SeaStar Medical, Inc.
Eric Schlorff, CEO
3513 Brighton Boulevard, Suite 410
Denver, CO 80216

February 21, 2024

Re: BH220740
HUD Number: DEV-2019-434
Trade/Device Name: Selective Cytopheretic Device (SCD-PED)
Product Code: QZV
Filed: July 1, 2022
Amended: August 11, 2022; August 12, 2022, August 19, 2022; August 29, 2022; September 19, 2022; September 20, 2022; September 27, 2022; September 30, 2022; October 7, 2022; October 11, 2022; October 13, 2022; December 19, 2022; February 21, 2023; March 2, 2023; April 3, 2023; April 11, 2023; May 15, 2023; June 9, 2023; September 26, 2023; October 17, 2023; October 25, 2023; December 8, 2023; December 22, 2023; January 24, 2024; January 26, 2024; January 31, 2024; February 9, 2024; February 13, 2024; February 15, 2024; February 20, 2024 and February 21, 2024.

Dear Eric Schlorff:

The Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) has completed its review of your humanitarian device exemption (HDE) application for the Selective Cytopheretic Device (SCD-PED). This device is indicated to treat acute kidney injury (AKI) in pediatric patients (weight ≥10kg and age ≤22 years) with acute kidney injury (AKI) due to sepsis or a septic condition on antibiotic therapy and requiring renal replacement therapy (RRT). Based upon the information submitted, the HDE is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act).

Expiration dating for this device has been established and approved at three years from the date of sterilization for SCD Tubing Set and at three years from the date of manufacturing for SCD-PED Cartridge.

Continued approval of the HDE is contingent upon the submission of periodic reports, required under 21 CFR 814.126, at intervals of one year (unless otherwise specified) from the date of approval of the original HDE. This report, identified as "Annual Report" and bearing the applicable HDE reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and must include the information required by 21 CFR 814.126.

In accordance with 21 CFR 814.124, an HDE holder is responsible for ensuring that a humanitarian use device (HUD) under an approved HDE is administered only in facilities having institutional review board (IRB) oversight. In addition, approval by an IRB or an appropriate local committee is required before the HUD can be used at a facility, with the exception of emergency use. An HDE holder is also required to maintain records of the names and addresses of the facilities to which the HUD has been shipped, correspondence with reviewing IRBs as well as any other information requested by a reviewing IRB or FDA (21 CFR 814.126(b)(2)).

You have agreed to provide the following non-clinical information **in a report**, which may be followed by an HDE supplement where applicable.

1. **Device Performance Bench Testing:** Bench testing will be conducted to establish the performance of the approved SCD-PED device and used as design controls to support any potential future changes to the device. The test protocol will include, but will not be limited to, description and justification of the test methods (including how the test parameters are representative of the clinical conditions of use) and acceptance criteria. The data in the test report will demonstrate the performance of the approved SCD-PED device and demonstrate the testing and acceptance criteria are acceptable to use for design controls.

   The study milestones are as follows:

   - April 21, 2024: Final Study Protocol
   - August 21, 2024: Final Study Report

2. In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

A Humanitarian Device Exemption (HDE) Surveillance Registry: The surveillance registry will be carried out to collect safety data on clinical use of SCD-PED under the HDE. The study outcomes include new (secondary) blood stream infections within 28 days from the time of SCD-PED initiation or through hospital discharge, whichever is sooner. All patients initiated on SCD-PED therapy under the HDE-approved indication will be enrolled into the surveillance registry. A closely matched comparator cohort will be identified from the Worldwide Exploration of Renal Replacement Outcomes Collaborative in Kidney Disease (WE-ROCK) registry. A minimum of 300 patients will be enrolled in the registry within two years from the HDE approval. All patients will be followed for 90 days following treatment.

The study milestones are as follows:

- Final Study Protocol: February 20, 2024 (submitted)
- From the date of study protocol approval, you must meet the following timelines for
  - First subject enrolled within 6 months: August 20, 2024
  - 20% of subjects enrolled within 12 months: February 20, 2025
  - 50% of subjects enrolled within 18 months: August 20, 2025
  - 100% of subjects enrolled within 24 months: February 20, 2026
- Study Completion date: May 30, 2026
- Final Study Report: August 31, 2026

PAS Progress Reports must be submitted every six months from the date of the HDE approval letter, unless otherwise specified by FDA. The Final PAS Report should be submitted no later than three (3) months after study completion.

Each PAS report should be submitted to the address below identified as an "HDE Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable HDE reference number.

Be advised that failure to comply with any post-approval requirement, including the SCD-PED Surveillance Registry and Device Performance Bench Testing constitutes grounds for FDA withdrawal of approval of the HDE in accordance with 21 CFR 814.118(a) and 21 CFR 814.126.

Be advised that protocol information, interim, and final results will be published on the Post-Approval Studies Program Database Webpage, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

In addition, the results from any post approval study should be included in the labeling as these data become available. Under 21 CFR 814.108, any updated labeling must be submitted to FDA in the form of an HDE Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by Premarket Approval Application Order" (https://www.fda.gov/media/71327/download).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For more information on these requirements, please see the UDI website available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production and process controls (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Before making any change affecting the safety or probable benefit of the HDE device, you must submit an HDE supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.108 and 814.39 except a request for a new indication for use of a humanitarian use device (HUD). A request for a new indication for use for an HUD shall comply with the requirements set forth in 21 CFR 814.110 which includes obtaining a new designation of HUD status for the new indication for use and submission of an original HDE application in accordance with §814.104. The application for the new indication for use may incorporate by reference any information or data previously submitted to the agency.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or post-marketing safety reporting (21 CFR Part 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product post-marketing safety reporting is available at https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products.

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing safety reporting requirements (21 CFR Part 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

FDA has determined that this device meets the conditions of either (I) or (II) under section 520(m)(6)(A)(i) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This device may be

sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (i.e., for profit) as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). The ADN for this device is determined to be (b) (4). You must immediately notify the agency whenever the number of devices shipped or sold in a year exceeds the ADN; we recommend submitting this information in an HDE report (See section 520(m)(6)(A)(iii)). FDA may also inspect the records relating to the number of your devices distributed during any calendar year. See section 520(m)(6)(B) of the FD&C Act. If you notify the FDA that the ADN has been exceeded, or if FDA discovers through an inspection that the ADN has been exceeded, then you are prohibited to sell your device for profit for the remainder of the year. See section 520(m)(6)(D) of the FD&C Act. If additional information arises regarding the ADN for your device, you may submit an HDE supplement (21 CFR 814.108) requesting that FDA modify the ADN based upon this additional information. See section 520(m)(6)(C) of the FD&C Act.

This device is indicated and labeled for use in pediatric patients or in a pediatric subpopulation and is permitted by FDA to be sold for profit in accordance with section 520(m)(6)(A)(i)(1) of the FD&C Act, and therefore will be subject to annual review by the agency's Pediatric Advisory Committee (PAC). As stated in section 520(m)(8) of the FD&C Act, the PAC annually reviews all HUDs described in section 520(m)(6)(A)(i)(1) of the FD&C Act, which are HUDs approved under an HDE that are intended for the treatment or diagnosis of a disease or condition that occurs in pediatric patients or in a pediatric subpopulation, and such device is labeled for use in pediatric patients or in a pediatric subpopulation in which the disease or condition occurs, and that are exempt from the profit prohibition, in accordance with section 520(m)(6) of the FD&C Act. See section 520(m)(8) of the FD&C Act, as amended by FDASIA.

The PAC reviews these devices to ensure that the HDE remains appropriate for the pediatric populations for which it is approved, in accordance with 520(m)(2) of the FD&C Act. The requirements under section 520(m)(2) of the FD&C Act include that (1) the target population of the device not more than 8,000 individuals in the United States; (2) the device would not be available to a person with the disease or condition without the HDE and there is no comparable device to available to treat or diagnose such disease or condition; and (3) the device does not expose patients to an unreasonable risk or significant risk of illness or injury and the probable benefit to health from the use of the device outweighs risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. The PAC will also conduct periodic review of adverse events for this device.

CBER does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading. CBER will notify the public of its decision to approve your HDE by making available, among other information, a summary of the safety and probably benefit data upon which the approval is based. The information can be found at https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/premarket-approvals-and-humanitarian-device-exemptions-supporting-documents . Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the HDE number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may

seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a HDE. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit a Product Correspondence to this HDE submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the Product Correspondence.

All required documents should be submitted in the same manner as your original submission to either the CBER Document Control Center at https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/regulatory-submissions-electronic-and-paperor the Electronic Submission Gateway at https://www.fda.gov/electronic-submissions-gateway. Failure to submit an electronic correspondence in the format originally submitted may result in processing delays.

If you have any questions concerning this approval order, please contact Shalini Seetharaman at (240) 672-8158 or Shalini.Seetharaman@fda.hhs.gov or Hosna Keyvan at (240) 762- 8645 or Hosna.Keyvan@fda.hhs.gov.

Sincerely,

Nicole Verdun, MD
Director
Office of Therapeutic Products
Center for Biologics Evaluation and Research