



October 17, 2024

Life Technologies Corporation  
Chelsea Pfaff  
Sr. Manager Regulatory Affairs  
Thermo Fisher Scientific  
7305 Executive Way  
Frederick, MD 21704

Re: P160045/S046

Trade/Device Name: Oncomine™ Dx Target Test

Product Code: PQP

Filed: February 29, 2024

Amended: March 18, 2024, March 25, 2024, May 3, 2024, July 19, 2024, September 18, 2024

Dear Chelsea Pfaff:

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 for expanding the indications to include a companion diagnostic indication for the identification of IDH1 and IDH2 mutations in patients with astrocytoma (AC) and oligodendroglioma (OG) that may benefit from the targeted drug therapy, VORANIGO (vorasidenib). This device is indicated for:

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), deletions, and insertions in 23 genes from DNA and fusions in ROS1 and RET from RNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue samples from patients with non-small cell lung cancer (NSCLC), IDH1 SNVs from FFPE tumor tissue samples from patients with cholangiocarcinoma (CC), BRAF V600E mutations from FFPE tumor tissue samples from patients with anaplastic thyroid cancer (ATC), IDH1 and IDH2 SNVs from FFPE tumor tissue samples from patients with astrocytoma (AC) and oligodendroglioma (OG), RET SNVs, multi-nucleotide variants (MNVs), and deletions from DNA isolated from FFPE tumor tissue samples from patients with medullary thyroid cancer (MTC) and RET fusions from RNA isolated from FFPE tumor tissue samples from patients with thyroid cancer (TC) using the Ion PGM™ Dx System.

The test is indicated as a companion diagnostic to aid in selecting NSCLC, CC, ATC, AC, OG, MTC and TC 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 by indication**

| Tissue type | Gene              | Variant                                                                                                                                                                                                    | Targeted therapy                                                  |
|-------------|-------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| NSCLC       | <i>BRAF</i>       | <i>BRAF</i> V600E mutations                                                                                                                                                                                | TAFINLAR® (dabrafenib) in combination with MEKINIST® (trametinib) |
|             | <i>EGFR</i>       | <i>EGFR</i> L858R mutation, <i>EGFR</i> exon 19 deletions                                                                                                                                                  | IRESSA® (gefitinib)                                               |
|             | <i>EGFR</i>       | <i>EGFR</i> exon 20 insertions                                                                                                                                                                             | RYBREVANT™ (amivantamab-vmjw)                                     |
|             | <i>ERBB2/HER2</i> | <i>ERBB2/HER2</i> activating mutations (SNVs and exon 20 insertions)                                                                                                                                       | ENHERTU® (fam-trastuzumab deruxtecan-nxki)                        |
|             | <i>RET</i>        | <i>RET</i> fusions                                                                                                                                                                                         | GAVRETO™ (pralsetinib)<br>RETEVMO® (selpercatinib)                |
|             | <i>ROSI</i>       | <i>ROSI</i> fusions                                                                                                                                                                                        | XALKORI® (crizotinib)                                             |
| CC          | <i>IDH1</i>       | <i>IDH1</i> R132C, <i>IDH1</i> R132G, <i>IDH1</i> R132H, <i>IDH1</i> R132L, and <i>IDH1</i> R132S mutations                                                                                                | TIBSOVO® (ivosidenib)                                             |
| ATC         | <i>BRAF</i>       | <i>BRAF</i> V600E mutations                                                                                                                                                                                | TAFINLAR® (dabrafenib) in combination with MEKINIST® (trametinib) |
| MTC         | <i>RET</i>        | <i>RET</i> mutations (SNVs, MNVs, and deletions)                                                                                                                                                           | RETEVMO® (selpercatinib)                                          |
| TC          | <i>RET</i>        | <i>RET</i> fusions                                                                                                                                                                                         | RETEVMO® (selpercatinib)                                          |
| AC and OG   | <i>IDH1, IDH2</i> | <i>IDH1</i> R132C, <i>IDH1</i> R132G, <i>IDH1</i> R132H, <i>IDH1</i> R132L, <i>IDH1</i> R132S, <i>IDH2</i> R172M, <i>IDH2</i> R172K, <i>IDH2</i> R172W, <i>IDH2</i> R172S, and <i>IDH2</i> R172G mutations | VORANIGO® (vorasidenib)                                           |

Safe and effective use has not been established for selecting therapies using this device for the variants listed in 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/type | Amino acid change | Nucleotide Change |
|---------------|-----------------|-------------------|-------------------|
| <i>KRAS</i>   | COSM512         | p.Gly12Phe        | c.34_35delGGinsTT |
| <i>KRAS</i>   | COSM516         | p.Gly12Cys        | c.34G>T           |
| <i>MET</i>    | COSM707         | p.Thr1010Ile      | c.3029C>T         |
| <i>PIK3CA</i> | COSM754         | p.Asn345Lys       | c.1035T>A         |

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

Based upon the information submitted, 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 available 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 all other applicable requirements, including those 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 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 must 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, under 21 CFR 814.82(a)(9), 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, which may be followed by a PMA supplement within one year of the date of this letter.

1. Life Technologies Corporation must provide data from additional IDH1 and IDH2 negative/wild type glioma and glioblastoma samples screened with a representative local immunohistochemistry (IHC) assay, to identify an additional negative population for inclusion into the clinical concordance evaluation between the LLT and the final CDx ODxT Test. This information must be provided to confirm the negative percent agreement (NPA, Pr(ODxTT- | LLT-)) and the clinical effectiveness of the ODxT Test as a companion diagnostic device for identification of patients with astrocytoma (AC) and oligodendroglioma (OG) with IDH1/IDH2 mutations who may benefit from treatment with VORANIGO (vorasidenib).

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 21 CFR 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 Part 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 available at <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. Additional information about changes that may require a PMA supplement are provided in 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>.

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production and process controls (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 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 <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 Part 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 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 Jahan Ara at 301-796-3241 or [Jahan.Ara@fda.hhs.gov](mailto:Jahan.Ara@fda.hhs.gov).

Sincerely,

**Soma Ghosh-S**

Soma Ghosh, Ph.D.  
Acting Director  
Division of Molecular Genetics and Pathology  
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