4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA-2025-N-4622]

Immunology and Microbiology Devices; Reclassification of Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product; Proposed Amendment; Proposed Order; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed amendment; proposed order; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is proposing to reclassify certain postamendments class III nucleic acid-based test systems indicated for use with a corresponding approved oncology therapeutic product (product codes OWD, PJG, PQP, and SFL) from class III (premarket approval) into class II (special controls), subject to premarket notification. FDA is also proposing a new device classification regulation, along with the special controls that FDA believes are necessary to provide a reasonable assurance of safety and effectiveness for these devices.

DATES: Submit electronic or written comments on the proposed order by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Please see section X of this document for the proposed effective date when the new requirements apply and for the proposed effective date of a final order based on this proposed order.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The https://www.regulations.gov electronic filing system will accept comments until midnight 11:59 p.m. Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments

received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal Rulemaking Portal:* https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2025-N-4622 for "Immunology and Microbiology Devices; Reclassification of Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product; Proposed Amendment; Proposed Order; Request for Comments." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday Eastern Time, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents, the plain language summary of the proposed order of not more than 100 words consistent with the "Providing Accountability

Through Transparency Act," or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Soma Ghosh, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 3316, Silver Spring, MD 20993, 240-402-5333, Soma.Ghosh@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background--Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended, establishes a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) establishes three classes of devices reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three classes of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Section 513(a)(1) of the FD&C Act defines the three classes of devices. Class I devices are those devices for which the general controls of the FD&C Act (controls authorized by or under section 501, 502, 510, 516, 518, 519, or 520 (21 U.S.C. 351, 352, 360, 360f, 360h, 360i, or 360j) or any combination of such sections) are sufficient to provide reasonable assurance of safety and effectiveness of the device; or those devices for which insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of safety and effectiveness or to establish special controls to provide such assurance, but because the devices are not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and do not present a potential unreasonable risk of illness or injury, are to be regulated by general controls (section 513(a)(1)(A) of the FD&C Act). General controls include, but are not limited to,

provisions that relate to establishment registration and device listing; premarket notification; prohibitions against adulteration and misbranding (*e.g.,* labeling that fails to bear adequate directions for use); recordkeeping and reporting, including adverse event reporting and reporting of corrections and removals initiated to reduce a risk to health posed by the device or to remedy a violation of the FD&C Act caused by the device which may present a risk to health; and current good manufacturing practice (CGMP) requirements. These controls apply to all devices unless an exemption applies.

Class II devices are those devices for which general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but for which there is sufficient information to establish special controls to provide such assurance, including the issuance of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines, recommendations, and other appropriate actions FDA deems necessary to provide such assurance (section 513(a)(1)(B) of the FD&C Act).

Class III devices are those devices for which insufficient information exists to determine that general controls and special controls would provide a reasonable assurance of safety and effectiveness, and are purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or present a potential unreasonable risk of illness or injury (section 513(a)(1)(C) of the FD&C Act).

Devices that were not introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976 (generally referred to as "postamendments devices") are classified automatically by section 513(f)(1) of the FD&C Act into class III without any action taken by FDA (Agency or we). Those devices remain in class III and require approval of a premarket approval application (PMA), unless and until: (1) FDA reclassifies the device into class I or II, or (2) FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to

predicate devices by means of the premarket notification procedures in section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807, subpart E, of the regulations (21 CFR part 807).

A postamendments device that has initially been classified into class III under section 513(f)(1) of the FD&C Act may be reclassified into class I or class II under section 513(f)(3) of the FD&C Act. Section 513(f)(3) of the FD&C Act provides that FDA, acting by administrative order, can reclassify the device into class I or class II on its own initiative, or in response to a petition from the manufacturer or importer of the device. To change the classification of the device, the proposed new class must have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.[1]

FDA relies upon "valid scientific evidence" as defined in section 513(a)(3) of the FD&C Act and 21 CFR 860.7(c)(2) in the classification process to determine the level of regulation for devices.[2] In general, to be considered in the reclassification process, the "valid scientific evidence" upon which the Agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information, e.g., the contents of a pending PMA (see section 520(c) of the FD&C Act (21 U.S.C. 360j(c))). Section 520(h)(4) of the FD&C Act provides that FDA may use, for reclassification of a device, certain information in a PMA 6 years after the application has been approved. This includes information from clinical and preclinical tests or studies that demonstrate the safety and effectiveness of the device, but it does not include the descriptions of methods of manufacture and product composition and other trade secrets.

In accordance with section 513(f)(3) of the FD&C Act, FDA is issuing this proposed order to reclassify postamendments class III nucleic acid-based test systems indicated for use with a corresponding approved oncology therapeutic product (product codes OWD, PJG, PQP,

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[1] See generally section 513 of the FD&C Act.
[2] See generally *id.*

and SFL),[3] hereafter collectively referred to as oncology therapeutic nucleic acid-based test systems, into class II (special controls) subject to premarket notification under a new device classification regulation with the name "Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product."

The identification in the proposed classification regulation characterizes oncology therapeutic nucleic acid-based test systems as prescription in vitro diagnostic (IVD) devices intended for the detection of specific genetic variant(s) and/or other nucleic acid biomarkers in human clinical specimens using nucleic acid amplification technology (NAAT) and/or sequencing technology, and are indicated for use with a corresponding approved oncology therapeutic product. These test systems include companion diagnostic (CDx) test systems, which are devices that provide information that is essential for the safe and effective use of a corresponding approved therapeutic product and the use of which is stipulated in the instructions for use in the labeling of both the diagnostic device and the approved therapeutic product (Ref. 1). These test systems also include those test systems that provide information about known benefits and/or risks of an approved therapeutic product, where the use of the test system is referenced in the product labeling of the corresponding approved therapeutic product but the test system is not essential for the safe and effective use of the approved therapeutic product.

As discussed further throughout this proposed order, FDA has issued PMAs for various oncology therapeutic nucleic acid-based test systems designated under product codes OWD, PJG, PQP, or SFL. The oncology therapeutic nucleic acid-based test systems within the different product codes have distinct characteristics in certain respects, for example, each product code generally represents devices with a distinct technology used (e.g., NAAT and/or sequencing technology) and/or specific analyte(s) detected by the test system. FDA has considered the

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[3] FDA's Center for Devices and Radiological Health (CDRH) uses product codes to help categorize and ensure consistent regulation of medical devices. A product code consists of three characters that are assigned at the time a product code is generated and is unique to a product type. The three characters carry no other significance and are not an abbreviation.

distinctions of these test systems across the four product codes and has determined that these test systems, including those devices that provide information that is essential for the safe and effective use of a corresponding approved oncology therapeutic product, as well as test systems that, while not essential to the safe and effective use of the corresponding approved oncology therapeutic product, provide information about known benefits and/or risks related to the use of the approved oncology therapeutic product, have the same or a similar risk profile and sufficiently similar purposes, design considerations, functions, and other features related to safety and effectiveness such that the same or similar regulatory controls are necessary and sufficient to provide reasonable assurance of safety and effectiveness.[4] For these reasons and considering that FDA did not identify any unique risks associated with the distinctions across these devices, FDA is proposing a single classification regulation to classify all oncology therapeutic nucleic acid-based test systems into class II. There would generally not be changes to the product codes (i.e., OWD, PJG, PQP, and SFL) for previously approved oncology therapeutic nucleic acid-based test systems, and future oncology therapeutic nucleic acid-based test systems would either be assigned to one of the currently existing product codes or a new product code, as appropriate. The new classification regulation would apply to both current and new devices that are oncology therapeutic nucleic acid-based test systems.

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[4] For example, a specific device could be indicated for and approved to provide information that is essential for the safe and effective use of a corresponding approved oncology therapeutic product and to provide information about known benefits and/or risks related to the use of a corresponding approved oncology therapeutic product that is not essential to the safe and effective use of a corresponding approved oncology therapeutic product. The distinction is determined by the data from the clinical development program of the corresponding therapeutic product and how the therapeutic product is labeled (i.e., whether the use of the IVD device is essential for the safe and effective use of the therapeutic product or not essential for the safe and effective use of the therapeutic product but provides information about known benefits and/or risks related to the use of the therapeutic product). The devices have sufficiently similar purposes, design considerations, functions, and other features related to safety and effectiveness such that the same or similar regulatory controls are necessary and sufficient to provide reasonable assurance of safety and effectiveness and the devices can be part of the same device type.

Based upon the extensive PMA data available to FDA in accordance with section 520(h)(4) of the FD&C Act,[5,6] published peer-reviewed literature studying the longstanding and well-understood technologies, and data available to the Agency demonstrating a lack of significant postmarket safety signals with oncology therapeutic nucleic acid-based test systems, FDA believes there is sufficient information to reclassify these devices from class III (premarket approval) into class II (special controls). FDA believes the standard in section 513(a)(1)(B) of the FD&C Act is met as there is sufficient information to establish special controls, which, in addition to general controls, would provide reasonable assurance of the safety and effectiveness of these devices.[7] Therefore, FDA is proposing to establish a new device classification regulation, "Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product," and classify this device type into class II along with the special controls that the Agency believes are necessary to provide a reasonable assurance of the safety and effectiveness for these devices.

Under the FD&C Act, premarket notification (510(k)) submissions are required to provide a reasonable assurance of the safety and effectiveness of class II devices unless FDA determines that the device type should be exempt from 510(k) requirements under section

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[5] In proposing to reclassify oncology therapeutic nucleic acid-based test systems from class III to class II, FDA, on its own initiative, is relying on data from relevant PMAs and a relevant PMA panel-track supplement (under product codes OWD, PJG and PQP) available to FDA in accordance with the six-year rule (see section 520(h)(4) of the FD&C Act (21 U.S.C. 360j(h)(4)) (see also, FDA, "Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997 - Guidance for Industry and for FDA Reviewers," August 9, 2000. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-section-216-food-and-drug-administration-modernization-act-1997-guidance-industry-and-fda). This data was from relevant PMAs and a PMA panel-track supplement approved after November 28, 1990 and before January 27, 2019 for devices that would fall under this specific proposed reclassification as noted in section II of this proposed order. See also, FDA's premarket approval database, available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm.

[6] For the purpose of this proposed order, PMA data considered in accordance with section 520(h)(4) includes only that data which was submitted to and therefore considered by FDA at the time the PMA was reviewed and approval was issued.

[7] FDA notes that the "ACTION" caption for this proposed order is styled as "Proposed amendment; proposed order; request for comments" rather than "Proposed order." Beginning in December 2019, this editorial change was made to indicate that the document "amends" the Code of Federal Regulations. The change was made in accordance with the Office of the Federal Register's (OFR) interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

510(m) of the FD&C Act.[8] FDA has not made this determination for oncology therapeutic nucleic acid-based test systems and, therefore, FDA is not proposing for this class II device type to be exempt from 510(k) requirements.

If this proposed order is finalized, persons who intend to market this type of device must submit to FDA a premarket notification under section 510(k) of the FD&C Act prior to marketing the device.

II. Regulatory History of the Devices

In accordance with section 513(f)(1) of the FD&C Act, oncology therapeutic nucleic acid-based test systems are automatically classified into class III because they were not introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, have not been reclassified into class I or II, and have not been found substantially equivalent to a device placed in commercial distribution after May 28, 1976, which was subsequently classified or reclassified into class I or class II. Therefore, these devices are subject to the PMA requirements under section 515 of the FD&C Act (21 U.S.C. 360e).

On August 17, 2011, FDA approved an original PMA for the first oncology therapeutic nucleic acid-based test system, the cobas 4800 BRAF V600 Mutation Test (P110020) (product code OWD), a real-time polymerase chain reaction (PCR) IVD device intended for the qualitative detection of the BRAF V600E mutation in DNA extracted from human melanoma tissue and intended to be used as an aid in selecting melanoma patients for treatment with vemurafenib (Ref. 2). In a January 13, 2012, *Federal Register* notice (77 FR 2071), FDA

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[8] In considering whether to exempt class II devices from premarket notification, FDA considers whether premarket notification for the type of device is necessary to provide reasonable assurance of safety and effectiveness of the device. FDA generally considers the factors initially identified in the January 21, 1998 *Federal Register* notice (63 FR 3142) and further explained in FDA's guidance issued on February 19, 1998, entitled "Procedures for Class II Device Exemptions from Premarket Notification, Guidance for Industry and CDRH Staff" in determining whether premarket notification is necessary for class II devices. FDA also considers that, even when exempting devices from the 510(k) requirements, these devices would still be subject to certain limitations on exemptions, for example, the general limitations set forth in 21 CFR 866.9.

announced the approval order and availability of the Summary of Safety and Effectiveness Data (SSED) for the device.

Subsequently, on December 19, 2014, FDA approved an original PMA for the BRACAnalysis CDx under product code PJG (P140020). The BRACAnalysis CDx is an oncology therapeutic nucleic acid-based test intended for the qualitative detection and classification of variants in the protein coding regions and intron/exon boundaries of the BRCA1 and BRCA2 genes using genomic DNA obtained from whole blood specimens. Single nucleotide variants and small insertions and deletions (indels) are identified by PCR and Sanger sequencing. Large deletions and duplications in BRCA1 and BRCA2 are detected using multiplex PCR. Results of the test are intended to be used as an aid in identifying ovarian cancer patients eligible for treatment with Lynparza (olaparib) (Ref. 3). In an April 22, 2015, *Federal Register* notice (80 FR 22527), FDA announced the approval order and availability of the SSED for the device.

FDA subsequently approved an original PMA for FoundationFocus CDx$_{BRCA}$ Assay under the product code PQP on December 19, 2016 (P160018). FoundationFocus CDx$_{BRCA}$ Assay is an oncology therapeutic nucleic acid-based test system using next generation sequencing (NGS) technology, intended for the qualitative detection of BRCA1 and BRCA2 alterations in formalin-fixed paraffin-embedded (FFPE) ovarian tumor tissues, with results of the test intended to be used as an aid in identifying ovarian cancer patients for whom treatment with Rubraca (rucaparib) is being considered (Ref. 4). In a September 25, 2017 *Federal Register* notice (82 FR 44626), FDA announced the approval order and availability of the SSED for the FoundationFocus CDx$_{BRCA}$ Assay. FDA subsequently approved a panel-track supplement[9] (P160018/S001), on April 6, 2018, expanding the indications for use of this test to include the qualitative detection of genomic loss of heterozygosity (LOH) from FFPE ovarian tumor tissue

[9] The term "panel-track supplement" is defined in section 737(4)(B) of the FD&C Act as, “a supplement to an approved premarket application or premarket report under section 515 that requests a significant change in design or performance of the device, or a new indication for use of the device, and for which substantial clinical data are necessary to provide a reasonable assurance of safety and effectiveness.”

for which positive homologous recombination deficiency (HRD) status (defined as tBRCA-positive or LOH high) in ovarian cancer patients is associated with improved progression-free survival (PFS) from Rubraca (rucaparib) maintenance therapy (Ref. 5).[10] This new indication for use, while not essential to the safe and effective use of the corresponding approved oncology therapeutic product, is to provide information about known benefits related to the use of the approved oncology therapeutic product. With the approval of P160018/S001, FDA has thus far approved four oncology therapeutic nucleic acid-based test systems that provide information about known benefits and/or risks of an approved oncology therapeutic product, where the use of the test system is referenced in the product labeling of the corresponding approved therapeutic product but the test system is not considered to be essential for the safe and effective use of the approved therapeutic product.

Finally, on August 15, 2025, FDA approved an original PMA for the Idylla CDx MSI Test under product code SFL (P250005). The Idylla CDx MSI Test is an oncology therapeutic nucleic acid-based test intended for the qualitative detection of a panel of seven monomorphic biomarkers (ACVR2A, BTBD7, DIDO1, MRE11, RYR3, SEC31A and SULF2) for identification of microsatellite instability (MSI) in colorectal cancer (CRC) tissue. The Idylla CDx MSI Test uses FFPE tissue sections from patients with CRC, from which nucleic acids are extracted and then analyzed using PCR amplification and subsequent melt-curve analysis.[11] The Idylla CDx MSI Test reports MSI status as either Microsatellite Stable (MSS), Microsatellite Instability-High (MSI-H), or invalid. The test is intended as a companion diagnostic to identify CRC patients with MSI-H status, who may benefit from treatment with OPDIVO (nivolumab) as

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[10] The original device was approved under the trade name FoundationFocus CDx$_{BRCA}$ Assay (P160018). The sponsor originally submitted the panel-track PMA supplement application (P160018/S001) for the same test with an expanded indication for use under the trade name FoundationFocus CDx$_{BRCA\ HRD}$. However, through the review process, the sponsor decided to change the name to FoundationFocus CDx$_{BRCA\ LOH}$. Consistent with the authorized device trade name for P160018/S001, the name used throughout this reclassification proposed order is FoundationFocus CDx$_{BRCA\ LOH}$.

[11] As noted above, FDA has determined that the tests assigned to product codes OWD, PJG, PQP, and SFL all utilize NAAT and/or sequencing-based technology for use with a corresponding approved oncology therapeutic product, and have sufficiently similar purposes, design considerations, functions, and other features related to safety and effectiveness such that all oncology therapeutic nucleic acid-based test systems have the same or a similar risk profile. Further, FDA has not identified any unique risks associated with the distinctions across these tests.

a monotherapy and/or treatment with OPDIVO (nivolumab) in combination with YERVOY (ipilimumab).[12]

Since the first approval order for an oncology therapeutic nucleic acid-based test system, FDA has reviewed and approved an additional 18, 2, 13, and 1 original PMAs under the product codes OWD, PJG, PQP, and SFL, respectively, and approximately 200, 29, 174, and 0 PMA supplements, respectively, for therapeutic nucleic acid-based test systems under product codes OWD, PJG, PQP, and SFL.[13]

In accordance with the "six-year rule" described in section 520(h)(4) of the FD&C Act (21 U.S.C. 360j(h)(4)) (Ref. 6), FDA considered data contained in the following 17 original PMAs and one panel-track supplement to an original PMA, representing oncology therapeutic nucleic acid-based test systems from three of the four product codes (i.e., OWD, PJG, and PQP) for oncology therapeutic nucleic acid-based test systems: cobas 4800 BRAF V600 Mutation Test (P110020)(product code OWD)(Ref. 2), therascreen KRAS RGQ PCR Kit (P110027)(product code OWD)(Ref. 7), therascreen KRAS RGQ PCR Kit (P110030)(product code OWD)(Ref. 8), THxID BRAF Kit (P120014)(product code OWD)(Ref. 9), cobas EGFR Mutation Test (P120019)(product code OWD)(Ref. 10), therascreen EGFR RGQ PCR Kit (P120022)(product code OWD)(Ref. 11), BRACAnalysis CDx (P140020)(product code PJG)(Ref. 3), cobas KRAS Mutation Test (P140023)(product code OWD)(Ref. 12), cobas EGFR Mutation Test v2 (P150044)(product code OWD)(Ref. 13), cobas EGFR Mutation Test v2 (P150047)(product code OWD)(Ref. 14), FoundationFocus CDx$_{BRCA}$ Assay (P160018)(product code PQP)(Ref. 4), FoundationFocus CDx$_{BRCA\ LOH}$ (P160018/S001)(product code PQP)(Ref. 5), Praxis Extended

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[12] As of the date of issuance of this proposed order, fewer than 6 years have transpired since FDA's approval of the Idylla CDx MSI Test (PMA P250005). Therefore, no information from this document has been used in support of this proposed order to reclassify oncology therapeutic nucleic acid-based test systems into class II (see section 520(h)(4) of the FD&C Act (21 U.S.C. 360j(h)(4))).

[13] FDA has determined that the tests assigned to product codes OWD, PJG, PQP, and SFL all utilize NAAT and/or sequencing-based technology for use with a corresponding approved oncology therapeutic product, and have sufficiently similar purposes, design considerations, functions, and other features related to safety and effectiveness such that all oncology therapeutic nucleic acid-based test systems have the same or a similar risk profile. Further, FDA has not identified any unique risks associated with the distinctions across these tests.

RAS Panel (P160038)(product code PQP)(Ref. 15), LeukoStrat CDx FLT3 Mutation Assay (P160040)(product code OWD)(Ref. 16), Oncomine Dx Target Test (P160045)(product code PQP)(Ref. 17), Abbott RealTi*m*e IDH2 (P170005)(product code OWD)(Ref. 18), FoundationOne CDx (P170019)(product code PQP)(Ref. 19), and Abbott RealTi*m*e IDH1 (P170041)(product code OWD)(Ref. 20). No information from PMAs and PMA supplements for which fewer than six years have passed since FDA's approval has been used in support of this proposed order to reclassify oncology therapeutic nucleic acid-based test systems into class II (see section 520(h)(4) of the FD&C Act (21 U.S.C. 360j(h)(4))).[14]

A review of data from FDA's Manufacturer and User Facility Device Experience (MAUDE) database, which contains Medical Device Reports (MDRs) of adverse events, indicates that as of September 8, 2025 there have been 147 reported events for oncology therapeutic nucleic acid-based test systems under product codes OWD (N= 139 MDRs), PJG (N= 1 MDR), PQP (N= 7 MDRs), and SFL (N= 0 MDR) since the approval of the first oncology therapeutic nucleic acid-based test system in 2011.

After review of the data, the Agency has determined that false positive results account for the device problem associated with a significant number (over 80 percent) of the MDR reported events. Other device problems that were less frequently reported include, for example, incorrect, inadequate or imprecise result or readings, non-reproducible results, output problem, and false negative results. Notably, a significant majority (over 95 percent) of the MDRs reported under these product codes listed identified no clinical signs, symptoms, or conditions; no known impact or consequence to the patient; and/or no patient involvement. Other less frequently reported health impacts, include, for example, inadequate/inappropriate treatment or diagnostic exposure; minor injury/illness/impairment; and delay to treatment/therapy.

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[14] In accordance with section 520(h)(4) of the FD&C Act, FDA has not relied on information in PMAs and PMA supplements approved within the last 6 years to develop the proposed special controls or to otherwise inform this proposed reclassification action.

A search of these product codes in FDA's Medical Device Recalls database indicates that as of September 8, 2025, there have been four class III recalls, 23 class II recalls,[15] and no class I recalls[16] involving oncology therapeutic nucleic acid-based test systems. Of the 23 class II recalls, 12 occurred between 2014 and 2022, have since been terminated, and were determined to be due to non-specific molecular interactions or fluorescence artifacts, nonconforming material/component, and a process control issue, all of which led to or could lead to false positive test results. There is 1 class II recall that was terminated on July 19, 2021, for which the manufacturer's reason for the recall was potential false positive test results, but the root cause is still under investigation by the firm. Other reasons for the class II recalls include erroneous translation of the approved English labeling to Hungarian, an incorrect or lack of expiration date, and erroneous test results caused by off-label use or a manufacturing or design issue of the device.

Of the four class III recalls, three occurred between 2012 and 2015, have since been terminated, and were determined to be due to a device design issue leading to the device generating invalid results and a mix up of materials/components (i.e., incorrect packaging of internal-use only components and released for distribution). The remaining class III recall was terminated on December 11, 2017, for which the manufacturer's reason for the recall was the device generating false positive results, however, the root cause is still under investigation by the firm.

This postmarket data, coupled with the relatively low number of reported events that caused patient harm, indicate a generally good safety record for these device types. The MDR and recall events provide information on the risks to health (identified in section V of this

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[15] The database searches initially identified 13 class II recalls reported under the product code OWD. However, after manual review of the data it has been determined that there is one recall that was improperly coded under the product code OWG although the product listed should fall within the product code OWD. As such, for the purpose of this proposed order the data related to this recall has been included in the Agency's postmarket surveillance analysis and discussion surrounding recall data.

[16] Class I, II, and III recalls are defined in 21 CFR 7.3(m).

proposed order), which FDA believes can be effectively mitigated through general controls and the special controls proposed herein.

In response to FDA's announcement that the Agency intended to initiate the reclassification process for certain IVDs including companion diagnostic tests (Ref. 21), FDA received a petition on July 25, 2024 from Foundation Medicine Inc., (Docket No. FDA-2024-P-3484) requesting FDA to reclassify next-generation sequencing oncology panel devices used for somatic or germline variant detection that include one or more companion diagnostic indications (under product code PQP) from class III to class II. As discussed in this proposed order, FDA has considered the information available to the Agency and believes that there is sufficient information available to establish special controls, and that the special controls proposed in section VII, together with general controls, would provide a reasonable assurance of the safety and effectiveness of such devices under the PQP product code, as well as other similar devices under product codes OWD, PJG and SFL, and is proposing, on its own initiative, that oncology therapeutic nucleic acid-based test systems, including those under product code PQP, be reclassified from class III to class II.

III. Device Description

Oncology therapeutic nucleic acid-based test systems are postamendments devices classified into class III under section 513(f)(1) of the FD&C Act. These oncology therapeutic nucleic acid-based test systems are prescription IVDs intended for the detection of specific genetic variant(s) and/or other nucleic acid biomarkers in human clinical specimens using NAAT (e.g., PCR) and/or sequencing technology (e.g., NGS), and are indicated for use with a corresponding approved oncology therapeutic product. These oncology therapeutic nucleic acid-based test systems include IVD CDx devices which are devices that provide information that is

essential for the safe and effective use of a corresponding approved therapeutic product.[17] The use of an IVD CDx device with a therapeutic product is stipulated in the instructions for use in the labeling of both the diagnostic device and the corresponding approved therapeutic product, including the labeling of any generic equivalents of the therapeutic product.[18] An IVD CDx device could be essential for the safe and effective use of a corresponding approved therapeutic product to:

- Identify patients who are most likely to benefit from the therapeutic product;
- Identify patients likely to be at increased risk for serious adverse reactions as a result of treatment with the therapeutic product;
- Monitor response to treatment with the therapeutic product for the purpose of adjusting treatment (e.g., schedule, dose, discontinuation) to achieve improved safety or effectiveness;
- Identify patients in the population for whom the therapeutic product has been adequately studied, and found safe and effective, i.e., there is insufficient information about the safety and effectiveness of the therapeutic product in any other population.

FDA does not include in this definition of a CDx device IVD devices that are not essential to the safe and effective use of a therapeutic product.[19] For more information on CDx devices, see FDA's guidance titled "In Vitro Companion Diagnostic Devices – Guidance for Industry and Food and Drug Administration Staff" (Ref. 1).

Additionally, the oncology therapeutic nucleic acid-based test systems in this proposed order include IVD test systems that provide information about known benefits and/or risks of

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[17] FDA, "In Vitro Companion Diagnostic Devices – Guidance for Industry and Food and Drug Administration Staff," August 6, 2014. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/in-vitro-companion-diagnostic-devices.
[18] *Id.*
[19] *Id.*

patient populations related to the use of a corresponding approved therapeutic product and are referenced in the labeling for the corresponding approved therapeutic product but are not essential for the safe and effective use of the therapeutic product. For example, such devices can be used to assess a biomarker-defined population of patients and provide information regarding the overall survival (OS) rate or objective response rate for those patients compared to the broader population of patients for whom the corresponding therapy is indicated. The use of these devices is not a prerequisite for receiving treatment with the corresponding therapeutic product but can aid in the benefit-risk assessment as to the use of the corresponding therapy for those biomarker-defined patients.

FDA proposes to revise 21 CFR part 866 to create a new device classification regulation with the name "Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product." Nucleic acid-based test systems indicated for use with a corresponding approved oncology therapeutic product are identified as prescription IVD devices intended for the detection of specific genetic variant(s) and/or other nucleic acid biomarkers in human clinical specimens using NAAT and/or sequencing technology to provide information related to the use of a corresponding approved oncology therapeutic product. These test systems provide information that is essential for the safe and effective use of a corresponding approved oncology therapeutic product and/or are test systems that, while not essential to the safe and effective use of the corresponding approved oncology therapeutic product, provide information about known benefits and/or risks related to the use of the corresponding approved oncology therapeutic product.

IV. Proposed Reclassification and Summary of Reasons for Reclassification

In accordance with section 513(f)(3) of the FD&C Act and 21 CFR part 860, subpart C, FDA is proposing to reclassify oncology therapeutic nucleic acid-based test systems from class III into class II, subject to 510(k) requirements. FDA believes that there is sufficient information available to establish special controls, and that these special controls, together with general

controls, would effectively mitigate the risks to health identified in section V and are necessary to provide a reasonable assurance of the safety and effectiveness of therapeutic nucleic acid-based test systems.

Under this proposed order, if finalized, oncology therapeutic nucleic acid-based test systems will be identified as prescription IVD devices. If the proposed order is finalized, these devices will be subject to the prescription labeling requirements for IVD products (see 21 CFR 809.10(a)(4) and (b)(5)(ii)). Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For oncology therapeutic nucleic acid-based test systems, FDA has not made this determination and, therefore, the Agency is not proposing to exempt these proposed class II devices from 510(k) requirements.[20] If this proposed order is finalized, persons who intend to market an oncology therapeutic nucleic acid-based test system will need to submit a 510(k) to FDA and receive clearance prior to marketing the device.

This proposed order, if finalized, will decrease regulatory burden on industry, as manufacturers will no longer have to submit a PMA for these types of devices but can instead submit a 510(k) to the Agency for review prior to marketing their device. The 510(k) pathway is less burdensome and generally more cost-effective for industry and FDA than the PMA pathway, the most stringent type of device marketing pathway. A 510(k) typically results in a shorter premarket review timeline compared to a PMA, which ultimately may provide more timely access of these types of devices to patients. FDA expects that the reclassification of these devices would enable more manufacturers to develop these types of devices such that patients would benefit from increased access to appropriately safe and effective tests.

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[20] See *supra* note 8.

Additionally, manufacturers may wish to use predetermined change control plans (PCCPs) as a way to implement future modifications to their devices without needing to submit a new 510(k) for each significant change or modification[21] while continuing to provide a reasonable assurance of device safety and effectiveness.[22] FDA reviews a PCCP as part of a marketing submission for a device to ensure the continued safety and effectiveness of the device without necessitating additional marketing submissions for implementing each modification described in the PCCP. When used appropriately, PCCPs authorized by FDA are expected to be least burdensome for manufacturers and FDA.[23]

FDA believes that there is sufficient information available to FDA through the 17 original PMAs and 1 panel-track supplement for cobas 4800 BRAF V600 Mutation Test (P110020; product code OWD), therascreen KRAS RGQ PCR Kit (P110027; product code OWD), therascreen KRAS RGQ PCR Kit (P110030; product code OWD), THxID BRAF Kit (P120014; product code OWD), cobas EGFR Mutation Test (P120019; product code OWD), therascreen EGFR RGQ PCR Kit (P120022; product code OWD), BRACAnalysis CDx (P140020; product code PJG), cobas KRAS Mutation Test (P140023; product code OWD), cobas EGFR Mutation Test v2 (P150044; product code OWD), cobas EGFR Mutation Test v2 (P150047; product code OWD), FoundationFocus CDx$_{BRCA}$ Assay (P160018; product code PQP), FoundationFocus CDx$_{BRCA\ \mathrm{LOH}}$ (P160018/S001; product code PQP), Praxis Extended RAS Panel (P160038; product code PQP), LeukoStrat CDx FLT3 Mutation Assay (P160040; product code OWD), Oncomine Dx Target Test (P160045; product code PQP), Abbott RealTi*m*e IDH2

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[21] For the purpose of this proposed order reference to "modification" means a significant change or modification that would generally require a new premarket notification under 21 CFR 807.81(a)(3).
[22] Section 3308 of the Food and Drug Omnibus Reform Act of 2022, Title III of Division FF of the Consolidated Appropriations Act, 2023, Pub. L. No. 117-328 ("FDORA"), enacted on December 29, 2022, added section 515C "Predetermined Change Control Plans for Devices" to the FD&C Act. Section 515C has provisions regarding predetermined change control plans (PCCPs) for devices requiring premarket approval or premarket notification. Under section 515C, supplemental applications (section 515C(a)) and new premarket notifications (section 515C(b)) are not required for a change to a device that would otherwise require a premarket approval supplement or new premarket notification if the change is consistent with a PCCP approved or cleared by FDA.
[23] Sections 513 and 515 of the FD&C Act. See also, FDA, "The Least Burdensome Provisions: Concept and Principles – Guidance for Industry and FDA Staff," February 5, 2019. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.

(P170005; product code OWD), FoundationOne CDx (P170019; product code PQP), and Abbott RealTi*m*e IDH1 (P170041; product code OWD)[24] (Refs. 2-5, and 7-20), published peer-reviewed literature on nucleic acid-based detection methods, including NAAT and sequencing technologies, and FDA's publicly available MAUDE and Medical Device Recalls databases to establish special controls that effectively mitigate the risks to health identified in section V. More specifically, in evaluating these data sources, FDA has identified the risks to health for inclusion in the overall risk assessment for oncology therapeutic nucleic acid-based test systems. The Agency has considered the risks to health identified by these sources and used certain information from these sources in developing proposed special controls that include mitigation measures for each of the risks to health identified in section V. Accordingly, there would continue to be a reasonable assurance of safety and effectiveness for the devices upon their reclassification from class III to class II when there is conformity with general and special controls. Absent the special controls identified in this proposed order, general controls applicable to these devices are insufficient to provide reasonable assurance of the safety and effectiveness of oncology therapeutic nucleic acid-based test systems.

V. Risks to Health

FDA is providing a substantive summary of the valid scientific evidence concerning the public health benefits of the use of oncology therapeutic nucleic acid-based test systems, and the risks to health of these devices (see further discussion of the special controls being proposed to mitigate these risks in section VII of this proposed order). FDA considered data from 17 PMAs and 1 panel-track supplement available to FDA under section 520(h)(4) of the FD&C Act, published peer-reviewed literature on nucleic acid-based detection methods, including NAAT

[24] In accordance with section 520(h)(4) of the FD&C Act. FDA has not relied on information in PMAs and PMA supplements approved within the last 6 years to develop the proposed special controls or to otherwise inform this proposed reclassification action.

and sequencing technologies, and postmarket information regarding oncology therapeutic nucleic acid-based test systems.

Cancer continues to be one of the two leading causes of death in the United States (Ref. 22). Biomarker tests for molecularly targeted therapies aim to provide information for health care providers to target and/or tailor cancer treatment based on identifiable molecular differences between patients, with the goal of improving patient outcomes while minimizing risks related to treatment side effects. Oncology therapeutic nucleic acid-based test systems provide a benefit to the public health by aiding in oncology therapeutic product treatment decisions. These test systems may provide information that is essential for the safe and effective use of a corresponding approved therapeutic product and/or provide information about known benefits and/or risks related to the use of a corresponding approved therapeutic product that is not essential for its safe and effective use. For example, health care providers may use a relevant oncology therapeutic nucleic acid-based test system to identify specific patients who are eligible for the safe and effective use of a corresponding oncology therapeutic product, including those patients for which the drug is contraindicated, or monitor a particular patient's response to an approved oncology therapeutic product for the purpose of optimizing a dosing regimen. These devices can be used to enable personalization of oncology care by identifying patients who are most likely to benefit from a specific therapy and yield improved clinical outcomes, or who are at varying degrees of risk for a particular side effect related to the use of a specific therapy. Ultimately, the use of such devices informs treatment decisions and has a significant public health impact for cancer patients.

The Agency has identified the following risks to health associated with the use of oncology therapeutic nucleic acid-based test systems.

- *False negative test results or false positive test results.* False negative test results or false positive test results may negatively influence oncology therapeutic product treatment decisions for patients. For those test systems intended to provide information that is

essential for the safe and effective use of a corresponding approved oncology therapeutic product, this risk may result in the withholding of appropriate oncology therapeutic treatment, delayed treatment from an available appropriate alternative therapy, or receiving inappropriate therapy with varying degrees of consequence (e.g., failing to adjust therapy to achieve optimal clinical outcome or exposing a patient to otherwise avoidable serious adverse health risks caused by the therapeutic product). For those test systems that provide information about known benefits and/or risks related to the use of a corresponding approved oncology therapeutic product but are not essential for the safe and effective use of the corresponding approved oncology therapeutic product, this risk may negatively influence patient management based on a misinformed benefit-risk assessment related to the use of a corresponding oncology therapeutic product and could lead to many of the same negative patient outcomes associated with test systems intended to provide information that is essential for the safe and effective use of a corresponding approved oncology therapeutic product as previously described.

- *Failure of the test system to perform as intended or indicated.* For test systems intended to provide information that is essential for the safe and effective use of a corresponding approved oncology therapeutic product, failure of the test system to perform as intended or indicated may result in inappropriate clinical management, due to, among other things, the potential need to rerun the test, leading to a delay in effective treatment or inappropriate treatment for a patient based on delayed results that are essential for the safe and effective use of a corresponding approved oncology therapeutic product. Similarly, for those test systems that provide information about known benefits and/or risks related to the use of a corresponding approved oncology therapeutic product but are not essential for the safe and effective use of the corresponding approved oncology therapeutic product, this risk may result in the potential need to rerun the test, leading to a delay in treatment or inappropriate treatment for a patient based on delayed results that

would provide important benefit-risk information for a health care provider to aid in the clinical decision making related to the use of a corresponding oncology therapeutic product.

- *Failure to correctly interpret test results.* Failure to correctly interpret test results, such as incorrect interpretation of the biomarker classification or information provided regarding the therapeutic product, may result in the same negative outcomes associated with false negative or false positive test results as previously discussed. For example, for test systems intended to provide information that is essential for the safe and effective use of a corresponding approved oncology therapeutic product, incorrectly interpreting the test results as positive (i.e., false positive test results) may lead to a patient receiving ineffective or unnecessary treatment that may unnecessarily expose them to treatment toxicities. Similarly, for those test systems that provide information about known benefits and/or risks related to the use of a corresponding approved oncology therapeutic product but are not essential for the safe and effective use of the corresponding approved oncology therapeutic product this risk may, for example, lead to inappropriate patient management decisions made by a health care provider, such as, selecting a suboptimal treatment for a patient, and failure for the patient to realize benefit from a different therapy based on inaccurate benefit-risk information related to the use of a corresponding oncology therapeutic product.

VI. Summary of Data Upon Which the Reclassification Is Based

The safety and effectiveness of this device type has become well established since the initial approval of the first oncology therapeutic nucleic acid-based test system in 2011. FDA believes that oncology therapeutic nucleic acid-based test systems should be reclassified from class III (premarket approval) into class II (special controls) because special controls can be established to mitigate the risks to health identified in section V and are necessary, in addition to general controls, to provide a reasonable assurance of the safety and effectiveness of these

devices. The proposed special controls are identified by FDA in section VII of this proposed order.

Taking into account the health benefits of the use of these devices and the nature and known incidence of the risks to health of the devices, FDA, on its own initiative is proposing to reclassify these postamendments class III devices into class II. FDA believes, that when used as indicated, oncology therapeutic nucleic acid-based test systems can provide significant benefits to health care providers and patients.

In proposing to reclassify and establish special controls for oncology therapeutic nucleic acid-based test systems, FDA has considered and analyzed the following information: (1) data from 17 PMAs and 1 PMA panel-track supplement for oncology therapeutic nucleic acid-based test systems available to FDA in accordance with section 520(h)(4) of the FD&C Act, (2) published peer-reviewed literature on nucleic acid-based detection methods, including NAAT and sequencing technologies, and (3) MDR and recall data from the Agency's publicly available MAUDE and Medical Device Recalls databases. The available evidence demonstrates that there are public health benefits derived from the use of oncology therapeutic nucleic acid-based test systems which provide information related to the use of a corresponding approved oncology therapeutic product. In addition, the nature of the associated risks to health are known, and special controls can be established to sufficiently mitigate these risks.

FDA considered the safety and effectiveness of oncology therapeutic nucleic acid-based test systems through review of PMA data dating back to the initial approval of the first oncology therapeutic nucleic acid-based test system in 2011, under product code OWD (P110020) (Ref. 2). Subsequently, between August 17, 2011 and September 8, 2025, FDA approved 35 PMAs and 403 supplements for oncology therapeutic nucleic acid-based test systems under the product codes OWD, PJG, PQP, and SFL. For the purpose of this reclassification, FDA was able to consider data from the following 17 original PMAs and 1 panel-track supplement to an original PMA in accordance with section 520(h)(4): cobas 4800 BRAF V600 Mutation Test (P110020),

therascreen KRAS RGQ PCR Kit (P110027), therascreen KRAS RGQ PCR Kit (P110030), THxID BRAF Kit (P120014), cobas EGFR Mutation Test (P120019), therascreen EGFR RGQ PCR Kit (P120022), BRACAnalysis CDx (P140020), cobas KRAS Mutation Test (P140023), cobas EGFR Mutation Test v2 (P150044), cobas EGFR Mutation Test v2 (P150047), FoundationFocus CDx$_{BRCA}$ Assay (P160018), FoundationFocus CDx$_{BRCA\ LOH}$ (P160018/S001), Praxis Extended RAS Panel (P160038), LeukoStrat CDx FLT3 Mutation Assay (P160040), Oncomine Dx Target Test (P160045), Abbott RealTi*m*e IDH2 (P170005), FoundationOne CDx (P170019), and Abbott RealTi*m*e IDH1 (P170041) (Ref. 2-5, and 7-20).[25]

As part of the Agency's analysis for the proposed reclassification of oncology therapeutic nucleic acid-based test systems, FDA reviewed and considered information provided within each of these applications, including information available in the SSEDs and device labeling for each application, which demonstrated a reasonable assurance of safety and effectiveness of the devices. In developing the proposed special controls, the Agency considered the analytical and clinical studies and device performance data, all of which demonstrated appropriate performance of the device and supported each approval. FDA believes the proposed special controls can effectively mitigate the risks to health identified in section V and, along with general controls, can provide a reasonable assurance of the safety and effectiveness for oncology therapeutic nucleic acid-based test systems. Additionally, FDA identified the probable adverse effects or risks to health of the tests based on information provided within the applications. As diagnostic tests, oncology therapeutic nucleic acid-based test systems generally do not pose additional safety hazards or direct adverse effects to the patients being tested beyond those associated with routine procedures typical for a diagnostic workup of the disease. The risks to health identified within the applications include false test results (i.e., false negative or false positive test results),

[25] In accordance with section 520(h)(4) of the FD&C Act. FDA has not relied on information in PMAs and PMA supplements approved within the last 6 years to develop proposed special controls or to otherwise inform this proposed reclassification.

failure to correctly interpret test results or incorrect test results interpretations, and failure of the device to perform as intended or indicated. Based on data collected in the clinical and non-clinical studies conducted, the safety profile for the devices was generally deemed acceptable in supporting the approvals of these devices.

While the oncology therapeutic nucleic acid-based test systems that are the subject of the 17 PMAs and 1 PMA panel-track supplement have unique test attributes in certain respects (e.g., the use of a specific technology and/or the type of analyte(s) detected by the test system), FDA has determined that these tests have sufficiently similar purposes, design considerations, functions, and other features related to safety and effectiveness such that the information and data reviewed and analysis conducted by FDA was analogous across all 18 applications available to the Agency in accordance with section 520(h)(4) of the FD&C Act. As such, and in order to avoid redundancy, the following three summaries are intended to provide examples that are representative of the PMA information and data that was reviewed and considered by FDA across the 18 applications in proposing to reclassify oncology therapeutic nucleic acid-based test systems from class III (premarket approval) into class II (special controls).

For example, FDA reviewed the original PMA data for the first FDA-approved oncology therapeutic nucleic acid-based test system, which was approved on August 17, 2011, through an original PMA (P110020) (product code OWD) (Ref. 2), for a CDx test, cobas 4800 BRAF V600 Mutation Test, intended for the qualitative detection of the BRAF V600E mutation in DNA extracted from FFPE human melanoma tissues and to be used as an aid in selecting melanoma patients whose tumors carry the BRAF V600E mutation for treatment with vemurafenib. The Agency considered the submitted studies and data provided in the approved submission, which demonstrated reasonable assurance of safety and effectiveness of this test when used in accordance with the indications for use. Such studies and data include the results of the international, randomized, open-label, controlled, multicenter, Phase III clinical study N025026 (BRIM3) for which the cobas 4800 BRAF V600 Mutation Test was used as a CDx test for

selecting patients for treatment with vemurafenib (Zelboraf). Results from this clinical study demonstrated that patients who received treatment with vemurafenib (Zelboraf) based on a BRAF V600E positive test result as detected by the cobas 4800 BRAF V600 Mutation Test met the study's two co-primary efficacy endpoints, OS and PFS as compared to dacarbazine. Therefore, the results of this clinical study helped to demonstrate a reasonable assurance of the safety and effectiveness of the cobas 4800 BRAF V600 Mutation Test for its indicated use, as an aid in selecting melanoma patients whose tumors carry the BRAF V600E mutation for treatment with vemurafenib. The performance of the test was also supported by the analytical validation studies. For example, reproducibility studies demonstrated very good agreement to support analytical performance of the test. The adverse effects of the test are based on data collected in the BRIM3 clinical study. As a diagnostic test, the cobas 4800 BRAF V600 Mutation Test involves testing on FFPE human melanoma tissue sections, which are routinely removed as part of the diagnosis of melanoma by pathologists. The test, therefore, presents no additional safety hazard to the patient being tested. Potential adverse effects of the cobas 4800 BRAF V600 Mutation Test include failure of the device to perform as expected, failure to correctly interpret test results, and/or false positive test results or false negative test results which may lead to improper patient management decisions in melanoma treatment.

Additionally, FDA considered the original PMA studies and data from the Oncomine Dx Target Test PMA, which FDA approved on June 22, 2017 (P160045) (product code PQP) (Ref.17). The Oncomine Dx Target Test is a qualitative 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 FFPE tumor tissue samples from patients with non-small cell lung cancer (NSCLC) using the Ion PGM Dx System. The test system is indicated to aid in selecting NSCLC patients with V600E and EGFR (Ex. 19del or L858R variant) mutations in DNA, and ROS1 fusions in RNA for the targeted therapies of Tafinlar (dabrafenib) in combination with Mekinist (trametinib), Xalkori (crizotinib), and Iressa

(gefitinib), respectively, in accordance with the approved therapeutic product labeling. The Agency considered the submitted studies and data in the approved submission, which demonstrated reasonable assurance of safety and effectiveness of the Oncomine Dx Target Test when used in accordance with the indications for use. Such studies and data include the retrospective analyses of patients enrolled in two clinical studies (BRF113928 for BRAF V600E mutations and A8081001 for ROS1) and safety and efficacy data obtained from these trials. The clinical outcomes, based on objective response rate (ORR), observed for both clinical studies were maintained based on the ORR estimated from the respective bridging studies supporting the effectiveness of the Oncomine Dx Target Test to select NSCLC patients whose tumors are positive for BRAF V600E or ROS1 fusions for treatment with Tafinlar (dabrafenib) in combination with Mekinist (trametinib), Xalkori (crizotinib), respectively. The safety and effectiveness of the Oncomine Dx Target Test for the selection of NSCLC patients with an EGFR (Ex. 19del or L858R variant) mutation was demonstrated in a retrospective analysis of concordance between the Oncomine Dx Target Test and the FDA-approved QIAGEN therascreen EGFR RGQ PCR Kit. Results demonstrating a high concordance between the Oncomine Dx Target Test and the QIAGEN therascreen EGFR RGQ PCR Kit and comparable reproducibility performance observed between the two tests supported the effectiveness of the Oncomine Dx Target Test to identify NSCLC patients whose tumors are positive for the EGFR (Ex. 19del or L858R variant) mutations for treatment with Iressa (gefitinib). Further, analytical performance studies were conducted with the Oncomine Dx Target Test using DNA and RNA extracted from FFPE tissue of NSCLC patients which demonstrated acceptable sensitivity for the tested variants when used in accordance with the directions provided. The risks of the test or potential adverse effects of the test include failure of the device to perform as expected, failure to correctly interpret test results, and/or false positive test results or false negative test results that could lead to improper patient management decisions in NSCLC treatment. Therefore, the clinical and analytical data in this application supported the reasonable assurance of safety and

effectiveness of the Oncomine Dx Target Test when used in accordance with the approved indications for use.

As a final example, FDA considered PMA studies and data from the FoundationFocus CDx*BRCA* LOH[26] panel-track PMA supplement, which FDA approved on April 6, 2018 expanding the indications for use of this test (P160018/S001) (product code PQP) (Ref. 5) to include an indication for use to provide information that while not essential to the safe and effective use of a corresponding approved oncology therapeutic product, provides information about known benefits and/or risks related to the use of an approved oncology therapeutic product. FoundationFocus CDx*BRCA* LOH was originally indicated for the qualitative detection of BRCA1 and BRCA2 alterations in FFPE ovarian tumor tissue to aid in identifying ovarian cancer patients with deleterious tumor BRCA variants (tBRCA-positive) who may be eligible for treatment with Rubraca (rucaparib), providing information that is essential for the safe and effective use of Rubraca (rucaparib). The panel-track PMA supplement expanded the indications for use to include the qualitative detection of genomic LOH from FFPE ovarian tumor tissue to determine HRD status (defined as tBRCA-positive and/or LOH high) in ovarian cancer patients, and positive HRD status in such patients is associated with improved PFS from Rubraca (rucaparib) maintenance therapy. This new indication for use is to provide information about known benefits related to the use of the approved oncology therapeutic product, although the information provided is not essential to the safe and effective use of the corresponding approved oncology therapeutic product. In accordance with the six-year rule[27] and to support this proposed reclassification action, the Agency considered the submitted studies and data in the approved

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[26] The original device was approved under the trade name FoundationFocus CDxBRCA (P160018). The sponsor originally submitted the panel-track PMA supplement application (P160018/S001) for the same device with an expanded indication for use under the trade name FoundationFocus CDx*BRCA* HRD. However, through the review process, the sponsor decided to change the name to FoundationFocus CDx*BRCA* LOH. For the purpose of providing example summaries that are representative of the PMA information and data that was reviewed and considered by FDA to support the proposed reclassification action in accordance with the six-year rule (see section 520(h)(4) of the FD&C Act), the name used throughout this paragraph is FoundationFocus CDx*BRCA* LOH.

[27] In accordance with section 520(h)(4) of the FD&C Act, FDA has not relied on information in PMAs and PMA supplements approved within the last 6 years to develop the proposed special controls or to otherwise inform this proposed reclassification action.

submission, which demonstrated reasonable assurance of safety and effectiveness of this test when used in accordance with the indications for use. For example, the clinical performance of the test for its new indication was established based on results from ARIEL3, a Phase 3, global, randomized, double-blind clinical study of Rubraca (rucaparib) maintenance therapy demonstrating an improved PFS in patients selected by the FoundationFocus CDx$_{BRCA\ LOH}$ and a clinical bridging study that included an analysis of the concordance of the LOH results between the FoundationFocus CD x$_{BRCA\ LOH}$ and the clinical trial assay (CTA) used in the therapeutic product trial. The primary objective of the therapeutic product clinical trial was to evaluate PFS by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. The bridging study, which supports extrapolating the clinical performance characteristics of the CTA to a candidate device (in this case, the FoundationFocus CDx$_{BRCA\ LOH}$) to support the clinical validity of the candidate device, includes retrospective testing of clinical trial samples using the FoundationFocus CDx$_{BRCA\ LOH}$. To support that the FoundationFocus CDx$_{BRCA\ LOH}$ is clinically meaningful and provides information about known benefits and/or risks related to the use of the approved oncology therapeutic product, the clinical trial data were analyzed using a Cox Proportional Hazard model to demonstrate that there is an interaction between the test results (HRD status) and the corresponding therapeutic product in the intent-to-treat (ITT) population. The Proportional Hazard model showed a statistically significant improvement in PFS for patients randomized to Rubraca as compared with placebo in all patients, including the biomarker positive subgroups (i.e., HRD and tBRCA subgroups). Thus, results demonstrate there is overall probable clinical benefit of the FoundationFocus CDx$_{BRCA\ LOH}$ for its approved indication for use. However, the approved oncology therapeutic product drug is intended for all comers, irrespective of biomarker results, therefore, the information provided is not essential to the safe and effective use of the corresponding approved oncology therapeutic product. Further, the performance of the FoundationFocus CDx$_{BRCA\ LOH}$ was also supported by analytical validation studies, such as reproducibility and repeatability studies, which demonstrated acceptable analytical performance

of the assay. The risks of the test are based on data collected in the validation studies conducted to support the test approval. The FoundationFocus CDx$_{BRCA\ \mathrm{LOH}}$ involves testing on FFPE ovarian cancer tumor tissue. The risks of the test or potential adverse effects of the test include failure of the device to perform as expected, failure to correctly interpret test results, and/or false positive test results or false negative test results which could lead to improper patient management decisions in ovarian cancer treatment. Therefore, the clinical and analytical data in this panel-track PMA supplement supported the reasonable assurance of safety and effectiveness of this test when used in accordance with the indications for use.

In addition to the original PMA data from the 17 available PMAs and one PMA panel-track supplement, FDA further considered that nucleic acid-based detection methods, including NAAT and sequencing, are well-established technologies, for example, with NAAT, such as PCR, first described in the 1980s (Ref. 23). These technologies have been commonly used in both research and clinical settings for decades and their general principles are well understood and widely published in the literature at this time (Ref. 24). There have been significant scientific developments aimed at addressing certain limitations for NAAT and sequencing technologies and expanding the applications of these technologies, such as the introduction of a thermostable DNA polymerase in PCR and the emergence of high throughput or next generation sequencing techniques (Ref. 25-26). These developments further demonstrate the maturity of these technologies, and FDA considered the breadth of knowledge available regarding NAAT and sequencing technologies in proposing to reclassify oncology therapeutic nucleic acid-based test systems from class III (premarket approval) into class II (special controls). This includes, for example, the establishment of special controls that FDA believes can effectively mitigate those identified risks to health (discussed in section V) and, along with general controls, are necessary to provide a reasonable assurance of the safety and effectiveness for these devices.

Finally, a search of FDA's publicly available MAUDE database revealed 147 reported events for oncology therapeutic nucleic acid-based test systems under product codes OWD, PJG,

PQP, and SFL, a significant majority of which did not cause patient harm per the reports. A search of FDA's publicly available Medical Device Recalls database revealed that there have been four class III recall, 23 class II recalls, and no class I recalls involving oncology therapeutic nucleic acid-based test systems. The lack of class I recalls, and relatively few numbers of class II and class III recalls,[28] coupled with the relatively low number of reported events that caused patient harm, indicate a generally good safety record for this device type (see further discussion of the MDR and recall data in section II of this proposed order).

Based on the Agency's review of the information described in this proposed order, FDA has determined that special controls, in addition to general controls, are necessary to provide a reasonable assurance of safety and effectiveness for these devices, and that sufficient information exists to establish such special controls. Therefore, FDA, on its own initiative, is proposing to reclassify oncology therapeutic nucleic acid-based test systems from class III (premarket approval) into class II (special controls) subject to 510(k) requirements.

VII. Proposed Special Controls

FDA believes that the following proposed special controls would mitigate each of the risks to health described in section V and that these special controls, in addition to general controls, would provide a reasonable assurance of safety and effectiveness for oncology therapeutic nucleic acid-based test systems.

Risks of false positive test results or false negative test results, failure of the test system to perform as intended or indicated, and failure to correctly interpret test results can be mitigated by special controls, including certain design verification and validation activities. For example, documentation of clinical performance testing which must include clinical data demonstrating acceptable performance of the device for its intended use based on data generated using a dataset

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[28] As defined in 21 CFR 7.3(m), the numerical designation, i.e., I, II, or III, assigned by the FDA to a particular product recall indicates the relative degree of health hazard presented by the product being recalled. Class I recalls are those classified as the highest level of risk in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death.

representative of the intended use population. This may include, for example, data from use of the device as the clinical trial enrollment assay in the therapeutic product clinical trial or data from a method comparison study to an appropriate FDA-authorized device. The analytical performance testing must include data demonstrating appropriate analytical performance of the device such as the precision, analytical accuracy, analytical sensitivity, analytical specificity, and sample and reagent stability of the test system. In addition, device design verification and validation information must include the specification for risk mitigation elements intended to mitigate risks associated with testing and results interpretation including, controls, procedures, and user training requirements.

The risks of false test results, failure to correctly interpret test results, and failure of the device to perform as intended or indicated can be further mitigated by special controls that require specific information in the labeling for these test systems. For example, a requirement to provide a device description that includes a description of relevant limitations with regard to target/genomic region(s) that cannot be targeted and/or detected by the test system, as applicable. In addition, these risks can be further mitigated by labeling special controls that require an appropriate, as determined by FDA, summary of the performance studies performed and the results of those studies, thus informing the user of the expected performance of the device. Table 1 shows how FDA believes such risks to health described in section V would be mitigated by the proposed special controls.

Table 1.--Risks to Health and Mitigation Measures for Oncology Therapeutic Nucleic Acid-Based Test Systems

Identified Risks to Health	Mitigation Measures
False positive test results or false negative test results	Certain design verification and validation activities, including certain analytical validation and clinical validation data. Certain labeling information, including certain performance information.
Failure of the test system to perform as intended or indicated	Certain design verification and validation activities, including certain analytical validation and clinical validation data.

	Certain labeling information, including certain performance information.
Failure to correctly interpret test results	Certain design verification and validation activities, including certain analytical validation and clinical validation data. Certain labeling information, including certain performance information.

If this proposed order is finalized, oncology therapeutic nucleic acid-based test systems will be identified as prescription IVD devices. Therefore, these devices would be subject to the prescription labeling requirements for IVD products (see 21 CFR 809.10(a)(4) and (b)(5)(ii)).

If this proposed order is finalized, oncology therapeutic nucleic acid-based test systems will be reclassified into class II (special controls) and will be subject to premarket notification requirements under section 510(k) of the FD&C Act. As discussed in this proposed order, the intent is for the reclassification to be codified in the new classification regulation 21 CFR 866.6075. If finalized, firms will be required to comply with the particular mitigation measures set forth in the special controls. Adherence to the special controls, in addition to the general controls, is necessary to provide a reasonable assurance of the safety and effectiveness of oncology therapeutic nucleic acid-based test systems.

VIII. Analysis of Environmental Impact

We have determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

While this proposed order contains no new collections of information, it does refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 820 (Quality System Regulation) have been approved under OMB control

number 0910–0073; the collections of information in part 807, subpart E (Premarket Notification Procedures), have been approved under OMB control number 0910-0120; and the collections of information in 21 CFR parts 801 and 809 (Device Labeling) have been approved under OMB control number 0910-0485.

X. Proposed Effective Date

FDA proposes that any final order based on this proposal become effective 30 days after the date of its publication in the *Federal Register.*

XI. Codification of Orders

Under section 513(f)(3) of the FD&C Act, FDA may issue final orders to reclassify devices. FDA will continue to codify classifications and reclassifications in the Code of Federal Regulations (CFR). Changes resulting from final orders will appear in the CFR as newly codified orders. Therefore, under section 513(f)(3) of the FD&C Act, in the proposed order, we are proposing to codify Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product in the new 21 CFR 866.6075, under which these oncology therapeutic nucleic acid-based test systems would be reclassified from class III into class II.

XII. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at https://www.regulations.gov. References without asterisks are not on public display at https://www.regulations.gov because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. Although FDA verified the website addresses in this document, please note that websites are subject to change over time.

* 1. In Vitro Companion Diagnostic Devices – Guidance for Industry and Food and Drug Administration Staff, issued August 6, 2014 (available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/in-vitro-companion-diagnostic-devices).

* 2. P110020 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P110020

* 3. P140020 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P140020

* 4. P160018 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P160018

* 5. P160018S001 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P160018S001

* 6. "Guidance for Industry and for FDA Reviewers: Guidance on Section 216 of the Food and Drug Administration Modernization Act of 1997," issued on August 9, 2000. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-section-216-food-and-drug-administration-modernization-act-1997-guidance-industry-and-fda.

* 7. P110027 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P110027

* 8. P110030 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P110030

* 9. P120014 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P120014

* 10. P120019 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P120019

* 11. P120022 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P120022

* 12. P140023 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P140023

* 13. P150044 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P150044

* 14. P150047 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P150047

* 15. P160038 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P160038

* 16. P160040 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P160040

* 17. P160045 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P160045

* 18. P170005 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P170005

* 19. P170019 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P170019

* 20. P170041 Summary of Safety and Effectiveness, available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?ID=P170041

* 21. FDA, “CDRH Announces Intent to Initiate the Reclassification Process for Most High Risk IVDs,” January 31, 2024. Available at https://www.fda.gov/medical-devices/medical-devices-news-and-events/cdrh-announces-intent-initiate-reclassification-process-most-high-risk-ivds.

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List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 866 be amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

1. The authority citation for 21 CFR part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360*l*, 371.

2. Add § 866.6075 to subpart G to read as follows:

§ 866.6075 Nucleic Acid-Based Test Systems for Use with a Corresponding Approved Oncology Therapeutic Product.

(a) *Identification*. Nucleic acid-based test systems indicated for use with a corresponding approved oncology therapeutic product are identified as prescription in vitro diagnostic devices intended for the detection of specific genetic variant(s) and/or other nucleic

acid biomarkers in human clinical specimens using nucleic acid amplification (e.g., polymerase chain reaction) and/or sequencing technology (e.g., next generation sequencing) to provide information related to the use of a corresponding approved oncology therapeutic product. These test systems include devices that provide information that is essential for the safe and effective use of a corresponding approved oncology therapeutic product and devices that, while not essential to the safe and effective use of the corresponding approved oncology therapeutic product, provide information about known benefits and/or risks related to the use of the corresponding approved oncology therapeutic product.

(b) *Classification*: Class II (special controls). The special controls for this device are:

(1) Design verification and validation must include:

(i) A summary of the empirical evidence that establishes the appropriate analytical quality metrics and thresholds for the test system.

(ii) Device performance data demonstrating appropriate, as determined by FDA, analytical and clinical performance of the device for the intended use. This must include:

(A) Data demonstrating the precision, analytical accuracy, analytical sensitivity, analytical specificity, and sample and reagent stability of the test system. Analytical performance data must be evaluated for each gene/variant, or alternatively, justification for an alternative approach must be provided and determined by FDA to be appropriate, such as the use of a representative set of genes and/or variants.

(B) Data demonstrating all targeted region(s) that can be detected by the test system and disclosure of any region(s) not targeted or detected by the test system and/or with limited detection by the test system, as applicable.

(C) Clinical data generated using clinical specimens representative of the intended use population demonstrating appropriate, as determined by FDA, clinical performance of the device for its intended use.

(D) Data demonstrating appropriate validation of the intended specimen handling protocol and specimen preparation (e.g., nucleic acid extraction and purification) as described in the labeling.

(iii) Specifications and data that appropriately demonstrate the validity of the biomarker classification process, including any bioinformatic pipeline. This information must include a description of the classification process, including protocol(s) and criteria used for classification and reporting, and detailed documentation of the basis for biomarker interpretation with appropriate references.

(iv) Specification for risk mitigation elements intended to mitigate risks associated with testing and results interpretation including controls, procedures, and user training requirements, as appropriate.

(2) Labeling must include the following:

(i) A device description which includes:

(A) The biomarker(s) detected by the test system;

(B) Relevant limitations with regard to target/genomic region(s) that cannot be targeted or detected by the test system and/or with limited detection by the test system, as applicable;

(C) A description of the analysis algorithms used for biomarker detection and annotation, evaluation, and classification;

(D) A description of the quality metrics, thresholds, and filters utilized at each step of the test system, as applicable.

(ii) An appropriate summary, as determined by FDA, of the performance studies conducted and the results of those studies, including those that relate to all design verification and validation special controls.

(iii) For those test systems intended to provide information that is essential for the safe and effective use of a corresponding approved oncology therapeutic product, language indicating that the test system is indicated for use with a corresponding FDA-approved oncology

therapeutic product. Device labeling must be consistent with the information set forth in the corresponding FDA-approved oncology therapeutic product labeling.

(iv) For those test systems intended to provide information about known benefits and/or risks related to the use of a corresponding FDA-approved oncology therapeutic product but are not essential for the safe and effective use of the corresponding approved oncology therapeutic product, language summarizing the benefits and/or risks related to the use of a corresponding FDA-approved oncology therapeutic product that must be consistent with the information set forth in the corresponding FDA-approved oncology therapeutic product labeling.

Lowell M. Zeta,

Acting Deputy Commissioner for Policy, Legislation, and International Affairs.

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