



U.S. Food & Drug Administration
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To: Administrative File BL 125812/0

From: Zainab Mansaray-Storms, Consumer Safety Officer, CBER/OCBQ/DMPQ/MRB2

Through: Anthony Lorenzo, Branch Chief, CBER/OCBQ/DMPQ/MRB2
Carolyn Renshaw, Division Director, CBER/OCBQ/DMPQ

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Applicant: Humacyte Global, Inc. (Lic. # 2336)

Facility: Humacyte Global, Inc., Durham, North Carolina (FEI# 3014294024)

Product: Acellular tissue engineered vessel (SYMVESS), intended for surgical implantation

Subject: Review of the responses to the post-marketing commitment for the sterilization validation of the bioreactor disposable set of the drug product of acellular tissue engineered vessel

RECOMMENDATION

The responses from Humacyte Global, Inc. to the post-marketing commitment (PMC) for the sterilization validation of the bioreactor disposable set appear to be acceptable. PMC fulfilled.

SIGNATURE BLOCK

Reviewer, Title, Affiliation	Concurrence	Signature and Date
Zainab Mansaray-Storms, Consumer Safety Officer CBER/OCBQ/DMPQ/MRB3	Concur	
Anthony Lorenzo, Branch Chief CBER/OCBQ/DMPQ/MRB3	Concur	
Carolyn Renshaw, Division Director CBER/OCBQ/DMPQ	Concur	

SUMMARY

Humacyte Global Inc., (Humacyte) submitted BLA 125812/0 for a novel acellular tubular implant composed of human extracellular matrix proteins typically found in human blood vessels, termed as acellular tissue engineered vessel, for the treatment of urgent arterial repair

following extremity vascular trauma (b) (4) when autologous vein graft is not feasible.

In the original BLA 125812/0 submission, sterilization validation of the bioreactor disposable set (BDS) was not provided. Humacyte committed to the following post-marketing commitment (PMC) from DMPQ in response to Information Request #21 on 10 May 2024 (BLA 125812/0.30, eCTD 0031):

“Humacyte commits to perform sterilization validation of the commercial bioreactor disposable set and provide the final report, including a summary of the dose verification study and the applicable data. Humacyte commits to continue performing aseptic process simulation of the full manufacturing process (b) (4) every (b) (4) (b) (4) until this post-marketing commitment is fulfilled. Humacyte will submit the final study report by September 30, 2024.”

Humacyte submitted a response to the above PMC on 22 Aug 2024 (STN 125812/0.69, eCTD 0070) to provide the complete BDS sterilization validation. At the time of the PMC receipt, the Agency had yet to determine an action on the original application.

The information provided in the amendment was reviewed and found to be acceptable. While Humacyte conveyed the information as a PMC, approval of the original BLA 125812/0 is pending at the time of this review.

REVIEW OF RESPONSES TO THE POST MARKETING COMMITMENT

Humacyte commits to perform sterilization validation of the commercial bioreactor disposable set and provide the final report, including a summary of the dose verification study and the applicable data. Humacyte commits to continue performing aseptic process simulation of the full manufacturing process (b) (4) every (b) (4) until this post-marketing commitment is fulfilled. Humacyte will submit the final study report by September 30, 2024.

PMC Review

In response to the PMC, Humacyte provided the final report for the commercial bioreactor disposable set (BDS) sterilization validation.

The BDS is manufactured and sterilized by (b) (4) by (b) (4) and provided as ready-to-use BDS to Humacyte. (b) (4) performed the sterilization validation using the complete BDS (b) (4) used as the (b) (4) (b) (4) drug product. The sterilization validation used a (b) (4) design of the full BDS assembly; meaning it did not contain (b) (4)

The validation activities included an installation qualification (IQ), operational qualification (OQ) and a process performance qualification (PPQ).

For the IQ study, the sample item portion (SIP) value was verified. (b) (4) bioreactors from (b) (4) BDS set was used for the study. The acceptance criterion was the bioburden of the SIP must be designed to adequately represent the intended design space while considering guidance from (b) (4) (b) (4) Section (b) (4). The results of the IQ met the acceptance criteria.

For the OQ study, (b) (4) BDSs from (b) (4) different lots were used and sampled for bioburden pursuant to (b) (4) (b) (4). The acceptance criteria for the OQ were “The bioburden of the SIP shall be such that either (b) (4) of the (b) (4) SIPs yield positive tests of sterility, or a bioburden of (b) (4) or more is found on at (b) (4) of (b) (4) or more SIPs.” The results of the OQ indicated that (b) (4) of (b) (4) from (b) (4) lots yield positive test for sterility, meeting the acceptance criteria.

For the PPQ, (b) (4) BDSs from (b) (4) different lots were used. First, bioburden was determined from each sample according to (b) (4) (b) (4). Then, a calculation of the correct SIP (b) (4) value per (b) (4) was determined. And finally, a verification dose experiment was executed. The delivered (b) (4) dosage range was (b) (4) (b) (4) (the specified (b) (4) dosage range was (b) (4)).

The below acceptance criteria were in place for the PPQ:

- The bioburden of the SIP must be less than (b) (4) to utilize (b) (4)
- The calculation of correct SIP (b) (4) value per of (b) (4) section (b) (4)
- Accept the verification dose if there is (b) (4) test of sterility obtained from the (b) (4) tests carried out.
 - If there are (b) (4) tests of sterility, perform a confirmatory verification dose test.
 - If there are (b) (4) tests of sterility, do not accept verification as the dosage may be inadequate,

The bioburden results from the PQ are provided in the tables below.

Samples from lot # (b) (4)	Raw Count	Correction Factor Applied
(b) (4)	(b) (4)	(b) (4)

There is growth present on (b) (4) of samples from lot (b) (4)

Samples from lot # (b) (4)	Raw Count	Correction Factor Applied
(b) (4)	(b) (4)	(b) (4)

There is growth present on (b) (4) of samples from lot (b) (4)

Samples from lot # (b) (4)	Raw Count	Correction Factor Applied
(b) (4)	(b) (4)	(b) (4)

There is growth present on (b) (4) of samples from lot # (b) (4)

All PPQ test results met the predetermined acceptance criteria. There were (b) (4) test of sterility in the (b) (4) tests carried out.

Per the firm, the study confirms that the validation was successfully completed and confirms that the (b) (4) process for the BDS assembly is effective.

In response to an information request (STN 125812/0.74; received 08 Nov 2024), Humacyte stated that (b) (4) performs (b) (4) dose audits as required by (b) (4) for the BDS. In

addition, Humacyte confirmed the routine sterilization dose for the BDS is required to be (b) (4) (b) (4).

Reviewer's comment: Results from the sterilization validation by (b) (4) (b) (4) were provided. All results met the predetermined acceptance criteria. For the verification dose, the specified range of (b) (4) dosage range of (b) (4) was used. Routine sterilization dose for the BDS is (b) (4) The sterilization validation of the BDS appears acceptable.