



U.S. FOOD & DRUG
ADMINISTRATION

DATE: June 16, 2023

FROM: Haecin Chun, MS, Consumer Safety Officer
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Division of Inspections and Surveillance (DIS)
Office of Compliance and Biologics Quality (OCBQ)

THROUGH: Dennis T. Cato, Chief BMB

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TO: Taruna Khurana, PhD, Chair
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SUBJECT: Bioresearch Monitoring Final Review Memo
SPONSOR: Emergent Product Development Gaithersburg Inc.
PRODUCT: Anthrax Vaccine Adsorbed, Adjuvanted (CYFENDUS)
APPLICATION: BLA STN 125761/0

FINAL SUMMARY STATEMENT:

Bioresearch Monitoring (BIMO) inspection assignments were issued for one nonclinical laboratory that conducted two animal efficacy studies: 3580-100069467 and 3655-100072763, under the Animal Rule, and for six clinical study sites that participated in the conduct of two safety studies conducted in humans: Protocols EBS.AVA.210 and EBS.AVA.212. The inspections did not reveal substantive issues impacting the information and data submitted in the BLA.

BACKGROUND:

Anthrax Vaccine Adsorbed, Adjuvanted (CYFENDUS) was evaluated under the Animal Rule because human efficacy studies were not ethically feasible. In consultation with the review committee, two non-clinical efficacy studies and two clinical studies were identified for BIMO inspections.

The following table lists the selected non-clinical and clinical studies and their corresponding FDA's BIMO Compliance Program (CP):

BIMO Compliance Program	Study Number	Study Title
7348.007: Inspection of Nonclinical Laboratories Conducting Animal Rule-Specific Studies	Protocol 3580-100069467	Evaluation of the Efficacy and Toxin Neutralizing Antibody (TNA) Threshold of Protection in Guinea Pigs Immunized with A V7909 14 Days Apart and Challenged with Bacillus anthracis on Days 28 or 70 Post-First Immunization
7348.007: Inspection of Nonclinical Laboratories Conducting Animal Rule-Specific Studies	Protocol 3655-100072763	GLP Study Evaluating the Efficacy and Toxin Neutralizing Antibody (TNA) Threshold of Protection in Nonhuman Primates Immunized with A V7909 14 Days Apart and Challenged with Bacillus anthracis on Days 28 or 70 Post First Immunization
7348.811: Clinical Investigators and Sponsor-Investigators	Protocol EBS.AVA.210	A Phase 2 Drug-Vaccine Interaction Study to Examine Whether Coadministering AV7909 with Ciprofloxacin or Doxycycline Affects Antibiotic Pharmacokinetics or AV7909 Immunogenicity in Healthy Adults
7348.811: Clinical Investigators and Sponsor-Investigators	Protocol EBS.AVA.212	A Phase 3, Randomized, Double-blind, Parallel-group Trial to Evaluate the Lot Consistency, Immunogenicity, and Safety of AV7909 for Postexposure Prophylaxis of Anthrax in Healthy Adults

NON-CLINICAL LABORATORY AND CLINICAL INVESTIGATOR INSPECTIONS CONDUCTED IN SUPPORT OF THIS BLA:

One non-clinical laboratory inspection assignment was issued for a nonclinical laboratory that conducted the two Animal Rule-specific efficacy studies. The inspection was conducted according to CP 7348.007, Inspection of Nonclinical Laboratories Conducting Animal Rule-Specific Studies. The inspection of these studies included a review of the quality and integrity of the data contained in the final reports of the Animal Rule-specific studies.

For the two clinical studies listed above, a total of six clinical study sites were selected for inspection based on subject enrollment, previous inspection history, review committee concerns, as well as the data and information submitted in the BLA. These inspections were conducted in accordance with CP 7348.811, Inspection Program for Clinical Investigator (CI), and the inspection assignments included specific questions related to the study protocols. During the inspection, the information and data submitted in the BLA were compared to source documents at each inspected site.

INSPECTION SUMMARY AND OUTCOME:

The table below summarizes the BIMO inspections:

Protocol ID	Study Species	Study Site Name and Location (Site ID, if assigned)	FDA Form 483 Issued?	Final Inspection Classification
3580-100069467	Guinea pig	(b) (4)	No	No Action Indicated (NAI)
3655-100072763	Non-human primate	(b) (4)	No	NAI
EBS.AVA.210 & EBS.AVA.212	Human	Meridian Clinical Research, LLC, Omaha, NE (US2002 and US1006)	No	NAI
EBS.AVA.212	Human	Optimal Research, LLC Peoria, IL (US1008)	No	NAI
EBS.AVA.212	Human	Christie Clinic, LLC Champaign, IL (US1026)	No	NAI
EBS.AVA.212	Human	Advanced Clinical Research West Jordan, UT (US1003)	Yes	Voluntary Action Indicated (VAI)
EBS.AVA.212	Human	Benchmark Research San Angelo, TX (US1019)	Yes	VAI
EBS.AVA.212	Human	The Iowa Clinic, PC* West Des Moines, IA (US1027)	Yes	VAI

***This was a For-Cause (Directed) inspection assignment that was issued as result of noncompliance issues noted in the sponsor's audit report submitted in the BLA.**

INSPECTIONAL FINDINGS:

No significant inspectional findings were observed for the above studies conducted in humans and non-human primates. However, the following noteworthy observations were revealed during the inspection of the three clinical study sites listed below:

Site # US1003: Observations noted during the inspection and discussed with the CI include failure to report adverse events and concomitant medications for a few subjects, and failure to maintain adequate case histories for several subjects.

Site # US1019: Several subjects' source records were not documented contemporaneously and accurately. The source documentation for Safety Calls at Day 394 was observed as missing but was documented in the EDC (the study site stated in their 483 response that when this issue was identified, the site contacted each subject and completed another safety call out of window).

Site # US1027: This For-Cause (Directed) inspection was issued to evaluate the degree of impact on the integrity of the data collected from Site 1027 due to the noncompliance issues reported by the sponsor, and to determine the adequacy of the study site's corrective actions taken to remediate the problems noted in the sponsor's audit report. The inspection also included a review of source documents for any other missing adverse event data not reported to the sponsor. The inspection revealed additional instances of incorrectly calculated BMIs and enrollment of one ineligible subject who was on two antihypertensive medications. The inspection found no other unreported significant adverse events.

SPONSOR/MONITORING ISSUES:

No significant sponsor or monitoring issues were identified during the above inspections.

FINANCIAL DISCLOSURE:

The CI CP directs the FDA investigator to ask the CI if and when he/she disclosed information about his/her financial interests to the sponsor and/or interests of any sub-investigators, spouse(s) and dependent children, and if and when the information was last updated. The information submitted to the BLA was verified for each of the inspected sites.

Should you have any questions or comments about the contents of this memo or any aspect of Bioresearch Monitoring, please contact me at 240-402-8038.

Haecin Chun
Consumer Safety Officer