



November 30, 2017

Foundation Medicine, Inc.  
Christine Vietz, PhD, RAC  
Sr. Director Regulatory Affairs  
150 Second Street, 1st Floor  
Cambridge, MA 02141

Re: P170019  
Trade/Device Name: FoundationOne CDx™  
Filed: June 6, 2017  
Amended: November 22, 2017  
Product Code: PQP

Dear Dr. Vietz:

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 FoundationOne CDx™. This device is indicated for the following:

FoundationOne CDx™ (F1CDx) is a next generation sequencing based *in vitro* diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling. Additionally, F1CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms. The F1CDx assay is a single-site assay performed at Foundation Medicine, Inc.

**Table 1: Companion diagnostic indications**

<b>Indication</b>	<b>Biomarker</b>	<b>Therapy</b>
Non-small cell lung cancer (NSCLC)	<i>EGFR</i> exon 19 deletions and <i>EGFR</i> exon 21 L858R alterations	Gilotrif® (afatinib), Iressa® (gefitinib), or Tarceva® (erlotinib)
	<i>EGFR</i> exon 20 T790M alterations	Tagrisso® (osimertinib)
	<i>ALK</i> rearrangements	Alecensa® (alectinib), Xalkori® (crizotinib), or Zykadia® (ceritinib)

	<i>BRAF</i> V600E	Tafinlar <sup>®</sup> (dabrafenib) in combination with Mekinist <sup>®</sup> (trametinib)
Melanoma	<i>BRAF</i> V600E	Tafinlar <sup>®</sup> (dabrafenib) or Zelboraf <sup>®</sup> (vemurafenib)
	<i>BRAF</i> V600E and V600K	Mekinist <sup>®</sup> (trametinib) or Cotellic <sup>®</sup> (cobimetinib) in combination with Zelboraf <sup>®</sup> (vemurafenib)
Breast cancer	<i>ERBB2</i> (HER2) amplification	Herceptin <sup>®</sup> (trastuzumab), Kadcyca <sup>®</sup> (ado-trastuzumab-emtansine), or Perjeta <sup>®</sup> (pertuzumab)
Colorectal cancer	<i>KRAS</i> wild-type (absence of mutations in codons 12 and 13)	Erbix <sup>®</sup> (cetuximab)
	<i>KRAS</i> wild-type (absence of mutations in exons 2, 3, and 4) and <i>NRAS</i> wild type (absence of mutations in exons 2, 3, and 4)	Vectibix <sup>®</sup> (panitumumab)
Ovarian cancer	<i>BRCA1/2</i> alterations	Rubraca <sup>®</sup> (rucaparib)

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.

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 device is to be distributed only with serial number-controlled instruments and only to Foundation Medicine, Inc., a single laboratory site located at 150 Second Street, Cambridge, MA 02141. 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 as follows: library construction reagents, hybrid capture reagents and sequencing reagents may be stored between 4°C and -20°C for up to 90 days; DNA samples may be stored at 4°C for up to 6 weeks; and -20°C for up to 3 months. This is to advise you that the protocols you used to establish this expiration dating are considered approved protocols 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. Two copies of 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. This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of

the final 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. For more information on these requirements, please see the UDI website, <http://www.fda.gov/udi>.

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 information in a report(s) which may be followed by a PMA supplement(s) when applicable.

1. Provide additional clinical concordance data to support the performance of your device within the appropriate clinical contexts. Please perform concordance testing against additional approved CDx devices for their respective approved clinical indications.
2. Provide clinical response data for NSCLC patients with an EGFR T790M mutation detected with mutant allele frequency (MAF) < 5% who were subsequently treated with Tagrisso® (osimertinib). This will support the clinical performance of your device for patients detected as positive by F1CDx (with MAF <5%) who were considered negative by another approved CDx.
3. Provide results from additional testing of clinical samples to establish the analytical performance characteristics of your device for all variant types and genomic signatures that may be detected. Please ensure that the samples adequately represent the ranges of CNAs, rearrangements, MSI and TMB that are detected by your device, with consideration given to the fusion partners (for rearrangements) and the reportable ranges (for MSI and TMB).
4. Provide software documentation for validating and implementing software changes required to generate the test report.

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" <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm>.

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, 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 <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm>.

In accordance with the recall requirements specified in 21 CFR 806.10, 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 <http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm>.

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 HomePage located at <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm>. 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 copies 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 in 6 copies, 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  
PMA 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 Hisani Madison, Ph.D., MPH at 301-796-6162 or [Hisani.Madison@fda.hhs.gov](mailto:Hisani.Madison@fda.hhs.gov).

Sincerely,

Reena Philip-S

Reena Philip, Ph.D.  
Director  
Division of Molecular Genetics and Pathology  
Office of *In Vitro* Diagnostics and  
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Center for Devices and Radiological Health