



Our STN: BLA 125812/0

**MID-CYCLE COMMUNICATION
SUMMARY**

April 2, 2024

Humacyte Global, Inc.

Attention: (b) (4)

(b) (4)

Dear Dr. (b) (4)

Attached is a copy of the summary of your March 28, 2024 Mid-Cycle Communication Teleconference with CBER. This memorandum constitutes the official record of the Teleconference. If your understanding of the Teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER as soon as possible.

Please include a reference to STN BLA 125812/0 in your future submissions related to Human Acellular Vessel (under review).

If you have any questions, please contact Helen Sansone at (240) 549-2276 or Helen.Sansone@fda.hhs.gov.

Sincerely,

Mara Miller, MA
Director
Division of Review Management and Regulatory Review 2
Office of Review Management and Regulatory Review
Office of Therapeutic Products
Center for Biologics Evaluation and Research

Mid-Cycle Communication Teleconference Summary

Application Type and Number: BLA 125812/0

Proposed Product Name: Human Acellular Vessel (under review)

Proposed Indication for Use: Urgent arterial repair following extremity vascular trauma (b) (4) when autologous vein is not feasible (under review)

Applicant: Humacyte Global, Inc.

Meeting Date & Time: March 28, 2024; 2:00 pm - 3:00 pm ET

Committee Chair: Jin Sung Hong

RPM: Helen Sansone

FDA Attendees:

Colleen Caldwell, MS, MPH, CBER/OTP/ORMRR

CDR Leah Crisafi, MD, CBER/OTP/OCE

Maryna Eichelberger, PhD, CBER/OCBQ/DBSQC

Lola Fashoyin-Aje, MD, MPH, CBER/OTP/OCE

Alifiya Ghadiali, PhD, RAC, CBER/OCBQ/DMPQ

Salil Ghosh, MS, PhD, CBER/OCBQ/DBSQC

Jin Sung Hong, PhD, CBER/OTP/OCTHT

Guo-Chiuan Hung, PhD, CBER/OTP/OGT

Hyesuk Kong, PhD, CBER/OCBQ/DBSQC

Pratima Labroo, PhD, CBER/OTP/OCTHT

Wei Liang, PhD, CBER/OTP

Heather Lombardi, PhD, CBER/OTP/OCTHT

Zainab Mansaray Storms, PhD, CBER/OCBQ/DMPQ

Adamma Mba-Jonas, MD, MPH CBER/OBPV/DPV/PB

Lori Peters, CBER/OCBQ/DMPQ

Vaishali Popat, MD, MPH, CBER/OTP/OCE

Joseph Quander III, CBER/OCBQ/DMPQ

Carolyn Renshaw, CBER/OCBQ/DMPQ

Laura Ricles, PhD, CBER/OTP/OCTHT

Helen Sansone, CBER/OTP/ORMRR

Andrey Sarafanov, PhD CBER/OTP/OPPT/DH/HB2

Prateek Shukla, MD, CBER/OTP/OCE

Ramani Sista, PhD, CBER/OTP/ORMRR

Lisa Stockbridge, PhD, CBER/OCBQ/DCM/APLB

Zehra Tosun, PhD, CBER/OTP/OCTHT

Wei Tu, CBER/OCBQ/DBSQC/LBVI

Triet Tran, PharmD, BCSCP, CBER/OCBQ/DIS

Boguang Zhen, PhD, CBER/OBPV/DB

Thomas Zhou, PhD, CBER/OBPV/DB

Applicant Attendees:

Harold Alterson, SVP, Quality, Humacyte
Cindy Cao, PhD, Chief Regulatory Officer, Humacyte
Emmanuelle Hugentobler, MD, Vice President, Scientific Affairs, Humacyte
Jeff Jones, MS, Global Head of CMC Regulatory Affairs, Humacyte
Zak Khondker, PhD, Executive Director and Head of Biometrics, Humacyte
Rob Kirkton, PhD, Director, New Product Development, Humacyte
Rubina Mondal, MS, Sr. Director, Regulatory Affairs, Humacyte
Laura Niklason, MD, PhD, Founder and Chief Executive Officer, Humacyte
Shamik Parikh, MD, Chief Medical Officer, Humacyte
Heather Prichard, PhD, Chief Operations Officer, Humacyte
Manira Rayamajhi, PhD, Sr. Director, Regulatory Affairs, Humacyte
Mark Tulchinsky, MD, Head of Pharmacovigilance and Safety, Humacyte
Matt Udelhofen, Associate Director, MSAT, Humacyte
(b) (6) Director, Regulatory Affairs, (b) (4)

Agenda:

Discussion Summary:

1. Any significant issues/major deficiencies, categorized by discipline, identified by the Review Committee to date.
 - Extractables evaluation of the primary container closure: The information provided in response to CMC IR #6, received March 19, 2024, regarding the extractables study is based on a simulated leachable study with accelerated conditions of product storage but not the required information. Thus, no extractables study, as required by (b) (4) (b) (4) is provided for the (b) (4) bag (i.e., bioreactor bag and final container closure). An extractables study is required to support the safety of the final container closure. Additional information (e.g., extractables study results from the (b) (4) bag manufacturer or from Humacyte) or a plan to conduct an extractables evaluation of the final container closure is needed.

Meeting Discussion for Agenda item 1:

The Applicant acknowledged the comments sent in the CMC information request and committed to submit available extractables study data for the final container closure (components) or performing this study if the data are not available. FDA reminded the Applicant that the extractables study is usually performed first and the leachables study is designed based on the results of the extractables study. Therefore, when the extractable study data are available, the Applicant should align the results (retrospectively) with the data from the already performed leachables

study to ensure that any leachables in the drug product are not missed from detection. The Applicant confirmed that they will do this accordingly.

The Applicant asked FDA if it is acceptable to change the (b) (4) (b) (4) test to the (b) (4) test. FDA said this change would be acceptable but asked the Applicant to submit an amendment to the BLA to update the (b) (4) method and submit a qualification report for the (b) (4) testing. The Applicant agreed and stated they anticipate submitting the information within a month and a half.

In addition, the Applicant asked FDA if the review team could expedite the review for the Lot Release Protocols of each batch with a 15-business day approval window. FDA stated that at this time, we cannot commit to completing the review within 15-business days. FDA said the review will most likely be completed within 30-days. FDA clarified that we only expedite reviews if there is a product shortage.

2. Information regarding major safety concerns.

- At this time, no major safety concerns have been identified.

Meeting Discussion for Agenda item 2:

There was no discussion of this question during the meeting.

3. Preliminary Review Committee thinking regarding a.) risk management, b) the potential need for any post-marketing requirement(s) (PMRs), and/or safety-related PMCs, and c.) the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk.

- Risk Evaluation and Mitigation Strategies (REMS) are not anticipated at this time.
- The review of the BLA is on-going. If PMRs are anticipated, we will notify the applicant.

Meeting Discussion for Agenda item 3:

There was no discussion of this question during the meeting.

4. Any information requests sent, and responses not received.

- On March 25, 2024, FDA issued an IR requesting updated efficacy reports/data for the 12 subjects who were ongoing in study CLN-PRO-V005 at time of data cutoff on June 30, 2023; requested an explanation between Extremity Set Flag and Limb Cohort Flag; further information

regarding patient (b) (6) initial injury and specifically, any liver related abnormalities; and time to event graphs for primary patency, secondary patency and mortality. In addition, FDA requested an excel table to document all subjects enrolled in studies CLN-PRO-V005 and CLN-PRO-V017 (ClinicalIR1table.xlsx). FDA asked the applicant to provide responses by April 15, 2024.

Meeting Discussion for Agenda item 4:

The Applicant acknowledged the pending clinical IR and requested clarification regarding the expected contents for the column titled “disrupted” in the excel table. FDA advised that this refers to any loss of HAV integrity such as loss of integrity due to rupture or dehiscence of the anastomosis with adjacent blood vessels. The Applicant was further advised that they may add additional columns as necessary for any distinctions they may wish to make. This table should include data through January 15, 2024.

In addition, the Applicant confirmed that their 120-day safety update is expected to be submitted on April 11, 2024, and will include safety and efficacy data through January 15, 2024, in the same SDTM and ADAM format as the original application. The Applicant also plans to provide follow-up data on extremity vs. non-extremity groups and justifications for patients with no follow-up data.

5. Any new information requests to be communicated.

- CMC plans to ask for additional information regarding reagent identity testing and identity testing validation or qualification data; (b) (4) identity testing; stability of (b) (4) (b) (4) validation information of (b) (4) testing methods; manufacturing and controls of the bioreactor bag and its components (b) (4) narrowing DP release specifications; and DP in-use stability (b) (4)
- As the review continues, new information request(s) will be conveyed as needed.

Meeting Discussion for Agenda item 5:

There was no discussion of this question during the meeting.

6. Proposed date(s) for the Late-Cycle meeting (LCM).

- The Late Cycle Meeting between you and the review committee is scheduled on **May 20, 2024 from 3:00 pm to 4:00 pm ET.**

- We intend to send the Late Cycle meeting materials to you approximately 10 days in advance of the meeting, on **May 10, 2024**.

Meeting Discussion for Agenda item 6:

There was no discussion of this question during the meeting.

7. Updates regarding plans for the AC meeting.

- There are currently no plans for an AC meeting.

Meeting Discussion for Agenda item 7:

There was no discussion of this question during the meeting.

8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates.

Milestones	Date
Communicate Anticipated PMR (if applicable)	June 29, 2024
Communicated PMCs (if applicable) and Start Labeling Negotiations	July 12, 2024
PDUFA Date:	August 10, 2024

Inspection Schedule:

- BIMO inspections are currently pending.
- The Pre-License Inspection will take place from April 1- 5, 2024 at the Humacyte Global, Inc. facility in Durham, North Carolina.

Meeting Discussion for Agenda item 8:

There was no discussion of this question during the meeting.