Soon to be required: current susceptibility testing breakpoints

Valerie Neff Newitt

October 2023—A CAP accreditation program requirement that microbiology laboratories use current antimicrobial susceptibility testing breakpoints, which was added to the checklist in 2021, will go into effect Jan. 1, 2024.

Three other microbiology laboratory requirements in the 2023 checklist edition, released in August, are new, expanded, or revised.

The antimicrobial susceptibility testing requirement, MIC.11385, calls for laboratories to use current breakpoints for the interpretation of antimicrobial minimum inhibitory concentration and disk diffusion test results. For laboratories subject to U.S. regulations, new breakpoints must be implemented within three years of the date of publication of an update by the Food and Drug Administration.

For laboratories not subject to U.S. regulations, new breakpoints must be implemented within three years of publication of an update by the standards development organization the laboratory uses, such as the Clinical and Laboratory Standards Institute or European Committee on Antimicrobial Susceptibility Testing.

“This is an important and big change,” says Carol A. Rauch, MD, PhD, adjunct associate professor of pathology, microbiology, and immunology at Vanderbilt University School of Medicine, a member of the CAP Checklists Committee, and a member until recently of the CAP Microbiology Committee.

Dr. Rauch

“That’s why laboratories were given advance notice,” she says. “This gave them time to read it, understand it, and think about what it means as well as what they have to do to comply.”

The reason for the new requirement: “Organisms are evolving faster than our regulatory framework has evolved,” she says.

“Imagine the FDA approved a device 15 years ago with an automated instrument, panels, and software, and your lab still uses that device to test and issue results. In the meantime, organisms have developed resistance, and there’s new data about outcomes and pharmacokinetics, findings that can lead to a change in breakpoints used to interpret results. When this happens, the old breakpoints are then considered obsolete.” If the lab fails to detect resistance and reports to the clinician that the organism is susceptible to the drug, the clinician may choose that drug for therapy and the patient may not do well because the reported test result was erroneous.

“Unfortunately, nothing has compelled device manufacturers to update breakpoints for their systems, and labs often rely on manufacturers for guidance,” Dr. Rauch says.

“If we’re using a device that was FDA approved or cleared a long time ago with breakpoints that were current at that time, and underneath us the ground has changed, patients are at risk.”

Dr. Rauch recently worked with the CDC's Antibiotic Resistance Laboratory Network, where she observed that efforts to track resistance and contain outbreaks are hindered if the laboratory did not use current breakpoints.

"The resistance is not detected, and that resistant organism can spread to other patients within a facility and beyond as the patient moves to long-term care and then back to the ICU, et cetera. The labs doing the initial testing really have to do that right in order for our systems to work at containing resistance and making sure infections are treated appropriately."

Step one for labs is to "know your breakpoints," she says. "You can't implement new ones until you've identified which ones need it." A phase two requirement in the microbiology checklist, MIC.11380 Antimicrobial Susceptibility Test Interpretation Criteria, says there must be written criteria for determining and interpreting MIC or zone diameter sizes as susceptible, intermediate, resistant, nonsusceptible, or susceptible dose-dependent, and the criteria must be reviewed annually. This requirement was significantly revised in 2021 and, unlike MIC.11385, went into effect at that time.

"It expects labs to go through a process and find every organism, every method they use and every result they issue, and ask why they're calling it susceptible or what basis underlies their ability to say it's resistant," Dr. Rauch says. That is, how are the determinations made? Sounds simple, she says, because "everybody should know that for every laboratory test"—if the result is positive, for example, what makes it a positive result.

"But in this case, if you're using automated instruments, people may have been doing this for years and maybe weren't even working in the lab when it was set up," and don't necessarily have the information on hand. In talking with others in recent years about this problem and the need to determine if breakpoints are current, she knows many labs have had "'aha' moments" about an outdated breakpoint. Laboratories have been contacting their manufacturers to find out "what breakpoints are hidden in that big black box."

The CAP, CLSI, CDC, American Society for Microbiology, and Association of Public Health Laboratories created a seven-part breakpoint implementation toolkit, which became available recently, to help labs update MIC breakpoints (https://clsi.org/bit-toolkit). "Luckily, 11385 has had a fair amount of support from partner organizations," Dr. Rauch says of the collaboration and the resources that are online.

MIC.11385 doesn't require that every drug that exists be tested using the current breakpoints because each lab chooses which drugs its institution or clients need. "If you have something that is out of date because it won't detect current resistance in the world of microbes, you can choose to not report that erroneous result. You can test it by another method in your laboratory, such as a manual method," she says, noting that much of this issue is related to the large, automated commercially available instruments. "Or you could send it to another laboratory."

She advises working with clinicians and other antimicrobial stewardship partners to determine which drugs are the priorities. "There might be some drugs you don't report for a while or send out." The requirement's phase one status means if the laboratory receives a citation because it hasn't completed all of this work, "it can respond with the status of its plans," she says.

Of the activity the new requirement catalyzed in 2021, Dr. Rauch says: "There's work for manufacturers, work for professional organizations, and work for the labs. This work must be done, however.

"Patient safety is at risk here."

MIC.22050 Culture Media and Incubation Conditions is a new requirement in the checklist edition released in August.

It requires laboratories to use defined media and incubation conditions to allow for the recovery of potential pathogens for each culture type, specimen, and/or body site. It consolidates and replaces prior microbiology checklist requirements and says at minimum, media and incubation conditions must allow for isolation and identification of potential pathogens for the following: respiratory specimens (*Streptococcus pneumoniae* and

Haemophilus species), urine specimens (Gram-positive and -negative bacteria), genital specimens for *Neisseria gonorrhoeae* (selective media designed for its recovery, such as Thayer-Martin), and cerebrospinal and other sterile fluids (fastidious bacteria such as *N. meningitidis, S. pneumoniae,* and *H. influenzae*).

MIC.11350 Morphologic Observation Evaluation requires the lab to evaluate, at least annually, the consistency of morphologic observation among personnel who perform microscopic analysis from direct specimens and cultured organisms. The requirement now applies to all microscopic analysis, not just stains, and quantitation if applicable.

“The previous version of the checklist requirement focused on stains but now applies to anything you’re looking at under the microscope, including wet preparations. We want all of the staff doing it the same way,” Dr. Rauch explains, adding that the aim is consistency of result reporting.

MIC.16605 Mass Spectrometer Controls requires the laboratory to test appropriate control organisms on each day of patient testing. The revision specifies that the same protein extraction method used for clinical testing must be used when testing the microorganisms for quality control assessment.

“If it’s going to serve as a control, you have to do exactly what you would do for a patient,” Dr. Rauch says. For laboratory-developed tests, the choice and use of control organisms is at the lab director’s discretion. “But they have to make sure that whatever they are doing for controls matches what they are doing for patient specimens,” she says. “That’s the bottom line.”

New and revised requirements in other checklists were reported in the August issue (https://bit.ly/CT-082023) and in the September issue (https://bit.ly/CT-0923-visco).

CAP-accredited labs can access compliance-related resources on www.cap.org (in e-Lab Solutions Suite, log-in required, under Accreditation Resources), including the Oct. 18 Focus on Compliance webinar and other past Focus on Compliance webinars, as well as lab inspection preparation videos. Also online are answers to the most common checklist-related questions, a self- and post-inspection toolbox, and customizable templates and forms for, among other things, competency assessment and quality management.n

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