

Bioresearch Monitoring Mid-Cycle Review Memo, May 16, 2012 - Octaplas

- **MEMORANDUM**

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

DATE May 16, 2012

FROM Christine Drabick, Bioresearch Monitoring Branch, HFM-664
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Bioresearch Monitoring Branch Chief,
HFM-664

TO Nancy Kirshbaum, HFM-343, Chair
Pratibha Rana, HFM-380, RPM

SUBJECT Bioresearch Monitoring Mid-Cycle Review Memo
SPONSOR: Octapharma AG
PRODUCT: Octaplas LG™ (Human Coagulation Active Plasma for Infusion,
Solvent/Detergent Treated)
BLA: STN 125416/0

Mid-Cycle Summary:

Bioresearch Monitoring inspection assignments were issued for two clinical investigators and two study protocols. The pivotal study, LAS-203, was conducted at a single site in Vienna, Austria.

LAS-201: A Sequential Cohort Study to Compare Tolerability and Efficacy in Patients Receiving *octaplas* or *octaplas LG*

LAS-203: A Comparative, Open-Label, Randomized, Cross-over Phase I Trial in Healthy Volunteers to Investigate the Relative Efficacy, Safety and Tolerability of Octaplas LG™ vs. Octaplas® SD

Protocol	Study Site	Location	Form FDA 483 Issued	Inspection Final Classification	IND#

Protocol	Study Site	Location	Form FDA 483 Issued	Inspection Final Classification	IND#
LAS-201	Institute of Transfusion Medicine	Nordhausen, Germany	No	EIR Pending	None
LAS-203	Medical University of Vienna	Vienna, Austria	Yes	EIR Pending	13956

The Bioresearch Monitoring inspections at both sites are complete. The Establishment Inspections Reports (EIRs) for both inspections are pending.

STUDY PROTOCOL 201

Study Protocol 201 was a non-interventional, sequential cohort, observational, open, prospective, multi-center study. Treatment was administered according to normal clinical practice, rather than protocol-specified treatment parameters. This study was not conducted under an IND.

The inspection of this observational study was limited due to European data protection regulations (European Parliament and Council Directive [95/46/EC](#)), which state “neither the sponsor, nor authorised representatives from the sponsor or representatives from regulatory authorities are authorised to access and review confidential patient information. For observational studies we do not have an agreement with the patients authorising the entities listed above to access their medical data”. Informed consent was not required for this observational study and as a result, source documents were not permitted to be reviewed. Information submitted in the BLA was compared to Case Report Forms (CRFs) and other records available for inspection.

During the inspection the FDA investigator was informed that the investigational product was administered by physicians who were not participating in the study and subjects were not enrolled in the study prior to treatment. The study physicians reviewed the records provided by the treating physicians and retrospectively selected subjects to enroll in the study.

The Establishment Inspection Report is pending for this inspection. Based on the information received from the FDA investigator, the source documents for the data submitted in the BLA for study 201 were not available for review, consequently the data submitted in the BLA could not be verified.

STUDY PROTOCOL LAS 203

Study Protocol LAS 203 was conducted at a single site in Vienna, Austria. A four-item Form FDA 483 was issued to the investigator. The Form FDA 483 observations included: failure to maintain adequate and accurate case histories and study records;

failure to provide the sponsor with sufficient financial information regarding a sub-investigator; failure to ensure the study was conducted in accordance with the general investigational plan and protocol; and failure to document reasons for early termination of subjects. A letter responding to the Form FDA 483 was received from the investigator providing explanations and corrective actions. These findings will be evaluated upon receipt of the EIR.

Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at 301-827-6323.

Christine J. Drabick
Consumer Safety Officer