When implementing molecular testing in the microbiology laboratory at OSF Saint Francis Medical Center, we started with the more difficult laboratory-developed testing and then moved to the United States Food and Drug Administration (FDA)-approved assays, which are equally important but require a less rigorous evaluation process. FDA-approved molecular testing can be less difficult because the assays in question have already been developed and validated. Our responsibility is to make sure that these assays work for our laboratory, write up the protocol with our specifications, and perform training before we turn out results on patients. Using FDA-approved testing usually involves following certain guidelines, which takes most of the guesswork out of the evaluation process.

In 2007, the Illinois legislature passed a law known as the MRSA Screening and Report Act, which required all hospitals in Illinois to implement screening criteria for patients to determine whether they are carriers of methicillin-resistant Staphylococcus aureus (MRSA) on admission. This did not involve all patients but included those that were, according to the MRSA Screening and Report Act, “in all intensive care units, and other at-risk patients identified by the hospital”.

OSF established guidelines for screening that have change slightly over the years. The most current screening criteria are as follows:

- Patient being admitted into an intensive care unit
- Patient resides in a nursing home, assisted-living facility, prison, jail, or shelter, or is homeless
- Patient lives with a person who carries MRSA
- Patient has been hospitalized within the past 3 months
- Patient has received intravenous (IV) and/or oral (PO) antibiotics in the past 3 months
- Patient has a history of MRSA infection or colonization
- Patient has a history of IV drug abuse
- Patient is human immunodeficiency virus (HIV) positive
- Patient receives hemodialysis
- Patient uses an existing, functional percutaneous endoscopic gastrostomy (PEG) feeding tube, tracheostomy (trach) tube, or catheter
- Patient has open wounds and/or skin abrasion

At first, it seemed as though this new law would create a lot more work for the average microbiology technologist, depending on the size of the facility in which he or she works. At OSF in particular, this would have meant a significant increase in the number of cultures performed per week, not including post-treatment follow-up for patients whose specimens had yielded positive results on initial testing. This would also have resulted in a greater workload for the nursing staff because any patient with positive test results would have needed to be placed in isolation. OSF is not fully equipped with private rooms; hence, it was possible that patients would need to be moved in accordance with their MRSA status.

At the time, we were performing MRSA cultures with CHROMagar media (CHROMagar, Paris, France), which revealed a color change when MRSA was growing in the media. This type of testing has a turnaround time of 24 to 48 hours, which was unacceptable. We verified an FDA-approved assay on the Cepheid SmartCycler (Cepheid,
Sunnyvale, CA), which included a manual extraction option, and then real-time polymerase chain reaction (PCR) on the SmartCycler for amplification and detection. This process had to be batched; testing was only performed during the first shift, so the turnaround time was approximately 24 hours. This method was more useful than the culture method but was still not ideal. We discovered that certain samples yielded invalid results, which meant that we had to perform repeat testing. This method also took 3 to 4 hours of technician time, which was cumbersome compared with the mere minutes it takes to read a culture.

At approximately the time when we were starting to get accustomed to performing MRSA testing on the SmartCycler, we learned about the new GeneXpert molecular instrument (Cepheid), which performed real-time PCR from a direct sample in a simplified closed system within approximately 1 hour. The company had recently revealed that it had created an FDA-approved test to screen for MRSA in the nares on this instrument. My manager, along with infectious-disease physicians and other key stakeholders that included (but were not limited to) our infection-control team, persuaded hospital administrators why our current testing method, using the SmartCycler, was not ideal and that it was impractical to use the culture method as a basic screening tool. For the number of patients that would require screening, based on the new law, it was necessary for us to use a system that was quick, accurate, and could be performed during any shift. Based on this explanation, we received approval to purchase the GeneXpert system and to verify the FDA-approved MRSA screening assay.

We quickly ordered and received the GeneXpert instrument. While we awaited its arrival, we worked with Cepheid to schedule on-site training for the employees who would use the new instrument. Training personnel from Cepheid came to OSF for 2 days and provided complete, thorough training on the functionality of the GeneXpert instrument (including maintenance and cleaning). The trainer also helped me to upload the necessary software for MRSA testing and trained our team on performing that particular test. The procedure includes collecting samples properly (so that we can educate the nursing staff), ensuring sample integrity, performing the assay, reading results accurately, and troubleshooting invalid results.

As I mentioned earlier, the MRSA test performed on the GeneXpert instrument is an FDA-approved assay (for specimens collected from the nares only); hence, the evaluation requirements are quite different than the laboratory-developed assay evaluation requirements that I discussed in the most recent article in this series. The main difference is that an FDA-approved assay has already been validated by the manufacturer. It is now up to the consuming laboratory to verify that the product works effectively (and in the manner intended). In reference to guidelines from an online article published in 2006 in the journal Clinical Microbiology Reviews (published by the American Society for Microbiology), I established guidelines to follow in verifying the effectiveness of this MRSA assay. See Table 1 for suggested guidelines on verification of a qualitative FDA-approved assay.

<table>
<thead>
<tr>
<th>Table 1. Verification Elements for Qualitative FDA-Approved Test</th>
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<td><strong>Elements</strong></td>
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<tr>
<td>Accuracy</td>
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<tr>
<td>Precision, qualitative</td>
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<tr>
<td>Reportable range</td>
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<td>Reference intervals (normal values)</td>
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We successfully went live with the new MRSA screening assay on the GeneXpert instrument in February 2008; the assay quickly proved itself to be valuable. Using this assay and instrument, we were able to provide screening results within 2 to 4 hours of collecting the specimen. This allowed for a more efficient isolation process and the ability to treat colonization of MRSA much more quickly. We could never have experienced this level of efficiency and accuracy by using culture as a screening tool. However, we still use culture as a follow-up after treatment; PCR is too sensitive and will still yield positive results even after treatment.

When we started screening for MRSA by PCR, performed on the GeneXpert instrument, we performed approximately 800 tests per month. Now, we perform approximately 1000 to 1200 per month, not only on inpatients. We also perform testing for outpatient clinics and sister hospitals and have upgraded to a larger GeneXpert System, the GeneXpert Infinity (Cepheid). The methodology for this instrument is the same; however, the analyzer is more automated than the smaller system. It can be interfaced, and has the capability to run up to 48 cartridges at one time, versus the conventional 16 that can be run by the smaller GeneXpert instrument. Having the capacity to run more tests keeps us busy.

In addition to MRSA screening on the GeneXpert System, we have also been performing other FDA-approved assays. We converted from enzyme immunoassay (EIA) testing for *Clostridium difficile* A/B combination antigen to testing for *Clostridium difficile* toxin B. We also run an *Enterovirus* cartridge on cerebrospinal fluid (CSF) specimens and an assay that detects influenza types A and B and subtype H1N1. In addition, we perform an assay that detects MRSA and *S. aureus* in the nares; this test is mainly used for presurgical testing of patients undergoing orthopedic surgery. We are currently in the process of verifying the MRSA/*S. aureus* blood-culture, Factor II Prothrombin, and Factor V Leiden assays. LMc

References