Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research

MEMORANDUM

From:	Shaokui Wei, MD, MPH Epidemiologist, Pharmacovigilance Branch 3 (PB3) Division of Pharmacovigilance (DPV) Office of Biostatistics and Pharmacovigilance (OBPV) Center for Biologics Evaluation and Research (CBER)
To:	Craig Zinderman, MD, MPH Associate Director for Medical Policy, OBPV, CBER
Through:	Meghna Alimchandani, MD Acting Director, DPV, OBPV, CBER
Subject:	Safety and Utilization Review for the Pediatric Advisory Committee (PAC)
Applicant:	SeaStar Medical
Product:	Selective Cytopheretic Device for Pediatrics (SCD-PED)
STN:	HDE# BH 220740.12
Indication:	Intended to treat 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 continuous kidney replacement therapy (CKRT)
Meeting Date:	Pediatric Advisory Committee Meeting, November 2025

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I. INTRODUCTION

In accordance with the Pediatric Medical Device Safety and Improvement Act, this review provides a safety update for the Pediatric Advisory Committee (PAC), based on the postmarket experience with the use of a humanitarian use device, Selective Cytopheretic Device for Pediatrics (SCD-PED), manufactured by SeaStar Medical with the trade name, QUELIMMUNE. This review provides updated postmarket safety data, so the Committee can advise the Food and Drug Administration (FDA) on potential safety concerns associated with the use of this device in children. This memorandum documents FDA's complete evaluation, including review of postmarket medical device reporting (MDR) of adverse events, annual reports from the manufacturer, post-approval study report, and the peer-reviewed literature associated with the device.

II. BACKGROUND

Acute Kidney Injury (AKI) may become a critical and life-threatening condition that profoundly affects pediatric patients, particularly those in the pediatric intensive care unit (PICU) requiring Continuous Kidney Replacement Therapy (CKRT) and those with concomitant sepsis or a septic condition. The confluence of sepsis and AKI in children presents a particularly challenging clinical scenario, marked by a heightened risk of poor outcomes, including increased mortality rates.

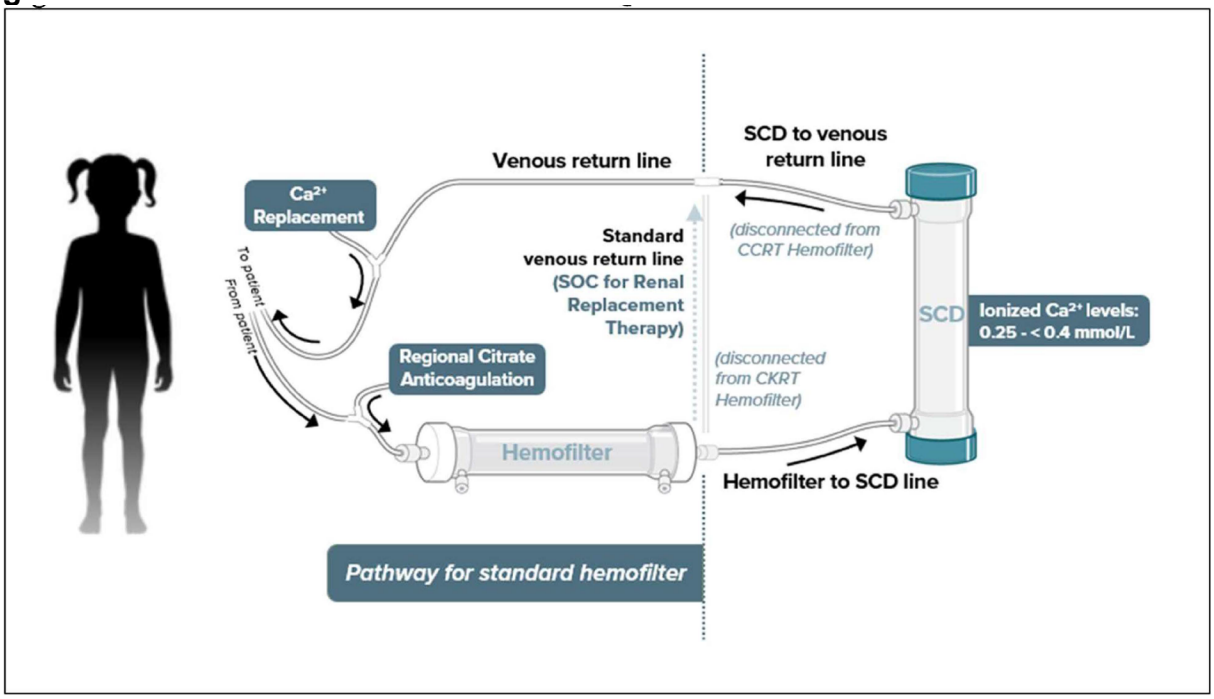
Patients with AKI experience a systemic inflammatory response with activated circulating leukocytes playing a central role in this process. The response includes increased production of cytokines, activation of polymorphonuclear leukocytes (PMNs), and increased expression of leukocyte adhesion molecules, which further contributes to AKI and other organ dysfunction.

Pediatric sepsis associated AKI is characterized by a dysregulated immune response, systemic inflammation, and endothelial dysfunction, all of which contribute to the historically poor outcomes observed in this population.

III. DEVICE DESCRIPTION

The SCD-PED is comprised of tubing, connectors, and a synthetic hollow-fiber membrane cartridge. The SCD-PED is connected in-line to an existing, commercially available CKRT circuit device as outlined in Figure 1 below. After the CKRT hemofilter, blood is diverted to the extra capillary space (ECS) of the SCD. Blood circulates through this space, and then returns to the patient via the venous return line of the CKRT circuit. Of note, the blood flow path in the SCD-PED is non-sterile. A therapeutic post-cartridge ionized calcium level (of < 0.40 mmol/L for > 90% of treatment time) is achieved with Regional Citrate Anticoagulation (RCA) for the entire CKRT and SCD blood circuits.

Figure 1: Schematic of the CKRT circuit and SCD-PED



The diagram illustrates the technical configuration and flow pathways used in advanced renal replacement therapy, specifically showing how the SCD-PED system integrates with standard CKRT equipment to provide enhanced treatment capabilities for patients requiring intensive kidney support. The CKRT circuit displayed has the following components: a line representing the pathway for blood flow from the patient to the hemofilter followed by a line for the venous return for blood flow back to the patient in standard CKRT equipment; for SCD therapy, there is a line for blood flow from the patient to the SCD cartridge, a specialized component for enhanced detoxification therapy, and the venous return line from the SCD cartridge back to the patient; and multiple interconnected lines and connections that facilitate the flow of blood and dialysate through the treatment system.

The SCD-PED cartridge incorporates a synthetic hollow fiber membrane which can bind activated leukocytes to its extracapillary surface.

Patients with AKI can experience cytokine storm and hyperinflammation from activated neutrophils that can release cytokines and other pro-inflammatory mediators, which may worsen clinical outcomes. The fiber membrane lining the walls of the cartridge, together with the low ionized calcium level is intended to promote binding of activated neutrophils and monocytes to the fibers, resulting in overall decrease in inflammatory mediators.

IV. INDICATIONS FOR USE

The SCD-PED is intended to treat 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 continuous kidney replacement therapy (CKRT).

V. REGULATORY HISTORY

The pediatric clinical study SCD-PED-01 to support this Humanitarian Device Exemption (HDE) was approved to proceed under investigational device exemption (IDE # G150179) on September 15, 2015, by the Center for Devices and Radiological Health (CDRH)[1]. CDRH had original jurisdiction over the HDE, and the study was conducted in accordance with 21 CFR Parts 50, 56, and 812.

The IDE was subsequently transferred to Center for Biologics Evaluation and Research (CBER) in October 2021, based on determination that the device output includes more than minimally manipulated biologic products (leukocytes).

The SCD-PED was approved in the US on February 21, 2024. The initial approval letter (BH220740/0) included the following conditions of approval (CoA):

> "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"

VI. ANNUAL DISTRIBUTION NUMBER/ANNUAL SALES NUMBERS

Section 520(m)(6)(A)(ii) of the FD&C allows HDEs indicated for pediatric use to be

[1] This started as a pilot study and then changed to pivotal study for HDE after HUD was granted in June 2020.

sold for profit as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN).

The currently approved ADN for SCD-PED is [redacted] SCD-PED sets. The ADN was calculated as [redacted] SCD-PED sets x 8,000 individuals = [redacted] SCD-PED sets; where the SCD-PED sets is derived from [redacted] of therapy where the cartridge and tubing set are replaced every 24 hours (the duration of use for the SCD-PED device ranged from 1-7 days and the SCD-PED Cartridge and SCD blood tubing set are to be replaced every 24 hours of use throughout the duration of therapy); 8000 individuals represent the target population per the HDE definition at the time the labeling was approved (February 2024).

The number of SCD-PED sets distributed has not exceeded the ADN. The number of SCD-PED sets distributed during:

- Calendar year 2024: [redacted] sets
- Calendar year 2025: Not yet available, however, from January 1, 2025, through June 30, 2025, SeaStar distributed [redacted] sets

Note: These estimates were provided by the manufacturer for FDA review. Distribution data is protected as confidential commercial information and may require redaction from this review.

During the PAC review period, February 21, 2024, to June 30, 2025, [redacted] pediatric patients and [redacted] adult were treated with SCD-PED.

VII. LABEL CHANGES IN REVIEW PERIOD

There were no safety related label changes during the PAC review period (February 21, 2024, to June 30, 2025).

VIII. MEDICAL DEVICE REPORTS (MDRs)

A. Strengths and Limitations of MDR Data

The FDA receives MDRs of suspected device-associated deaths, serious injuries, and malfunctions from mandatory reporters (manufacturers, importers, and device user facilities) and voluntary reporters such as health care professionals, patients, and consumers. The FDA uses MDRs to monitor device performance, detect potential device-related safety issues, and contribute to benefit-risk assessments of these products.

MDR reports can be used to:

- Establish a qualitative snapshot of adverse events for a device or device type
- Detect actual or potential device problems including:
    - rare or unexpected adverse events;
    - adverse events that occur during long-term use;
    - adverse events associated with vulnerable populations;
    - off-label use; and use error.

Although MDRs are a valuable source of information, this Medical Device Reporting is a passive surveillance system and has limitations, including the submission of incomplete, inaccurate, untimely, unverified and/or additionally biased data. In addition, the incidence of an event cannot be determined from MDRs alone due to under-reporting of events and lack of information about frequency of device use.

Limitations of MDRs include:

- MDR data alone cannot be used to establish rates of events, evaluate a change in event rates over time, or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices.
- Confirming whether a device actually caused an event can be difficult based solely on information provided in MDRs. Establishing a cause-and-effect relationship is especially difficult if circumstances surrounding the event have not been verified or if the device in question has not been directly evaluated.
- MDR data is subjected to reporting bias due to, reporting practices, increased media attention, and/or other agency regulatory actions.
- MDR data does not represent all known safety information for a reported medical device and should be interpreted in the context of other available information when making device-related or treatment decisions.

B. MDRs Associated with SPC-PED

The MDR database was searched on July 9, 2025, to identify postmarket adverse event reports associated with the use of SPC-PED submitted to FDA during the PAC review period, February 21, 2024, to June 30, 2025. There were no MDRs identified in FDA Manufacturer and User Facility Device Experience (MAUDE) database.

IX. ANNUAL REPORT REVIEW

The sponsor's first annual report was received on February 21, 2025, which covered the 1-year reporting period following the HDE approval (February 21, 2024).

The annual report states that the sponsor has not received any reports of device-related events, as of the date of the report (2/21/2025). Additionally, the report notes that there

has been [redacted] treated under Emergency Use at [redacted] Hospital. According to the report, this patient has improved clinically and continues to do well.

Reviewer comments: There was no safety concern identified in the reporting period.

X. POST-APPROVAL STUDY (PAS) REPORT REVIEW

SeaStar Medical is conducting a PAS per the requirements set forth in the February 21, 2024, HDE Approval Order for HDE Surveillance Registry (see Section V Regulatory History). This study is an observational registry of patients who are treated with QUELIMMUNE as part of routine clinical care for their condition. The study is currently in delayed status due to challenges with patient enrollment and study updates related to enrollment are under ongoing FDA review. As of the sponsor's most recent progress report, received August 20, 2025, there were no adverse events related to QUELIMMUNE reported. There were no secondary bloodstream infections reported as adverse events.

XI. POSTMARKET LITERATURE REVIEW

A PubMed literature search conducted on July 10, 2025, using the search term "QUELIMMUNE" OR "Selective Cytopheretic Device for Pediatrics" for articles published between February 21, 2024, and June 30, 2025, retrieved 5 articles (listed below). Titles and abstracts were reviewed for relevance to safety information specifically for SCD-PED and its labeled indication. No new safety concern was identified.

Article	**Author's conclusions**
1: Goldstein SL, Ollberding NJ, Askenazi DJ, et al. Selective Cytopheretic Device Use in Continuous Kidney Replacement Therapy in Children: A Cohort Study With a Historical Comparator. Kidney Med. 2024 Feb 15;6(4):100792.	The authors report aggregate data from two pediatric studies using the SCD to support critically ill children with AKI, multi-organ dysfunction syndrome who received CRRT as part of their standard of care. Twenty-two patients received CRRT-SCD treatments. Fifteen serious adverse events were recorded; none were SCD-related as per the authors.
2: Goldstein SL, Humes HD. Current Experience Using the Selective Cytopheretic Device for Continuous Immunomodulation in Acute Kidney	This article reviews the history of the SCD and use experience, from discovery to preclinical testing to translational research application at the bedside. It discusses the SCD mechanism of

Article	Author's conclusions
Injury and Multiorgan Failure. Blood Purif. 2025 May 3.	action, its immunomodulatory effect, and the human studies involving critically ill adult pediatric patients with AKI who require CKRT as part of the standard of care.
3: Pino CJ, Johnston KA, Westover AJ, Humes HD. Selective Cytopheretic Device (QUELimmune): A Leukocyte Processing, Immunomodulatory Device. J Am Soc Nephrol. 2025 Jan 1;36(1): 144-146.	This article describes the SCD (QUELimmune) approved by FDA for pediatric patients with acute kidney injury (AKI) requiring CKRT.
4: Iyer SPN, Pino CJ, Yessayan LT, et. Al. Increasing Eligibility to Transplant Through the Selective Cytopheretic Device: A Review of Case Reports Across Multiple Clinical Conditions. Transplant Direct. 2024 May 16;10(6): e1627.	This article presents 4 patients with improved eligibility for transplantation and device implantation through use of the SCD: a pediatric patient with hemophagocytic lymphohistiocytosis who successfully underwent stem cell transplant, two adults with hepatorenal syndrome who became eligible for liver transplantation, and an adult with cardiorenal syndrome who qualified for left ventricular assist device implantation.
5: Humes HD, Luckritz K, Gorga S, et.al. Management dilemma in choosing evolving treatments in neutropenic septic shock. Pediatr Nephrol. 2025 Jun 21.	This case report describes a 10-year-old kidney transplant recipient with Burkitt lymphoma who developed neutropenic septic shock with multiorgan failure and a 95% mortality risk. The authors state that after initial SCD treatment followed by therapeutic plasma exchange, continued SCD therapy led to significant improvements in inflammatory markers, organ function recovery, and patient survival to discharge.

XII. SUMMARY

FDA did not identify new safety signals during this comprehensive postmarketing safety review that included review of the manufacturer's annual report, the PAS report, and the literature published during the PAC review period. There were no

MDRs received by FDA during this review period. The HDE for this device remains appropriate for the pediatric populations for which it was granted. FDA will continue routine monitoring of the safety and distribution data for this device.