Meeting Summary

Applicant: **OCTAPHARMA Pharmazeutika Produktionsges.m.b.H.**

Product: **Human Fibrinogen**

STN: **125612**

Meeting Date: August 23, 2016 at 10:30 am

From: Karen Campbell

Attendees: Ze Peng, Tao Pan, Grainne Tobin, Obinna Echeozo, Lokesh Bhattacharyya, Varsha Garnepudi and Lorraine Wood

Cc: William McCormick, James Kenney, Jackie Glen, Marie Anderson

Summary of Product and Proposed Indication

- Treatment of acute bleeding episodes (b) (4) in adult and pediatric patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

Purpose/Goals:

- Clarification of DBSQC's review responsibilities
- In-Support Testing requirements

General understanding

DBSQC should review the lot release tests and method validations only for lot release tests of drug substances and drug product to be agreed upon with the product reviewer(s)

1. Review the test methods to ensure that they are detailed enough to carry out the same tests in our lab following the sponsor's method.
2. Appropriate system suitability criteria and/or assay validity criteria are included in the procedure.
3. Review assay validation reports to ensure that the methods are appropriately validated for its intended use.

NOTE: DBSQC will not review anything regarding manufacturing, product characterization, stability studies, labeling etc.

DBSQC Review Assignments

Reviewers assigned to 125612 are: Karen Campbell, Varsha Garnepudi, Tao Pan, Obinna Echeozo, and Grainne Tobin (this may be changed to Leslyn Aaron)

The items with DBSQC reviewers below are typical of DBSQC review assignments and may be altered as needed

Test	DP/DS	Reviewer	In Support Testing?
Sterility	DP	Echeozo	Undecided
(b) (4)	DS	Echeozo	No
Endotoxin	DP	Echeozo	Yes
General Safety	DP	Echeozo	No
(b) (4)	DP/DS	Pan/Tobin/Aaron	Yes
(b) (4)	DP	Pan	No
(b) (4)	DP	Pan	No
Solubility	DP	Pan/Tobin/Aaron	Yes
Stability of solution	DP	Pan	No
Water (Moisture)	DP	Pan	Yes
(b) (4)	DP/DS	Tobin/Aaron	Yes
(b) (4)	DP	Tobin/Aaron	calculated
(b) (4)	DP/DS	Pan	No
(b) (4)	DP/DS	Tobin/Aaron	Yes
Glycine	DP	Pan	No
Citrate	DP	Pan	No
Chloride	DP	Pan	No
L-Arginine HCl	DP	Pan	No
(b) (4)	DP	Pan	No
(b) (4)	DP	Pan	No

Note: DS is (b) (4)

Discussion:

Sterility – In-support sterility testing might be needed. Obinna will confer with Jim about how many samples would be needed. Ze will look at the batch analysis information related to sterility to see if there are any OOS results, and will discuss with the DMPQ reviewer(s) to see if the in-support sterility test is needed.

Fibrinogen by (b) (4) – Octapharma uses (b) (4) as the reference standard, which has been calibrated to the (b) (4) for fibrinogen in plasma ((b) (4)). DBSQC uses a different international standard (b) (4)), but will use the same international standard for the testing of fibrinogen as Octapharma did ((b) (4)).

There are (b) (4) conformance lots mentioned in the BLA. (b) (4) of them were manufactured using Planova 20N filter, and the last (b) (4) lots were manufactured using Pegasus SV4 filter.

If all (b) (4) lots are intended for release, we should test all of them. Ze will check the expiration dates to see if any will still be in-date when approval is expected. Any meant for release at approval must be tested and any other lots as determined by the product office (Ze Peng) will be tested.

The number of samples needed for DBSQC testing:

Endotoxin – 1 container
Clottable protein and Fibrinogen – 1 container
Moisture content – 2 containers
Sterility – to be determined

- **Discuss which of the tests from the specifications for DS and DP (above) will have in-support testing conducted**
    - **Will any testing be needed post licensure for lot release?** Yes, testing post approval is expected. The tests will be determined later in the review process after testing has been completed.

Post meeting updates from Ze Peng

All (b) (4) conformance lots ((b) (4)) need to be tested. They were manufactured in 2014 and the shelf life Octapharma proposed in this submission is (b) (4) years.

Ze discussed the sterility testing with the DMPQ reviewer and they decided that because of the large number of final containers needed we will not test for sterility. In addition, (b) (4) lots (technical/commercial) have been manufactured using the proposed commercial process with no sterility issues.