November 17, 2017

VIA Electronic Mail to NCDRequest@cms.hhs.gov

Tamara Syrek Jensen
Director, Coverage and Analysis Group
Center for Medicare & Medicaid Services
Mail stop # S3-02-01
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Formal Request for an NCD:
Comprehensive Genomic Profile Testing with FoundationOne CDx™

Dear Ms. Jensen:

On behalf of Foundation Medicine, Inc. (FMI), the developer of the FoundationOne CDx™ comprehensive genomic profiling test (F1CDx), I am formally requesting that CMS establish a new National Coverage Determination (NCD) for comprehensive genomic profile testing for the management of cancer patients with solid tumors that are metastatic, including Stage IV and recurrent, with F1CDx. Comprehensive genomic profile testing falls under the Medicare benefit category for "diagnostic laboratory tests."[1]

Attached, please find documentation supporting this request – i.e., the information outlined in the September 26, 2003 *Federal Register* notice entitled "Revised Process for Making Medicare National Coverage Determinations".[2] As set forth in the attached documents, FMI requests that CMS publish an NCD that establishes the following coverage for comprehensive genomic profile testing:

A. *F1CDx is medically reasonable and necessary for the management of cancer patients with solid tumors of the following tissue types that are metastatic, including Stage IV and recurrent, when comprehensive genomic profile testing is ordered to inform patient management by the treating physician:*

   1. *Bladder*
   2. *Breast (female)*
   3. *Cancer of Unknown Primary*
   4. *Colon and rectum*
   5. *Endometrial*
   6. *Lung cancer—non-small cell*
   7. *Melanoma of the skin*
   8. *Ovary*
   9. *Pancreas*
   10. *Stomach/Gastric*

B. *F1CDx is medically reasonable and necessary for solid tumors of tissue types not listed above that are metastatic, including Stage IV and recurrent,*

[1] Soc. Sec. Act §1861(s)(3).

[2] 68 Fed. Reg. 55,634, 55,637 (Sept. 26, 2003) [CMS-3062-N].

when comprehensive genomic profile testing is performed within a clinical study that fulfills all the following:

1. *As a fully-described, written part of its protocol, the clinical research study must include a comparison of patients who have undergone F1CDx with a parallel group of Medicare beneficiaries who did not, matched for certain clinical characteristics, including cancer type, stage of disease, age, socio-economic status, and sex and must evaluate:*

    a. *The subset with a matched therapy or clinical trial on the F1CDx report*
    b. *The frequency that a match on F1CDx leads to receipt of the matched therapy (when data on receipt of matched therapies are available)*
    c. *The frequency that clinical trial potential eligibility determined by F1CDx leads to clinical trial enrollment (as determined through analysis of clinical trial claims)*

2. *Outcome comparisons must include time to disease progression and overall survival in the parallel groups as well as:*

    a. *Time to disease progression in those who received matched therapy consonant with the F1CDx report compared to matched patients on both the outcome of time to disease progression and overall survival.*

3. *The clinical study must adhere to the following standards of scientific integrity and be relevant to the Medicare population:*

    a. *The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.*
    b. *The research study is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.*
    c. *The research study does not unjustifiably duplicate existing studies.*
    d. *The research study design is appropriate to answer the research question being asked in the study.*
    e. *The research study is sponsored by an organization or individual capable of executing the proposed study successfully.*
    f. *The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found in the Code of Federal Regulations (CFR) at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it also must be in compliance with 21 CFR Parts 50 and 56.*
    g. *All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).*
    h. *The research study has a written protocol that clearly addresses, or incorporates by reference the standards listed as Medicare coverage requirements.*

i. *The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.*

j. *The clinical research study is registered on the www.ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.*

k. *The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org). However, a full report of the outcomes must be made public no later than three (3) years after the end of data collection.*

l. *The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.*

m. *The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.*

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

4. *The principal investigator must submit the complete study protocol, identify the relevant CMS research question(s) that will be addressed and cite the location of the detailed analysis plan for those questions in the protocol, plus provide a statement addressing how the study satisfies each of the standards of scientific integrity (a. through m. listed above), as well as the investigator's contact information, to the address below. The information will be reviewed, and approved studies will be identified on the CMS website.*

Director, Coverage and Analysis Group
Re: F1CDx CED
Centers for Medicare & Medicaid Services (CMS)
7500 Security Blvd., Mail Stop S3-02-01
Baltimore, MD 21244-1850

C. *F1CDx is not covered for cancer patients under the age of 18, those with hematologic malignancies, and/or those receiving only palliative care, including those in hospice care.*

Please contact Gary Martucci at 1-610-256-9182 (or by e-mail at gmartucci@foundationmedicine.com) if you have any questions regarding this request. We look forward to working with you and your staff on this request.

Sincerely yours,

Vincent A. Miller, MD
Chief Medical Officer
Foundation Medicine, Inc.

SUPPORTING DOCUMENTATION – NCD FOR COMPREHENSIVE GENOMIC PROFILE TESTING WITH FOUNDATIONONE CDX™

1. A full and complete description of the item or service in question.

F1CDx is a next generation sequencing based in vitro diagnostic device for detection of base substitutions, insertion and deletion alterations (indels), copy number alterations (CNAs) and select gene rearrangements in 324 genes, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB), using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. F1CDx is medically reasonable and necessary for the management of cancer patients with solid tumors that are metastatic, including Stage IV and recurrent, when comprehensive genomic profile testing is ordered to inform patient management by the treating physician.

2. A specific, detailed description of the proposed use of the item or service, including the target Medicare population and the medical condition(s) for which it can be used.

F1CDx is a next generation sequencing based in vitro diagnostic device for detection of base substitutions, insertion and deletion alterations (indels), copy number alterations (CNAs) and select gene rearrangements in 324 genes, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB), using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. F1CDx is medically reasonable and necessary for the management of cancer patients with solid tumors that are metastatic, including Stage IV and recurrent, when comprehensive genomic profile testing is ordered to inform patient management by the treating physician.[3] More specifically, F1CDx is used to accurately identify patients likely to benefit from a targeted and/or immunotherapy to improve patient outcomes.

The target population includes Medicare beneficiaries with solid tumors that are metastatic, including Stage IV and recurrent. In 2014, Medicare enrollees included 54,095,565 individuals (Centers for Medicare & Medicaid Services 2014). Among Medicare enrollees, an estimated 895,870 (1.7%) had solid tumor cancers, and approximately 26% of those enrollees (232,926; 0.43% of total Medicare enrollees) are estimated to have had metastatic solid tumor cancers eligible for testing with F1CDx based on SEER incidence rates for distant tumor diagnoses among individuals ≥ 65 years. Current experience

[3] The clinical terms defined in this coverage statement are defined as follows:

Term	Definition	Source
Solid tumor	An abnormal mass of tissue that usually does not contain cysts or liquid areas.	National Cancer Institute. Definition of solid tumor - NCI Dictionary of Cancer Terms. 2017 (link). Accessed August 11, 2017.
Stage IV	The cancer has spread to distant parts of the body at the time the patient is initially diagnosed with cancer.	National Cancer Institute. Cancer Staging. 2017 (link). Accessed August 11, 2017.
Metastatic	Having to do with metastasis, which is the spread of cancer from the primary site (place where it started) to other places in the body.	National Cancer Institute. Definition of metastatic - NCI Dictionary of Cancer Terms. 2017 (link). Accessed August 11, 2017.
Recurrent cancer	Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumor or to another place in the body.	National Cancer Institute. Definition of recurrent cancer - NCI Dictionary of Cancer Terms. 2017 (link). Accessed August 11, 2017.

indicates that approximately 12% of all solid tumors receive NGS biomarker testing with testing rates expected to double by 2020. Therefore, the actual utilization of NGS testing is expected to be between 12-24% of the eligible population.

Cancer patients under the age of 18, those with hematologic malignancies, and/or those receiving only palliative care, including those in hospice care, would not be eligible for F1CDx.

3. **A compilation of the supporting medical and scientific information currently available that measures the medical benefits of the item or service. This may include portions of primary study data that have been separately submitted to the FDA as part of its submission package and are deemed most relevant for our review.**

We are submitting a comprehensive dossier separately that summarizes the currently available medical and scientific information relevant to F1CDx (see Tab [insert tab number]). As requested, the dossier is organized consistent with the "ACCE Model List of 44 Targeted Questions Aimed at Comprehensive Review of Genetic Testing",[4] and includes information regarding the disorder(s) for/setting(s) in which F1CDx is intended for use, the analytic validity, clinical validity, and clinical utility of F1CDx, and an overview of the ethical, legal, and social implications associated with the provision of F1CDx. In addition, as F1CDx is undergoing review through the FDA/CMS parallel review program, CMS also has access to FMI's modular PMA submission to the FDA.

In the dossier, we have highlighted a subset of studies that demonstrate improved clinical outcomes across multiple tumor types when:

- Patients are treated with genomically-matched FDA-approved drugs or biologics that are identified as appropriate from testing of biomarker(s) included in FDA-approved companion diagnostics' labeling and/or that are otherwise used on-label consistent with results of genomic matching; or
- FDA-approved drugs or biologics are used off-label in an anticancer chemotherapeutic regimen that are identified as medically accepted due to the presence of a marker supported by one or more citations that are included (or approved for inclusion) in one or more of the CMS-recognized compendia (e.g., the American Hospital Formulary Service-Drug Information and other authoritative compendia as identified by the Secretary), supported by clinical evidence in CMS-recognized peer-reviewed publications, or are otherwise used off-label by study investigators; or
- Patients are treated with genomically-matched investigational agents.

4. **If the requestor has submitted an application to the FDA for market approval of the product for which coverage is sought, then a copy of the "integrated summary of safety data" and "integrated summary of effectiveness data," or the combined "summary of safety and effectiveness data," portions of the FDA application should be included in the request for an NCD. These documents will ensure that our review is comprehensive.**

FDA regulates F1CDx as a Class III medical device. F1CDx is FDA-approved (*see* P[insert PMA number]; approved [insert approval date], 2017) (see Tab [insert tab number]) as a next generation sequencing based in vitro diagnostic device for detection of base substitutions, insertion and deletion alterations (indels), copy number alterations (CNAs) and select gene rearrangements in 324 genes, as well

[4] *See* Centers for Disease Control and Prevention, ACCE Model List of 44 Targeted Questions Aimed at a Comprehensive Review of Genetic Testing (Dec. 28, 2010), https://www.cdc.gov/genomics/gtesting/acce/acce_proj.htm.

as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. F1CDx is intended to be used by physicians for patient management according to professional guidelines in oncology for cancer patients with any solid tumor and to inform molecular eligibility for clinical trials. Additionally, F1CDx is intended to be used as a comprehensive companion diagnostic to identify patients that may benefit from treatment following detection of:

Indication	Biomarker	Therapy
Non-small cell lung cancer (NSCLC)	*EGFR* exon 19 deletions and *EGFR* exon 21 L585R alterations	Gilotrif® (afatinib), Iressa® (gefitinib), or Tarceva® (erlotinib)
	EGFR exon 20 T790M alterations	Tagrisso® (osimertinib)
	ALK rearrangements	Alecensa® (alectinib), Xalkori® (crizotinib), or Zykadia® (ceritinib)
	BRAF V600E	Tafinlar® (dabrafenib) in combination with Mekinist® (trametinib)
Melanoma	*BRAF* V600E	Tafinlar® (dabrafenib) or Zelboraf® (vemurafenib)
	BRAF V600E and V600K	Mekinist® (trametinib) or Cotellic® (cobimetinib), in combination with Zelboraf® (vemurafenib)
Breast	*ERBB2* (HER2) amplification	Herceptin® (trastuzumab), Kadcyla® (ado-trastuzumab-emtansine), or Perjeta® (pertuzumab)
Colorectal cancer	*KRAS* wild-type (absence of mutations in codons 12 and 13)	Erbitux® (cetuximab) or Vectibix® (panitumumab)
	KRAS wild-type (absence of mutations in exons 2, 3, and 4) or *NRAS* wild type (absence of mutations in exons 2, 3, and 4)	Vectibix® (panitumumab)
Ovarian cancer	*BRCA1/2* alterations	Rubraca® (rucaparib)

In addition, as F1CDx is undergoing review through the FDA/CMS parallel review program, CMS also has access to FMI's modular PMA submission to the FDA.

5. An explanation of the design, purpose, and method of using the item or equipment, including whether the item or equipment is for use by health care practitioners or patients.

F1CDx involves the furnishing, by FMI, of a test report that summarizes the results of the F1CDx comprehensive genomic profiling test to licensed physicians. F1CDx is intended to be used by physicians for the management of cancer patients with solid tumors that are metastatic, including Stage IV and recurrent, when comprehensive genomic profile testing is ordered to inform patient management by the treating physician. Specifically, F1CDx is used to accurately identify patients likely to benefit from a targeted and/or immunotherapy to improve patient outcomes consistent with FDA-approved therapeutic labeling, CMS-recognized compendia (e.g., the American Hospital Formulary Service-Drug Information and other authoritative compendia as identified by the Secretary), peer-reviewed publications, and/or professional guidelines in oncology.

F1CDx can be ordered by a physician or non-physician practitioners as outlined in 42 C.F.R. § 410.32(a)(2).

6. A statement from the requestor containing the following:

a. An explanation of the relevance of the evidence selected.

The evidence summarized in (and attached to) this document establishes F1CDx as medically reasonable and necessary for the management of cancer patients with solid tumors that are metastatic, including Stage IV and recurrent, when comprehensive genomic profile testing is ordered to inform patient management by the treating physician. This evidence supports the use of F1CDx to accurately identify patients likely to benefit from a targeted and/or immunotherapy to improve patient outcomes consistent with FDA-approved therapeutic labeling, CMS-recognized compendia (e.g., the American Hospital Formulary Service-Drug Information and other authoritative compendia as identified by the Secretary), peer-reviewed publications, and/or professional guidelines in oncology.

b. Rationale for how the evidence selected demonstrates the medical benefits for the target Medicare population.

The outcome measures reported in the clinical studies referenced in the above-referenced dossier include well-established clinical outcomes measures for cancer patients with solid tumors that are metastatic, including Stage IV and recurrent, including response rate (complete or partial), time to treatment failure, progression-free survival, and/or overall survival.[5] The dossier also provides information on the populations included in the studies supporting the reasonable and necessary use of F1CDx, including information showing that F1CDx demonstrates medical benefit to the Medicare population.

c. Information that examines the magnitude of the medical benefit.

As noted above, the clinical outcome measures reported in the clinical studies referenced in the above-referenced dossier include well-established indications of medical benefit, including response rate (complete or partial), time to treatment failure, progression-free survival, and/or overall survival. The dossier also provides information on the populations included in the studies supporting the reasonable and necessary use of F1CDx, including information showing that F1CDx demonstrates medical benefit to the Medicare population.

d. Reasoning for how coverage of the item or service will help improve the medical benefit to the target population.

[5] *See, e.g.*, U.S. Food and Drug Administration, Guidance for Industry: Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (May 2007), https://www.fda.gov/downloads/Drugs/Guidances/ucm071590.pdf.

Establishing coverage for F1CDx will benefit cancer patients with solid tumors that are metastatic, including Stage IV and recurrent, by facilitating the accurate identification of patients with genomic alterations that make them likely to benefit from a targeted and/or immunotherapy to improve patient outcomes consistent with FDA-approved therapeutic labeling, CMS-recognized compendia (e.g., the American Hospital Formulary Service-Drug Information and other authoritative compendia as identified by the Secretary), peer-reviewed publications, and/or professional guidelines in oncology.

e. In the case of an aggrieved party, how that party is "in need" of the item or service.

Not applicable.

7. A description of any clinical trials or studies currently underway that might be relevant to a decision regarding coverage of the item or service.

As outlined in the above-referenced dossier (see Tab [insert number]), F1CDx is medically reasonable and necessary for the management of cancer patients with solid tumors that are metastatic, including Stage IV and recurrent, when comprehensive genomic profile testing is ordered to inform patient management by the treating physician. FMI supports several active clinical trials that may generate additional data further supporting F1CDx as medically reasonable and necessary. The following table identifies representative examples of such trials:[6]

Study title	Clinicaltrials.gov identifier	Enrollment (estimated)
Molecular Profiling in Tissue Samples From Patients With Cancer Who Are Exceptional Responders to Treatment	NCT02243592	300
S1400 Lung-MAP: Biomarker-Targeted Second-Line Therapy in Treating Patients With Recurrent Stage IV Squamous Cell Lung Cancer	NCT02154490	10,000
Comprehensive Genomic Analysis in Tissue and Blood Samples From Young Patients With Lung Cancer	NCT02273336	60
A Prospective Randomized Trial Comparing the Effectiveness of Physician Discretion Guided Therapy Versus Physician Discretion Guided Plus Next-Generation Sequence Directed Therapy	NCT02132845	100
Study of Molecular Profile-Related Evidence to Determine Individualized Therapy for Advanced or Poor Prognosis Cancers (I-PREDICT)	NCT02534675	225
Olaparib in Men With High-Risk Biochemically-Recurrent Prostate Cancer Following Radical Prostatectomy, With Integrated Biomarker Analysis	NCT03047135	50

[6] This table identifies studies supported by FMI that include comprehensive genomic profile testing with F1CDx or the FoundationOne® laboratory-developed test.

Study title	Clinicaltrials.gov identifier	Enrollment (estimated)
Study to Assess the Activity of Molecularly Matched Targeted Therapies in Select Tumor Types Based on Genomic Alterations	NCT02795156	160
A Phase III, Open Label, Randomized Study to Assess the Efficacy and Safety of Olaparib (Lynparza™) Versus Enzalutamide or Abiraterone Acetate in Men With Metastatic Castration-Resistant Prostate Cancer Who Have Failed Prior Treatment With a New Hormonal Agent and Have Homologous Recombination Repair Gene Mutations (PROfound)	NCT02987543	340
TRITON2: A Multicenter, Open-label Phase 2 Study of Rucaparib in Patients With Metastatic Castration-resistant Prostate Cancer Associated With Homologous Recombination Deficiency	NCT02952534	160
TRITON3: A Multicenter, Randomized, Open Label Phase 3 Study of Rucaparib Versus Physician's Choice of Therapy for Patients With Metastatic Castration Resistant Prostate Cancer Associated With Homologous Recombination Deficiency	NCT02975934	400
An Open Label, Single Arm, Multicentre Study to Assess the Clinical Effectiveness and Safety of Lynparza (Olaparib) Capsules Maintenance Monotherapy in Platinum Sensitive Relapsed Somatic or Germline BRCA Mutated Ovarian Cancer Patients Who Are in Complete or Partial Response Following Platinum Based Chemotherapy (ORZORA).	NCT02476968	275
A Phase III, Open Label, Randomised, Controlled, Multi-Centre Study To Assess the Efficacy and Safety of Savolitinib Versus Sunitinib in Patients With MET-Driven, Unresectable and Locally Advanced, Or Metastatic Papillary Renal Cell Carcinoma (PRCC)	NCT03091192	180
A Multi-arm, Phase Ib, Open-Label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumour Activity of AZD9291 in Combination With Ascending Doses of Novel Therapeutics in Patients With EGFRm+ Advanced NSCLC Who Have Progressed Following Therapy With an EGFR TKI (TATTON)	NCT02143466	298
A Modular Phase I, Open-Label, Multicentre Study to Assess the Safety, Tolerability, Pharmacokinetics and Preliminary Anti-tumour Activity of AZD6738 in Combination With Cytotoxic Chemotherapy and/or DNA Damage Repair/Novel Anti-cancer Agents in Patients With Advanced Solid Malignancies.	NCT02264678	230

Study title	Clinicaltrials.gov identifier	Enrollment (estimated)
ARIEL4 (Assessment of Rucaparib In Ovarian CancEr TriaL): A Phase 3 Multicenter, Randomized Study of Rucaparib Versus Chemotherapy in Patients With Relapsed, BRCA Mutant, High Grade Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer	NCT02855944	345
A Phase 1, Open-Label, Dose-Escalation and Expansion, Safety and Tolerability Study of INCB062079 in Subjects With Advanced Hepatocellular Carcinoma and Other Malignancies	NCT03144661	100
A Phase 2 Efficacy and Safety Study of Niraparib in Men With Metastatic Castration-Resistant Prostate Cancer and DNA-Repair Anomalies	NCT02854436	160
A Phase 2a Study to Evaluate The Clinical Efficacy of JNJ-42756493, A Pan-Fibroblast Growth Factor Receptor (FGFR) Tyrosine Kinase Inhibitor, In Asian Patients With Advanced Non-Small-Cell Lung Cancer, Urothelial Cancer, Gastric Cancer, Esophageal Cancer Or Cholangiocarcinoma	NCT02699606	55
A Phase I Dose Finding Study of Oral LXH254 in Adult Patients With Advanced Solid Tumors Harboring MAPK Pathway Alterations	NCT02607813	174
A Phase II Multicenter, Single Arm Study of Oral BGJ398 in Adult Patients With Advanced or Metastatic Cholangiocarcinoma With FGFR2 Gene Fusions or Other FGFR Genetic Alterations Who Failed or Are Intolerant to Platinum-based Chemotherapy	NCT02150967	120

8. **Information involving the use of a drug or device subject to FDA regulation as well as the status of current FDA regulatory review of the drug or device involved. An FDA regulated article would include the labeling submitted to the FDA or approved by the FDA for that article, together with an indication of whether the article for which a review is being requested is covered under the labeled indication(s). (We recognize that the labeling on FDA-approved products sometimes changes. For purposes of our review, we are interested in the labeled indications at the time a requestor submits a formal request. If, during our review, the labeled indication or status of a pending FDA approval or clearance changes, we expect the requestor to notify us.)**

FDA regulates F1CDx as a Class III medical device. Attached, please find the premarket approval notice for F1CDx (P[insert PMA number]; approved [insert approval date], 2017) (see Tab [insert tab number]), as well as the FDA-approved labeling for F1CDx (see Tab [insert tab number]).

9. **In the case of items that are eligible for a 510(k) clearance by the FDA, identification of the predicate device to which the item is claimed to be substantially equivalent.**

Not applicable (the FDA approved F1CDx under a PMA).