U.S. FOOD & DRUG ADMINISTRATION

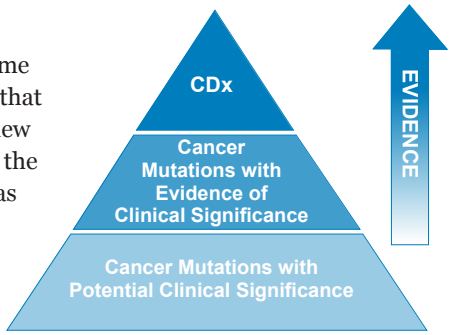
FDA FACT SHEET

CDRH'S APPROACH TO TUMOR PROFILING NEXT GENERATION SEQUENCING TESTS

The Food and Drug Administration (FDA) has recently announced the marketing authorization of three tumor profiling next generation sequencing (NGS) tests, Thermo Fisher Scientific's Oncomine Dx Target Test,[1] MSK-IMPACT[2] and Foundation Medicine's FoundationOne CDx[3] which are important advancements in the real-world application of precision oncology. The approach taken to the regulation of these tumor profiling NGS tests includes several key features described below.

Three-Tiered Approach for Reporting Biomarkers in Tumor Profiling NGS Tests

FDA is committed to and works individually with test developers to use the least burdensome approach for its review of tests. Multiplexed tumor profiling tests assess many biomarkers that may have a range of clinical evidence associated with them that is constantly changing as new science emerges. Below, we discuss the three levels of biomarkers addressed collectively in the Oncomine Dx Target TestMSK-IMPACT, and FoundationOne CDx authorizations, as well as the analytical and clinical evidence used to support claims for those biomarkers.



Level 1: Companion Diagnostics

Companion diagnostics (CDx) are test that provide information that is essential for the safe and effective use of a corresponding therapeutic product4 , such as a drug. Tumor profiling NGS tests may include CDx claims that are prescriptive for a specific therapeutic product, such as the Table 1 claims listed in the intended use for the Oncomine Dx Target Test and FoundationOne CDx. Such claims are supported by analytical validity of the test for each specific biomarker and a clinical study establishing either the link between the result of that test and patient outcomes or clinical concordance to a previously approved CDx.

New Level 2: Cancer Mutations with Evidence of Clinical Significance

Tests for biomarkers described as cancer mutations with evidence of clinical significance enable health care professionals to use information about their patients' tumors in accordance with the clinical evidence, such as clinical evidence presented in professional guidelines, as appropriate. Such claims are supported by a demonstration of analytical validity (either on the mutation itself or via a representative approach, when appropriate) and clinical validity (typically based on publicly available clinical evidence, such as professional guidelines and/or peer-reviewed publications).

Level 3: Cancer Mutations with Potential Clinical Significance

Mutations not considered biomarkers in Level 1 or Level 2 can be described as cancer mutations with potential clinical significance. These mutations may be informational or used to direct patients towards clinical trials for which they may be eligible. Such claims are supported by analytical validation, principally through a representative approach, when appropriate, and clinical or mechanistic rationale for inclusion in the panel. Such rationales would include peer-reviewed publications or in vitro pre-clinical models.

A Fluid Approach to Reporting within Levels 2 and 3

Following FDA review and authorization of a tumor profiling NGS test, the test developers will be able to report additional variants of the same type post-market within the existing analytically validated genes in the panel, for claims consistent with the clinical criteria established in the original submission, without an additional FDA submission. As evidence of clinical significance becomes recognized by the clinical community, and provided that the analytical validity of the test was reviewed and established in the initial or a subsequent submission, mutations can be moved from Level 3 to Level 2 without an additional FDA submission.

[1] Additional information on the premarket approval for the Oncomine Dx Target Test is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma. cfm?id=P160045

[2] Additional information on the marketing authorization of the MSK-IMPACT is available at https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm585347.htm

[3] Additional information on the premarket approval for the FoundationOne CDx is available at https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm587273.htm

[4] Additional information regarding companion diagnostics is available in FDA's guidance entitled "In Vitro Companion Diagnostic Devices," available at https://www.fda.gov/ downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM262327.pdf

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