November 6, 2023

STEMCELL Technologies Canada Inc.
Jason Peng
Associate Director, Regulatory Affairs
1618 Station Street
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Canada

Re: DEN220090
Trade/Device Name: EasySep Human Bone Marrow CD138 Positive Selection Kit
Regulation Number: 21 CFR 866.6120
Regulation Name: Hematopoietic cell enrichment kit
Regulatory Class: Class II
Product Code: QYO
Dated: December 7, 2022
Received: December 12, 2022

Dear Jason Peng:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the EasySep Human Bone Marrow CD138 Positive Selection Kit, a prescription device with the following indications for use:

> EasySep Human Bone Marrow CD138 Positive Selection Kit is an in vitro diagnostic device intended to enrich CD138+ cells from bone marrow collected from patients diagnosed with multiple myeloma. The CD138+ cells are enriched by immunomagnetic positive selection for use in validated downstream assays. The end-user is responsible for validation of this kit for use with the assay. For in vitro diagnostic use by laboratory professionals.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the EasySep Human Bone Marrow CD138 Positive Selection Kit, and substantially equivalent devices of this generic type, into Class II under the generic name hematopoietic cell enrichment kit.

FDA identifies this generic type of device as:

> **Hematopoietic cell enrichment kit.** A hematopoietic cell enrichment kit is an in vitro diagnostic device intended for the selection and enrichment of specific hematopoietic cells from human whole blood and/or bone marrow collected from patients with hematological malignancies using immunomagnetic bead-based selection. It is intended for use with diagnostic assays as part of the pre-analytical workflow.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On December 12, 2022, FDA received your De Novo requesting classification of the EasySep Human Bone Marrow CD138 Positive Selection Kit. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the EasySep Human Bone Marrow CD138 Positive Selection Kit into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the EasySep Human Bone Marrow CD138 Positive Selection Kit can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Risks to Health	Mitigation Measures
Failure to perform as expected due to errors in enrichment, contributing to false positive or false negative results, or failure to produce results in downstream assays	Use of certain specimen collection devices. Certain design verification and validation, including certain studies and risk mitigation analysis. Certain labeling information, including limitations, device descriptions, methodology and protocols, and performance information.
Incorrect interpretation of enrichment results by the lab	Certain labeling information, including limitations, device descriptions, methodology and protocols, and performance information. Certain design verification and validation, including certain studies and risk mitigation analysis.

In combination with the general controls of the FD&C Act, the hematopoietic cell enrichment kit is subject to the following special controls:

(1) Any sample collection device used must be FDA-cleared, -approved, or -classified as 510(k) exempt (standalone or as part of a test system) for the collection of the sample types with which this device is intended to be used; alternatively, the sample collection device must be cleared in a premarket submission as a part of this device.

(2) The intended use statement must include:
  (i) The intended use specimen type (e.g., human whole blood and/or bone marrow) for each malignancy for which acceptable enrichment has been demonstrated and documented using the minimum volume required to ensure a 95% accurate call rate when the cell concentration is at the limit of detection, per the device labeling.
  (ii) A detailed description of the cell enrichment target(s).
  (iii) A statement that the end-user is responsible for validation of this device for use with the assay.

(3) The labeling required under 21 CFR 809.10(b) must include:
  (i) Detailed specifications and procedures, appropriately supported by replicate and stability data, for sample collection, processing, and storage, including acceptable ranges of deviation.
  (ii) A detailed device description, including all device parts (e.g., instruments and associated user manuals, antibody(ies), reagents, and consumables) and their use within the enrichment procedure.
  (iii) Prominent and conspicuous limiting statements clearly explaining:
    (A) Any end user validation required for use with specific tests and collection devices.
    (B) Bone marrow stability is severely compromised after 48 hours (or, alternatively, a different timeframe supported by appropriate specimen stability data under paragraph (4)(i)(E)).
    (C) The device is intended only for enriching hematopoietic cell specimens for use in further processing or analysis using additional independent methods.
    (D) Results from the device do not provide information regarding any health conditions.
    (E) The device is not intended for cell enumeration.
    (F) A detailed summary of the studies required under paragraph (4).

(4) Design verification and validation must include:
  (i) Detailed documentation of the following studies for each intended specimen type and malignancy combination, including the study protocols containing descriptions of the test methods, prescribed methods of data analysis and acceptance criteria, final study reports, and data line listings:
    (A) Recovery study data demonstrating the range of the device.
    (B) A study demonstrating the device limit of detection by demonstrating the minimum number of cells within a prespecified volume that the device is capable of enriching and the percent enrichment when the concentration of cells is established, using a flow cytometry reference method determined to be acceptable by FDA.
    (C) A study demonstrating device reproducibility, including multiple operators at each site using the specified enrichment method(s) and protocol. The evaluation must include multiple runs, different instruments, and three different reagent lots. The study must include specimens with low, medium, and high starting enrichment target levels and result in enrichment and acceptable precision at each level. The study must include specimens containing different genetic alterations representative of the cancer indication or condition.
    (D) A study demonstrating device specificity, including interference, to evaluate the impact on cell enrichment.

(E) Studies performed to support the stability of samples using the indicated specimen collection method(s) under various storage times, as applicable.

(ii) Detailed documentation of studies performed to demonstrate on-board and in-use reagent stability, including studies to demonstrate reagent shelf life.

(iii) A shipping stability study, separate from the on-board and in-use reagent stability study, must be performed that demonstrates acceptable stability of the parts that comprise the device.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the hematopoietic cell enrichment kit they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD&C Act; 21 CFR 1000-1050).

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-

regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Allen Williams at 301-796-4806.

Sincerely,

Donna M. Roscoe -S

Donna Roscoe, Ph.D.
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