First Committee Meeting, January 28, 2013 - Kcentra

Attendees:
Ze Peng (ZP)—Chair/CMC/Product
Beth Walton (BW)—RPM
Iftekhar Mahmood (IM)—Clinical Pharmacology
La'Nissa Brown-Baker (LBB)—Pharm-Tox
Rebecca Olin (RO) and Kelly Lewis (KL)—CMC/Facility
Tony Hawkins (TH)—BIMO
Ross Pierce (RP) and Nisha Jain (NJ)—Clinical
Amy Malla (AM)—Study Data Tabulation Model (STDM)
Joe Quander (JQ) and Erica Heit (EH)—Lot Release
Sukhminder Sandhu (SS)—Epidemiology
Jessica Hu (JH)—Biostat
Roman Drews (RD)—Consultant on CMC/Product

Not Present (Cc :)
Kristine Khuc (KK)—APLB
Lokesh Bhattacharyya and Karen Campbell (KC)—Lot Release (Assigned on 4/20/12)

Purpose/Goals:

- Timelines
- Ensure a reviewer is assigned to each section of the submission
- Confirm the reviewers can access their sections of the submission. Any issues opening the datasets
- Sponsor is seeking Orphan Drug Designation in Office of Orphan Products Development (OOPD) *(*Review schedule is subject to change*). The team needs to decide if this submission qualifies for Priority Review
- Identify if consult reviewers are needed in the review process
- Verify if the product is New Molecular Entity (NME)
- Identify follow-up activities to be completed before the next meeting (Filing Meeting). See SOPP 8404 for RTF information
- Evaluate which inspections are needed
- Determine if a Press Release is required

Summary of Product and Proposed Indication

- The proposed indication for CSL Behring's Prothrombin Complex Concentrate (Human), Beriplex, is for the urgent reversal of vitamin K antagonist (i.e., warfarin) therapy in patients with acute major bleeding.

Introductions (Team**)**
Reviewer Assignment:
Action: Follow up with Ms. Karen Campbell to ensure that a DBSQC reviewer is assigned to the file
Review of the Meeting Schedule (BW)

- Due date for this submission is January 28th, 2013

- Filing Meeting is May 9th, 2012;
- There will be interim Labeling meetings scheduled. The first Labeling meeting will be scheduled shortly after the Mid-cycle meeting on August 30th, 2012
- The sponsor requested a Proprietary Name Review (PNR) - Letter must be issued within 90 days (by June 30th, 2012)
- The sponsor requested Orphan Drug designation and Priority Review. The team has 45 days to decide if Priority Review will be granted.

Accessibility to Submission Files:

- There were a couple of reviewers who had difficulty accessing the data files for the submission; however, the issues were resolved by eliciting the help from IT/EDR support.

Follow-up Activities to be Completed before Filing Meeting on 9 May 2012

Orphan Drug Designation

Actions: Follow-up OOPD to determine how long it will take to review CSL Behring's request for Orphan Drug designation. *Follow-up: OOPD usually takes between 60-90 days for the first review cycle. However, as in a previous case with CSL Behring, OOPD may request additional information and review cycles.*

Priority Review (Discussion)

- ZP noted that similar licensed products currently exist in the market. Therefore, Beriplex is **not considered NME** based on the compositions of the final container.
- RP recommended denying the sponsor's request for priority review because the sponsor has not demonstrated either superior efficacy or greater safety for Beriplex vis-à-vis plasma (current standard of care in the U.S.).
  - Data provided in BLA did not establish safety and effectiveness of serious and life threatening illness
  - The sponsor has not demonstrated an advantage in terms of safety and efficacy
  - The superiority testing did not meet the criteria.
  - The respiratory and chemical AEs are not clear in Beriplex to offer a superior safety profile (RP).
- LBB and JH also agreed that a priority review should not be granted.
- NJ noted that the severity of AEs or moderate AEs are more frequent in Beriplex

Inspections (DMPQ and BIMO)

- RO noted that the manufacturing facility was last inspected in January 2012. A recent waiver memo stated that inspections back in 2005 were Voluntary Action Indicated (VAI). DMPQ is planning to waive the inspection unless the Product Office has compelling issue(s) which warrant an inspection.
- BIMO inspections are required to support the clinical review. TH will continue his review of the clinical data and recommend specific clinical study sites for BIMO inspections. BIMO inspection dates TBD.

Administrative

Review Memos and Supervisory Concurrence

- BW outlined the following administrative requirements and guidelines for this submission:
  - Reviewers are required to complete two memos –a Mid-cycle and a Final memo
  - The chair should be copied on **all** communications to the firm. The Chair should be appraised of all activities related to the submission.
  - According to OBRR office policy, all Information Request (IRs) should contain **supervisor concurrence** and such memos should be communicated to the sponsor via the OBRR RPM IRs. Supervisory concurrence can be obtained by copying one's supervisor on the information request memo (or email). OBRR RPMs can not initiate an IR without supervisory concurrence.

Press Release

- RP agreed that a press release is required.

BPAC

- The team needs to decide if a presentation at BPAC is required.