Instrumentation and analytical methods

By James W. Jacobson, PhD, and Sherry A. Dunbar, PhD

Instrument systems and analytical methods for clinical diagnostics must provide accuracy and precision, speed and convenience for the quantification of specific molecular and particulate species, ideally with no or minimum system downtime. In addition, laboratory management has to address the requirements and costs of sample handling, chemical or physical processing, assay kinetics, sample throughput, data processing, and staffing needs as well as regulatory standards.

In recent years, new technologies and contributions to the life sciences and chemical analysis have included DNA microarray technologies, polymer-based microfluidics, time-of-flight mass spectrometer technologies, bioinformatics, and systems biology technologies. Experienced laboratorians also keep their eye on future developments that may be only two or three years away from availability to the clinical laboratory.

The current diverse and dynamic technology-innovation environment reveals researchers working on nucleic acid chemistry, bioinformatics, microfluidics, new molecular-diagnosics tests, and robotics. Incorporating technological advances into the lab, however, must be weighed with cost-reduction efforts and regulatory implementations.

A balance of factors

Gary W. Procop, MD, section head and clinical microbiology laboratory director, The Cleveland Clinic, says, “The acquisition of new instrumentation is an important laboratory decision that has to balance technical performance of the instrument, its ease-of-use, and cost. In some instances, the laboratorian may find it beneficial to lease or enter a reagent-rental agreement, particularly if changes in technology are expected in the near future.”

James Versolavic, MD, PhD, director, division of molecular pathology, Texas Children’s Hospital, says, “The rapid evolution from single- or oligonucleotide testing to multi-analyte testing and systems biology has created the need for more sophisticated instrumentation for molecular diagnostics. Technologies such as spectrally addressable liquid-bead arrays can provide the tools to examine multiple mutations and pathogens simultaneously and take advantage of advances in functional genomics. Laboratories will be challenged with incorporating these new highly parallel diagnostic technologies, and technical personnel must adapt to more complex quality-assessment systems.”

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The promise of the molecular-diagnostics market has finally begun to come to fruition. The development of reliable technologies that can deliver reliable nucleic-acid-based assays, both DNA and RNA, and are also consistent with traditional good laboratory practice, has been elusive. But, technologies are meeting these standards. That, combined with research to establish the clinical utility of multiplexed nucleic-acid assays, is creating — finally — a real molecular-diagnostics market. The future will likely mean results from multiplexed tests — a few to several hundred — that can be used to aid diagnostics and guide therapeutic decisions.

The emerging trends in diagnostics — not just in molecular-diagnostic testing, but also in multiplexed protein assays — indicate that multiplexing, especially focused multiplexing, is the future of the industry.

Adopting new technologies

A consequence of this current breakneck pace of technology innovation is the availability of a bewildering variety of exciting new analytical methods and platforms ranging from the “not ready for prime time” start-up to products at the full development stage. Opportunities to evaluate new technologies, instruments, and methods abound.

Adopting a new platform can be transforming for workflow, throughput, and business growth — and change is important, but it can also be expensive (e.g., cash, labor, time, and opportunity cost) if the laboratory fails to fully consider which technologies are best suited as solutions to specific problems it needs to solve. Many laboratories have evidence of less-than-stellar technology decisions gathering dust under cabinets or in closets.

In choosing to implement, or even evaluate, new technologies for the laboratory, management must ensure that the problem being addressed is the problem...
As laboratorians, what questions should be asked in evaluating a new method for implementation in the laboratory? Some questions are obvious ones — how does the method compare to what the lab is currently using? Assessment of performance characteristics in method comparisons and platform evaluations is well defined and has been published by numerous authors (i.e., Burtis & Ashwood, 1999; Murray, 2003), and within CLSI standards.

Other parameters are not nearly as obvious but are equally important — if we adopt this technology today, will the company be around tomorrow to support this decision to acquire the instrumentation? Clinical laboratories know that they require strong support from instrument vendors. Figure 1 is a reference checklist for the assessment of new instruments and/or analytical methods. The checklist includes due-diligence questions and issues worthy of serious consideration.

Complex decisions simplified
The complexity of the needs and requirements of the clinical laboratory means that the decision-making process for new instrumentation and/or analytical methods is equally complex. Laboratorians want to bring to their labs the highest level of technical sophistication in instrumentation and analytical testing that they can afford and have the space to operate. This includes increased testing capacity and reduced labor costs; reduced re-runs, calibrations, and missed holding times; reduced sample processing and multianalyte testing; and minimum downtime.

Quality and performance have always been critically important in the clinical-laboratory market as are the issues of cost and efficiency. The ability to make informed medical decisions is paramount, as is the ability to do so in a highly reliable, accurate, precise, and cost-efficient way. The right instrumentation needs
to have technology that addresses all of these points. Technology that delivers very high performance and does so in a way that impacts cost in real terms, including reducing labor costs, is key. Looking to the future, the technology choice should have versatility and flexibility to easily expand or reduce assay panels as needed to deliver fast, accurate, and cost-effective bioassay results.

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References