Our STN: BL 125761/0 **BLA APPROVAL – ANIMAL RULE**

July 20, 2023

Emergent Product Development Gaithersburg Inc.
Attention: Preeya Lowe
300 Professional Drive
Gaithersburg, MD 20879

Dear Ms. Lowe:

Please refer to your Biologics License Application (BLA) received April 20, 2022, submitted under section 351(a) of the Public Health Service Act (PHS Act) for Anthrax Vaccine Adsorbed, Adjuvanted.

LICENSING

We have approved your BLA for Anthrax Vaccine Adsorbed, Adjuvanted effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Anthrax Vaccine Adsorbed, Adjuvanted under your existing Department of Health and Human Services U.S. License No. 2089. Anthrax Vaccine Adsorbed, Adjuvanted is indicated for post-exposure prophylaxis of disease following suspected or confirmed exposure to *Bacillus anthracis* in persons 18 through 65 years of age when administered in conjunction with recommended antibacterial drugs.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT01263691, NCT01770743, NCT04067011, NCT03877926.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Anthrax Vaccine Adsorbed, Adjuvanted drug substance at Emergent BioDefense Operations, 3500 N. Martin Luther King Junior Blvd., Lansing, Michigan. The CpG 7909 adjuvant component of the vaccine will be manufactured at (b) (4) . The final formulated product will be manufactured at Emergent BioDefense Operations, 3500 N. Martin Luther King Junior Blvd., Lansing, Michigan, filled at (b) (4) , and labeled and packaged at Emergent BioDefense Operations, 3500 N. Martin Luther King Junior Blvd., Lansing, Michigan.

You may label your product with the proprietary name CYFENDUS and market it in a multiple-dose vial containing ten doses of 0.5 mL.

ADVISORY COMMITTEE

We did not refer your application to the Vaccines and Related Biological Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for Anthrax Vaccine Adsorbed, Adjuvanted shall be 48 months from the date of manufacture when stored at 2 °C to 8 °C. The date of manufacture shall be defined as the date the CpG 7909 adjuvant component is mixed with Anthrax Vaccine Adsorbed drug substance. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency.

FDA LOT RELEASE

Please submit protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations :

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of Anthrax Vaccine Adsorbed, Adjuvanted, or in the manufacturing facilities.

LABELING

We are approving this application, under the provisions of 21 CFR 601, Subpart H (Approval of Biological Products When Human Efficacy Studies Are Not Ethical or Feasible), for use as recommended in the agreed-upon labeling text and required patient labeling. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced animal efficacy regulations.

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft content of labeling including Package Insert, submitted under amendment 64, dated July 20, 2023, Patient Information Sheet, submitted under amendment 63 dated July 19, 2023, and the draft carton and container labels submitted under amendment 59, dated July 13, 2023.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the: Package Insert submitted on July 20, 2023 and the Patient Information Sheet submitted on July 19, 2023. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on July 13, 2023, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125761 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
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10903 New Hampshire Ave.
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You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). In addition to the reporting requirements in 21 CFR 600.80, you must submit adverse experience reports for all potentially immune-mediated adverse events as 15-day expedited reports to the Vaccine Adverse Event Reporting System (VAERS) at https://vaers.hhs.gov/. Potentially immune-mediated adverse event reports must be submitted as 15-day expedited reports for 3 years following the date of product licensure. You must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports for Vaccines* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports-vaccines. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.

SUBPART H APPROVAL REQUIREMENTS

Approvals under 21 CFR Part 601, Subpart H (Approval of Biological Product When Human Efficacy Studies Are Not Ethical or Feasible) are subject to three requirements:

a. *Approval with restrictions to ensure safe use.*

This subsection permits the Agency to require postmarketing restrictions as are needed to ensure safe use of the drug product, commensurate with the specific safety concerns presented by the drug product. We have concluded that Anthrax Vaccine Adsorbed, Adjuvanted can be safely used without restrictions on distribution or use.

b. *Information to be provided to patient recipients.*

This subsection requires applicants to prepare labeling to be provided to patient recipients for drug products approved under this subpart. We have concluded that the FDA-Approved Patient Labeling for Anthrax Vaccine Adsorbed, Adjuvanted meets the requirements of this subsection. We remind you that the Patient Labeling must be available with the product to be provided, when possible, prior to administration or dispensing of the drug product for the use approved under this subpart.

c. *Postmarketing Studies.*

This subsection requires you to conduct postmarketing studies, such as field studies, to verify and describe the biological product's clinical benefit and to assess its safety when used as indicated when such studies are feasible and ethical. We note that a postmarketing study is required to assess the clinical benefit and safety of Anthrax Vaccine Adsorbed, Adjuvanted in a post-exposure setting should an anthrax event occur in the United States.

We remind you of your postmarketing requirement specified in your submission dated April 20, 2023. This requirement, along with agreed upon completion dates, is listed below.

Subpart H Approval Required Study

1. To conduct a field study to evaluate the clinical benefit and safety of CYFENDUS when administered in conjunction with recommended antibacterial drugs for post-exposure prophylaxis following a *Bacillus anthracis* mass exposure event. The study will be conducted as a Postmarketing Requirement (PMR) under regulations for products approved under the Animal Rule, 21 CFR 601.91(b)(1).

    - Final Protocol Submission: March 31, 2024
    - Study Completion: To be determined should an event occur
    - Final Report Submission: To be determined should an event occur

Please submit the protocol to your IND 14451, with a cross-reference letter to this BLA, STN BL 125761, explaining that this protocol was submitted to the IND.

Please submit a final report as a supplement to this BLA, STN BL 125761. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart H Postmarketing Requirements**."

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because the biological product for this indication has an orphan drug designation, you are exempt from this requirement.

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

David C. Kaslow, MD
Director
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research