



November 05, 2024

Caris Life Sciences
Peggy Carter, Ph.D., RAC
Corporate Vice President, Regulatory
4610 South 44th Place
Phoenix, AZ 85040

Re: P240010
Trade/Device Name: MI Cancer Seek™
Product Code: PQP
Filed: April 1, 2024
Amended: August 5, 2024

Dear Dr. Peggy Carter:

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 MI Cancer Seek. This device is indicated for:

MI Cancer Seek is a next-generation sequencing (NGS) based in vitro diagnostic (IVD) device using total nucleic acid (TNA) isolated from formalin-fixed paraffin-embedded (FFPE) tumor tissue specimens for the detection of single nucleotide variants (SNVs) and insertions and deletions (indels) in 228 genes, microsatellite instability (MSI), tumor mutational burden (TMB) in patients with previously diagnosed solid tumors, and copy number amplification (CNA) in one gene in patients with breast cancer.

MI Cancer Seek is intended as a companion diagnostic to identify patients who may benefit from treatment with the targeted therapies listed in **Table 1** below, in accordance with the approved therapeutic product labeling.

Additionally, MI Cancer Seek is intended to provide tumor mutational profiling to be used by qualified healthcare professionals in accordance with professional oncology guidelines for cancer patients with previously diagnosed solid malignant neoplasms. Genomic findings other than those listed in **Table 1** are not prescriptive or conclusive for labeled use of any specific therapeutic product.

Table 1. MI Cancer Seek Companion Diagnostic Indications

Indication	Biomarker	Therapy
Breast Cancer	<i>PIK3CA</i> (C420R; E542K; E545A, E545D [1635G>T only], E545G, E545K, Q546E, Q546R; and H1047L, H1047R, H1047Y)	PIQRAY® (alpelisib)
	<i>KRAS</i> wild-type (absence of mutations in exons 2, 3, and 4) and	VECTIBIX® (panitumumab)

Colorectal Cancer (CRC)	<i>NRAS</i> wild type (absence of mutations in exons 2, 3, and 4)	
	<i>BRAF</i> V600E	<i>BRAFTOVI</i> ® (encorafenib) in combination with <i>ERBITUX</i> ® (cetuximab)
Melanoma	<i>BRAF</i> V600E	<i>BRAF</i> Inhibitors approved by FDA*
	<i>BRAF</i> V600E or V600K	<i>MEKINIST</i> ® (trametinib) or <i>BRAF/MEK</i> Inhibitor Combinations approved by FDA*
Non-small cell lung cancer (NSCLC)	<i>EGFR</i> exon 19 deletions and exon 21 L858R alterations	<i>EGFR</i> Tyrosine Kinase Inhibitors approved by FDA*
Solid Tumors	MSI-H	<i>KEYTRUDA</i> ® (pembrolizumab), <i>JEMPERLI</i> (dostarlimab-gxly)
Endometrial Carcinoma	Not MSI-H	<i>KEYTRUDA</i> ® (pembrolizumab) in combination with <i>LENVIMA</i> ® (lenvatinib)
*For the most current information about the device indications for the therapeutic products in this group, go to: https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools#Group_Labeling		

MI Cancer Seek is a single-site assay performed at Caris Life Sciences, Phoenix, AZ.

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 Caris Life Sciences located at Phoenix, AZ. 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 3.5 months of shelf life for the assay reagents at the recommended storage conditions. 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. Caris Life Sciences must provide data evaluating the effects of endogenous interfering substances including high level presence of necrotic tissue, melanin and fatty acids. The samples for this assessment should represent a range of solid tumors across the intended use population including companion diagnostic and tumor profiling biomarkers. The data from this study must be adequate to demonstrate that the potential endogenous interfering substances in patients with solid tumor do not adversely impact companion diagnostic and tumor profiling biomarker detection.
2. Caris Life Sciences must provide the results from well-designed FFPE block and slide stability studies in which DNA yield, DNA quality, variant calling and invalid rates in aged samples are assessed by running samples through the entire assay workflow. The baseline or time zero (T0) must represent a freshly collected sample. The samples for this assessment should represent a range of solid tumors across the intended use population including companion diagnostic and tumor profiling biomarkers. Invalid rate and biomarker agreement rates must be assessed at each timepoint tested using the baseline measurement as reference. The data from this study must be adequate to support the MI Cancer Seek FFPE block and slide stability duration claims.

The final study protocol and study report should be submitted within 12 months of the PMA approval date.

Be advised that failure to comply with any post-approval requirement 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 Erdem Coskun at (301) 796-3513 or Erdem.Coskun@fda.hhs.gov.

Sincerely,

Soma Ghosh -S

Soma Ghosh, Ph.D.
Acting Director
Division of Molecular Genetics and Pathology
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health