

Review Memorandum

January 9, 2023

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Subject: STN 125761/0

Product Name Cyfendus, Anthrax Vaccine Adsorbed, Adjuvanted (AV7909)

Applicant Emergent BioDefense Operations Lansing LLC (EBOL)

Proposed Indication 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 regimen.

Cross-reference(s) DMF (b) (4) Description of (b) (4)

DMF (b) (4) CpG 7909 Container Closure (Polypropylene screw cup), (b) (4)

DMF (b) (4) High Density Polypropylene Bottle (HDPE), (b) (4)

Review of the Chemistry, Manufacturing, and Control information relevant to CPG 7909 adjuvant Drug Substance submitted as part of the Initial Biologics License Application

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1.0 EXECUTIVE SUMMARY

1.1 AV7909 DRUG PRODUCT (DP)

AV7909 Anthrax Vaccine Adsorbed, Adjuvanted (AV7909) is a pre-formulated bacterial vaccine containing the Anthrax Vaccine Adsorbed (AVA) (b) (4) composed of a cell-free filtrates of microaerophilic cultures of an avirulent nonencapsulated strain of *Bacillus anthracis* (strain (b) (4))

(b) (4) absorbed to aluminum hydroxide and the (b) (4) agonist, oligodeoxynucleotide adjuvant, CPG 7909.

The AVA DS is manufactured by Emergent BioDefense Operations Lansing LLC (EBOL), Lansing, MI, USA; the CPG 7909 adjuvant DS is manufactured by (b) (4) US; the AV7909 is formulated at Emergent.

The AVA DS in AV7909 is produced using the (b) (4) manufacturing process as AVA in the licensed anthrax vaccine, BioThrax® (Anthrax Vaccine Adsorbed), License No. 1755; STN 103821. The AVA DS contains a (b) (4)

Addition of CPG 7909 adjuvant to AVA DS has been shown to enhance immune response when compared to AVA alone in both nonclinical and clinical studies by accelerating development of toxin-neutralizing antibodies.

AV7909 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. AV7909 is to be administered via intramuscular injection in the deltoid muscle in two doses (0.5 mL each) given two weeks apart. Each 0.5 mL dose of AV7909 contains 0.5 mL of AVA DS and (b) (4) of CPG 7909 adjuvant.

Emergent is seeking approval under FDA's Animal Rule pathway 21 CFR Part 601, Subpart H, "Approval of Biological Products When Human Efficacy Studies Are Not Ethical or Feasible". Additionally, AV7909 has been procured by the United States Government under a BARDA procurement contract and is being distributed to the US Strategic National Stockpile (SNS) since August 2019 under a pre-Emergency Use Authorization (EUA), sponsored by the Centers for Disease Control and Prevention (submitted 21 December 2018). For licensure of AV7909 under the Animal Rule, clinical efficacy is based on the bridging of immunogenicity responses and survival outcomes from animal efficacy studies and observed immunogenicity responses from clinical studies.

The following nonclinical and clinical studies were conducted to support licensure: a guinea pig model development study and a proof-of-concept post-exposure prophylaxis (PEP) immunogenicity and efficacy study in guinea pigs; two Good Laboratory Practices (GLP) and four supportive pre-exposure prophylaxis immunogenicity and efficacy studies in nonhuman primates (NHPs) and guinea pigs; four GLP rat toxicology studies; a Phase 1 dose range-finding clinical study; two Phase 2 clinical studies (a regimen-finding and an antibiotic-vaccine interaction study), and a Phase 3 pivotal immunogenicity, lot consistency and safety study.

This review covers the CPG 7909 adjuvant Drug Substance.

63 pages determined to be not releasable: (b)(4)