRP template – Combined Vaccine and Buffer received April 20, 2016 in 125597/0.31 are acceptable. This template may be used for future lot release submissions.