



DBSQ/OCBQ ANALYTICAL METHOD REVIEW MEMO

To The file: STN 125789

From Simleen Kaur, M.S.
Laboratory of Microbiology, *In-Vivo* Testing and Standards (LMIVTS)
Division of Biological Standards and Quality Control (DBSQ)

Through Maryna Eichelberger, Ph.D., Director, DBSQ
James Kenney, D.Sc., Chief, LMIVTS

Applicant Adaptimmune

Subject Review of Mycoplasma, Endotoxin, and Sterility Analytical Methods for afamitresgene autoleucel

Recommendation: Approval

Executive Summary:

The mycoplasma, endotoxin, and sterility analytical methods used for testing and release of afamitresgene autoleucel and the associated analytic method qualifications or validations, were reviewed. The assays were adequately described and shown to be suitable for their intended purpose, however, the sponsor recently decided to perform the (b) (4) method for (b) (4) sterility testing and has not completed the verification testing. On July 8, 2024 (Amendment # 64) Adaptimmune committed to providing this information as a post marketing commitment (PMC). In addition, data were not provided to demonstrate (b) (4) of the (b) (4)) and (b) (4) methods. The sponsor has committed to providing this information for drug product testing as stated in their response received on July 21, 2024 (Amendment # 56). The report for (b) (4) sterility test is expected to be submitted by October 31, 2024, and a report of the (b) (4) study is expected by December 2024.

Conclusion: The analytical methods and their qualifications or validations reviewed for afamitresgene autoleucel drug substance and drug product were found to be adequate for their intended use.

Documents Reviewed



Information in sections of the original submission that describe control of Drug Substance (DS) and Drug Product (DP) (3.2.S.4 and 3.2.P.5, respectively), including descriptions of DS and DP specifications, analytical procedures of DS and DP and

qualifications or validation of these analytical procedures were reviewed. In addition, responses to CBER's Information Requests (IRs) received on January 31, 2024 (Amendment # 6), June 10, 2024 (Amendment # 46), June 17, 2024 (Amendment # 52), June 21, 2024 (Amendment # 56), July 8, 2024 (Amendment # 64) and July 24, 2024 (Amendment # 85), were also reviewed as mentioned below.

(b) (4)



(b) (4)



4. Mycoplasma Method (DP)

Introduction

Mycoplasma testing for (b) (4) sample is performed at Adaptimmune in Philadelphia, PA. Specification of (b) (4) must be met for release of (b) (4) sample.

Method

The test for mycoplasma is performed in accordance with (b) (4). The (b) (4) mycoplasma test is a (b) (4) method where (b) (4) from a test sample followed by (b) (4). The mycoplasma (b) (4) is

performed in accordance with (b) (4) [REDACTED] The method is described in more detail below together with the tests performed to determine the validation of the test method for its intended use.


The original validation reports for mycoplasma lacked sufficient information to complete the review. Therefore, IRs were sent requesting clarification and responses were received on January 31, 2024 (Amendment # 6), June 17, 2024 (Amendment # 52), and June 21, 2024 (Amendment # 56), which were found acceptable and explained below.

Mycoplasma Validation



(b) (4) [REDACTED]

Specificity

(b) (4)

Robustness and Ruggedness

(b) (4)


Conclusion

The mycoplasma (b) (4) validation was performed, and the test results indicate there is no product interference from the test sample. However, (b) (4) testing, as required by (b) (4) was found incomplete since it did not include (b) (4) method testing and no comparison with the sensitivity of (b) (4) system to provide assurance that the (b) (4) system is equal to or greater than the (b) (4) method. Therefore, an IR was sent on June 20, 2024, requesting a PMC on the (b) (4) testing. Adaptimmune PMC was received on June 21, 2024 (Amendment # 56) commits to the requested study and report will be submitted by December 2024.

5. Endotoxin Method (DP)Introduction

Endotoxin testing for afamitresgene autoleucel DP is performed at Adaptimmune in Philadelphia, PA. Specification of (b) (4) must be met for release of afamitresgene autoleucel DP.

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

Conclusion




The method suitability test was performed and compliant with (b) (4) and the test results indicate there is no product interference from DP test samples, thus indicating the (b) (4) BET test method is appropriate under the actual conditions of use.

6. Sterility Method (DP)Introduction


Sterility testing for afamitresgene autoleucel DP is performed at Adaptimmune in Philadelphia, PA. Specification of 'Not Detected' must be met for release of afamitresgene autoleucel DP.

Method

(b) (4)



(b) (4)



Conclusion

The method validation tests were performed and compliant with (b) (4) and the test results indicate there is no product inhibition of microorganism growth. The (b) (4) sterility test method was demonstrated to provide assurance equal to or greater than the (b) (4) method and is appropriate under the actual conditions of use.