

Meeting Minutes, January 13, 2010 - Flublok

Meeting Date: January 13, 2010

Meeting Time: 4 – 5:30 PM

Meeting Location: Woodmont Office Complex, Conference Room 300N

File: BLA 125285

Product Name: FluBlok

Sponsor: Protein Science Corporation (PSC)

FDA Attendees:

Jerry Weir, Maryna Eichelberger, Matthew Sandbulte, Arifa Khan, Katherine Matrakas, Timothy Fritz

Purpose of Meeting:

To identify define what information Protein Sciences Corporation (PSC) will need to provide in response to the Complete Response letter issued January 11, 2010.

Discussion:

The review team members discussed, item by item, the requests in the Complete Response letter to reduce the letter to a bulleted list of information that PSC would need to provide to address CBER's concerns. The bulleted list is provided below.

1a.

- A Process Validation Protocol for the manufacture of recombinant HA from B/Brisbane/60/2008
- A Process Validation Report for the manufacture of 3 consecutive lots of HA from B/Brisbane/60/2008
 - The Report should include:
 - Process parameters and in-process results for all downstream steps
 - -----(b)(4)-----
 - If any process parameters or in-process test results were added as specifications to control the manufacturing process, these should be noted.
 - The data should demonstrate that corrective action(s) have resolved the inconsistency in yield and -----(b)(4)-----.

1b.

- Because data provided in PSC's December 11, 2009 submission (including Reports 09-073 and 09-075) do not support (b)(4) chromatography for purification of H1 hemagglutinin, a report is needed for investigations that were done to identify discrepancies in (b)(4) column performance
 - This report should be completed prior to conducting the (b)(4) validation runs described below and should include:
 - An assessment of differences in elution profiles for H1 validation runs
 - A re-assessment of investigation 09-073
 - A reassessment of the out-of-trend potency result for lot ----(b)(4)----
 - The report should also acknowledge the problem(s), provide a thorough investigation and, if possible, identify root cause(s).
- A Process Validation Report for the (b)(4) chromatography purification step for 3 consecutive lots of H1 hemagglutinin
 - The report should include:
 - Process parameters and in-process test results for all downstream steps
 - -----(b)(4)-----
 - A description of changes implemented to obtain consistent column performance.

1c.

- The Drug Product Blend and Fill Validation report and data summaries for runs #2 and #3 as requested in CBER's October 1, 2009 Information Request
 - The report should include:
 - Batch records for each lot
 - A summary report of deviations and corrective actions
 - Summary tables of parameters, quality control and lot release results
- Validation reports and data summaries for shipping and any hold times associated with the bulk Drug Substance.

2.

- The final ----(b)(4)----- report for (b)(4) testing of 2 trivalent, vialled batches of FluBlok
- Results of PSC's repeat testing of -----(b)(4)-----
- Discussion of the strategy for investigating the origin and nature of the ----(b)(4)-----, prior to study initiation
 - Depending upon review of the b(4) results and of PSC's strategy to resolve the (b)(4) issue, CBER would be able to provide PSC with guidance for addressing safety concerns related to the ----(b)(4)-----

3.

- Results of the investigation into the specificity and identity of --(b)(4)----- detected in the ----(b)(4)----- assays of the ----(b)(4)----- cells
- A table of -(b)(4)- assays in place for adventitious agent testing of the ----(b)(4)----- with limit of detection for each assay

4.

- A synopsis of the study performed to evaluate particle characteristics as described in the August 24, 2009 response to CBER's July 30, 2009 Information Request
 - The synopsis should include:
 - Data to characterize the nature of the aggregates and changes to these aggregates that occur with time
 - The impact of changes in aggregates on product potency

5.

- Results of antigenic analysis of B/Brisbane/60/2008 rHA similar to the analysis provided in amendment submitted 11 December, 2009 (Figure 1).
 - Assays of antigenic analysis should include:
 - Recombinant HA from the test article (B/Brisbane/60/2008)
 - rHA from a prior influenza B vaccine strain AND/OR B/Brisbane/60/2008 containing the original reported Asn197 residue
 - Whole influenza viruses corresponding to the recombinant HA molecules tested (and as per usual protocol, other reference viruses that are representative of antigenic drift)
 - The reference antisera used in this analysis needs to include anti-B/Brisbane/60/2008 and sera specific for each of the other antigens used in the assay

6.

- Results of repeat container closure integrity testing
 - These results should include:
 - Test results under dynamic conditions (i.e., exposure to differential pressures)
 - Sensitivity data for the test method

7a.

- Data submitted appears to be acceptable. No further requests expected.

7b.

- Data regarding -----(b)(4)----- submitted by PSC on December 18, 2009 needs review by DPQ.

7c.

- Data regarding Tween 20 quantitation submitted by PSC on December 18, 2009 needs review by DPQ.

7d.

- Data submitted appears to be acceptable. No further requests expected.

Action Items

- Reviewers should finalized their reviews of PSC's original BLA submission, PSC's response to the August 29, 2009 Complete Response letter and subsequent amendments submitted by PSC.
- Route PSC's December 18, 2009 submission to DPQ for review of responses related to ----(b)(4)----- and Tween 20 quantitation.
- OCBQ has a January 28, 2010 meeting with PSC and Hospira scheduled regarding (b)(4) testing and will inquire whether PSC needs additional guidance regarding item 1c.