December 12, 2022

Resolution Bioscience, Inc.
Chris Pretzinger
Senior Director, Regulatory Affairs
550 Kirkland Way, Suite 200
Kirkland, WA 98033

Re: P210040
Trade/Device Name: Agilent Resolution ctDx FIRST
Product Code: PQP
Filed: January 10, 2022
Amended: March 10, 2022, September 6, 2022, December 12, 2022

Dear Chris Pretzinger:

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 Agilent Resolution ctDx FIRST. This device is indicated for:

> The Agilent Resolution ctDx FIRST assay is a qualitative next generation sequencing-based, *in vitro* diagnostic test that uses targeted hybrid-capture sequencing technology to detect and report single nucleotide variants (SNVs) and deletions in two genes. The Agilent Resolution ctDx FIRST assay utilizes circulating cell-free DNA (cfDNA) isolated from plasma of peripheral whole blood collected in Streck Cell-Free DNA Blood Collection Tubes (BCTs). The test is intended as a companion diagnostic to identify patients with non-small cell lung cancer (NSCLC) who may benefit from treatment with the targeted therapy listed in Table 1, in accordance with the approved therapeutic labeling.

Table 1. Companion Diagnostic Indication

Indication	Biomarker	Therapy
Non-small cell lung cancer (NSCLC)	*KRAS* G12C	KRAZATI™ (adagrasib)

> A negative result from a plasma specimen does not assure that the patient's tumor is negative for genomic findings. Patients with NSCLC who are negative for the biomarker listed in Table 1 should be reflexed to tissue biopsy testing for Table 1 biomarker using an FDA-approved tumor tissue test, if feasible.
>
> Additionally, the test is intended to provide tumor mutation profiling for SNVs and deletions in the *EGFR* gene for use by qualified health care professionals in accordance with professional guidelines

in oncology for patients with NSCLC. The test is for use with patients previously diagnosed with NSCLC and in conjunction with other laboratory and clinical findings.

Genomic findings other than those listed in Table 1 are not prescriptive or conclusive for labeled use of any specific therapeutic product.

The Agilent Resolution ctDx FIRST assay is a single-site assay performed at Resolution Bioscience, Inc.

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 Resolution Bioscience, 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 seven (7) months of shelf life for the Agilent Resolution ctDx FIRST assay reagents at the recommended storage conditions; used Agilent Resolution ctDx FIRST assay reagents are stable for at least two (2) freeze-thaw cycles and 30 days at -20°C ± 10°C; whole blood specimens may be stored in Cell-Free DNA blood collection tubes for up to seven (7) days after blood collection and prior to plasma isolation; cfDNA may be stored at -20°C ± 10°C for 30 days; and Agilent Resolution ctDx FIRST assay intermediates may be stored at -20°C ± 10°C for 30 days. 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. Resolution Bioscience must provide data from a well-designed and well-controlled short-term frozen plasma stability using intended use clinical samples for *KRAS* G12C and *EGFR* level 2 variants. The data from this study must be adequate to support short-term frozen plasma stability claims for *KRAS* G12C and *EGFR* level 2 variants.

2. Blood Collection Tubes
    a. Resolution Bioscience must demonstrate clinically insignificant variability when different lots of the Agilent Resolution ctDx FIRST Blood Collection tube are used with the Agilent Resolution ctDx FIRST assay. Resolution Bioscience must provide data from a robust and high confidence precision study. This study must confirm the Agilent Resolution ctDx FIRST assay's precision when the Agilent Resolution ctDx FIRST cfDNA Blood Collection tubes are used, and must use replicate samples from each of multiple different patients. Each patient who donates specimens for this study must have plasma collected in a total of four tubes, each from two tube lots; three lots are required to be represented in the study. This is important to assess variability between tube lots and across patient specimens. Each replicate must be run at or near the minimum standardized cfDNA input (*i.e.,* at a target concentration of 15 ng). The samples must be collected from intended use patients with *KRAS* G12C and *EGFR* level 2 variants that are identified by the Agilent Resolution ctDx FIRST assay. The data from this study must be adequate to minimize clinically significant inaccurate results when used on specimens collected in the Agilent Resolution ctDx FIRST Blood Collection tubes in the intended use population.
    b. Resolution Bioscience must provide robust and high confidence data from a well-designed and well-controlled study to evaluate potential interference caused by underfilling the Agilent Resolution ctDx FIRST Blood Collection tubes. Replicates must be run at or near the minimum standardized cfDNA input (i.e., at a target concentration of 15 ng). The samples must be collected from intended use patients with *KRAS* G12C and *EGFR* variants that are identified by the Agilent Resolution ctDx FIRST assay. The data from this study must be adequate to evlaute the potential interference caused by underfilling the Agilent Resolution ctDx FIRST Blood Collection tubes in the intended use population.
    c. Resolution Bioscience must evaluate the impact of variations in mixing after blood collection (incomplete mixing). Replicates must be run at or near the minimum standardized cfDNA input (i.e., at a target concentration of 15 ng). The samples must be collected from intended use patients with *KRAS* G12C and *EGFR* variants that are identified by the Agilent Resolution ctDx FIRST assay. The data from this study must be adequate to demonstrate the impact of inadequate or overmixing on the performance of Agilent Resolution ctDx FIRST Blood Collection tubes in the intended use population.
    d. Resolution Bioscience must provide robust and high confidence data from a stability study which demonstrates acceptable stability of whole blood collected from the intended use patients (NSCLC), stored, and shipped in the Agilent Resolution ctDx FIRST cfDNA Blood Collection tubes. The study must confirm the claimed whole blood shipping and storage stability for the intended use population.

e. Resolution Bioscience must demonstrate clinically insignificant variability on the performance of the Agilent Resolution ctDx FIRST assay when specimens collected in Agilent Resolution ctDx FIRST cfDNA Blood Collection tubes at modified plasma spinning protocol from that of the manufacturer's recommendations. The study must confirm that the Resolution Bioscience's modified centrifugation protocol has not impacted sample QC metrics and variant calling.

The final study data, study conclusions, and labeling revisions should be submitted within one (1) year of the PMA approval date.

Be advised that failure to comply with any of the above post-approval requirements 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 Rama Kamesh Bikkavilli at 301-796-2826 or RamaKamesh.Bikkavilli@fda.hhs.gov.

Sincerely,

Donna M. Roscoe -S

Donna Roscoe, 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