



ADDENDUM to DBSQC/OCBQ ANALYTICAL METHOD REVIEW MEMO

To The file: STN 125812/0/71

From Hyesuk Kong, Ph.D.
Laboratory of Microbiology, *In-Vivo* Testing and Standards (LMIVTS)
Division of Biological Standards and Quality Control (DBSQC)

Through James L. Kenney, D. Sc., Acting Director DBSQC, for Maryna Eichelberger
James L. Kenney, D.Sc., Chief, LMIVTS

Product SYMVESS (acellular tissue engineered vessel - ATEV)

Applicant Humacyte Global, Inc. (Humacyte)

Subject STN 125812/0/71 Addendum – Updated Sterility Test Method and the Use
of Environmental Isolates for Sterility Suitability Testing for SYMVESS

Recommendation: Information Request #8/Post-Marketing Commitment #4: Risk
Assessment of Environmental Isolates Related to Sterility Method Qualification;
Fulfilled.

Executive Summary:

The original sterility method qualification studies did not include evaluation of environmental (EM) isolates; therefore, an information request was sent on February 8, 2024, asking for qualification study be performed with EM isolates from the manufacturing facility for sterility test. The firm addressed the risk assessment of in-house EM isolates related to sterility method qualification in Amendment 71 on August 30, 2024, providing clarification that EM isolates (b) (4) [REDACTED] (b) (4) [REDACTED] for their drug product (DP) manufacturing facility are similar to the (b) (4) [REDACTED] indicator microorganisms and the risk estimation determined that not including the EM isolates would be 'low risk'.

Conclusion: Based on risk assessment of the EM isolates from 2023, EM isolates will not need to be included in a sterility suitability assessment for sterility testing. Following the selection of the annual EM isolates, an assessment of additional sterility method qualification will be incorporated into their environmental monitoring annual report. This reviewer determined this amendment has been satisfied, is acceptable, and this item be removed from the list of Post-Marketing Commitment.

Documents Reviewed

Information in sections of Amendment 71: response to the CBER's Information Request (IR) received on August 30, 2024, including a risk assessment of EM isolates and perform necessary sterility method qualification using in-house EM isolates was reviewed.

Background

On December 8, 2023, Humacyte submitted this original BLA for SYMVESS product indicated for 'urgent arterial repair following extremity vascular trauma (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. DBSQC completed the review of analytical methods and associated analytic method qualifications/validations. Please refer to review memo dated July 26, 2024.

In response to an information request (IR, #8: dated 02/08/2024), requesting EM isolates to be qualified as part of sterility method qualification to ensure they can be detected in addition to the indicated (b) (4) microorganisms, Humacyte committed to submitting a risk assessment of EM isolates or perform the necessary sterility method qualification using in-house EM isolates as a Post-marketing Commitment (PMC) by August 30, 2024.

On August 30, 2024, Humacyte submitted a risk assessment of in-house EM isolates for their sterility method. This review focuses on the risk assessment report of EM isolates and perform necessary sterility method qualification using in-house EM isolates, to determine if EM isolates will be used to perform additional sterility method suitability.

EM Isolate Risk Assessment Review

At the time IR #8 was submitted, Humacyte was in the process of preparing their 2023 Annual Environmental Monitoring Trend Report. A risk assessment was performed on EM isolates identified in the report to determine the risk associates with using only (b) (4) indicator organisms during sterility method qualification. Humacyte opened a corrective and preventive action (i.e., CAPA-2024-011) to capture this commitment with a completion date of August 30, 2024.

Humacyte performed a Risk Estimation following SOP-0321, 'Quality Risk Management', to determine the risk level of not including the 2023 EM isolates (i.e., (b) (4) in an additional sterility suitability test and provided

clarification that EM isolates from their manufacturing facility are similar to the (b) (4) indicator microorganisms (b) (4)

(b) (4)

Based on this risk assessment of the EM isolates recovered from the manufacturing facility, which assured CBER that the (b) (4) indicator microorganisms used in this qualification are representative of potential bioburden contaminants and the inclusion of environmental isolates in this qualification was not necessary.

Conclusion

This reviewer concludes, Humacyte successfully fulfilled their IR/PMC commitment for the risk assessment of environmental isolates and perform necessary sterility method qualification using in-house environmental isolates and successfully notified the FDA that the final study report, which includes a risk assessment by August 30, 2024.