Put It on the Board, 11/14

For Ebola cases, weighing broader, faster diagnostics

November 2014—Amid initial confusion over Ebola-related safety protocols for health professionals providing direct patient care, laboratory professionals report hearing a consistent message from the CDC on proper specimen handling. The pressing question for laboratories is how best to approach testing with potential Ebola patients given the dual imperatives of preventing exposure and offering faster diagnostic answers.

Pathologists tell CAP TODAY that a smart strategy on Ebola has to involve getting clinicians, lab professionals, and administrators on the same page. That multidisciplinary approach to the disease was taken at University of Chicago Medicine, which in October saw one case of suspected Ebola at its medical center. The patient tested negative.

Dr. Beavis

Kathleen G. Beavis, MD, is interim director of the academic medical center's laboratories and medical director of the microbiology and immunology laboratories. In early discussions with other U. of C. stakeholders, Dr. Beavis pushed hard to make a wider menu of tests available to patients suspected of Ebola while they awaited definitive results from the Centers for Disease Control and Prevention.

Dr. Beavis says she was "not satisfied" with a protocol that would mean waiting the 12 to 48 hours it could take to get a conclusive Ebola result before offering "broader diagnostics." By September, she and her colleagues were able to persuade administrators and others to pursue a different strategy. When a patient who meets criteria for potential Ebola virus disease arrives, a special room near the isolation area is set up with instrumentation including BioFire's FilmArray to run the company's rapid respiratory, gastrointestinal, and blood culture identification panels. Thin-smear malaria testing also will be done when appropriate.

A similar approach was taken at Emory University Hospital, which by early November had successfully treated four Ebola patients. The hospital created "a self-contained POC laboratory" within its quarantine facility, which involved use of the FilmArray to "detect a panel of viral, bacterial, fungal, or parasitic pathogens" (Hill CE, et al. *Lab Med*. 2014; 45: e109–e111).

Dr. Beavis hopes this kind of protocol will yield better care for patients.

"It is much likelier the patient has one of the bacterial causes of diarrhea, for example, than Ebola. Let's get that diagnosed. . . . This is our challenge as pathologists, and as physicians—to offer the broadest range of diagnostic testing that we can," says Dr. Beavis, a member of the CAP's Microbiology Resource Committee.

Another member of that committee, Benjamin Pinsky, MD, PhD, directs the clinical virology laboratory at Stanford Healthcare and Stanford Children's Health. He says the notion of offering additional testing options for potential Ebola patients is "something we've been thinking about."

"We will be offering malaria testing by rapid antigen, as well as thin smears," he says. "That will be available. But at this point, we are not planning to perform respiratory virus testing with the anticipation that if the physicians believe the patient is sick enough, then they will just empirically treat them with Tamiflu."

The CDC does not advise the exclusive use of POC testing while awaiting Ebola test results, says Nancy E. Cornish, MD, a medical officer in the agency's Division of Laboratory Science and Standards.

Dr. Cornish

"There are a lot of things that need to be taken into consideration before deciding how you're going to handle these specimens," she tells CAP TODAY. "Laboratorians are well equipped to sit down and look at their laboratory, look at their instrumentation, and determine how they are going to handle this kind of testing."

Dr. Cornish says the CDC's lab-specific guidance on Ebola has remained consistent, unlike the shift seen in the agency's recommendations on personal protective equipment to be donned by health professionals in direct contact with patients. In October, the CAP published an Ebola update on its website that consolidates the agency's advice on handling specimens that have or may have Ebola. The document, along with several pertinent links to other CDC guidance, is at http://j.mp/capebola.

Suspected Ebola specimens must be sent to the CDC or one of about 30 labs that are part of the agency's Laboratory Response Network for testing with the Department of Defense's EZ1 real-time RT-PCR assay. A negative result with that test rules out Ebola, but a positive requires confirmation at the CDC using two additional RT-PCR assays: the CDC Ebola virus NP real-time RT-PCR and the CDC Ebola virus VP40 real-time RT-PCR. While the instrument time for that first rule-out test is between four and six hours, Dr. Cornish says, actual TAT varies depending on where the testing is done and how long it takes to transport the specimen there. Dr. Cornish advised laboratory professionals to consult with their state's public health laboratory to determine how quickly results can be available.

In late October, hospital labs got an option for faster results when the Food and Drug Administration gave emergency use authorization to a commercial Ebola test with an instrument time of about one hour. The Biothreat-E assay also runs on the FilmArray platform and was already being used at Emory. The emergency authorization makes it available to moderate- and high-complexity CLIA labs, and the test is priced at $185 per kit. The FilmArray instrument, already in place at more than 300 American hospitals, costs $39,500.

That one-hour turnaround time can make an impact that goes beyond clinical care, says Matt Scullion, vice president of sales and marketing at BioFire Defense, a division of BioMérieux.

"If you have to wait 12 to 48 hours to get answers back from the CDC lab, rather than have the results ready in one hour, that's time, stress, and patient care being held up because you don't have the diagnostics," Scullion says. "From a public, psychological perspective, knowing the answer in an hour… makes a huge difference."

Any laboratory using the Biothreat-E must still send specimens to an LRN lab or the CDC to rule in or rule out Ebola infection. Details about the emergency use authorization, instructions for use, guidance on interpretation, and more are available from BioFire at http://j.mp/biothreat-e.

Stanford's Dr. Pinsky says "we are absolutely considering performing the BioFire Biothreat-E assay." Dr. Pinsky is assistant professor in the Stanford University School of Medicine's Department of Pathology, as well as in the Department of Medicine's Division of Infectious Diseases and Geographic Medicine. He estimates it would take a week or two to validate the assay, if appropriate validation materials can be obtained.

"We could get that up and running in a relatively short amount of time, given the immediacy of this potential infection," Dr. Pinsky says. He adds that he would like to know more about the real-world clinical performance of

the assay, given that it was evaluated using specimens spiked with inactivated Ebola Zaire virus.

BioFire's Scullion notes that the company's Ebola test for defense applications—the NGDS BT-E assay—will be used as part of the Defense Department's deployment in West Africa. He says Emory University researchers are expected to publish their clinical experience with the Biothreat-E. Institut Mérieux, a philanthropic organization associated with BioMérieux, plans a study of 300 to 600 West African patient samples, Scullion says.

BioFire Defense's director of regulated products, Cynthia Phillips, PhD, says that head-to-head evaluations will be done to compare the Biothreat-E with an RT-PCR assay the CDC is using.

"We look forward to seeing those results published," she says. *–KBO'R*

LabCorp will buy CRO Covance for $6.1 billion

Laboratory Corp. of America has entered into a definitive agreement to acquire Princeton, NJ-based contract research organization Covance for cash and LabCorp shares valued at $105.12 per Covance share—an equity value of about $6.1 billion.

The aim is for Covance's risk-based patient monitoring tools to enhance LabCorp's predictive analytics capabilities to help at-risk patients, risk-bearing physicians, and payers. The combined company will leverage the scale of its central laboratory operations and collective data resources to drive greater research and development productivity for its clients, according to LabCorp.

"There's not a significant amount of overlap between our businesses," LabCorp CEO David P. King said in a conference call with investors and reporters. "We are adding approximately $900 million in high-margin central lab revenue to our base. This comes from a new payer, not from our current payer base."

King promised a "seamless integration of these two companies to create… a real powerhouse in health care services." He said the acquisition "will position us as the partner of choice for drug development," due in part to the 650,000 registered LabCorp patients who could be tapped for clinical trial recruitment.

King will serve as CEO of the combined company. The transaction is expected to close in the first quarter of 2015 and is subject to Covance shareholder approval, regulatory approvals, and customary closing conditions.

Chembio's POC HIV test lands CLIA waiver

The Food and Drug Administration recently granted a CLIA waiver for Chembio Diagnostics' DPP HIV 1/2 Assay.

The assay detects HIV antibodies in oral fluid or blood and uses the company's Dual Path Platform technology. The product's SampleTainer specimen collection bottle is a closed system.

The DPP HIV 1/2 Assay is one of only two FDA-approved, CLIA-waived oral fluid HIV 1/2 rapid tests available in the U.S. The other is made by OraSure Technologies.

$502 price for fecal DNA colorectal cancer test

The Centers for Medicare and Medicaid Services has issued its final National Coverage Determination for Cologuard, making it the first FDA-approved stool DNA test for the detection of colorectal cancer and precancer covered by Medicare. Coverage went into effect immediately, and the CMS has proposed payment of $502 for the test.

The decision was based on a comprehensive review as part of the FDA-CMS parallel review pilot program. Medicare says it will cover the test once every three years for average-risk, asymptomatic patients between 50 and 85 years old. Cologuard has been shown to find 92 percent of colorectal cancers in average-risk patients, with 87 percent specificity.

Biocare acquires CymoGen Dx

Biocare Medical has entered into an agreement to buy New Windsor, NY-based CymoGen Dx.

“CymoGen’s broad product line of next-gen FISH probes for detection of genetic anomalies in tissue samples adds to Biocare’s growing presence in the molecular diagnostics market,” Biocare CEO Roy Yih said in a statement. “Of particular importance are probes PTEN, TMPRSS-ERG, and AR, which will complement Biocare’s leading position in solid tissue IHC prostate markers.”

Biocare’s recently released Oncore Automated Staining platform has the capability to process slide-mounted, formalin-fixed, paraffin-embedded tissue samples through the entire in situ hybridization process.

CMS will cover test for ER+ breast cancer recurrence

BioTheranostics’ Breast Cancer Index test has been awarded Medicare coverage. The CMS posted a positive coverage and reimbursement policy after evaluation by Palmetto GBA, the Medicare administrator responsible for the MolDX molecular diagnostic technology assessment program.

Breast Cancer Index is a molecular genomic test that quantifies the risk of breast cancer recurrence and predicts which patients have a high likelihood of benefiting from extended endocrine therapy. The Medicare policy covers use of the test to predict the five- to 10-year recurrence risk in women with early stage, estrogen receptor-positive breast cancer.

In addition to new claims, Medicare coverage and payment for the Breast Cancer Index will be made retrospectively for previously submitted claims, according to the company.

Beckman, NEB automate NGS applications

Beckman Coulter Life Sciences, in partnership with New England Biolabs, offers automated methods to improve processes and throughput in next-generation sequencing sample preparation. Under the agreement, Beckman will develop, distribute, and support automation for NEB’s NEBNext sample prep reagent kits. NEB will provide technical expertise on the reagents, chemistry, and protocols.

Methods available now are NEBNext Ultra Directional RNA and NEBNext Ultra DNA (including for ChIP-Seq) for Illumina NGS and NEBNext Fast DNA Fragmentation and Library Prep for Ion Torrent. Other methods, including for NEBNext ribosomal RNA depletion and the NEBNext Small RNA reagent kits, are expected to follow.