



DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To The file: STN 125812/0

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Product SYMVESS (acellular tissue engineered vessel - tyod)

Applicant Humacyte Global, Inc. (Humacyte)

Subject Review of Sterility, Endotoxin, and (b) (4) Analytical Methods used for SYMVESS

Recommendation: Approval

Executive Summary

The sterility, bacterial endotoxin, and (b) (4) analytical methods used for testing and release of SYMVESS drug product (DP) and the associated analytic method qualifications, were reviewed. The assays were adequately described and shown to be suitable for their intended purpose.

Conclusion: The analytical methods and their qualifications reviewed for SYMVESS DP were found to be adequate for their intended use. Additionally, Humaycte commits to submit a report on the risk assessment of environmental isolates, by perform sterility method qualification using in-house environmental isolates. The final study report will be submitted as a 'Post-marketing Commitment (PMC) - final study report', by August 30, 2024.

Documents Reviewed

Information in the original submission that describe control of DP (3.2.P.5), including descriptions of DP specifications, analytical procedures of DP, and the qualification of these analytical procedures were reviewed. In addition, responses to CBER's information request (IR) received on February 22, 2024 (Amendment 11), April 15,

2024 (Amendment 19), April 29, 2024 (Amendment 23), May 7, 2024 (Amendment 28), and June 14, 2024 (Amendment 42) were also reviewed.

Background

On December 8, 2023, Humacyte submitted this original BLA for SYMVESS indicated for 'urgent arterial repair following extremity vascular trauma (b) (4) (b) (4) (b) (4) (b) (4) when autologous vein is not feasible'. SYMVESS is a sterile, tissue-engineered, acellular, tubular composed of organized extracellular matrix proteins typically found in human blood vessels. The SYMVESS has dimensions of approximately 6 mm in inner diameter and 42 cm in length. SYMVESS is immersed in (b) (4) Phosphate Buffered Saline (b) (4) within the final container package prior to implantation. (b) (4) is the only excipient and keeps the synthetic graft hydrated prior to implantation. Each final container package (i.e., box containing Tyvek-sealed tray) contains one SYMVESS unit for administration to a single patient.

The manufacturing process of SYMVESS starts by (b) (4)

(b) (4)

The final step of this decellularization process (b) (4) The bioreactors are then individually sealed becoming the sterile final container package for each product. Visual inspection is performed, and samples are taken for quality control release testing. The Applicant indicated that because the SYMVESS is manufactured (b) (4) they only submitted information in the drug product section but not in drug substance section.

This review focuses on qualification of the sterility, bacterial endotoxin, and (b) (4) tests to determine if these methods are suitable for testing the SYMVESS DP under the actual conditions of use. Note: Zainab Mansaray Storms - in CBER's OCBQ's Division of Manufacturing and Product Quality - will review the in-process bioburden testing for SYMVESS.

1. Sterility (DP)

Introduction

Sterility testing for (b) (4) (b) (4) from SYMVESS at end of the (b) (4) stage, just prior to final container, is performed at (b) (4) Acceptance criteria of 'No Growth' must be met for the lot release of SYMVESS DP.

Method

The (b) (4) sterility test is used in accordance with (b) (4)

(b) (4)

The approach of using excipient (b) (4) as an appropriate test sample for (b) (4) (b) (4) sterility testing was determined by (b) (4) (b) (4) which describe the acquisition of (b) (4) test articles from the interior of the syringe or device that are subsequently tested as directed in the section entitled (b) (4) It enables sterility testing to be performed within the (b) (4) that (b) (4) (b) (4) that would recover contaminants introduced into the system, which CBER finds acceptable.


The original qualification report for sterility lacked sufficient information to complete the review: 1) sterility testing of SYMVESS DP was performed using (b) (4) lot of SYMVESS DP and 2) the qualification studies did not include evaluation of environmental (EM) isolates; therefore, an IR was sent requesting: 1) a qualification study be performed with (b) (4) lots and EM isolates from the manufacturing facility be used in the qualification of the sterility test method. The responses for the verification of the (b) (4) lots were received on February 22, 2024 (Amendment 11) and April 29, 2024 (Amendment 23), which were found acceptable and reviewed as part of the DP sterility testing below.

Sterility Test Qualification for DP


(b) (4) qualified their (b) (4) method for the (b) (4) excipient SYMVESS DP sample by performing (b) (4) (b) (4) qualification studies to determine if the method is suitable under the actual conditions of use. The test performed using (b) (4) on (b) (4) batches (b) (4) (b) (4) of SYMVESS DP.

(b) (4)

(b) (4)

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(b) (4)

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Regarding qualification by EM isolates in an IR response (amendment 11) received by CBER on February 22, 2024, Humacyte agreed to test EM isolates from their manufacturing facility in the sterility test method qualification. Humacyte is in the process of preparing their 2023 Annual Environmental Monitoring Trend Report. A risk assessment will be performed on EM isolates identified in the report to determine the risk associates with using only USP indicator organisms during sterility method qualification. If it is determined that additional sterility method qualification is required using in-house EM isolates, this additional sterility method qualification will be completed. Humacyte opened a corrective and preventive action (i.e., CAPA-2024-011) to capture this commitment with a completion date of August 30, 2024. This completion date is after the action due date for this file. Therefore, CBER requested Humacyte to submit their CAPA completion report in a PMC.

Conclusion

The method suitability tests were performed and compliant with (b) (4) and the test results indicate there is no product interference from bioreactor excipient (b) (4) (b) (4) from SYMVESS product, thus indicating the (b) (4) sterility test method is appropriate under the actual conditions of use at (b) (4) (b) (4) Humaycte commits to submit their EM risk assessment completion report and perform any necessary sterility method qualification using in-house environmental isolates. The final study report will be submitted as a PMC by August 30, 2024.

2. Endotoxin (DP)

Introduction

Endotoxin testing is performed in the bioreactor excipient (b) (4) (b) (4) from SYMVESS product at end of the (b) (4) stage, (b) (4) final container, at (b) (4) facility in (b) (4). The acceptance criteria for SYMVESS DP is (b) (4) (b) (4).

Method

(b) (4)

The original qualification report for the endotoxin study did not include information required for completion of the review; therefore, two IRs were sent requesting missing information and a follow-up for their (b) (4) calculation. IR responses were received on February 22, 2024 (Amendment 11) and April 29, 2024 (Amendment 23), which were found acceptable and explained below.

(b) (4) Qualification for DP

(b) (4)

(b) (4)

Conclusion

The method suitability tests were performed and compliant with (b) (4) and (b) (4). Therefore, CBER determined their (b) (4) test method is appropriate under the actual conditions of use.

(b) (4)

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