



Food & Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993

MEMORANDUM

DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To: The file STN 125761/0

From:

Reviewer	Role	Date finalized	Stamp	Lab Chief	Stamp
Wei Tu, M.D.	Reviewer	5/23/23		Muhammad Shahabuddin, Ph.D.	
Seth Schulte, M.S.	Reviewer	3/17/23		Simleen Kaur, M.S. (Acting)	
Ritu Agarwal, Ph.D.	Lead Reviewer	6/5/23		Kenneth Scott Phillips, Ph.D.	
Kouassi Ayikoe, Ph.D.	Reviewer	6/7/23			

Through Maryna Eichelberger, Ph.D., Division Director, DBSQC/OCBQ

Applicant: Emergent BioSolutions Inc.

Subject: Review of Analytical Methods used for Anthrax Vaccine Adsorbed Adjuvanted (AV7909), drug substances and drug product

Recommendation: Approval

Executive Summary: The following analytical methods used for lot release of Anthrax Vaccine Adsorbed, Adjuvanted (CYFENDUS) drug substance, adjuvant and drug product, and the associated analytical method validations or qualifications, were reviewed:

1. (b) (4) (Wei Tu)
2. (b) (4) (Wei Tu)
3. (b) (4) (Wei Tu)
4. Identity of Protective Antigen (PA) in DP by (b) (4) (Wei Tu)
5. (b) (4) (Seth Schulte)
6. Endotoxin test of (b) (4) (Seth Schulte)
7. (b) (4) (Seth Schulte)
8. Sterility test of DP (Seth Schulte)
9. (b) (4) (R. Agarwal)

10. (b) (4) (R. Agarwal)
11. (b) (4) (R. Agarwal)
12. (b) (4) (R. Agarwal)
13. (b) (4) AV7909 DP) (R. Agarwal)
14. Formaldehyde Content (b) (4) AV7909 /DP) (R. Agarwal)
15. (b) (4) CPG 7909 content by (b) (4) (AV7909 DP) (R. Agarwal)
16. (b) (4) (AV7909 DP) (R. Agarwal)
17. Assay for Appearance (b) (4) AV7909 DP) (R. Agarwal)
18. (b) (4) (R. Agarwal)
19. Total Protein (b) (4) (K. Ayikoe)
20. (b) (4) (K. Ayikoe)
21. (b) (4) AV7909 DP) (K. Ayikoe)
22. Sodium Chloride (b) (4) AV7909 DP) (K. Ayikoe)
23. (b) (4) (K. Ayikoe)
24. (b) (4) (K. Ayikoe)
25. (b) (4) (K. Ayikoe)
26. (b) (4) (K. Ayikoe)

Conclusion

The analytical methods and their validations and/or qualifications reviewed for the CYFENDUS drug substance and drug product were found to be adequate for their intended use.

Background

On 18 April 2022, part 2 of a rolling BLA was submitted by Emergent BioSolutions Inc. for Anthrax Vaccine Adsorbed, Adjuvanted (AV7909) drug product (STN 125761/0). Anthrax Vaccine Adsorbed, Adjuvanted (AV7909) is a pre-formulated bacterial vaccine containing the Anthrax Vaccine Adsorbed (b) (4) consisting of cell-free filtrates of cultures of *Bacillus anthracis* adsorbed to aluminum hydroxide, and the immunostimulatory toll-like receptor 9 (TLR9) agonist oligodeoxynucleotide adjuvant, CPG 7909. The AVA (b) (4) used to produce AV7909 is made with the same ingredients, as in the licensed anthrax vaccine, BioThrax (Anthrax Vaccine Adsorbed, License No.1755; STN: BL103821). The (b) (4)

(b) (4) which may augment the protective efficacy of PA. For the manufacture of AV7909, AVA DS is further formulated with CPG 7909. The CPG 7909 adjuvant is a novel synthetic molecule, consisting of 24 nucleotides with a phosphorothioate backbone. The AV7909 DP is a new product developed by the sponsor. 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. The AV7909 is administered via intramuscular injection in the deltoid muscle in two doses (0.5 mL each), given two weeks apart.

Information Reviewed

Information in sections of the original submission that describe control of DS and DP (3.2.S.4 and 3.2.P.5, respectively), including analytical procedures of DS and DP, and validation of these analytical procedures were reviewed. Additional information in amendments as specified by each reviewer were also reviewed.

Review Narrative

(b) (4) [Redacted]

(b) (4) [Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

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

4. Identity of protective antigen (PA) by (b) (4) in DP, Wei Tu

Introduction:

The identity of PA, the main component in AV7909 DP is determined by (b) (4). This assay is performed at Emergent BioDefense Operations Lansing LLC (EBOL) in Lansing, MI, and has a specification of "positive".

Method:

(b) (4)



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

(b) (4)



Conclusion

The Identity by (b) (4) for detection of Protective Antigen (PA) in AV7909 DP was adequately validated and is suitable for its intended use

(b) (4)



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

(b) (4)

[Redacted]

[Redacted]

[Redacted]

(b) (4)

8. Sterility test of DP (Seth Schulte)

Introduction

Sterility testing is performed on the DP at the (b) (4) facility in (b) (4). Acceptance criteria of 'No Growth Detected' must be met for the lot release of CYFENDUS.

(b) (4)

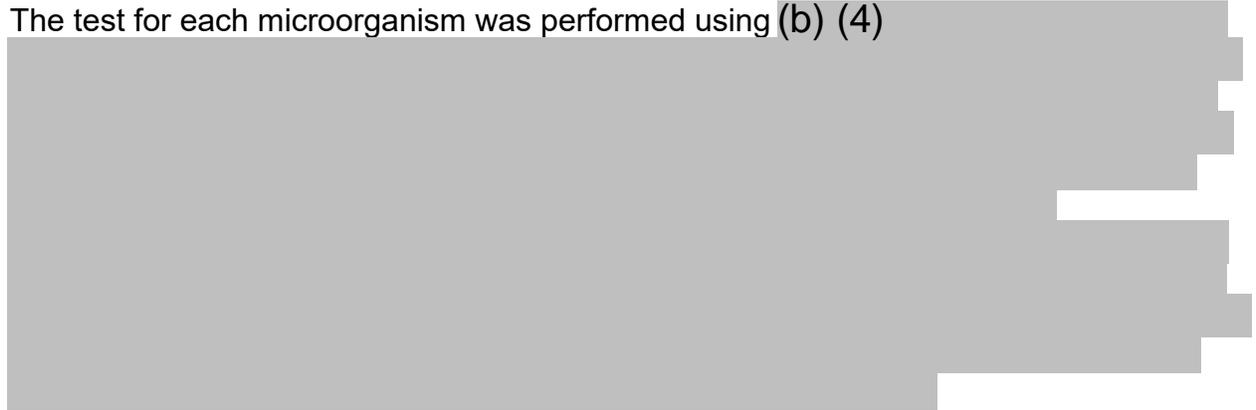
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CYFENDUS DP Sterility Test Qualification
Emergent qualified their compendial (b) (4)

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Sterility test report ExD040528 lacked sufficient information to complete a review of the method, therefore an IR was sent to Emergent on June 22, 2022, asking for clarification and additional data to supplement their report. The response to CBER's IR was received on July 26, 2022 (Amendment #8) and reviewed as part of the DP sterility test qualifications below.

The test for each microorganism was performed using (b) (4)

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(b) (4)

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(b) (4) [Redacted]

Conclusion

The method suitability tests were performed and compliant with (b) (4) and the test results indicate there is no product interference from the test sample, thus indicating the (b) (4) sterility test method is appropriate under the actual conditions of use for the DP at the (b) (4) facility.

(b) (4) [Redacted]

[Redacted]

[Redacted]

[Redacted]

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

(b) (4)

[Redacted]

[Redacted]

13. Benzethonium Chloride Content by (b) (4) AV7909 DP) (R. Agarwal)
The determination of Benzethonium chloride content is performed using (b) (4)
[Redacted] AV7909 drug
product. Benzethonium chloride is used as a (b) (4). The proposed
release specification is (b) (4)

(b) (4)

[Redacted]

[Redacted]

(b) (4) [Redacted]

[Redacted]

[Redacted]

[Redacted]

Conclusion: The method is clearly described and validated, and is suitable as a lot-release test for the determination of benzethonium chloride in (b) (4) AV7909 drug product.

14. Formaldehyde Content (b) (4) /AV7909 DP) (R. Agarwal)

The formaldehyde content is measured in (b) (4) AV7909 drug product using a (b) (4) method. The specification for formaldehyde, is set at (b) (4)

(b) (4)

[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

(b) (4)



Conclusion: The method is clearly described and validated, and is suitable as a lot-release test for the determination of formaldehyde in (b) (4) AV7909 drug product.

15. (b) (4) CPG 7909 content by (b) (4) (AV7909 DP) (R. Agarwal)

The (b) (4) CPG 7909 content in AV7909 drug product is determined by a (b) (4) . The specification for the (b) (4) CPG content is (b) (4) .

(b) (4)



1 page determined to be not releasable: (b)(4)

(b) (4)

Conclusion: The method is clearly described and validated, and is suitable as a lot-release test for determination (b) (4) CPG 7909 content of AV7909 drug product.

16. Identity of (b) (4) CPG 7909 by (b) (4) (AV7909 DP) (R. Agarwal)

The (b) (4) CPG 7909 in AV7909 drug product is determined by a (b) (4)

(b) (4) CPG 7909 is an identity test that is used to confirm the presence of CPG 7909 in DP at the time of release.

(b) (4)

(b) (4)

[Redacted]

[Redacted]

Conclusion: The method is clearly described and validated, and is suitable as a lot-release test for the identity of (b) (4) CPG 7909 in AV7909 drug product.

17. Appearance (b) (4) AV7909 DP) (R. Agarwal)

The appearance of (b) (4) is evaluated by visual inspection. The specification for appearance is (b) (4) milky-white suspension for AV7909 finished drug product.

Method

This procedure does not require sample preparation. The appearance of samples is (b) (4)

[Redacted]

The final product vials are inspected for product appearance (b) (4)

[Redacted]

The batch analysis data for the (b) (4) AV7909 final container product were within the specified limits. No additional validation is necessary.

Conclusion: The assay is suitable as a release test for (b) (4) AV7909 finished drug product.

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

(b) (4)



21. Aluminum content in (b) (4) AV7909 DP (K. Ayikoe)

Aluminum (from Aluminum hydroxide) serves as an adjuvant in (b) (4) (b) (4)

(b) (4) Emergent BioDefense Operations Lansing (EBOL); (b) (4) testing lab. The method is currently validated by (b) (4) of which approval and transfer to Emergent BioDefense request is provided in this current submission. The specifications for (b) (4) and AV7909 DP (release and stability) are (b) (4)

(b) (4)



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(b) (4)



Conclusion:

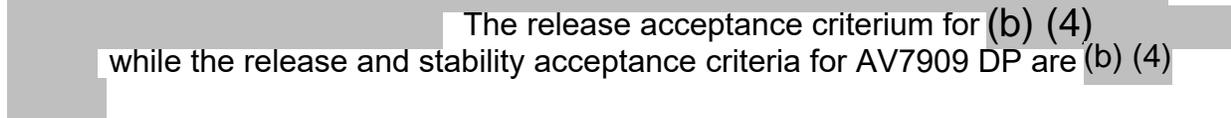
The (b) (4) assay for the quantitative determination of Aluminum in Anthrax Vaccine Adsorbed, (b) (4) DP (AV7909) and their validations are acceptable and therefore suitable for their intended purposes. The method transfer from (b) (4) to Emergent Lansing facility is acceptable.

22. Sodium Chloride Content in (b) (4) DP (K. Ayikoe)

Sodium chloride in (b) (4) AV7909 DP is an (b) (4)



The release acceptance criterium for (b) (4) while the release and stability acceptance criteria for AV7909 DP are (b) (4)



(b) (4)



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(b) (4) [Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

Conclusion:

The (b) (4) [Redacted] assay method for the quantitative determination of sodium chloride in (b) (4) [Redacted] AV7909 DP (and its validation) is acceptable and is therefore suitable for its intended purposes.

(b) (4) [Redacted]

[Redacted]

[Redacted]

[Redacted]

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