August 01, 2024

Personal Genome Diagnostics, Inc.
Jennifer Dickey, Ph.D., RAC
Head, Regulatory & Quality
3600 Boston Street
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Re: DEN230046
Trade/Device Name: PGDx elio plasma focus Dx
Regulation Number: 21 CFR 866.6085
Regulation Name: High throughput sequencing based tumor profiling test of circulating cell-free nucleic acids
Regulatory Class: Class II
Product Code: SBY
Dated: June 30, 2023
Received: June 30, 2023

Dear Dr. Jennifer Dickey:

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 PGDx elio plasma focus Dx, a prescription device under 21 CFR Part 801.109 with the following indications for use:

> PGDx elio plasma focus Dx is a qualitative next generation sequencing-based *in vitro* diagnostic device that uses targeted high throughput hybridization-based capture technology for detection of single nucleotide variants (SNVs), insertions and deletions (indels), copy number amplifications (CNAs), and translocations in human genomic circulating cell-free DNA (cfDNA) on the Illumina NextSeq 550Dx instrument. PGDx elio plasma focus Dx utilizes cfDNA from plasma of peripheral whole blood collected in Streck Cell-Free DNA blood collection tubes (BCTs). PGDx elio plasma focus Dx is a tumor mutation profiling test intended to provide information on mutations to be used by qualified health care professionals in accordance with professional guidelines in oncology for cancer patients with solid malignant neoplasms. The test is for use with patients previously diagnosed with cancer and in conjunction with other laboratory and clinical findings. A negative result from a plasma specimen does not assure that the patient's tumor is negative for genomic findings. Genomic findings are not prescriptive or conclusive for use of any specific therapeutic product.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the PGDx elio plasma focus Dx, and substantially equivalent devices of this generic type, into Class II under the generic name high throughput sequencing based tumor profiling test of circulating cell-free nucleic acids.

FDA identifies this generic type of device as:

> **High throughput sequencing based tumor profiling test of circulating cell-free nucleic acids.** A high throughput sequencing based tumor profiling test of circulating cell-free nucleic acids is a qualitative in vitro diagnostic test intended for next generation sequencing analysis of circulating cell-free nucleic acids from plasma samples collected from peripheral whole blood to detect mutations in a panel of targeted genes to aid in the management of previously diagnosed cancer patients by qualified health care professionals. The results of the test are not prescriptive or conclusive for use of any specific therapeutic product.

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 June 30, 2023, FDA received your De Novo requesting classification of the PGDx elio plasma focus Dx. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the PGDx elio plasma focus Dx 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 PGDx elio plasma focus Dx 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
Risk of false positive, false negative, or failure to provide a result.	Certain design verification and validation activities, including certain analytical studies Certain labeling information, including certain performance information
Incorrect interpretation of test results by the user	Certain design verification and validation activities, including certain analytical studies Certain labeling information, including certain performance information

In combination with the general controls of the FD&C Act, the high throughput sequencing based tumor profiling test of circulating cell-free nucleic acids is subject to the following special controls:

(1) Design verification and validation must include:
  (i) Information demonstrating analytical validity of the device according to analytical performance characteristics, evaluated either specifically for each gene/mutation or, when clinically and practically justified, using a representative approach based on other mutations of the same type, including:
    (A) Data that adequately supports the intended specimen type, specimen handling protocol, and nucleic acid purification.
    (B) A summary of the empirical evidence obtained to demonstrate how the analytical quality metrics and thresholds were optimized.
    (C) Detailed documentation of analytical performance studies conducted as appropriate to the technology, specimen types tested, and intended use of the device, including: accuracy, limit of detection, precision, nucleic acid input concentration range, and device stability.
  (ii) Information that adequately supports the clinical significance of the panel must include:
    (A) A description of the criteria (e.g., types and levels of evidence) used to establish the clinical significance of each mutation.
    (B) A description of the clinical evidence associated with each mutation with references, such as clinical evidence presented in professional guidelines and peer-reviewed publications.
  (iii) For devices with a predetermined change control plan (PCCP), include the planned modifications to the device, the risks of the planned modifications and corresponding risk mitigations, and the verification and validation activities, including pre-specified acceptance criteria, that will be performed for specified device modifications.
(2) The labeling required under 21 CFR 809.10, as well as any test report generated, must include the following, as applicable:
  (i) The intended use statement must specify the following:
    (A) A statement that the test is indicated for patients previously diagnosed with cancer.
    (B) A statement that the results of the test are not prescriptive or conclusive for use of any specific therapeutic product.
    (C) The intended specimen type(s) and matrix.
    (D) The mutation types (e.g., single nucleotide variant, insertion, deletion, copy number variation or gene rearrangement) for which validation data has been provided.
    (E) The name of the testing facility or facilities, as applicable.
    (F) The name of the sequencer used.
  (ii) A detailed device description including:
    (A) A description of the test in terms of genomic coverage, as follows:
      (1) A list of all genes, variant types, and target regions within each gene that the device detects.
      (2) A description of any within-gene targeted regions that cannot be reported and the data behind such conclusion.
    (B) A description of the methodology and protocols for each step of the test, including description of the quality metrics, thresholds, and filters at each step of the test that are implemented for final result reporting and a description of the metrics for run-failures, specimen-failures, invalids, as applicable.

(iii) A summary of the information that demonstrates the required analytical performance characteristics of the device.
(iv) A listing of all mutations that are intended to be detected by the device and that are reported in the test results, categorized based on criteria (e.g., levels of evidence) used to establish clinical significance of the mutations.
(v) For devices with a PCCP, labeling related to the PCCP, including:
  (A) A statement that the device has a PCCP;
  (B) A description of planned modification(s) to the device, including validation requirements; and
  (C) A version history, a description of how device modification(s) will be implemented, and a description of how users will be informed of device modification(s) made in accordance with the PCCP.

In addition, this is a prescription device and must comply with 21 CFR 801.109.

FDA's granting of your De Novo request also included the review and authorization of your Predetermined Change Control Plan (PCCP) titled "Pre-defined Change Control Plan for Variant Promotions and Un-masking" version 1. Under 21 CFR 807.81(a)(3), a new premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the authorized PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

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 high throughput sequencing based tumor profiling test of circulating cell-free nucleic acids 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 Part 801); 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 Catherine Fischer at catherine.fischer@fda.hhs.gov.

Sincerely,

Soma Ghosh -S

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