

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

DATE December 15, 2014

FROM Anthony Hawkins, Bioresearch Monitoring Branch
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

THROUGH Patricia Holobaugh, Chief, Bioresearch Monitoring Branch

THROUGH Gilliam Conley, Director, Division of Inspections and Surveillance

TO Robert Fisher, BLA Committee Chair
Ross Pierce, BLA Clinical Reviewer
Thomas Maruna, RPM
Tracy Tilghman, RPM

SUBJECT Bioresearch Monitoring Primary Discipline Review
BLA: STN 125562-0
IND: 11982
PRODUCT: Anthrax Immune Globulin Intravenous (AIGIV), NP-015
SPONSOR: Cangene Corporation (doing business as Emergent
Biosolutions)

PRIMARY DISCIPLINE REVIEW SUMMARY

A Good Laboratory Practice (GLP) inspection of one non-clinical laboratory conducting animal studies did not reveal significant problems that impact the data submitted in this biologics licensing application (BLA).

BACKGROUND

The Bioresearch Monitoring (BIMO) Branch requested one GLP inspection covering four animal studies conducted at the (b) (4), in support of this Biologics Licensing Application (BLA). The sponsor reported each of the inspected studies was conducted under The Animal Rule (21 CFR Part 314 Subpart I and 21 CFR Part 601 Subpart H). The BLA review committee concurred with the four proposed animal studies for inspection based upon various criteria including test system utilized, individual study animals of special interest and also numbers and types of adverse events and protocol deviations reported by the sponsor.

GLP studies inspected:

1. *Pharmacokinetic Evaluation of Anthrax Immune Globulin (AIG), NP-015 in Cynomolgus Macaques Following Single Intravenous Infusion* (Protocol (b) (4) 695-G005780)
2. *Determination of Pharmacokinetics of Anthrax Immune Globulin (AIG), NP-015 in Rabbits* (Protocol (b) (4) 694-G005681)
3. *Determination of Dose Range Efficacy of Anthrax Immune Globulin (AIG), NP-015 in Cynomolgus Monkeys Exposed to Inhalation Anthrax: GLP Study* (Protocol (b) (4) 828-G005780)
4. *Therapeutic Efficacy of Anthrax Immune Globulin Intravenous (AIGIV), NP-015 in Rabbit Model of Inhalation Anthrax: GLP Study* (Protocol (b) (4) 1207-100005104)

The inspection was conducted in accordance with FDA's Compliance Program Guidance Manual (CPGM) 7348.808, Good Laboratory Practice. Information submitted in the BLA was compared to source documents at the inspected non-clinical laboratory site. The inspection assignment included specific questions concerning the above GLP studies. During the inspection, two FDA investigators reviewed study records for 214 (100%) of the total study animals enrolled in the above four GLP studies inclusive.

INSPECTION FINDINGS

The results from the inspection covering the above GLP study protocols showed only a few minor problems.

Equipment:

Four animal cage/racks stored in the clean equipment area contained water in the lumen of the automatic watering system conduit in violation of (b) (4) operating procedures for sanitation of animal caging systems. The firm did not adhere to its own operating procedures for manual temperature monitoring of one cold storage unit (CSU) for storing samples, reagents and other articles (CSU did not contain retained materials from completed GLP studies).

Protocol Adherence:

One protocol 695-G005780 study animal with a documented history of continuing diarrhea or soft stool of unknown etiology was randomized and placed on study, in violation of the protocol.

Study Records:

Nineteen (19) protocol 694-G005780 study animals had at least one instance of missing documentation for weekly vascular access port flushing for blood draws. The animals were either extra animals (e.g., not on study) or animals who had completed their required blood draws for study related activities when the flushing was not documented as performed. There was no documentation showing required euthanasia criteria review involving four of the protocol 1207-10005104 study animals.

SPONSOR ISSUES

The inspection did not reveal any sponsor issues.

ADMINISTRATIVE FOLLOW-UP

We issued an information letter to the inspected firm. Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at 240-402-8950.

Anthony Hawkins
Consumer Safety Officer