

Subject: Filing Meeting: STN BL125577, Von Willebrand Factor (Recombinant), Baxter Healthcare Corporation, BLA Standard 12 Month Review

Location: WO71-4244

Start: Mon 2/2/2015 2:30 PM

End: Mon 2/2/2015 4:00 PM

Organizer: Ward-Peralta, Cherie

Attendees: Ward-Peralta, Cherie; Alimchandani, Meghna; Campbell, Karen M; He, Jie; Kimchi-Sarfaty, Chava; King, Colonious; Kong, Hyesuk; Lu, Shuya (Joshua); Mahmood, Iftekhar; Nguyen, Loan; Sauna, Zuben; Zhang, Jianmin (Jack) Chazin, Howard; Farshid, Mahmood; Jain, Nisha; Lee, Timothy; Rees, Renee; Anderson, Marie; Valencia, Iliana; Weinstein, Mark; Bhattacharyya, Lokesh

Attendees Did Not Attend: Baum, Victor; Bhattacharyya, Lokesh; Pilaro, Anne;

Filing Meeting for the following PDUVA V Program BLA:

STN: BL125577, BLA Standard 12 Month Review

Applicant: Baxter Healthcare Corporation

Product: Von Willebrand Factor (Recombinant)

Short Summary: Prevention and treatment of bleeding episodes in adults (age 18 and older) diagnosed with von Willebrand disease.

Please note the following agenda items for our filing meeting discussions and pending actions for this original BLA subject to PDUVA V Program guidelines:

At the filing meeting, each reviewer is expected to discuss the relevant content of the submission and present an overview that includes:

1. A summary of the submitted material:

Dr. Kimichi-Sarfaty with the DMPQ reviewer will perform one inspection at the Baxter (b) (4) site. This is new manufacturing site and need to observe the performance of the last testing of the drug product.

Mr. He informed that the application lists three sites and one site was recently inspected. The (b) (4) site is a new building and the office is still process the paper work to schedule the inspection.

Dr. Kimichi-Sarfaty informed that product is a recombinant made from the (b) (4) [redacted] The vwf is (b) (4) [redacted] The discussions

held during the review of the IND, we agreed that (b) (4)

Mr. He stated that there have been changes made to the referenced (b) (4) therefore he may need some additional information and may request a copy of the (b) (4) as this submission should stand alone.

2. A description of any required material that may have been omitted from the submission:

Mr. Zhang performed the validation test on the some of the SDTM data sets. There were no major issues with the validation but there were 28 errors and 40765 warnings in 27 SDTM datasets. A justification was provided within the report for the reasons of the errors and warning. An error example is missing data on the age of the subject. An example of a warning is the dataset is incorrectly labeled in comparison to the current standard data system. Dr. Jain agreed that this was fine as there are only 27 patients in the study.

3. Any substantive deficiencies or issues that potentially have significant impact on the ability to complete the review or approve the application - None
4. APLB - Proprietary Name Review (PNR) request was received on December 31, 2014; ADD is March 31, 2015

Dr. Nguyen informed that the submitted name (Vonvendi) was found tentatively acceptable in November 2014 in the IND; therefore, there should not have any issue with the review.

5. Propose whether product would be subject to Lot Release, Surveillance or Exempt from Lot Release. See SOPP 8408.1: Development of Testing Plans and Release of Lots as Part of the Approval Process

This will be exempt as this is a recombinant product.

- a. Confirm the batch analysis information was submitted in the application or send a request if not submitted
- b. Determine if any new instrumentation and/or testing personnel training is needed
- c. If needed, to prepare a communication on the requirements for the submission of samples and lot specific data

Ms. Campbell informed that Dr. Bhattacharyya will review the lot tests and their validations of the drug product, except sterility and endotoxin tests, which will be reviewed by Dr. Kong. DBSQC Reviewers proposed to use the typical testing plan for this type of product. A meeting will be scheduled between DBSQC and the review team to finalize the in-support tests to be performed by DBSQC and the testing plan. A request will be sent for Baxter to submit lots for testing at the time of mid-cycle.

6. Discuss the need for a RTF or deficiencies identified letter (Refer to SOPP 8404: Refuse to File) – No deficiencies or refuse to files.

7. Confirm decision by all assigned reviewers on filing, deficiencies identified or RTF action on this application.

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| a. Clinical Reviewer
No Filing Issues | Victor Baum |
| b. Clinical Pharmacology Reviewer
No Filing Issues | Istekhar Mahmood |
| c. Toxicology Reviewer
No Filing Issues | Anne Pilaro |
| d. CMC Reviewer
Sarfaty No Filing Issues | Chava Kimchi- |
| e. CMC – Analytical Methods Reviewer
No Filing Issues | Zuben Sauna |
| f. DMPQ Reviewer
No Filing Issues, but will request additional information | Jie He |
| g. Statistical Reviewer of clinical data
No Filing Issues | Shuya (Joshua) Lu |
| h. Postmarketing Safety Epidemiological Reviewer
Alimchandani No Filing Issues | Meghna |
| i. OCBQ/APLB Reviewer
No Filing Issues | Loan Nguyen |
| j. OCBQ/BIMO Reviewer
No Filing Issues | Colonious King |
| k. OCBQ/DBSQC or LIB Representative
Bhattacharyya; Karen Campbell; Marie Anderson
No Filing Issues | Hyesuk Kong; Lokesh |

8. Confirm decision regarding standard or priority review status – Standard Review

9. Confirm decision regarding need for an Advisory Committee – A memo to not take this to an Advisory Committee Meeting will be provided.

10. This is an Orphan product therefore there is no PREA.

11. There will be a press release with this approval.

Action Items After Meeting:

- If there are no filing issues, an email in response to this meeting can be sent to me including supervisor on cc line on your filing decision.
- If submission will be RTF, please try to finalize RTF memo with management concurrence by **February 10, 2015**

- Filing Letter Due to be Issued by **February 17, 2015**
- If there are deficiencies not identified during the filing of the submission, these can be issued in a letter by **March 3, 2015**

End of Meeting