

FILING MEETING AGENDA/SUMMARY

Application type and number: BLA 125683
Product name: Immune Globulin Subcutaneous (Human), 20% (IGSC 20%)
Proposed indication: Primary Humoral Immunodeficiency
Applicant: Grifols Therapeutics LLC
Meeting date & time: August 23, 2018; 10:00 a.m.
Meeting Chair: **Jennifer Reed, Ph.D.**
Meeting Recorder: **Patrick Riggins, Ph.D.**
Candido Alicea, Ph.D.

Background:

The applicant submitted this BLA for Immune Globulin Subcutaneous (Human), 20% (IGSC 20%); (b) (4) for the treatment of primary humoral immunodeficiency. The new IGSC 20% manufacturing process is based on the currently licensed process used for Immune Globulin Injection (Human), 10%, Caprylate/Chromatography Purified (Gamunex-C) but includes an additional (b) (4) step to increase the protein concentration to 20%. The (b) (4) (b) (4) for IGSC 20% includes the addition of polysorbate 80 for enhanced stability of the final drug product over shelf-life.

Table 1: Review Committee and Discipline Filing Decision Summary

Discipline/Organization	Name [with credentials (not title)]	Attended meeting	Fileable	RTF	Deficiencies Identified
Regulatory Project Manager (RPM)	Candido Alicea	X			
Chair	Jennifer Reed	X	X		No
Clinical Reviewer	Deborah Belsky	X	X		
Toxicology Reviewer	Evi Struble	X	X		No
Clinical Pharmacology	Iftexhar Mahmood	X	X		No
CMC Reviewer	Jennifer Reed; Tao Pan; Hsiaoling Wang; Claire Wernly; Pei Zhang; Maria Virata	X	X		No
OCBQ/DMPQ RPM	Sarah Lee				
OCBQ/DMPQ Reviewer	Bradley Dworak	X	X		No
OCBQ/DMPQ/PRB Reviewer	N/A				
OCBQ/APLB Reviewer	Oluchi Elekwachi/Alpita Papat				
OCBQ/BIMO Reviewer	Haecin Chun	X	X		No
OCBQ/DBSQC Reviewer	Varsha Garnepudi	X	X		No

Discipline/Organization	Name [with credentials (not title)]	Attended meeting	Fileable	RTF	Deficiencies Identified
	Charlene Wang	X	X		No
OCBQ/DMPQ/Lead Inspector	N/A				
CMC Inspector	N/A				
Statistical Reviewer of clinical data	Jiang Hu				
Postmarketing Safety Epidemiological/Pharmacology vigilance Reviewer	Faith Barash	X	X		No
Labeling Reviewer	Alpita Papat				
Office Director/Deputy	Wilson Bryan/Kimberly Benton				
Division Director/Deputy	Dov Golding/ Mahmood Farshid	X	X		No
Other Attendee(s)	Dot Scott	X	X		No
	Lisa Stockbridge	X	X		No
	Deborah Trout	X	X		No

REGULATORY CONCLUSIONS / DEFICIENCIES

1. Does the application, on its face, appear to be suitable for filing or is the application unsuitable for filing and will require an RTF letter?

All attendees indicated that the application is suitable for filing.

2. If fileable, list any substantive deficiencies or issues that have significant impact on the ability to complete the review or approve the application:

This BLA is fileable and has no substantive deficiencies only a few minor issues were discussed.

- a. BioStatistics –Jiang Hu: Fileable - The final disclosure amount given does not compromise the data.
- b. Clinical – Deborah Belsky: Fileable – There are studies on going that have not listed the endpoint.

3. If RTF, list any substantive deficiencies or issues that would make this application unsuitable for filing:

N/A

FILING MEETING DISCUSSION, IF FILED:

4. Indicate any comments on the status of the proprietary name review (PNR).

Applicant has been advised that (b) (4) is not an approvable PNR, and that they should submit an alternate PNR.

5. Indicate whether the product sh/would be subject to lot release, surveillance, or exempt from lot release. Verify sample availability.

No decision yet, no stopping issues at this date and time.

6. Confirm review schedule of this application.

The attendees confirmed that this submission will be conducted under Standard Review.

7. Indicate the decision regarding the need for an Advisory Committee.

No need for advisory committee.

8. Indicate whether the submission triggers PREA; if yes, a PeRC meeting is needed.

PREA triggered.

9. Is a comprehensive and readily located list of all clinical sites included or referenced in the application?

Yes

10. Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?

Yes, only one manufacturing facility.

11. Indicate any updates since the First Committee Meeting on pre-license inspection, pre-approval inspection, or BIMO sites requiring inspections (Is a pre-license inspection necessary? What is BIMO's status?)

BIMO would like concurrence from the committee (specifically from clinical and stats) on the facilities selected, the number of inspected sites will depend on available resources. We have until Mid-cycle meeting to assign inspection sites, this can be amended if necessary.

12. If the application is affected by the Application Integrity Policy (AIP), has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

N/A

13. Is the product an Original Biological Product or a New Molecular Entity (NME) for an NDA?

Original Biological Product

**FOR APPLICATIONS IN THE PDUFA PROGRAM (NME NDAs/Original BLAs),
IF FILED**

14. Confirm that any late submission components were submitted within 30 days. List any late submission components that arrived after 30 days.

N/A

15. Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?

Yes

ADMINISTRATIVE DETAILS, IF FILED:

16. Review the Milestone Schedule and indicate if there are any issues with the schedule. Note: This is a confirmation to capture any changes made since the First Committee Meeting.

Application Received 09-Jul-2018
Committee Assignment 23-Jul-2018
First Committee Meeting 02-Aug-2018
Filing Meeting 23-Aug-2018
Filing Action (Day 60) 07-Sep-2018
Deficiencies Identified (Day 74) 21-Sep-2018
Proprietary Name Review 18-Oct-2018
Internal Mid-Cycle Meeting 21-Dec-2018
Mid-Cycle Communication with Sponsor 08-Jan-2019
Late-Cycle Meeting Internal 21-Mar-2019
Late-Cycle Meeting with Sponsor TBD
PMC Study Target 05-May-2019
Labeling Target 05-May-2019

17. Action Due Date - The internal target date for sending the filing letter will be September 7, 2018. The Action Due date that will be communicated to the Applicant in the filing letter will be July 9, 2019.