



DBSQ/OCBQ ANALYTICAL METHOD REVIEW MEMO

To The file: STN 125813

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Applicant Autolus

Subject Review of Mycoplasma, Endotoxin, and Sterility Analytical Methods for
obecabtagene autoleucel (obe-cel)

Recommendation: Approval

Executive Summary:

The mycoplasma, endotoxin, and sterility analytical methods used for testing and release of obe-cel and the associated analytic method qualifications or validations, were reviewed. The assays were adequately described and shown to be suitable for their intended purpose.

Conclusion: The analytical methods and their qualifications or validations reviewed for obe-cel 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 5, 2024 (Amendment #7), January 31, 2024 (Amendment # 16), March 26, 2024 (Amendment # 27) and June 11, 2024 (Amendment # 40) were also reviewed as mentioned below.

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

(b) (4)



(b) (4)



(b) (4)



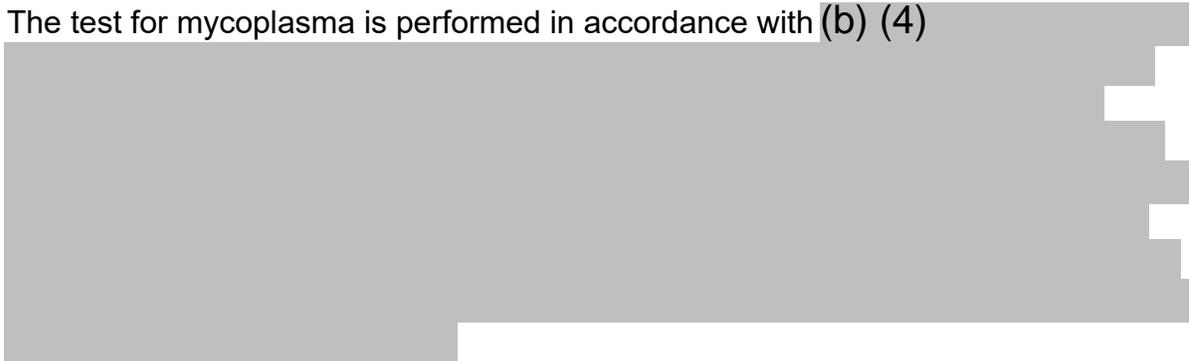
4. Mycoplasma Method (DP)

Introduction

Mycoplasma testing for (b) (4) sample is performed at Autolus in Steyennege, UK. Specification of 'Not Detected' must be met for release of (b) (4) sample.

Method

The test for mycoplasma is performed in accordance with (b) (4)



The validation study was performed on obe-cel positive control matrix prepared using healthy donor leukapheresis starting material instead of patient leukapheresis samples but since the manufacturing process and matrix for obe-cel positive control is same as final patient drug product sample, CBER found this acceptable. The

mycoplasma test should be performed on (b) (4) [redacted] to ensure mycoplasma is detected if the material is contaminated. Therefore, IRs were sent requesting (b) (4) and (b) (4) testing be repeated using (b) (4) [redacted] of different mycoplasma species. However, Autolus re-evaluated validation study using (b) (4) [redacted] of different mycoplasma species. The responses were received on January 5, 2024 (Amendment # 7) and January 31, 2024 (Amendment # 16) and June 11, 2024 (Amendment # 40) which were found acceptable and explained below.

Mycoplasma Validation

(b) (4) [redacted]

[redacted]

[redacted]

[redacted]

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

(b) (4)



Conclusion

The mycoplasma (b) (4) validation was performed, and compliant with (b) (4) and the test results indicate there is no product interference from the test sample. The sensitivity of the (b) (4) method is equivalent or greater than the (b) (4) method, thus indicating the test method is suitable under the actual conditions of use.

5. Endotoxin Method (DP)

Introduction

Endotoxin testing for obe-cel DP is performed at Autolus in Steyennege, UK. Specification of (b) (4) must be met for release of obe-cel DP.

Method

(b) (4)



The submission lacked sufficient information to complete review of endotoxin test, therefore, an IR was sent requesting missing information and a response was received on January 5, 2024 (Amendment #7), which was found acceptable and explained below.

(b) (4)-BET Validation

(b) (4)



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(b) (4)

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Conclusion

The ^{(b) (4)} BET validation was performed, and compliant with (b) (4) and the test results indicate there is no product interference from the test sample. The ^{(b) (4)} BET method was demonstrated to provide assurance equal to or greater than the (b) (4) method and is appropriate under the actual conditions of use thus indicating the test method is appropriate under the actual conditions of use.

6. Sterility Method (DP)

Introduction

Sterility testing for obe-cel DP is performed at Autolus in Steyennege, UK. An acceptance criterion of 'No Growth Detected' must be met for the release of obe-cel DP.

Method

(b) (4)



The original validation reports for sterility lacked sufficient information to complete the review. Therefore, IRs were sent requesting data and clarification to fulfill these deficiencies. Responses were received January 5, 2024 (Amendment #7), January 31, 2024 (Amendment # 16) and March 26, 2024 (Amendment # 27) which were found acceptable and explained below.

Sterility Test Validation for DP

(b) (4)



1 page determined to be not releasable: (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 thus indicating the test method is appropriate under the actual conditions of use.