



U.S. FOOD & DRUG
ADMINISTRATION

Memorandum

DATE: November 27, 2017

TO: Lilia Bi, BLA Committee Chair
Yao-Yao Zhu, Clinical Reviewer
Nevitt Morris, RPM

FROM: Carla Jordan
Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH: Dennis T. Cato, Chief, Bioresearch Monitoring Branch

THROUGH: Carrie M. Mampilly, Director, Division of Inspections and Surveillance

SUBJECT: Bioresearch Monitoring Final Discipline Review Memo
BLA: STN125610/o
PRODUCT: Voretigene Neparvovec (AAV2-hRPE65v2)
SPONSOR: Spark Therapeutics

REVIEW SUMMARY

Bioresearch Monitoring (BIMO) inspections were conducted at two clinical sites in support of this Biologics Licensing Application (BLA). The inspections did not reveal significant problems that impact the data submitted in the application.

BACKGROUND

Spark Therapeutics submitted this BLA to obtain a marketing approval for AAV2-hRPE65v2 to be used to treat subjects with Leber Congenital Amaurosis (LCA) due to RPE65 mutations. The following study was conducted to support this application:

STUDY # AAV2-hRPE65v2-301

A Safety and Efficacy Study in Subjects with Leber Congenital Amaurosis (LCA) Using Adeno-Associated Viral Vector to Deliver the Gene for Human RPE65 to the Retinal Pigment Epithelium (RPE)

This study was conducted at two domestic sites. Both sites were inspected in support of this Biologics License Application (BLA). The inspections were conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.811, Inspection Program for Clinical Investigators. Information submitted in the BLA was compared to source documents at each clinical study site. The BIMO inspection assignment also included specific questions concerning the clinical study.

There were 31 subjects enrolled in the study. Random data was reviewed for 15 subjects, which represented approximately 50% of the enrolled subjects.

SIGNIFICANT INSPECTION FINDINGS

No significant inspectional findings were noted from the BIMO inspection.

The table below summarizes the BIMO inspections:

Study Site	Form FDA 483 Issued?	Final Classification
University of Iowa Hospitals and Clinics Department of Ophthalmology and Visual Sciences Iowa City, IA 52242	NO	No Action Indicated
Children's Hospital of Philadelphia Ophthalmology Department Philadelphia, PA 19104	NO	No Action Indicated

SPONSOR ISSUES

No significant sponsor or monitoring issues were noted at the inspected study sites; however, there were two instances at the Iowa site where the Case Report Form and source data for the presence or absence of "bleb subfoveal" did not match the data submitted by the Sponsor in the BLA. This information was discussed with the appropriate review committee members.

FINANCIAL DISCLOSURE

The Clinical Investigator Compliance Program directs the FDA investigator to verify that the clinical investigator disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children, and provided updates, as necessary. The information submitted to the BLA was verified for each of the inspected clinical sites.

ADMINISTRATIVE FOLLOW-UP

Information letters were issued to both clinical investigators.

Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at (240) 402-8975.

Carla Jordan
Consumer Safety Officer