DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

June 22, 2017

Life Technologies Corporation
Jody Schulz
Senior Manager, Regulatory Affairs
5781 Van Allen Way
Carlsbad, CA 92008

Re: P160045
Trade/Device Name: Oncomine Dx Target Test
Filed: October 17, 2016
Amended: October 17, 2016; October 31, 2016; November 1, 2016; December 14, 2016; March 7, 2017; April 17, 2017; May 17, 2017; and May 26, 2017
Product Code: PQP

Dear Jody Schulz:

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 Oncomine Dx Target Test. 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) and deletions in 23 genes from DNA and fusions in ROS1 from RNA isolated from formalin-fixed, paraffin-embedded (FFPE) tumor tissue samples from patients with non-small cell lung cancer (NSCLC) using the Ion PGM™ Dx System.

The test is indicated to aid in selecting NSCLC 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

Gene	Variant	Targeted therapy
BRAF	BRAF V600E	TAFINLAR®(dabrafenib) in combination with MEKINIST® (trametinib)
ROS1	ROS1 fusions	XALKORI® (crizotinib)
EGFR	L858R, Exon 19 deletions	IRESSA® (gefitinib)

Safe and effective use has not been established for selecting therapies using this device for the variants in Table 1 in tissue types other than NSCLC.

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
KRAS	COSM512	c.34_35delGGinsTT
KRAS	COSM516	c.34G>T
MET	COSM707	c.3029C>T
PIK3CA	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 is approved. You may continue commercial distribution of the device upon receipt of this letter.

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 professionals need in order to use the device and insofar as the sale and distribution of the device are restricted to professionals who have completed the specific training, have the specific experience, or have the combination thereof identified in the labeling. 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 6 months when the Oncomine™ 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 Oncomine™ 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. 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 non-clinical information in a report(s) which may be followed by a PMA supplement where applicable.

1. Final study data, study conclusions, and labeling revisions within 9 months of the PMA approval date for:

    a. Results from a three site reproducibility study using clinical samples with allelic frequencies near the established limit of detection (i.e., 1x LoD) to confirm the values from the limit of detection study.

    b. Results from an interference study using variant positive clinical samples in order to confirm that the presence of necrotic tissue does not interfere with the performance of the Oncomine™ Dx Target Test.

    c. Results from a study using clinical specimens to demonstrate that 3 different lots of each of the components of the Oncomine™ Dx Target Test and Controls Kit may be used interchangeably, in order to confirm that the interchangeability demonstrated using control samples reflects performance with clinical samples as well.

    d. Results from an additional guard-banding study using fusion positive clinical samples to verify the tolerance ranges of the critical elements of the RNA workflow for the Oncomine™ Dx Target Test.

2. Validation testing, results, and associated software documentation within 3 months of the PMA approval date from regression testing on the commercial release configuration [Torrent Suite Dx Software v5.6.4 and Assay Definition File (ADF) v1.8)] to confirm there are no defects for ADF and no new defects other than those listed in Torrent Suite Dx v5.6.4 Software Release Note (Rev. D).

3. Validation testing, results, and associated software documentation within 6 months of the PMA approval date to confirm the resolution of existing unresolved anomalies 2519 and 2520.

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 Home Page 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.

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If you have any questions concerning this approval order, please contact Karen Bijwaard at 301-796-6162 or Karen.Bijwaard@fda.hhs.gov.

Sincerely,

Reena Philip -S

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