

Memorandum

Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Compliance and Biologics Quality
Division of Manufacturing and Product Quality

To: File STN BL STN 125354 amendment 6 and 7

From: Deborah Trout, Committee Member, CBER, OCBQ, DMPQ, HFM-675

Through: Carolyn Renshaw, Branch Chief, MRB1, DMPQ, OCBQ, HFM-675

Subject: Review of response to letters date May 27, 2010 (amendment 6) and August 26, 2010 (amendment 7).

Recommendation: Approval

CR Letter Question 34

It is unclear from your response dated October 15, 2009 whether a process validation protocol was executed for critical manufacturing steps. Please note the objective of process validation is to ensure that the manufacturing process will consistently yield product with specific quality attributes. Further, a process validation protocol is a prospectively written plan pre-approved by the quality unit that specifies critical steps, controls, and measurements. The process validation protocol states how validation will be conducted, identifying sampling, assays, specific acceptance criteria, production equipment, and operating ranges. Results obtained for each study described in the protocol should be evaluated in an associated process validation report. Please comment.

Response (amendment 6)

Alarmed performed process validation as required; however it was not summarized in one document. A summary of the manufacturing process is shown below:

----- (b)(4) -----

----- (b)(4) -----

----- (b)(4) -----

----- (b)(4) -----

----- (b)(4) -----

----- (b)(4) -----

----- (b)(4) -----

The critical manufacturing steps include ----- (b)(4) -----
-----, Since the diluent is tested ----- (b)(4) -----
-----, validation of this step is unnecessary. There are no unknown qualities at that
step. Diluent that is not within specifications will be discarded. ----- (b)(4) ----- has been
validated. ----- (b)(4) -----
-----,
excipients are measured and the product is tested for identity and potency. The identity
test and the potency test have been validated as discussed in other parts of this
submission. The product will be rejected and discarded if it does not pass the identity
and/or potency tests and if the excipients are outside specifications.

The firm's response appears acceptable

CR Letter Question 35

It appears from your response dated October 15, 2009 that the media fill procedure does
not include ----- (b)(4) ----- . Please provide
validation data to support ----- (b)(4) -----
-----.

Response (amendment 6)

----- (b)(4) ----- . SOP 911-003 documents this
procedure. Validation 1010 was submitted in support of ----- (b)(4) -----
----- . This provides evidence to support ----- (b)(4) ----- , since it
was done with coccidioidin (Spherusol). ----- (b)(4) -----
----- . It is intended that potency and identity
and visual inspection will be conducted ----- (b)(4) -----
-----.

The firm's response is not complete.

*You have not provided the requested information. Please note ----- (b)(4) -----
----- . Please supply validation data to support the
----- (b)(4) -----
----- data is unavailable please explain how ----- (b)(4) ----- was validated to*

ensure its capacity for excluding contamination for the longest hold period encountered during routine production.

Response (amendment 7)

(b)(4)

The firm's response appears acceptable.

CR Letter Question 36

Please provide data demonstrating that you have achieved -----(b)(4)-----
-----.

Response (amendment 6)

(b)(4)

The firm's response is not complete.

*Data provided did not address -----(b)(4)-----, Please provide data demonstrating that you have achieved -----(b)(4)-----
-----.*

Response (amendment 7)

CR Letter Question 38

Please provide method validation for the -----(b)(4)----- used to test container closure integrity.

Response (amendment 6)

The -----(b)(4)----- Test was performed in accordance with Validation 1034. This study was designed to detect -----(b)(4)-----

The firm's response appears acceptable

CR Letter Question 39

The regulation cited under Section 4, Environmental Assessment for your Categorical Exclusion made in pursuant to 21 CFR 25.31(f), is not appropriate. Please submit a corrected citation.

Response (amendment 6)

The correct reference is 21 CFR 25.31(c).

The firm's response appears acceptable.