Put It on the Board, 6/16

Guidance seen as sign of FDA openness to digital pathology

The Food and Drug Administration has issued final guidance for industry and agency staff on how to assess the technical performance of whole-slide imaging devices. During a Digital Pathology Association webinar on the FDA action, experts said the guidance is another strong sign of the agency's working to detail the standards manufacturers will need to meet to earn approval for WSI's use in primary diagnosis.

The document ("Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices," available at http://1.usa.gov/1Xxw5iu) comes on the heels of presubmission discussions with WSI manufacturers and the DPA that cleared the road for submissions to go through the de novo pathway instead of the more cumbersome premarket approval process. See "FDA open to whole-slide imaging as class II device," CAP TODAY, February 2016, page 86.

"Previously, whole-slide imaging was considered class III with no predicate device available," said Esther Abels, director of quality and regulatory and medical affairs at Philips and chair of the DPA's regulatory task force. "And in December, the agency recommended we could follow the de novo pathway. I think this is great, and this also helps us put the TPA [technical performance assessment] into perspective for your applicant submission files."

The FDA's final guidance sets common standards for how the technical aspects of different technologies can be tested and assessed, Abels said.

"Whole-slide imaging devices all have similar purposes and intended uses, but they are differently designed," she said during the May 25 DPA webinar. "We need to ensure that all the elements and components representing the whole design, affecting the safety and effectiveness, are reasonably assured. This is for the end-user, so they know the device was tested thoroughly and that it's robust enough, that it's reproducible and repeats itself over and over again in the same way."

The FDA issued its draft guidance in February 2015. The final guidance was changed in response to outside comments on scope, specifications, and descriptions. It covers components such as the light source, imaging optics, processing software, scanning, file formats, and display as well as how the system functions as a whole. The TPA represents another move toward regulatory acceptance of digital pathology, Abels said.

"By taking this step, the agency recognizes that whole-slide imaging is an essential innovation that can have a significant impact on the current practice of pathology and medicine," she said. "The TPA is really helping us. It's the agency suggesting how to best characterize the technical aspects, and it takes a standardized and harmonized approach on testing."

As for the million-dollar question—when will the FDA approve use of WSI for primary diagnosis—no one yet knows

the answer. When the first submission for that intended use reaches the FDA, “there is no assurance it will be successful,” said Jeffrey Gibbs. He is director of the Hyman, Phelps, and McNamara law firm and an expert on FDA law and regulation of in vitro diagnostics.

“From the date of submission to the date of approval of de novo could be many months,” Gibbs said during the webinar. “Until someone submits the de novo and the clock starts ticking, the FDA doesn’t have to take action. But once that de novo is approved, then other submissions will become 510(k)s.”

Abels said decisions likely will turn on the quality of manufacturers’ submissions.
“It all depends on how much scientific evidence is generated and whether it gives probable assurance of safety and effectiveness,” she said. “The timelines are not known.”
[hr]

Eco effort cuts biohazard waste, saves money

An environmental initiative at the Cleveland Clinic laboratories has increased recycling by 20 percent and reduced biohazardous waste hauling charges by an estimated $10,000 a year. The effort succeeded by expanding the categories of items that could be tossed in recycling bins instead of into biohazard containers, and by working to educate laboratory professionals through a “know where to throw” campaign.

Ilyssa Gordon, MD, PhD, led the initiative. She is assistant professor of pathology at Cleveland Clinic and holds what may be a one-of-a-kind title in laboratory medicine: medical director for sustainability.

“Physician involvement is key in all of this,” she says. “While anybody can create interest in an [environmental] program for laboratories, we’re in a position to be able to make our voices heard and help make decisions with patients’ best interests in mind.”

Building on previous work in the Cleveland Clinic operating rooms, Dr. Gordon worked with the health system’s sustainability office and sanitation department to add another disposal option to laboratory spaces in the form of purple-bagged bins intended for hard plastics that lack recycling symbols as well as bulk, white Styrofoam. The items in those purple bags go to a local organization, Buckeye Industries, that employs people with disabilities to sort them for reuse.

In April 2014, the effort was piloted in the Cleveland Clinic’s cytogenetics laboratory and accompanied by a required educational module. Before the pilot, about 80 percent of waste went into biohazard containers and 20 percent went to containers destined for landfills. After the purple-bagged bins were introduced, 20 percent of the biohazardous waste shifted to the new disposal option. That change, multiplied across other laboratory spaces in the subsequent years, has added up to organizational savings because biohazardous waste is the priciest kind to dispose of.

“These savings accrue to the organization as a whole,” Dr. Gordon says. “It takes some convincing, and making the point that it’s not just about saving money but that it’s the right thing to do.”

Vendors supplying laboratories have an obligation to reduce waste upstream, she adds, noting a common hindrance to recycling efforts.

“The package insert in a kit is a folded-up piece of paper in shrink- wrap in a little square. That’s difficult for us, because we’re asking people to unwrap and throw the plastic wrapping in one bin and then throw the paper into another bin. We want companies to think about what they are sending us. They need to move ahead with the times. They should consider having a website [for the insert] listed on the box.”

Dr. Gordon would like to hear from leaders at other laboratories working to reduce their environmental footprint. If you have a story to share, please contact her at gordoni@ccf.org.—*Kevin B. O’Reilly*
[hr]

EGFR mutation liquid biopsy OK'd as companion Dx

The FDA has approved the Cobas EGFR Mutation Test v2, a blood-based companion diagnostic for the cancer drug Tarceva (erlotinib). This is the first FDA-approved, blood-based genetic test that can detect epidermal growth factor receptor gene mutations in non-small cell lung cancer patients. Such mutations are present in about 10 to 20 percent of such cancers.

With the Cobas EGFR Mutation Test v2, the presence of specific NSCLC mutations—exon 19 deletion or exon 21 (L858R) substitution mutations—detected in patients' blood samples aids in selecting those who may benefit from treatment with Tarceva. However, if such mutations are not detected in the blood, then a tumor biopsy should be performed to determine if the NSCLC mutations are present. The test may benefit patients too ill or otherwise unable to provide a tumor specimen for *EGFR* testing.

The efficacy of the Cobas EGFR Mutation Test v2 using blood samples was determined by using the test to identify the *EGFR* mutation status in patients enrolled in a clinical trial whose tumor biopsies were previously confirmed positive for the EGFR exon 19 deletion or L858R mutations as determined by the Cobas EGFR Mutation Test v1. The Cobas EGFR Mutation Test v2 is manufactured by Roche Molecular Systems in Pleasanton, Calif.
[hr]

Qiagen adds Horizon QC to next-generation system

Horizon Discovery Group announced that Qiagen will be offering an extensive package of quality control data, generated through the application of Horizon's reference standards, with its GeneReader NGS System.

As part of the project, Qiagen validated its platform using Horizon's molecular reference standards. By incorporating this data set into the GeneReader NGS System workflows, Qiagen is able to reinforce the accuracy of its NGS platform, facilitating system setup, quality assurance, and training for laboratories.

Qiagen markets the GeneReader platform, introduced in late 2015, as a solution to address fragmented NGS workflows and bottlenecks that have hindered many research labs from achieving actionable insights from next-generation sequencing.

[hr]

Siemens enters molecular oncology services market

Siemens has expanded its diagnostics portfolio with the acquisition of NEO New Oncology of Cologne, Germany. The company's cancer genome diagnostic platform NEO will support pathologists and oncologists with comprehensive molecular information to help select targeted cancer therapies.

NEO New Oncology is developing molecular profiling assays based on next-generation sequencing for tissue specimens and body liquids.

The acquisition of NEO New Oncology is intended to provide Siemens—whose health care division now operates as Siemens Healthineers—an entry point into NGS-based genomic testing and expands its capabilities in precision medicine and companion diagnostics. Furthermore, the acquisition aims to establish a business prospect in the field of molecular services, with the plan to provide testing services to physicians, hospitals, and laboratories.
[hr]

Roche PD-L1 tabbed as complementary test

The FDA has approved Roche's Ventana PD-L1 (SP142) Assay as a complementary diagnostic for patients who are

considering treatment with the FDA-approved Roche immunotherapy Tecentriq (atezolizumab) for metastatic urothelial cancer. This test is the first to evaluate patient PD-L1 status using immune cell staining and scoring within the tumor microenvironment.

The assay can identify patients most likely to respond to treatment with Tecentriq, as demonstrated by higher overall response rates in cohort two of the IMvigor 210 clinical trial. The novel approach uses immunohistochemistry technology designed to visually enhance and score PD-L1 protein on tumor-infiltrating immune cells. In an analysis based on 14.4 months of median follow-up, Tecentriq shrank tumors in 15 percent of people evaluable for efficacy whose disease progressed after platinum-based chemotherapy. Tecentriq shrank tumors in 26 percent of people whose disease had medium and high levels of PD-L1 expression.

PD-L1 testing is not required for the use of Tecentriq, but it may provide additional information for physicians and inform patient dialogue. [hr]