Put It on the Board, 12/17

FDA announces IMPACT authorization and path for authorization of other tumor profiling tests

The FDA on Nov. 15 authorized Memorial Sloan Kettering Cancer Center's IMPACT (Integrated Mutation Profiling of Actionable Cancer Targets) tumor profiling test. The IMPACT test uses next-generation sequencing to identify the presence of mutations in 468 unique genes, as well as other molecular changes in the genomic makeup of a tumor.

The FDA's action set forth a policy framework that paves the way for the efficient review and availability of other NGS-based cancer profiling tools. The FDA also announced the recent accreditation of the New York State Department of Health as an FDA third-party reviewer of in vitro diagnostics, including tests similar to the IMPACT test. Moving forward, laboratories whose NGS-based tumor profiling tests have been approved by NYSDOH do not need to submit a separate 510(k) application to the FDA. Instead, developers may choose to request that their NYSDOH application, as well as the state's review memorandum and recommendation, be forwarded to the FDA for possible 510(k) clearance. Other accredited third-party FDA reviewers also may become eligible to conduct such reviews and make clearance recommendations to the agency.

"The goal of allowing NGS-based tumor profiling tests to undergo review by accredited third parties is to reduce the burden on test developers and streamline the regulatory assessment of these types of innovative products. As this field advances, we are modernizing the FDA's approach to the efficient authorization of laboratory tests from developers that voluntarily seek 510(k) clearance," FDA commissioner Scott Gottlieb, MD, said in a statement.

The IMPACT test was reviewed by the FDA through the de novo premarket review pathway. Results indicated the assay is highly accurate (greater than 99 percent) and capable of detecting a mutation at a frequency of about five percent (range of two to five percent). Detection of certain molecular changes (microsatellite instability) using the IMPACT test was concordant more than 92 percent of the time across multiple cancer types in 175 cases, when compared with traditional methods of detection, according to an FDA statement.

Along with this authorization, the FDA is establishing a class II regulatory pathway for the review of other NGS-based tumor profiling tests for use in patients diagnosed with cancer. Class II designation allows these types of tests to be eligible to use the FDA's 510(k) clearance process, either by submitting the application to the FDA directly or through an accredited third-party reviewer such as the New York State Department of Health.

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FoundationOne CDx approved with proposed coverage

The FDA approved the FoundationOne CDx (F1CDx), the first breakthrough-designated, next-generation-sequencing-based IVD test that can detect genetic mutations in 324 genes and two genomic signatures in any solid tumor type. The Centers for Medicare and Medicaid Services at the same time proposed coverage of the F1CDx.

“The FDA’s Breakthrough Device Program and Parallel Review with CMS allowed the sponsor to win approval for this novel diagnostic and secure an immediate proposed Medicare coverage determination within six months of the FDA receiving the product application,” FDA commissioner Scott Gottlieb, MD, said in a statement.

Jeffrey Shuren, MD, director of the FDA’s Center for Devices and Radiological Health, said in the statement, “With the run of one test, patients and health care professionals can now evaluate several appropriate disease management options.”

The CMS issued a proposed national coverage determination of the F1CDx and other similar NGS IVDs for Medicare beneficiaries with advanced cancer (i.e., recurrent, metastatic, or advanced stage IV cancer) who have not been previously tested using the same NGS technology and continue to seek further cancer therapy.

This determination was made under the FDA-CMS Parallel Review Program, in which the agencies concurrently review medical devices to help reduce the time between the FDA’s approval of a device and Medicare coverage. This voluntary program is open to certain premarket approval applications for devices with new technologies and to medical devices that fall within the scope of a part A or part B Medicare-benefit category and have not been subject to a national coverage determination.

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FDA clears Ventana MMR IHC Panel for CRC

Roche announced in November FDA clearance of the Ventana MMR IHC Panel for patients diagnosed with colorectal cancer. The tests detect proteins associated with a DNA mismatch repair and aid in differentiating between sporadic CRC and probable Lynch syndrome.

The panel of five assays includes four that target MMR proteins MLH1, MSH2, MSH6, and PMS2, as well as the Ventana BRAF V600E (VE1) assay. It is the first test to be granted a de novo class II designation from the FDA for MMR testing.

The panel consists of Ventana anti-MLH1 (M1), Ventana anti-PMS2 (A16-4), Ventana anti-MSH2 (G219-1129), Ventana anti-MSH6 (SP93) antibodies, for patients diagnosed with colorectal cancers for the detection of MMR protein deficiency as an aid in identifying probable Lynch syndrome, and Ventana BRAF V600E (VE1) antibody as an aid in differentiating between sporadic CRC and probable Lynch.

The ready-to-use panel is optimized for use with the OptiView DAB IHC detection kit, OptiView amplification kit, and ancillaries on the fully automated BenchMark Ultra system.

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SeraCare issues NGS reference material for hematologic malignancies

SeraCare Life Sciences has launched its Seraseq Myeloid DNA and Myeloid RNA fusion reference materials, the first set of comprehensive myeloid cancer NGS reference materials. These materials include a wide range of mutation types, from simple but clinically important SNVs to gene fusions. To maximize compatibility with existing and emerging myeloid assays, the new products contain 23 DNA mutations (including FLT3 ITDs and NPM1) along with nine fusion RNAs (including BCR-ABL and PML-RARA). Variants are present against a single well-characterized

genomic background (GM24385) at clinically relevant allele frequencies that are precisely quantified using highly sensitive digital PCR assays.

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Sysmex offers two new hematology systems

Sysmex America introduced last month two hematology automation systems, the XN-9100 and XN-3100. Both systems integrate with the new SP-50 fifth-generation slidemaker-stainer.

The XN-9100 saves space over previous models with its new twin modularity, combining two neighboring XN units in one twin module. It offers enhanced adaptability with add-on modules for lab-specific modification to meet testing needs, including total lab automation connectivity that is compatible with major manufacturers' systems.

The XN-3100 is a compact benchtop unit for lower- to mid-volume testing facilities. The recommended workload is 250 to 400 samples per day.

Sysmex announced on Nov. 8 that its XW-100 CBC analyzer received FDA clearance, making it the first CLIA-waived CBC system.

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FDA approves Ventana ALK (D5F3) CDx assay

Roche has obtained FDA approval for the Ventana ALK (D5F3) CDx assay as a companion diagnostic to identify ALK-positive non-small cell lung cancer patients eligible for treatment with Roche's Alecensa (alectinib). The Ventana ALK (D5F3) CDx assay is the only test approved as a companion diagnostic for Alecensa.

The assay is intended for the qualitative detection of the anaplastic lymphoma kinase protein in formalin-fixed, paraffin-embedded non-small cell lung carcinoma tissue stained with a BenchMark XT or BenchMark Ultra automated staining instrument. It is indicated as an aid in identifying patients eligible for treatment with Xalkori (crizotinib), Zykadia (ceritinib), or Alecensa.

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Study: Fewer biopsies for men tested with phi

A study published in *Prostate Cancer and Prostatic Diseases* found that physicians elected to perform fewer biopsies when Prostate Health Index, or phi, testing was included in their overall routine clinical assessment.

Phi testing is for men presenting with elevated serum total PSA in the 4–10 ng/mL range and a non-suspicious digital rectal exam. The findings, published in the November online issue of the journal (doi:10.1038/s41391-017-0008-7), were based on a comparison of more than 500 men tested with phi to a historical control group of similar men seen by the same participating urologists within the previous 24 months, and prior to the commercial implementation of phi testing in their practice. The FDA-approved test is exclusive to Beckman Coulter.

According to the study, titled "Clinical utility of the Prostate Health Index *(phi)* for biopsy decision management in a large group urology practice setting," men receiving a phi test showed nearly a 24 percent reduction in biopsy procedures performed compared with the historical control group (36.4 percent versus 60.3 percent respectively, $P<0.0001$). Physicians reported that the phi score had a significant impact on their patient management plan in more than 73 percent of cases, including biopsy deferrals when the phi score was low, and decisions to perform biopsies when the phi score indicated an intermediate or high probability of prostate cancer (phi≥36).

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ArcherDx, Celgene sign CDx agreement

ArcherDx has signed an agreement to develop and commercialize a next-generation-sequencing-based oncology companion diagnostic for Celgene's investigational drug CC-122 for indications in diffuse large B-cell lymphoma.

Under the terms of the agreement, ArcherDx will use its Anchored Multiplex PCR technology combined with the Illumina MiSeqDx sequencing system and Archer Analysis bioinformatics software to develop the companion diagnostic. The assay is based on a proprietary gene expression signature developed by Celgene to identify DLBCL patients most likely to respond to CC-122, a cereblon-modulating agent currently under investigation in multiple disease settings.
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