New tests, technologies at center of 2016 CAP checklist revamp

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August 2016—Maybe laboratory accreditation checklists aren't the first reading you reach for when you want to unwind. But for an intriguing window into laboratory medicine and how it's changing, you might take a look at the revisions in the 2016 edition of the Laboratory Accreditation Program checklists, released in August.

"Just in the past few years, there's been an explosion in the ways that pathologists and laboratory folks are using new technologies to serve patients in familiar ways," says Gerald Hoeltge, MD, checklist commissioner and member of the CAP Council on Laboratory Accreditation. Many of the 2016 checklist revisions are geared to addressing this trend and related ones. Among the highlights: new standards for a just-emerging area of practice, a cogent recasting of one of the topics on which accreditation program staff field the most questions, revisions to keep pace with technology like mobile devices and robotic microscopy, and standards to catch up to the evolving role of telepathology.

Vocabulary updates, edits for concision and consistency, and streamlining are regular components of new checklist versions, and the 2016 checklist edition is no exception. For example, the word "documentation" has been changed to "records" throughout the checklists. But the 2016 checklists also feature notable additions and improvements to the requirements for record retention, in vivo microscopy, transfusion medicine, biorepositories, and telepathology. (For the 2016 revisions to the in situ hybridization checklist requirements, see page 60. The revisions to personnel checklist requirements will be covered next month.)

Record retention. The CAP had been receiving hints for some time that there was confusion about multiple different record retention requirements; accreditation program staff say they receive large numbers of questions on how long labs need to keep various types of records, Dr. Hoeltge notes. "These guidelines can apply to anything from tissue to cell samples to blood slides to plain old lab records," says Checklists Committee chair William W. West, MD, "but we've found they are in various places, sometimes buried in the middle of a note underneath a checklist requirement." They're often buried in text as well. "There might be a long paragraph listing the retention requirements for various records," says Dr. West, an associate professor and pathologist at the University of Nebraska Medical Center and Physicians Laboratory, PC, Omaha.

Dr. Hoeltge

The Checklists Committee hopes confusion will be stemmed by the reformatted and condensed record retention requirements, now in four convenient tables: one in the general checklist (GEN.20377), one in surgical pathology (ANP.12500), one in autopsy (ANP.33500), and one in cytogenetics. Says Dr. Hoeltge: "The staff and the committee carefully went through all 21 checklists and found every area where there was some kind of a record retention requirement and put them all together into a format that's easy to read and to identify whether your lab is utilizing best practices. The idea is that labs don't have to search all those vast resources on the CAP website to find the guidelines."

The tables will likely contain more detailed information in the future, and he considers the tabular format a model

for future checklist reformatting of other types of requirements.

Some record retention requirements were also updated, Dr. West notes. “Minor adjustments were made in the terminology, and the potential for longer retention requirements for minors’ records was added.”

Transfusion medicine. The checklist changes in transfusion medicine are related to the May 23, 2016 FDA final rule (specifically, 21 CFR 606.145, “Control of Bacterial Contamination of Platelets”), says Yara A. Park, MD, chair of the CAP Transfusion Medicine Resource Committee. A full review of the transfusion medicine checklist is not scheduled until 2017. “But this round was the kind of review and revision we do of the checklist when new rules come from the FDA or new things come on the market.”

Dr. Park

Development of the rule followed the FDA’s first approval of pathogen inactivation for platelets, which occurred in December 2014. With the rule, “I think what the FDA was trying to specify was exactly what they want suppliers to do with bacterial contamination testing. The idea is that now there is culture-based testing, rapid time of release testing, and the advent of pathogen inactivation on the scene and FDA approved. So there are different ways than we had thought of in the past of controlling for bacterial contamination,” says Dr. Park, an associate professor of pathology and laboratory medicine and medical director of transfusion medicine at the University of North Carolina at Chapel Hill.

The FDA final rule requires blood collection establishments and transfusion services to ensure that the risk of bacterial contamination of platelets is controlled adequately using FDA-cleared/approved devices or an equivalent system to detect the presence of bacteria in all platelet components. That requirement has been reflected in revised checklist requirement TRM.44955, which expands laboratories’ options for ensuring safe platelet components in line with new methods and technologies that are now approved by the FDA, including pathogen inactivation.

“I believe this is the first time we have specifically added pathogen inactivation into one of our checklist items,” Dr. Park says. While pathogen inactivation is popular in Europe, adoption in the U.S. has been slow, mainly due to the cost. “It’s quite expensive and platelets are already very expensive to buy. But pathogen inactivation has been coming into the headlines with illnesses such as Zika, so it’s appealing to more and more people.” She predicts use of pathogen inactivation will be more widespread in five years, although it can only be used on platelets and plasmas. “There’s no FDA-approved pathogen inactivation for red cells at this point.”

A new requirement (TRM.44957) was also added to the checklist to require laboratories to notify the collection facility if units are suspected of having bacterial contamination and to take steps to identify the organism. “I think most laboratories actually did this,” mostly using traditional culture-based microbiology testing, “but it wasn’t FDA-required until this year,” Dr. Park says.

TRM.44957 includes a requirement that records of testing of units be maintained as evidence of compliance. “Usually what the inspectors want to see at the time of inspection is not only evidence of standard operating procedures but also records that you’re actually doing the tests—for example, showing that a culture of platelets was done, here are the culture results, here is the time the culture was incubated, and so on.”

Notification to the blood supplier must also include information about the species identification where possible. “For example, if they can’t speciate it, we do give them the chance to say they tried but couldn’t identify the

organism. Alternatively, the laboratory may have an agreement with the blood supplier or a different lab to identify the organism."

The inclusion of pathogen inactivation as a method of controlling risk of contamination will help some labs right away, Dr. Park notes. "Before we added pathogen inactivation, people who chose to use pathogen inactivation and no longer used a culture-based method would have been found deficient. So the new checklist item allows people to have more choice in the way they approach contamination of platelets. If you're doing pathogen inactivation, culture is really unnecessary and just adds to your costs."

Dr. West

Telepathology and remote data assessment. Until this year, checklist requirements on telepathology were confined to anatomic pathology and cytopathology. "Now its use has expanded dramatically with our ability to transmit data to all kinds of locations," including to smartphones, Dr. West notes. So the Checklists Committee began in late 2015 to think of a broader concept of telepathology. This year, the checklist has been renamed "Telepathology and Remote Data Assessment."

Ordinarily, pathologists might review images and write interpretations in their offices, but many are turning to tablets and home computers to view those same images when out of the office. Or the pathologist might be in one location while the remote image is being generated by an internist doing an endoscopy at the hospital. "It's in the patient's best interest, of course, to get those diagnostic reports out in as timely a fashion as possible, so that needs to be encouraged. But it needs to be done right," Dr. Hoeltge says.

The telepathology checklist now specifically mentions flow cytometry, hematopathology, cytogenetics, and molecular pathology in addition to anatomic pathology. "In fact, the checklist addresses any lab situation where there's review of diagnostic material from a remote location," Dr. Hoeltge says. "It could be any place in the lab, as long as that review generates a formal report or becomes an entry into the patient's medical record."

Data transmission security and patient confidentiality are areas that generate concern and that the checklist strives to address, he says. But "these checklist requirements that have been around several years have been molded to address these other areas, and I think the revised 'remote data assessment' checklist items can be considered as helpful guideposts when a lab wants to roll an innovative idea into clinical practice."

Such innovations go beyond still images; they can include the video in an endomicroscopic procedure, or a "live" moving image generated by a microscope scanning a slide in a remote location. Some commercial systems allow a person sitting five miles away to control the instrument and cause a microscope to move the slide. "That's basically robotic microscopy," Dr. West says, "and how the slide gets moved is very complex." Or there might be a data file such as Sanger sequencing that wasn't initially an image but is displayed as an image on the screen for analysis purposes. To stay relevant to these and other new technologies, Dr. Hoeltge says, the aim is to make the checklist as inclusive as possible, "because we're recognizing it's not possible to predict what is going to happen."

Checklist requirement GEN.52842 has been updated to address the use of communication devices in public spaces. "This is becoming more of an issue simply because the data is becoming more mobile," Dr. West says. "Now I can take a picture of an image on the iPhone and transmit it to someone sitting at McDonald's having a cup of coffee. How do you protect patient data and patient privacy is the concern."

The CAP is getting a number of inquiries about different uses of new technologies. "Can you electronically submit orders from a remote site? Can you text in information? Can you text lab reports? These are complex issues

because of patient confidentiality and the requirement to retain medical records," Dr. West says. "You can't just order a test and not have a record of it six months later. You have to have some type of repository and some type of system to capture the data."

The only new item in the telepathology checklist is the section addressing telepathology system validation in the general checklist (GEN.50630). "Actually it isn't new in the sense that it was contained in other validation requirements," Dr. Hoeltge says. "But it was repeated in the data assessment section of telepathology items, just so everybody remembers that if you're coming up with a new way to do something, you've got to validate the process."

"What's really different is that it now says if you're going to validate, you have to use a real-world situation. In other words, if it's flow cytometry, you'll want to validate it with real or typical flow cytometry data," Dr. Hoeltge explains. "And secondly, the person validating has to be a pathologist or a person properly trained to assist them. Don't have the manufacturer's rep do it for you."

Biorepository. The CAP Biorepository Accreditation Program (BAP) was launched in 2012. Based on the principles of clinical laboratory accreditation programs, the BAP introduces multiple, scalable tools designed to improve and validate standard operating processes. It ensures consistent, industrywide verification of biospecimen quality and the proper implementation of regulatory efforts to protect the privacy and confidentiality of those from whom the biospecimens and data were obtained.

The primary change for 2016 is in the organization of the checklist, which lists requirements by category, such as biospecimen collection and handling, biospecimen processing and quality, and specialized techniques. This organization reflects the way in which inspection teams use the checklist to perform inspections, says Nilsa C. Ramirez, MD, chair of the Biorepository Committee and medical director of the Biopathology Center at Nationwide Children's Hospital in Columbus, Ohio.

"We were aware that biorepositories offered a large variety of services to investigators," she says. "However, evaluating the BAP applications and subsequently inspecting these biorepositories during the last four years provided us with a better picture of the variety and complexity of these services."

Biorepositories have a different set of challenges than do clinical laboratories, and the checklist will be modified over time to address them. "For example, biorepositories are constantly evolving to accommodate emerging research-based technologies in a cost-effective manner. Funding is also a challenge," Dr. Ramirez says, "as many rely on grant mechanisms that barely cover their budgetary needs."
She expects reorganization of the biorepository checklist to continue. "With the constant feedback we receive from the inspection teams, we are able to review and update checklist items on a regular basis. In addition, the CAP staff assigned to our program continues to support our efforts by offering valuable input. This process allows us to provide biorepositories with a checklist that can be customized to cover the constantly evolving field."

Future revisions are likely to address other issues. "We are always identifying new and unique services provided by biorepositories," Dr. Ramirez says. "Our goal is to incorporate items related to those services in future checklists. Considering our experiences so far, it is not uncommon for those unique services to become part of routine services offered by numerous biorepositories in a short period of time."

In vivo microscopy. Following the 2015 introduction of in vivo microscopy (IVM) requirements in the anatomic pathology checklist, the 2016 revisions include three new requirements that were added to the instruments and equipment section of the AP checklist for inspection of ex vivo uses of in vivo microscopy technologies. Ex vivo use of IVM technologies is the microscopic viewing of images or analog video for the evaluation of tissues or specimens that have been removed from the body.
The three new ex vivo microscopy (EVM) requirements address system validation (ANP.23560), function checks (ANP.23570), and method performance specifications availability (ANP.23580).

Sharad C. Mathur, MD, a member of the CAP In Vivo Microscopy Committee and chief of the pathology and

laboratory medicine service at Kansas City VA Medical Center, has been involved in standard setting for the field for some time. “One of the things we wanted to address right from the get-go was establishing best practices and guidelines for pathology institutions as well as non-pathologists who are using IVM. That led us to look at the concept of a checklist model.”

Various medical groups have used IVM, including cardiologists and gastroenterologists, as well as pathologists, he notes. But “it’s fairly new territory to look at IVM as the discipline of IVM. Within each application, an attempt at standardization has been made, with criteria for diagnosis and so forth, but globally there was no attempt to provide a framework for best practices. Every institution was doing its own thing.” Multiple groups were working on different organ systems, he says, but there was no single overarching group of practices.

The clinical practice of IVM is still limited, with only a few areas where it is routinely used clinically, Dr. Mathur says. “Some areas are on the cusp of becoming the standard of care and being used widely, but many areas are still investigational.”

That’s even more true of ex vivo microscopy, referring to use of imaging systems such as confocal microscopy, optical coherence tomography, multiphoton microscopy, optical spectroscopy/spectroscopic imaging, and similar technologies for evaluating tissues removed from the body. “In the ex vivo realm, everything is either in clinical trials or investigational; nothing is standard of care at this point. But there are a number of applications that can potentially be visualized for these types of techniques.”

For example, “To see if there is adequate representative diagnostic tissue in a small needle biopsy, sometimes we use touch preparations, and ex vivo applications could replace that. In other cases, we have to select tissue for tissue banking or special molecular studies. Right now, that’s being done by taking a small slice of tissue and doing a frozen section or some other type of visualization on it. That could also be performed by EVM technology.”

Since these applications are still investigational, the EVM checklist items could be somewhat premature, Dr. Mathur says. “The checklist will only apply to EVM for clinical care. So we do not anticipate that a large number of labs would use the checklist items at the moment. But I think it’s good to have that framework there, before these technologies become extremely widespread, so people have an idea of the kinds of best practices they should adopt.”
Many academic departments, he points out, are taking part in investigations of EVM and will gradually transition to clinical use—perhaps within the next year or two—and at that time the checklist items will apply. Having the EVM standards as part of the AP checklist, he believes, will spread awareness of the EVM technologies as on the horizon and recognized by the CAP.

While the IVM checklist items are a separate section of the AP checklist, the EVM applications were placed in the equipment and instruments section of the AP checklist because they are basically being used as new types of instruments within the AP lab, Dr. Mathur says. “We also modified a checklist requirement on retention of records, to include retention requirements for images from IVM and EVM.”

Within the new EVM checklist section, system validation is the most important item, he says. “If there are plans to put new imaging technologies in the pathology lab for ex vivo use, they need to ensure systems have been validated for that intended clinical use. And the validation has to be done by each lab for the clinical use intended for their lab. The same methodology might require different types of validation in different labs, depending on what they plan to do with it.” While the validation must emulate a real-world environment, the exact nature of the validation study is left up to the lab director.

The EVM function checks requirement refers to the need for regular function checks of the EVM system or instrument. “The manufacturer does have standard instructions for what checks need to be done to make sure the system is performing optimally. However, many of these systems are developed locally by labs, so they may not be standard off-the-shelf commercial systems and function checks would have to be defined for that system.”

The third checklist requirement relating to method performance specifications availability is to ensure that records

are maintained, Dr. Mathur notes. “Those records need to be available to ensure the system and any updates are correctly identified.”

The CAP Checklists Committee and scientific resource committee members say they are hopeful that this year’s substantive changes, streamlining, and more accessible format will enhance laboratories’ ability to meet the latest quality assurance challenges—as well as those that lie just around the corner.
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