September 19, 2025

Cytocell Limited
Steve Chatters
Executive Vice President of Regulatory, Medical, and Quality Affairs
Oxford Gene Technology, 418 Cambridge Science Park
Milton Road
Cambridge, CB4 0PZ
United Kingdom

Re: DEN240067
Trade/Device Name: KMT2A Breakapart FISH Probe Kit PDx (CDA-LPH013)
Regulation Number: 21 CFR 864.1885
Regulation Name: Revumenib eligibility detection system
Regulatory Class: Class II
Product Code: SFS
Dated: November 22, 2024
Received: November 22, 2024

Dear Steve Chatters:

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 KMT2A Breakapart FISH Probe Kit PDx (CDA-LPH013), a prescription device under 21 CFR Part 801.109 with the following indications for use:

> The CDA-LPH013 KMT2A Breakapart FISH Probe Kit PDx is a fluorescence *in situ* hybridization (FISH) test used to detect rearrangement of the *KMT2A* region on chromosome 11 at location 11q23.3 in 3:1 methanol/glacial acetic acid fixed bone marrow specimens from patients with acute leukemia with *KMT2A* rearrangement.
>
> The assay is indicated for detecting the presence of rearrangements involving the *KMT2A* region as a companion diagnostic to aid in identifying those patients for whom treatment with REVUFORJ® (revumenib) is indicated in accordance with the approved therapeutic product labeling. The CDA-LPH013 KMT2A Breakapart FISH Probe Kit PDx is not intended for monitoring of residual disease.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the CDA-LPH013 KMT2A Breakapart FISH Probe Kit PDx, and substantially equivalent devices of this generic type, into Class II under the generic name revumenib eligibility detection system.

FDA identifies this generic type of device as:

> **Revumenib eligibility detection system**: A revumenib eligibility detection system is identified as a prescription in vitro diagnostic device intended for the qualitative detection of structural abnormalities of chromosome 11 in specimens from patients with acute leukemia for the purpose of identifying patients who may benefit from treatment with revumenib, in accordance with the approved therapeutic product labeling..

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 November 22, 2024, FDA received your De Novo requesting classification of the CDA-LPH013 KMT2A Breakapart FISH Probe Kit PDx. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the CDA-LPH013 KMT2A Breakapart FISH Probe Kit PDx 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, in response to our request for additional information letter dated February 5, 2025, and during interactive review, FDA has determined that, for the previously stated indications for use, the CDA-LPH013 KMT2A Breakapart FISH Probe Kit PDx 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 and clinical studies. Certain labeling information, including certain limitation statements and performance information.
Incorrect interpretation of test results by the user.	Certain design verification and validation activities, including certain analytical studies and clinical studies.

Risks to Health	Mitigation Measures
	Certain labeling information, including certain limitation statements and performance information.

In combination with the general controls of the FD&C Act, the Revumenib eligibility detection system is subject to the following special controls:

(1) Labeling must include:

i. A detailed summary of the analytical and clinical performance testing, including results, as required under paragraph (2).

ii. The following limiting statements, as appropriate:

a. A statement indicating that the test is not intended for monitoring of residual disease, as a prenatal test, or as a population-based screening test;

b. A statement indicating that test results are intended to be interpreted by a qualified professional in conjunction with other diagnostic laboratory test results, and should take into consideration other clinical information.

(2) Design verification and validation must include:

i. Clinical data demonstrating appropriate clinical performance of the device using clinical specimens with structural anomalies of chromosome 11 (e.g., *KMT2A* rearrangements) representative of the intended use population to identify patients for whom revumenib would be effective, as determined to be appropriate by FDA.

ii. Specification of the criteria for test result interpretation and reporting, including device cut-off(s) [i.e., clinical threshold(s) or the medical decision point(s) between positive and negative results] or other relevant criteria that distinguishes positive and negative results. This information must include the rationale for the device cut-off(s) to include the upper reference of normal, or other relevant criteria and results supporting validation of the cut-off(s). Scoring criteria for all applicable signals must be provided.

iii. Device performance data demonstrating appropriate reproducibility of the device. The evaluation must include multiple runs, multiple readers, different days, and different reagent lots. Precision of the device must be evaluated per specimen and in aggregate. If the device will be used at more than one site, data must demonstrate adequate reproducibility across multiple intended use sites. Each site included in this study are required to undergo appropriate training of the device and result interpretation in order to demonstrate proficiency. The performance data must include clinical specimens from the intended use specimen type(s), intended use biomarker(s), and specimens near the clinical decision threshold(s).

iv. Device performance data demonstrating appropriate analytical sensitivity using interphase nuclei from a sufficient number (e.g., 25) of karyotypically normal male specimens and analytical specificity using metaphase chromosomes from a sufficient number (e.g., 5) of karyotypically normal male specimens.

v. Device performance data demonstrating appropriate specimen stability based on the intended use specimen type(s) (e.g., bone marrow) and samples using the indicated specimen collection method(s), as applicable.

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

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 Revumenib eligibility detection system 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.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System Rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

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 Deblina Banerjee at Reviewer Deblina.Banerjee@fda.hhs.gov.

Sincerely,

Soma Ghosh -S

Soma Ghosh, Ph.D.
Acting Director
Division of Molecular Genetics and Pathology
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