



ANGLE Europe Ltd.  
Martin Cooke  
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May 24, 2022

Re: DEN200062  
Trade/Device Name: Parsortix® PC1 Device  
Regulation Number: 21 CFR 866.6110  
Regulation Name: Circulating tumor cell enrichment device  
Regulatory Class: Class II  
Product Code: QSA  
Dated: September 25, 2020  
Received: September 28, 2020

Dear Martin Cooke:

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 Parsortix PC1 Device, a prescription device with the following indications for use:

The Parsortix® PC1 system is an in vitro diagnostic device intended to enrich circulating tumor cells (CTCs) from peripheral blood collected in K<sub>2</sub>EDTA tubes from patients diagnosed with metastatic breast cancer. The system employs a microfluidic chamber (a Parsortix cell separation cassette) to capture cells of a certain size and deformability from the population of cells present in blood. The cells retained in the cassette are harvested by the Parsortix PC1 system for use in subsequent downstream assays. The end user is responsible for the validation of any downstream assay. The standalone device, as indicated, does not identify, enumerate or characterize CTCs and cannot be used to make any diagnostic/prognostic claims for CTCs, including monitoring indications or as an aid in any disease management and/or treatment decisions.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Parsortix PC1 Device, and substantially equivalent devices of this generic type, into Class II under the generic name circulating tumor cell enrichment device.

FDA identifies this generic type of device as:

**Circulating tumor cell enrichment device.** A circulating tumor cell enrichment device is an in vitro diagnostic device used to enrich circulating tumor cells from the peripheral blood of patients diagnosed with cancer for subsequent in vitro diagnostic testing.

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 September 28, 2020, FDA received your De Novo requesting classification of the Parsortix PC1 Device. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Parsortix PC1 Device 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, has determined that, for the previously stated indications for use, the Parsortix PC1 Device 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:

Identified Risks to Health	Mitigation Measures
Failure to identify CTCs that are present in the sample leading to delays in patient management.	<ul style="list-style-type: none"> <li>• Use of certain specimen collection devices identified in special control (1).</li> <li>• Certain labeling information identified in special control (2), including limitations, device descriptions, training specifications, explanation of procedures, and performance information identified in special control (3).</li> <li>• Certain design verification and validation identified in special control (3), including documentation of certain analytical studies and clinical studies.</li> </ul>
No results obtained using downstream testing leading to delays in patient management.	<ul style="list-style-type: none"> <li>• Certain labeling information identified in special control (2), including limitations, device descriptions, training specifications, explanation of procedures, and performance information identified in special control (3).</li> </ul>
Incorrect evaluation of CTCs using downstream analyses leading to associated risk of false test results and improper patient management.	<ul style="list-style-type: none"> <li>• Certain labeling information identified in special control (2), including limitations, device descriptions, explanation of procedures, and performance information identified in special control (3).</li> </ul>

Identified Risks to Health	Mitigation Measures
Failure to correctly operate the device leading to delays in patient management and associated risk to downstream analyses resulting in false test results and improper patient management.	<ul style="list-style-type: none"> <li>• Certain labeling information identified in special control (2), including limitations, device descriptions, and explanation of procedures.</li> </ul>
Bloodborne pathogen transmission from blood waste/blood sample	<ul style="list-style-type: none"> <li>• Certain labeling information identified in special control (2), including limitations, device descriptions, and explanation of procedures.</li> </ul>

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

1. Any device used for specimen collection and transport must be FDA-cleared, -approved, or -classified as 510(k) exempt for the collection of human specimens; alternatively, the sample collection device must be cleared in a premarket submission as a part of this device.
2. The labeling required under 21 CFR 809.10(b) must include:
  - i. Detailed specifications and procedures for sample collection, processing, and storage.
  - ii. An intended use statement that includes:
    - (A) The intended specimen type(s) for which acceptable, as determined by FDA, validation data has been provided (e.g., peripheral whole blood).
    - (B) The identification of, or the specifications for, the collection device or devices to be used for sample collection.
    - (C) Information on the device output(s) (e.g., circulating tumor cells (CTCs), other blood cells, etc.).
    - (D) The specific tumor type(s) for which the device is intended to be used.
    - (E) A statement for general downstream diagnostic assays and that end users need to validate use with any subsequent tests and collection devices.
    - (F) A statement that the standalone device is not intended for diagnostic, prognostic, or monitoring use with CTCs, including as an aid in any disease management and/or treatment decisions.
  - iii. Prominent and conspicuous limiting statements clearly explaining:
    - (A) The use of the device is intended for the collection of CTCs from previously diagnosed cancer patients.
    - (B) The standalone device is not intended for cell enumeration.
    - (C) The users for whom the device is intended, including any training specifications.
    - (D) The performance characteristics of this device have not been established for general downstream diagnostic assays and that end users need to validate use with any subsequent tests and collection devices.
    - (E) An insufficient number of CTCs or even no circulating tumor cells may be collected.
    - (F) Results from the standalone device do not provide information to the patient regarding their current state of health.
    - (G) The standalone device does not diagnose any health conditions and is not a substitute for visits to a doctor or other healthcare professional.

- (H) The device is intended only for enriching CTC content in specimens so that the enriched specimens can then be used in further processing/analysis using additional independent methods.
  - (I) The variability of the number of CTCs and other cells harvested by the device may impact the success of any subsequent analysis.
  - iv. A troubleshooting section that includes clear instructions for resolving any common device-related issues.
  - v. A description of the device mechanism of action to enrich CTCs.
  - vi. A detailed summary of the analytical and clinical performance studies required under paragraph (3).
3. Design verification and validation must include the following:
- i. Documentation of studies that provide:
    - (A) Data demonstrating acceptable, as determined by FDA, analytical device performance using samples representative of the range of those with which the device is intended for use. The number of specimens tested must be sufficient to obtain estimates of device performance that is representative of the device performance within the full spectrum of the device's intended use.
    - (B) Data demonstrating acceptable precision, as determined by FDA, to adequately evaluate intra-run, inter-run, and total variability across operator, instrument, lot, day, and site, as applicable.
    - (C) Data demonstrating the detection limit of the device.
    - (D) Recovery study data demonstrating the range of the device.
    - (E) Data demonstrating appropriate validation of device design features and specifications such that it has been demonstrated that the device reproducibly and reliably collects and isolates CTCs. At a minimum, the data must include:
      - 1) Data, as appropriate for the intended use, including estimates of within-lot, within-device, and lot-to-lot variability, demonstrating that samples collected from the intended use population using the device provide CTCs that are suitable, as determined by FDA, for the intended downstream testing.
      - 2) Data demonstrating that the device output has no contamination or minimal levels of contamination from other sources, and that any such contamination does not interfere with the recovery of CTCs.
      - 3) Data demonstrating that the presence of clinically relevant levels of potential interfering substances in the intended specimen type(s) and intended use population, including endogenous and exogenous substances, does not interfere with the recovery of CTCs.
      - 4) Data demonstrating that blood samples collected for use with the device remain stable under certain storage conditions (e.g., temperature, time, etc.) and do not impact the output of representative downstream testing.
  - ii. Documentation of clinical studies using the device on intended use clinical specimens that demonstrate the device can enrich or capture an appropriate number of CTCs, as determined by FDA, to support the intended use of 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](mailto: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 Circulating tumor cell enrichment device 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](mailto: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 Timothy Schaefer at 301-796-6886.

Sincerely,

Wendy Rubinstein, MD, PhD  
Acting Director, Division of Molecular Genetics and  
Pathology  
Director, Personalized Medicine  
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OHT7: Office of In Vitro Diagnostics  
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