Our STN: BL 125606/0 **April 12, 2017**

CSL Behring GmbH
Attention: Kevin Darryl White, MBA, RAC
CSL Behring LLC
1020 First Avenue
PO Box 61501
King of Prussia, PA 19406-0901

Dear Mr. White:

Attached is a copy of the memorandum summarizing your March 13, 2017, Late-Cycle teleconference with CBER. This memorandum constitutes the official record of the teleconference. If your understanding of the teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER in writing as soon as possible.

Please include a reference to the appropriate Submission Tracking Number (STN) in future submissions related to the subject product.

If you have any questions, please contact Nannette Cagungun at (240) 402-8267 or at nannette.cagungun@fda.hhs.gov.

Sincerely,

Basil Golding, MD
Director
Division of Plasma Protein Therapeutics
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research

Late-Cycle Meeting Summary

Meeting Date and Time:	March 13, 2017
Meeting Location:	Telephone Conference
Application Number:	BL 125606/0
Product Name:	C1 Esterase Inhibitor Subcutaneous (Human)
Indication:	For routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients
Applicant Name:	CSL Behring GmbH
Meeting Chair:	Ewa Marszal, PhD
Meeting Recorder:	Nannette Cagungun, MS, PD, RAC

FDA ATTENDEES

Jaspal Ahluwalia, MD, Medical Epidemiologist, OBE/DE/AEB
Wilson Bryan, MD, Director, OTAT
Nannette Cagungun, MS, PD, RAC, Regulatory Project Manager, OTAT/DRPM
Dennis Cato, Consumer Safety Officer, CBER/OCBQ/DIS/BMB
Felice D'Agnillo, PhD, Research Biologist, OBRR/DBCD/LBVB
John Eltermann, RhP, MS, Division Director, OCBQ/DMPQ
Donald Ertel, MS, MT(ASCP), ASQ CQA, Regulatory Officer, OCBQ/DMPQ/BI
Mahmood Farshid, PhD, Deputy Division Director, DPPT/OTAT
Basil Golding, MD, Division Director, DPPT/OTAT
Lin Huo, PhD, Biostatistician, OBE/DB/TEB
Ilan Irony, MD, Deputy Division Director, OTAT/DCEPT
Michael Kennedy, PhD, Biologist/Team Lead, OTAT/DPPT/PDB
Hyesuk Kong, PhD, Biologist, OCBQ/DBSQC/LMIVTS
Ewa Marszal, PhD, Chemist, OTAT/DPPT/PDB
William McCormick, PhD, Division Director, OCBQ/DBSQC
Tejashri Purohit-Sheth, MD, Division Director, OTAT/DCEPT
Dorothy Scott, MD, Branch Chief, OTAT/DPPT/PDB

APPLICANT ATTENDEES

Iris Jacobs, MD, Senior Global Clinical Program Director, Clinical R&D
Henrike Feuersenger, PhD, Senior Statistician, Biostatistics
Dipti Pawaskar, PhD, Associate Director, Clinical Pharmacology and Early Development
Doerthe Vingerhoet, Senior Manager, CMC Team Lead
Sarah Mycroft, MD, Director, Clinical Safety Physician
Hartmut Landgrebe, PhD, Director, Therapeutic Area Lead, Global Regulatory Affairs
Michele Walsh, Manager, Global Regulatory Affairs

BACKGROUND

BLA 125606/0 was submitted on June 30, 2016 for C1 Esterase Inhibitor Subcutaneous (Human).

Proposed indication: For routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients

PDUFA goal date: June 30, 2017

In preparation for this meeting, FDA issued the Late-cycle Meeting Materials on March 1, 2017.

DISCUSSION

After introductions, CBER stated the review team has not found any substantive issues with the application. CBER noted CSL Behring (CSLB) had already responded to the information requests that were sent in February 2017 and that an additional information request would be provided soon. CBER further noted that the review team has not identified any issues related to risk management and labeling and that PMRs/PMCs are not anticipated at this time; however, non-reportable PMCs are possible. With the remaining review clock, the review team plans to finalize the review of the already submitted material; review the responses to the recent information requests; evaluate the product samples; and finalize the review of the labeling.

CSLB indicated samples (i.e., three vials of final product from each of the (b) (4) conformance lots) were still being held in Customs. They have provided all requested information and will follow up with Customs to see whether additional information is required to get the samples released. They asked whether CBER had any comments on the Lot Release Protocol Template. In January 2017, they proposed to ship samples of concurrent batches for release testing to CBER immediately following approval of the BLA.

CBER indicated that the Lot Release Protocol Template is still under review in the product office. CSLB will be informed if the review team identifies any issues with the template.

CSLB inquired about the additional information request that CBER indicated it would send. CBER responded that additional CMC information request would be sent shortly and would include the following items:

- Specifications for process control parameter (b) (4)
- SOPs for the (b) (4)
- Proposed storage temperature and supporting stability studies

- Characterization of protein (b) (4) since the concentration of the (b) (4)
- Risk evaluation for immunogenicity in relation to the presence of particulate matter
- Manufacturing changes affecting both Berinert and Haegarda should be submitted to both BLAs
- Request for additional samples of conformance lots

In response to CSLB's question, CBER indicated the review team has not identified substantive clinical issues with the application. The labeling target date is May 30, 2017 but in view of the holiday, CBER agreed to provide labeling comments to CSLB before that date.

This application has not yet been fully reviewed by the signatory authorities, Division Directors and Review Committee Chair and therefore, this meeting did not address the final regulatory decision for the application.