Pillar Biosciences, Inc.
% Gabriela Cook-DiDomenico
Vice President, Quality and Regulatory Affairs
Lakeside Life Science
36 Country Club Road, Unit 932
Gilford, NH 03249

July 30, 2021

Re: P200011
Trade/Device Name: ONCO/Reveal™ Dx Lung & Colon Cancer Assay (O/RDx-LCCA)
Product Code: PQP
Filed: February 18, 2020
Amended: October 15, 2020, January 15, 2021 and April 30, 2021

Dear Gabriela Cook-DiDomenico:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the ONCO/Reveal™ Dx Lung & Colon Cancer Assay (O/RDx-LCCA). This device is indicated for:

> The ONCO/Reveal™ Dx Lung and Colon Cancer Assay (O/RDx-LCCA) is a qualitative next generation sequencing based in vitro diagnostic test that uses amplicon-based target enrichment technology for detection of single nucleotide variants (SNVs) and deletions in 2 genes from DNA isolated from formalin-fixed paraffin-embedded (FFPE) non-small cell lung cancer (NSCLC) and colorectal cancer (CRC) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients with NSCLC or CRC who may benefit from treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling. The O/RDx-LCCA is intended to be used on the Illumina MiSeqDx® instrument.

Table 1. List of somatic variants for therapeutic use

Indication	Gene	Variant	Targeted therapy
Colorectal Cancer (CRC)	*KRAS*	*KRAS* wild-type (absence of mutations in codons 12 and 13)	ERBITUX® (cetuximab), or VECTIBIX® (panitumumab)
Non-Small Cell Lung Cancer (NSCLC)	*EGFR*	Exon 19 Deletions and Exon 21 L858R Substitution Mutations	EGFR Tyrosine Kinase Inhibitors approved by FDA*

*For the most current information about the therapeutic products in this group, go to: https://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ucm301431.htm

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below. Although this letter refers to your product as a device, please be aware that some approved products may instead be combination products. The Premarket Approval Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm identifies combination product submissions.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device and insofar as the sale and distribution of the device are restricted to Pillar Biosciences, Inc. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 13 months of shelf life for the O/RDx-LCCA reagent kits at the recommended storage conditions. No significant trend in poorer overall performance with increasing FFPE block age was observed, and robust assay performance was observed for samples over 10 years old in a retrospective analysis. FFPE curls may be stored at ambient conditions for thirty (30) days. DNA extracted from FFPE clinical samples may be stored at eight (8) months at 4°C and six (6) months at -20°C. The data supports a DNA freeze-thaw stability claim of 5 cycles. The gene-specific PCR products and indexed libraries may be stored for sixty (60) days and ninety (90) days at recommended storage condition between -15°C to -25°C, respectively. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of the PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. This report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the PMA device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

You have agreed to provide the following non-clinical information in a report, which may be followed by a PMA supplement where applicable.

1. In order to provide a more robust assessment of precision near the LoD levels for each CDx variant, Pillar Biosciences must provide robust and high-confidence data from a well-designed 3-site

reproducibility study using additional clinical samples carrying CDx biomarkers. The data from this study must be adequate to support precision near LoD for CDx variants in the intended use population.

2. Pillar Biosciences will provide results from the following stability studies using intended use specimen type as follows:

    i. Pillar Biosciences will provide robust and high confidence data from a stability study which uses FFPE blocks from the CDx intended use patients at low tumor content and close to the newly defined LoD levels, to the extent possible, starting from baseline measurement with stability data collected in a controlled prospective manner to support FFPE block stability claim.

    ii. Pillar Biosciences will provide robust and high confidence data from a stability study which uses FFPE-extracted DNA samples from the CDx intended use patients with allelic frequencies near the newly defined LoD (i.e., 1-1.5x LoD) and at low DNA inputs (30 ng) to supplement the DNA stability claim at -20°C for the CDx variants.

    The data from these studies must be adequate to support stability claims for the CDx variants in the intended use population.

3. Pillar Biosciences must provide robust and high confidence data from a study using clinical specimens to demonstrate that different lots of the O/RDx-LCCA reagent kit components may be used interchangeably. The data from these studies must be adequate to support that different lots of the O/RDx-LCCA reagent kit components do not impact the results of the assay.

Pillar Biosciences must provide detailed protocols, including acceptance criteria where appropriate, for the studies that are noted above as conditions of approval. These studies must be adequate to confirm the safety and effectiveness of the O/RDx-LCCA and must include a detailed description of the numbers of sample to be tested, the type of samples to be tested, the tumor types for each sample, the complete testing protocol, and a robust statistical analysis plan. These protocols must be submitted to FDA no later than 60 days after approval.

The final study data, study conclusions, and labeling revisions should be submitted within 1 year of the PMA approval date, unless stated otherwise.

Be advised that failure to comply with any post-approval requirement, including test protocol, sample size, completion/pass/fail requirements outlined above, and required timeline for data accrual and study completion per the above approved protocol, etc., constitutes grounds for FDA withdrawal of approval of the PMA in accordance with 21 CFR 814.82(c) and 814.46(a)(2).

This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final Unique Device Identification (UDI) rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24,

2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website, https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-udi-system.

Before making any change affecting the safety or effectiveness of the PMA device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" https://www.fda.gov/media/81431/download.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or post-marketing safety reporting (21 CFR 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems and on combination product post-marketing safety reporting is available at (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the post-marketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/industry-guidance-recalls.

CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet Home Page located at

https://www.fda.gov/medical-devices/device-approvals-denials-and-clearances/pma-approvals. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with a copy of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Haydar Celik at 301-348-1885 or Haydar.Celik@fda.hhs.gov.

Sincerely,

Reena Philip -S

Reena Philip, Ph.D.
Director
Division of Molecular Genetics
and Pathology
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