



Life Technologies Corporation
Fatima Khaiser
Regulatory Affairs Manager
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September 15, 2021

Re: P160045/S029

Trade/Device Name: Oncomine™ Dx Target Test (ODxT Test)

Product Code: PQP

Filed: May 4, 2021

Amended: May 10, 2021 and July 22, 2021

Dear Fatima Khaiser:

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) supplement for the Oncomine™ Dx Target Test (ODxT Test) to include a companion diagnostic indication for the detection of *EGFR* exon 20 insertions in non-small cell lung cancer patients who may benefit from treatment with EXKIVITY™ (mobocertinib). This device is indicated as follows:

The Oncomine™ Dx Target Test is a qualitative *in vitro* diagnostic test that uses targeted high throughput, parallel-sequencing technology to detect single nucleotide variants (SNVs), insertions, and deletions in 23 genes from DNA and fusions in *ROS1* and in *RET* from RNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor samples from patients with non-small cell lung cancer (NSCLC), and *IDH1* SNVs from FFPE tumor tissue samples from patients with cholangiocarcinoma using the Ion PGM™ Dx System.

The test is indicated as a companion diagnostic to aid in selecting NSCLC and cholangiocarcinoma patients for treatment with the targeted therapies listed in Table 1 in accordance with the approved therapeutic product labeling.

Table 1: List of Variants for Therapeutic Use

Tissue type	Gene	Variant	Targeted therapy
NSCLC	<i>BRAF</i>	BRAF V600E mutations	TAFINLAR® (dabrafenib) in combination with MEKINIST® (trametinib)
	<i>EGFR</i>	EGFR L858R mutation, EGFR Exon 19 deletions	IRESSA® (gefitinib)
	<i>RET</i>	RET Fusions	GAVRETO™ (pralsetinib)
	<i>ROS1</i>	ROS1 Fusions	XALKORI® (crizotinib)
	<i>EGFR</i>	EGFR exon 20 insertions	EXKIVITY™ (mobocertinib)

Cholangiocarcinoma	<i>IDH1</i>	IDH1 R132C, R132G, R132L, R132S, and R132H mutations	TIBSOVO® (ivosidenib)
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Safe and effective use has not been established for selecting therapies using this device for variants and tissue types other than those in Table 1.

Results other than those listed in Table 1 are indicated for use only in patients who have already been considered for all appropriate therapies (including those listed in Table 1).

Analytical performance using NSCLC specimens has been established for the variants listed in Table 2.

Table 2: List of Variants with Established Analytical Performance Only

Gene	Variant ID	Nucleotide Change
<i>KRAS</i>	COSM512	c.34_35delGGinsTT
<i>KRAS</i>	COSM516	c.34G>T
<i>MET</i>	COSM707	c.3029C>T
<i>PIK3CA</i>	COSM754	c.1035T>A

The test is not indicated to be used for standalone diagnostic purposes, screening, monitoring, risk assessment, or prognosis.

We are pleased to inform you that the PMA supplement 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. 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 5 months when the OncoPrint™ Dx Target DNA and RNA Panel and DNA Control Kit, the Ion PGM Dx Sequencing and Library Reagents Kits, and the Ion OneTouch™ Dx Template Reagents Kit are stored at -30°C to -10°C; the OncoPrint™ Dx Target RNA Control Kit is stored at -90°C to -60°C; the Ion OneTouch™ Dx Template Dx ES Beads and Ion PGM Dx Library Equalizer Kit are stored at 2°C to 8°C; and the Ion PGM Dx Sequencing Supplies and Solutions Kit and Ion OneTouch™ Dx Template Supplies and Solutions Kits are stored at 15°C to 30°C. 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 within 1 year of the date of this letter.

1. Thermo Fisher Scientific/Life Technologies Corp. must provide an additional LoD study using intended use clinical samples. The data from this study must be adequate to demonstrate an appropriate LoD for 3bp, 9bp, and 12bp *EGFR* exon 20 insertion variants.
2. Thermo Fisher Scientific/Life Technologies Corp. must provide data from well-designed and well-controlled precision studies:
 - i. Provide data from an external panel reproducibility and within-run repeatability study using intended use specimens carrying *EGFR* exon 20 insertions at or near the LoD levels (~1-1.5x LoD). The data from this study must be adequate to support precision near the LoD for *EGFR* exon 20 insertions in the intended use population.
 - ii. Provide data from an external sample processing reproducibility and within-run repeatability with an adequate number of replicates using intended use specimens carrying *EGFR* exon 20 insertions at or near the LoD levels (~1-1.5x LoD). The data from this study must be adequate to support precision (starting from sample processing) near the LoD for *EGFR* exon 20 insertions in the intended use population.
3. Thermo Fisher Scientific/Life Technologies Corp. must provide data from a well-designed and well-controlled endogenous interference substances study evaluating the effects of hemoglobin and tumor necrosis on the *EGFR* exon 20 insertion variant calling using intended use specimens near 1-1.5x LoD. The data from this study must be adequate to support the finding that the potential endogenous interfering substances in NSCLC do not adversely impact *EGFR* exon 20 insertion mutations calling.
4. Thermo Fisher Scientific/Life Technologies Corp. must provide additional data from a well-designed and well-controlled shelf-life stability study using *EGFR* exon 20 insertion or similar insertion intended use specimens. The data from this study must be adequate to support stability claims for insertions in the intended use population.

5. Thermo Fisher Scientific/Life Technologies Corp. will provide a final approved aggregation validation protocol for the merging of multiple assay definition files (ADF) associated with approved companion diagnostic indications and associated updates to the Torrent Suite Dx software for a final ADF and Torrent Suite Dx versions to be commercialized to support new approved indications within 60 days of approval of this PMA supplement.
6. Thermo Fisher Scientific/Life Technologies Corp. will provide results and software validation documentation from regression testing on the commercial release configuration to confirm there are no defects for the merged assay definition files based on the approved aggregation validation protocol and no new defects other than those listed in the approved Torrent Suite Dx versions within 6 months of approval of this PMA supplement.

Be advised that failure to comply with any post-approval requirement, including the LoD study, precision study, interference study, and software update, 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,

Reena Philip -S

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