Automation in the Clinical Microbiology Laboratory

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KEYWORDS

• Clinical microbiology • Preanalytical automation • Total laboratory automation
• Efficiency • Quality

KEY POINTS

- Today there are more skilled technicians leaving the workforce than entering, which has resulted in a looming critical shortage of skilled laboratory workers. At the same time, laboratory testing is expected to increase with universal health care and an aging baby boomer population.
- Automation will play a key role in addressing workforce shortages while improving efficiency and maintaining quality in the clinical microbiology laboratory.
- Automation options range from preanalytical specimen processors to total laboratory automation (TLA) with digital imaging that allows for remote work-up of specimens and diagnostic telemedicine that will have an impact on patient care.
- The cost of laboratory automation will depend on the level of automation required. Future studies are needed to fully understand the financial and clinical impact of total automation on clinical laboratory workflow and patient outcomes.

THE CLINICAL MICROBIOLOGY LABORATORY TODAY

The role of the clinical microbiology laboratory is to assist in the diagnosis of infectious diseases. This role is critical to patient care, patient outcomes, and infection control. This is an era of newly emerging and re-emerging pathogens and increasing antimicrobial resistance. Couple this with a global society that has allowed for increased mobility of emerging pathogens and antibiotic-resistant superbugs across continents, and the role of the clinical microbiology laboratory cannot be understated. Additionally, if a bioterrorism event were to occur, the clinical microbiology laboratory would be a front line of protection to accurately identify the presence of a looming threat to the community.

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An illustrative example of this is the case of Andrew Speaker, who in 2007 created a tuberculosis scare after he traveled from Atlanta, Georgia, to Paris, Greece, Italy, Prague, and Canada and then back across the United States border, all while infected with multidrug-resistant tuberculosis.[1] This diagnosis was made with techniques that were developed over 40 years ago and require weeks to yields answers. Much in microbiology is still manual and requires highly skilled technologists to analyze and interpret cultures to provide organism identification and antimicrobial susceptibility profile. Improved techniques are on the horizon, the Xpert MTB/RIF assay (Cepheid, Sunnyvale, California) is a fully automated molecular assay that can detect *Mycobacterium tuberculosis* as well as rifampicin resistance from a direct specimen in 2 hours. Currently this assay is labeled for research use only, but is close to United States Food and Drug Administration approval and already in use outside the United States.

Most of the traditional methods in clinical microbiology are culture based, which requires the plating of specimens to growth media as they are received into a laboratory. The manual processing and plating of specimens is a way of life for bacteriology. Culture work-up today is manual and subjective and depends on a skilled technologist to read the plates and identify the pathogens. Over the past several decades, automation has made some inroads into clinical microbiology laboratories. Automation has had impacts on the area of bacterial identification and susceptibility testing with the introduction of the Vitek (bioMérieux, Marcy l'Etoile, France), MicroScan (Siemens, Malvern, Pennsylvania, and Newark, Delaware), and Phoenix (Becton Dickinson and Company, Franklin Lakes, NJ (BD)) systems. These systems allowed microbiology to move most of the testing from tubed biochemical identification and susceptibility testing methods to plates and cards with wells that can be incubated, monitored, and read automatically. Additionally, automated blood culture instruments that allow for the continuous monitoring of incubated blood culture bottles and flag cultures when positive was a leap ahead of the manual method of detecting positive blood cultures, both in terms of sensitivity and time to detection of positive cultures and workflow in laboratories. The manual method of working up blood cultures requires visual examination of bottles, subculturing of negatives, and 7 days of incubation. The streamlined use of staffing resources and improved methodologies has made adoption of these instruments commonplace.

With the advance of modern molecular techniques, the implementation of methods from translational research to the clinical laboratory has become easier. The use of polymerase chain reaction (PCR)-based tests have become more integrated in the routine microbiology laboratory. Historically molecular testing in the clinical laboratory has required the use of typically 3 unidirectional separate PCR rooms which make testing more complex. Currently in the United States, there are Food and Drug Administration–approved PCR assays that fully automate nucleic acid extraction, amplification, and detection in a closed single-use device. These advances have made this technology not only more accessible to smaller laboratories and nearer to patients. These systems have gone from a single pathogen target with an internal control to systems that now have the ability to detect 15 or more pathogens in a single specimen as a panel with a turnaround time of approximately 1 hour. Genome sequencing and gene arrays, although not widely used in clinical microbiology, could result in a further transformation of traditional diagnostic approaches.

CHALLENGES IN THE CLINICAL LABORATORY

Operational challenges to clinical microbiology laboratories have also grown. In the midst of changing technology, laboratories are challenged with budget cuts, a

shrinking workforce, and legislation-mandated testing. At the same time, laboratories are expected to maintain quality for optimal patient care. Clinical laboratories and their role, however, are evolving. Laboratories are an active part of the way medicine is practiced. It has been estimated that as many as 70% of all medical decisions are based on laboratory results (Marc D. Silverstein, MD, unpublished data, 2003). Historically, microbiology laboratory results have relied on the growth of cultures that could delay patient results. New technology allows for rapid detection of pathogens directly from specimens. The tools now available are increasingly becoming more sophisticated and more accessible. These tools and the power behind them have the ability to substantially improve the quality and delivery of service, given that the necessary supporting teams (ie, infection prevention and antimicrobial stewardships) are in place. The pressure to become lean or eliminate waste along the entire stream of workflow, while maintaining quality, has left laboratories seeking ways to continually improve how patient care is delivered.

At the dawn of universal health care coverage in the United States, perhaps one of the most daunting challenges facing laboratories is who will perform the increasing volume of work and do so within budgetary constraints. The pipeline of laboratory workers is such that there are fewer skilled laboratory workers entering the workforce than leaving it, and the average medical technologist is approaching retirement age.[2–4] At the same time, there is a significant shortage of graduates from accredited laboratory science programs each year, so these programs simply cannot meet the demand to fill these positions.[2] There has also been a dramatic decline in the number of technologist training programs; 71% have closed from 1970 to 2007.[5] This decrease in technologist pool correlates with the projection that annually there is a greater than or equal to 70% shortfall of skilled laboratory workers.[3] These highly trained and skilled workers are college educated, certified, and/or licensed (depending in the state where they work) and a vanishing resource in this country. Similar to the nursing shortage this country faced more than a decade ago, the situation has hit the tipping point to becoming a crisis.

In part to mitigate this problem, in California, a medical laboratory technologist (MLT) licensure was implemented. MLTs are midlevel laboratory professionals. Under the supervision of a clinical laboratory scientist, an MLT can perform limited routine testing in a clinical laboratory and operate, maintain, and troubleshoot automated diagnostic instrumentation. MLTs can perform phlebotomy and moderately complex testing and supervise lower level laboratory workers. California currently has 6 approved MLT training programs in operation.[4]

Other solutions to improving the workforce crisis are to improve salary and increase public knowledge of laboratory science as a career choice. Change, however, will not happen quickly enough. Laboratories are increasingly asked to improve turnaround time and do more with less as budgets continue to shrink. TLA in clinical microbiology laboratories is one piece of the solution to addressing the workforce shortages that could improve efficiency and quality.

LIQUID MICROBIOLOGY—A PREREQUISITE TO PLATING AUTOMATION

Diagnosis of an infectious disease often requires the appropriate specimen collection from a clinically relevant site. Adequate specimen collection is extremely important to obtain quality results for patient care. Historically, collection swabs have been wound rayon-tipped swabs that are placed in a semisolid transport medium after collection. It is important to note about the rayon swab (**Fig. 1**) that, based on the tip structure, it is easy for a specimen to become trapped in the filaments that make up the tip of the

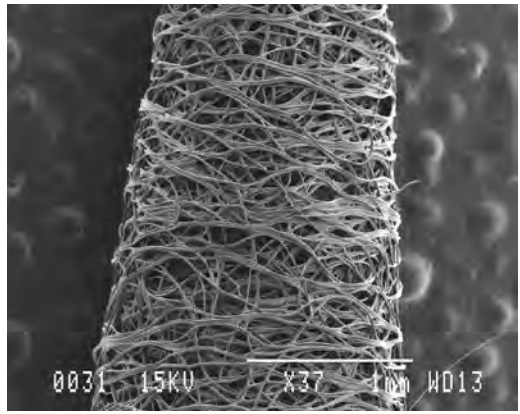

Fig. 1. Electron micrograph image of the tip of a rayon specimen collection swab. (*Courtesy of* Copan Diagnostics, Murrieta, CA; with permission.)

swab, thus reducing the amount of organism available for the plated media and pathogen recovery. Some culture types may require plating 5 or more different types of media, so little if any specimen may be remaining on the swab after being rolled across several plates.

To improve on the recovery of pathogens in a swab sample, Copan Diagnostics (Brescia, Italy) introduced the novel nylon flocked ESwab to microbiology in 2006. The ESwab is the only liquid based, multipurposed collection and transport system currently on the market. Perpendicular nylon fibers, as shown in **Fig. 2**, allow efficient collection and mitigate trapping of specimen due to the soft brush-like structure; hence, most of the available specimen attached to the flocked swab is eluted in the tube (approximately 90%) after it comes in contact with the liquid medium. Due to the homogenous nature of the specimen in the liquid Amies medium when plated, there is an equivalent distribution of the specimen on all plates, no matter how many plates are inoculated for a given specimen, contrary to conventional swabs. Because the transport medium is a liquid, the ESwab device is amenable for use on

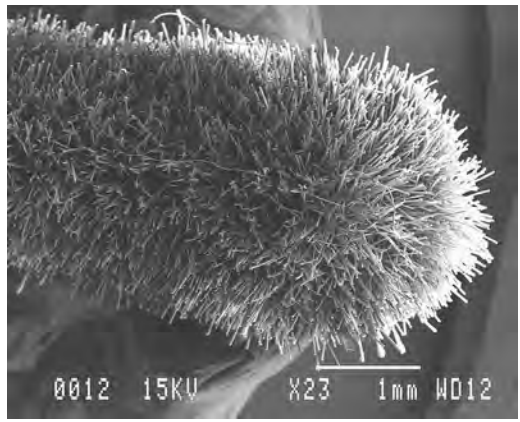

Fig. 2. Electron micrograph image of the tip of a flocked swab showing the increased surface area. (*Courtesy of* Copan Diagnostics, Murrieta, CA; with permission.)

automated plating instruments (**Fig. 3**). Studies show good viability of aerobic, anaerobic, and fastidious bacteria for up to 48 hours at room and refrigerated temperatures with the ESwab.[6–8] The performance of the ESwab compared with other swab systems for aerobic bacteria has been well documented.[7]

PREANALYTICAL AUTOMATION IN THE CLINICAL MICROBIOLOGY—HISTORICAL PERSPECTIVE

Historically, microbiology laboratories have been less automated than other clinical laboratories, such as chemistry. Laboratories in the United States and Europe have automated the preanalytical area of microbiology with the implementation of plating instruments. The reduction or elimination of repetitive tasks associated with manual plating can lead to efficiencies in labor savings and a reduction in ergonomic injuries.

The first semiautomated plating instrument, the Isoplater (Vista Technology, Edmonton, Alberta, Canada), was developed 23 years ago. Over the past several years, newer, more sophisticated plating instrumentation has been developed, such as the Innova (BD), InoqulA (part of TLA [discussed later] [BD Kiestra), Walk-Away Specimen Processor (WASP) (Copan Diagnostics), and PREVI Isola (bioMérieux). The newer instruments automate the plating of liquid specimens regardless of the specimen container type or size. All of these newer instruments can be interfaced with various laboratory information systems (LISs) that are currently available on the market. Interfaces with LISs are commonplace in laboratories for most instruments and can improve efficiency and patient safety in the laboratory setting. Reading of the primary specimen barcode and labeling of the plated media with patient identifiers allows for traceability and positive patient identification of all specimens. Some instruments are more versatile in that they have added features and functionality in addition to plating the primary specimen. These descriptions contained in this article are meant to highlight certain features on the various plating instruments and are not an exhaustive list of all the features available. **Fig. 4** summarizes and compares the fully automated preanalytical specimen processors currently on the market. For a more extensive list of instrument characteristics that should be taken into account when choosing a system, readers are referred to an article by Greub and Prod'hom.[9]

Fig. 3. Various ESwab collection and transport systems. White cap includes 1 regular-sized FLOQSwab (sampling sites: nose, throat, vaginal, and wounds). Green cap includes 1 minitip-sized FLOQSwab (sampling sites: eye, ear, nasal passages, and urogenital). Blue cap includes 1 flexible minitip-sized FLOQSwab (sampling sites: nasopharynx and pediatric sample collection). (*Courtesy of* Copan Diagnostics, Murrieta, CA; with permission.)

Comparison of Automated Specimen Processors

	PREVI Isola	Innova	WASP	InoqulA
De-cap/cap containers	No	Yes	Yes	Yes
# different media at once	5	6	9	12
# samples at once (max)	114	200	72	288
# plates streaked at once	1	1	1	Up to 5 at once
Streak only mode	No	Yes	Yes	Yes – MI module
Inoculate gram slide	No	No	Yes	Yes
Inoculate broth tube	No	No	Yes-Copan only	Yes
Detect ESwab presence	No	Yes	No	No
Method of Inoculation	Pipette	Re-useable loop	Re-useable loop	Pipette
Throughput	~180 inoculations/hr	~130 inoculations/hr	~130 inoculations/hr	250+ inoculations/hr
Integrate into track system	Future	No	Future	Yes - today
Sample vortex/agitation	No	Yes	Yes	Yes
Streaking Method	Spiral- plastic comb	Custom- loop	Custom- loop	Custom- rolling bead
Sort plates by incubator	Yes - standard	Yes - standard	Yes	Yes
Consumables/Waste	Streaking comb, pipette tip, extra cap	Re-useable loop	Re-useable loop	Re-useable bead, pipette tip

Fig. 4. Comparison of the fully automated plating instruments currently on the market.

ISOPLATER

The first semiautomated plating instrument developed was the Isoplater in 1989, and this device continues to be used in many laboratories. The instrument is semiautomated, meaning that the primary specimen must first be applied to the agar plate before placed on the instrument for streaking. Because specimens are planted onto the media before placed on the Isoplater, there is no requirement for a liquid sample. The streaking is performed with a wire loop and the pattern is a spiral streak (depicted in **Fig. 5**). This streaking pattern is unique and not the normal 4-quadrant streaking pattern that most technologists are familiar with in a clinical laboratory. There is a learning curve that technologists experience when moving from a 4-quadrant streak to a spiral streak pattern. With time and practice, technologists can easily make the transition to reading a spiral streak pattern. At Kaiser Permanente Regional Reference Laboratories, technologists adapted readily to the use of spiral streak pattern generated by the Isoplater. Other plating instruments in the authors' laboratory generate the 4-quadrant streak pattern but technologists have no problem reading plates that contain varied streak patterns. The Isoplater cannot be interfaced to an LIS, and barcodes or patient identifiers must be applied manually to the plates.

INOCULAB

In 2002, the InocuLAB (formerly Dynacon, now BD) was introduced to the market as an instrument that fully automated the plating process for liquid specimens (**Fig. 6**). The InocuLAB can decap the specimen container, inoculate the agar plate, and recap the container for future storage, adding to increased time savings and standardization within a laboratory. The InocuLAB can be programmed with several streaking patterns and a reusable wire loop is used for inoculating and streaking the specimen onto the plate. The InocuLAB can hold 40 specimens for primary plating. Becton Dickinson plans to phase out the InocuLAB and replace it in the market with Innova and InoqulA.

Fig. 5. Isoplater. The Isoplater is a first-generation semiautomated streak-only plating instrument. (*Courtesy of* Vista Technology Inc, Edmonton, Alberta Canada; with permission.)

Fig. 6. InocuLAB. The InocuLAB is the first plating instrument that fully automated the decapping/capping and plating process for liquid specimens. (*Courtesy of* Becton Dickinson, Franklin Lakes, NJ; with permission.)

INNOVA

The successor to the InocuLAB is the Innova (formerly Dynacon, now BD) (**Fig. 7**), which has been on the market since 2010. The instrument has a specimen capacity of 200 containers. The instrument contains 6 silos, which accommodate 270 plates and 6 different types of media. The instrument is 60 in $\times$ 50 in and the user only requires access to the front of the system. The Innova is similar to the InocuLAB in that a reusable wire loop is used to inoculate and streak the plate. Loops are available in various sizes, such as 1 μL, 10 μL, and 30 μL. To ensure inoculation quality, the Innova includes an agitator/shaker so that the specimen is homogenized before delivery to the plate/tube. An internal camera takes a picture of the loop to ensure the loop is straight for proper entry into the specimen container. An ultrasonic level senor ensures that there is sufficient volume in the specimen container. If there is not enough volume, the container is skipped and flagged so the operator can intervene when the other specimens are finished plating. The Innova was the first instrument to have a universal capper/decapper that can adjust to various-sized specimen transport containers. For example, the decapping/capping mechanism can uncap a urine boric acid tube and then adjust automatically to uncap a stool vial after the boric acid tube is recapped. Specimen containers are loaded in flexible metal racks, which allow the Innova to be loaded with many different-sized containers at the same time. The Innova can also be programmed with various plating protocols that can be configured by an end user based on laboratory need. To ensure flexibility, the user can program each drawer (a total of 5) with a unique plating protocol or the system can obtain the protocol information for each specimen container from the LIS. This is perhaps an

Fig. 7. Innova. The instrument has a specimen capacity of 200 containers and accommodates 270 plates and up to 6 different types of media. (*Courtesy of* Becton Dickinson, Franklin Lakes, NJ; with permission.)

important feature for smaller to medium-sized laboratories that might only have 1 plating instrument due to specimen volume and require added flexibility.

INOQULA

In 2012, BD acquired Kiestra, a Dutch company specializing in automation for the microbiology laboratory. Kiestra has been in the business of laboratory automation for 17 years, and installed its first system in a clinical microbiology laboratory in 2006. Kiestra has modular and full automation systems in operation with placements located in Europe, Australia, and the Middle East. The InoqulA (**Fig. 8**) has a dimension of 160 in $\times$ 36 in. The instrument has a capacity of 612 plates and can be loaded with 12 different media types. Compared with the other instruments discussed in this review, this system has the largest capacity. The system has customizable container racks and a flexible decapper so that different-sized containers can be processed by the system. A calibrated pipette is used to inoculate plates, broth tubes, and slides according to the sample protocol set by the end user. The instrument has a unique streaking technology that uses a magnetic rolling bead (shown in **Fig. 9**) to streak the plate using customizable patterns (spiral, 4 quadrant, biplate, and so forth). The beads can be reused after sterilization or disposed of. The instrument can streak up to 5 plates at one time with the rolling bead technology, enabling high throughput. So, for example, if a sample requires 7 plates to be inoculated, the InoqulA can streak 296 plates per hour.

The InoqulA also has a manual interactive mode that is designed for specimens that are not suitable for fully automated plating, such as tissues, catheter tips, and other

Fig. 8. InoculA. The InoculA is part of the Kiestra TLA line. The instrument has a capacity of 612 plates and can be loaded with 12 different media types. (*Courtesy of* Becton Dickinson, Franklin Lakes, NJ; with permission.)

nonliquid samples. In this mode, plates are automatically selected, barcoded, and streaked, while an operator manually inoculates the plates.

WASP

The WASP instrument (**Figs. 10** and **11**) is Copan Diagnostics' solution to preanalytical specimen processing automation, including plating and streaking, Gram slide preparation, and broth inoculation. The WASP has a footprint of 43.5 in $\times$ 81.5 in $\times$ 76 in and accommodates loading of up to 378 plates at once. There are 9 silos on the instrument that can accommodate up to 9 different types of media and can be loaded while the instrument is operating. The throughput of the instrument is approximately 180 bi-plates/hour. The instrument has a universal capping/decapping mechanism that allows for the plating of a wide variety of specimen types. The bidirectional interface allows for random loading of specimen types as the instrument queries the LIS to determine the specific plating protocol needed for that specimen type. The WASP includes a vortexer and a spinner so that the specimen is adequately homogenized for even specimen delivery and distribution during inoculation. Reusable metal loops are available in 3 sizes: 1 μL, 10 μL, and 30 μL. Each loop device comprises 2 individual loops, each of which (per the manufacturer) can process up to 15,000 plates. The

Fig. 9. Petri dish streaked with magnetic bead technology using the InoculA. (*Courtesy of* Becton Dickinson, Franklin Lakes, NJ; with permission.)

Fig. 10. WASP, front view. The instrument accommodates loading up to 378 plates at once. There are 9 silos on the instrument that can accommodate 9 different types of media. (*Courtesy of* Copan Diagnostics, Murrieta, CA; with permission.)

loops are incinerated between samples and inoculation is driven by specimen barcode. The WASP automatically selects the correct loop size based on the sample-type protocol. The WASP can use 2 loops on a single plate simultaneously, for example on a urine culture biplate, thus improving the throughput of the instrument. A variety of streak patterns can be programmed based on user need. For quality-control purposes, there is a camera that takes a picture of the loop each time an inoculation is made to assure a specimen is plated. The overall plating throughput varies depending on the streaking protocol.

In addition to plating functionality, the WASP includes a module that prepares a slide for Gram stain. The Gram SlidePrep Module (attached to the WASP, Copan) prepares not only the smear but will also ink jet the patient information directly onto the slide. The WASP contains another internal station called the warehouse carousel. This carousel can be loaded, for example, with Kirby-Bauer, optochin disks and bacitracin disks, to be planted on either primary or secondary plates for susceptibility testing or to aid in organism identification (**Fig. 12**). The WASP also includes a feature that allows inoculation of a mass spectrometer template. A study on the performance of the WASP was performed at Geisinger Health System,[10] which assessed cross-contamination, accuracy of the results, and quality of plating. Plated media results were comparable when WASP-inoculated plates were evaluated against routine plating methods.[10]

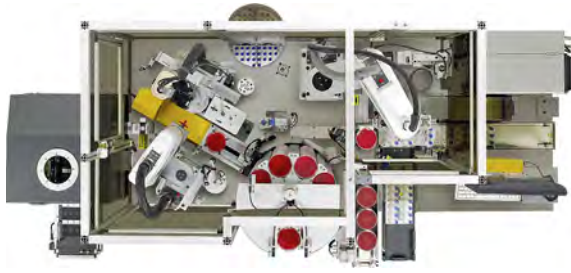

Fig. 11. WASP, top view. (*Courtesy of* Copan Diagnostics, Murrieta, CA; with permission.)

Fig. 12. WASP, warehouse carousel. (*Courtesy of* Copan Diagnostics, Murrieta, CA; with permission.)

PREVI ISOLA

The PREVI Isola (**Fig. 13**) is bioMérieux's product for preanalytical specimen plating. The instrument has a footprint of 66.5 in × 58.7 in × 35.7 in and accommodates 150 plates and 5 different types of media at once. The PREVI Isola has a unique streaking pattern, using a comb mimicking 16 loops streaking simultaneously, using a greater surface area of the agar that was shown to provide improved separation of organisms (**Fig. 14**). The spiral streaking pattern is similar to the Isoplater (described previously). Single-use, disposable specimen applicators (combs) are required for specimen inoculation of the primary specimen; the user also has the option to use 1 applicator per specimen. The throughput of the instrument is approximately 180 plates streaked per hour. The system also has the capability of streaking a biplate.

The PREVI Isola does not have the capability to decap and recap specimens, so these steps are manual. bioMérieux has in development an automated decapping/capping instrument that will be available in the future but is a stand-alone piece of equipment. In smaller-volume laboratories, this added step might not have an impact on efficiency but the necessary space needed for the decapping instrument might prove an issue for laboratories with limited floor space. In larger-volume laboratories, the impact of the lack of the capping/decapping functionality needs to be assessed but most likely will have an impact on efficiency savings. The PREVI Isola has the capability of querying the LIS similar to the other systems and can be programmed to segregate plates into separate canisters based on the atmospheric conditions the plates are to be incubated in. One study that compared the PREVI Isola to manual methods demonstrated decreased hands-on time and improved efficiency with the PREVI Isola.[11]

Fig. 13. PREVI Isola. The instrument accommodates 150 plates and 5 different types of media at once. (*Courtesy of* bioMérieux SA, Marcy l'Etoile, France.)

DIGITAL MICROBIOLOGY

Manufacturers have made progressive steps and have incorporated digital imaging into routine bacteriology incubators that have been in use for decades. The next generation of incubators will have a digital camera incorporated with an incubator for direct culture plate imaging. This digital imaging technology will allow clinical microbiology to develop and expand in ways that many would not have imagined. As part of the full automation package, the new incubators can be linked to the plating

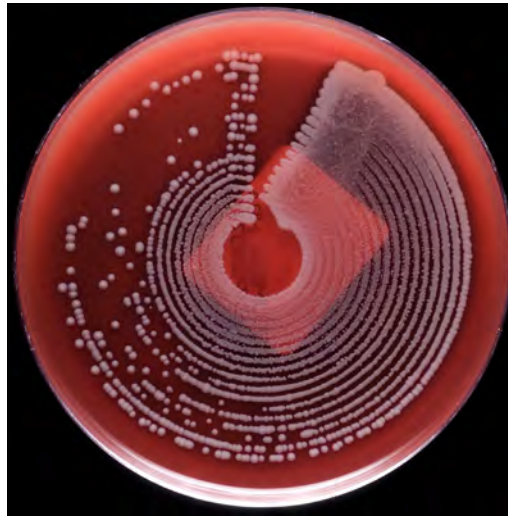

Fig. 14. Petri dish streaked using PREVI Isola. (*Courtesy of* bioMérieux SA, Marcy l'Etoile, France.)

instrument by a conveyor system that moves specimens into the incubators. Due to space constraints or workflow considerations, some laboratories may choose to forgo the conveyor belt/track systems and transfer plates into the incubators manually. The exact location where a plate is placed within the incubator will be determined by the software of the specific system.

The respective software systems can be programmed to take digital images of the media plates at operator-defined times and intervals. Digital images of the colony growth on the agar plate are taken and stored within the system. When technologists begin work on a culture, they call up images of a culture on a computer screen at a workbench and analyze the plates for growth/no growth from the screen (**Fig. 15**). The digital technology will allow technologists to observe the plates under different lighting conditions and magnify the colonies on the plate for better resolution during pathogen work-up. The optics of digital cameras allow better analysis of multiple morphotypes of bacteria that might be present in a specific sample The optics in digital cameras can observe colony growth on an agar plate that is invisible to the human eye. The WASPLab system, for example, has a camera that is capable of imaging a colony at 15 megapixels with a depth of 1 cm. For white colonies on a dark background, the limit of visualization is approximately 0.1 mm. Earlier recognition of growth could reduce turnaround time. According to BD, the European laboratories with Kiestra automation have adjusted their workflows based on the generation of results by digital imagers (BD Kiestra, personal communication, 2012). Laboratories have moved to working up the specimens when the cultures are available for work-up and scheduling technologists accordingly. As with any new technology, there will be a period of training and a learning curve that technologists go through. Productivity will increase gradually over time and as technologists become more comfortable with reading cultures digitally, so gains expected when automation is introduced will take time.

Digital microbiology brings clinical laboratories into the twenty-first century. Many institutions are already practicing and reaping the benefits of telemedicine. Laboratories that are in offsite locations with less-experienced technologists could receive assistance from more-experienced technologists when working up cultures. Another future application is that software could be programmed to read and discard negative cultures and transfer the results to an LIS for reporting without the need for a technologist to observe the plate. If chromogenic agar is used to work up specimens in a more timely fashion (where certain organisms turn a specific color on the medium), perhaps in the future software could be programmed to read the color of a colony and report a positive or negative result on that plate without technologist intervention.

Other benefits to digital microbiology are quality assurance and the ability to use stored images and cases for training purposes. When quality-related issues arise in a laboratory regarding cultures, frequently the plates are already discarded. As a result, little can be done to answer questions that might have been raised. With digital image collection, laboratory staff has the ability to review cultures for quality-assurance purposes that were worked up historically. Another advantage of being able to store images is for laboratories to develop a repository of unique isolates or challenging cultures for teaching and training purposes. bioMérieux is currently working with a laboratory in Berlin, Germany, to determine exactly what set of images is most useful to medical technologists. Studies of vary lighting conditions and backgrounds are under way so it can be determined which set of images is most useful to technologists on the bench (bioMérieux, personal communication, 2013).

Software developed to supplement digital microbiology will have functionality so that multiple cultures on the same patient can be viewed on 1 computer screen.

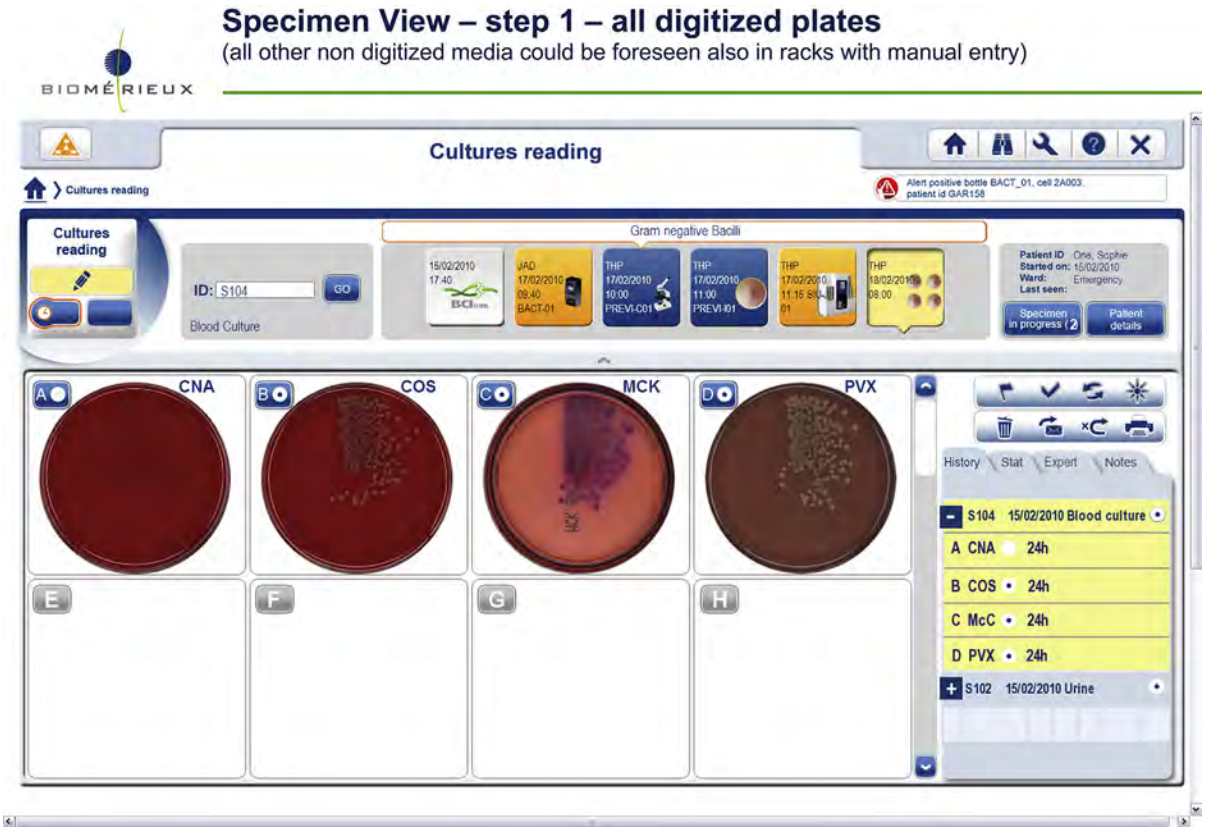

Fig. 15. Screen shot of MYLA courtesy of bioMérieux. Screen shots show an example of a computer screen with digital plate images. (*Courtesy of* bioMérieux SA, Marcy l'Etoile, France.)

This allows a broader-based assessment of all the cultures that are in a laboratory for a particular patient. For example, if both urine and blood cultures are growing a gram-negative rod, a technologist will be able to look at both cultures at the same time using the software and digital technology. This technology will allow a more integrated assessment of the culture work-up and allow for a more patient-centric process in the microbiology laboratory that is typically removed from the bedside. Work-up of microbiological cultures will never be the same.

TOTAL LABORATORY AUTOMATION

With health care reform comes the increased demand for not only high quality but cost effective laboratory services. Automation can result in efficiency and personnel cost savings, can reduce repetitive motion injuries, and perhaps can save organizations money in the area of workplace safety. Automation also allows for standardization in the way a task is performed, which can enhance quality and reproducibility. TLA occurs when several automation systems for microbiology come together.

TLA consists of several instrument components: (1) preanalytical plating instrumentation; (2) smart incubators containing digital cameras to incubate and photograph growth on plates for analysis; (3) track or conveyor systems to move plates to and from the plating instruments, incubators, and benches; and (4) other ancillary equipment for sample work-up. Depending on the size of the respective laboratory, the needs for TLA will be varied. Several schematics of the TLA systems manufactured by various vendors are shown in **Figs. 16–18**. Currently, bioMérieux and BD Kiestra have systems in Europe. All three companies are projecting placement of TLA in European, Canadian and US locations. With track systems loading the plates from the automated specimen processors, time savings will be realized in that laboratory personnel no longer will have to batch the plates in racks and manually place them in an incubator. Additionally, medical technologists will be working up cultures from a computer screen, eliminating the need to retrieve plates from incubators and manually screen them. As discussed previously, each system will have a unique software package that not only allows for digital culture work-up but also connects the

Fig. 16. WASPLab. Consists of WASP plating system, track, and incubator with digital camera. (*Courtesy of* Copan Diagnostics, Murrieta, CA; with permission.)

Fig. 17. BD Kiestra TLA. Consists of InoculA plating system, track system, and incubator with digital camera. (*Courtesy of* BD Kiestra B.V., 9207 JC Drachten, The Netherlands; with permission.)

various automation components that comprise a TLA solution for each vendor. bioMérieux is developing an ancillary instrument, called the Inoculum Preparation System, to inoculate the mass spectrometry template and tubes for susceptibility. Other vendors are developing similar instruments that can also inoculate a mass spectrometry template.

Mean time to failure data for track systems and digital incubators are not readily available because the instruments will be new to the market for bioMérieux and Copan, and BD Kiestra has been available solely in Europe. The Kiestra system tracks key performance indicators for their instruments, such as system availability, mean time between errors, and average time to repair. It is important with this instrumentation to ascertain reliability and mean time to failure before deployment in a laboratory setting for routine patient care. Poor reliability not only affects productivity in the workplace but also could have a significant negative impact on an operation that perhaps reduces personnel secondary to deployment of laboratory automation.

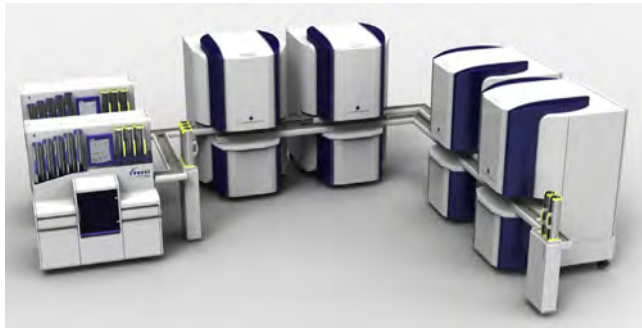

Fig. 18. bioMérieux. Full microbiology laboratory automation. Includes PREVI Isola, track system and smart incubator system with digital camera. (*Courtesy of* bioMérieux SA, Marcy l'Etoile, France.)

Patient care could be affected if processing and reading of cultures are delayed significantly. Instrument down time can also negatively affect the morale of laboratory personnel, which can result in mistrust of the automation in general and toward administration.

DEVELOPING A BUSINESS CASE

The complicated task of laboratories and manufacturers is to determine the automation necessity and provide a solid business case to support the acquisition of equipment. Automation manufacturers must realize that the relationship developed with customers will be more symbiotic than what exists today. Information that end users will need when making a decision about TLA solutions includes (but is not limited to) footprint of instruments, cost, mean time to failure of all the instrument components, labor savings, and potential decrease in turnaround time (or other quality indicators). These are just a few core components that must be considered when embarking on a solution for TLA. Many laboratories have varied solutions for automation. The question that remains is how the various TLA vendors will interface with automation, such as the Vitek, MicroScan, or Bactec (BD), already present in laboratories into a fully automated solution for each individual laboratory.

In 2010, health care expenditures in the United States approached $2.6 trillion. Compare this to 1980, when those costs were more than 10 times less, at $256 billion.[12] According to the Congressional Budget Office, laboratory spending is approximately 4% of health care expenditures, accounting for approximately $60 billion annually. Laboratory testing continues to grow every year because of newer, more specialized testing (that is often proprietary), consumer demand, and an aging population. It has been estimated that a majority, or approximately two-thirds, of health care decisions are based on laboratory results (Marc D. Silverstein, MD, unpublished data, 2003). Laboratories are unique, however, within the hospital setting. Conceivably, it is possible to run a hospital with most laboratory testing sent out. Consolidation of laboratory services and outreach programs has led to lower costs while generating revenue. Thus, hospital-based laboratories have competition. If there is a more cost-effective way to do something and address the lack of skilled laboratory workers, there is a threat that testing could be outsourced.

For laboratories to remain competitive, they must be able to make the case for new technology, namely automation, to administration. Part of the challenge is to know how to present a business case. In other words, technical directors have to learn how to present the data to business administrators to sell projects that are the best investments for their institutions. These are not skills readily taught in a laboratory or graduate science program. The first step to preparing a business case is to understand the factors driving the need for new technology/automation. In addition, it is important to understand who the stakeholders are (physicians, administration, technologists, and so forth) and educate them on the importance of laboratory automation. In the end, administrators will want to know what it will cost, what it will save, and how long it will take to get a return on investment (ROI).

Simply put, the key to selling the idea of automation in clinical microbiology laboratories is the cost difference between the manual and automated approaches. With the TLA components (described previously), the cost of consumables, reagents, and plates will, for the most part, remain constant. Factors, such as implementing ESwabs, to move to liquid microbiology could have an impact on cost analysis. The largest gain will be with the reduction in labor costs, with additional gains in quality, efficacy, reduced ergonomic injuries, and improved safety. The manual labor costs are

Table 1
Costs saved with automated microbiology specimen processor

Method	No. of FTEs/D	# D/Wk Plate	Annual Labor Costs[a]	Labor Savings/Y
Manual	2.5	7	$129,872.50	—
Automated	1.0	7	$51,949	$77,923.50

Abbreviation: FTE, Full Time Equivalent.
[a] Based on median laboratory assistant I cost with bonuses, benefits, and time off according to Salary.com, January 2013.

determined by calculating the total number of annual hours of staff time required to perform a procedure manually and multiplying those hours by the cost of labor (wages including benefits). The automated labor costs are determined by calculating the estimated annual hours of staff time required to perform a procedure in an automated fashion and multiplying those hours by the cost of labor (wages including benefits) (**Table 1**). Next, it is important to calculate the cost of acquisition; this includes the capital cost of the equipment, service contracts, cost of remodeling (if applicable), cost of interfacing equipment, and the cost of project planning/implementation/validation of the equipment (**Table 2**).

The ROI is calculated by determining the annual staff cost savings of the automated system (manual labor costs − automated labor costs) and dividing that by the cost of acquisition. This calculation determines how long it takes to recuperate the cost of converting to an automated process (**Table 3**). The ROI is meant to be a simplistic way to initially estimate if a project is worth the effort of a more-extensive cost analysis/pro forma.[13] This quantitative total has also been referred to as the economic justification index (EJI). An EJI of 0.5 equals 2 years, 1 is equal to 1 year, and 2 equals 6 months of a payback period for the reduction in costs.[14] Factors that are more difficult to quantify need to be monitored so gains to the organization due to reduced ergonomic injuries, quality, and turnaround time can be captured.

One approach to evaluating qualitative changes is to determine their strategic justification index (SJI). The SJI is determined by assigning a value of 0 to 2 (0 = not important, 1 = moderately important, and 2 = very important) to 6 change factors. These factors are quality, safety, procedure enhancement, audit trail, more timely decisions, and flexibility. The SJI is determined by dividing the sum of the 6 change factors by 12 (highest possible score). An SJI of 1 is equal to a very high value, indicating all 6 change factors are very important to the organization.[14]

To determine overall project justification, the EJI and SJI for the automation can be plotted on an X-Y graph, with a minimum of 0 and maximum of 1 (**Fig. 19**). This approach was originally proposed by the Zymar Corporation and later modified by Hamilton and colleagues[14,15] as a simple go/no-go tool for use before investing

Table 2
Cost of automated microbiology specimen processor

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Automation capital	$250,000					$250,000
LIS	$10,500					$10,500
Service Contract	—	$12,500	$12,500	$12,500	$12,500	$50,000
Total	$260,500	$12,500	$12,500	$12,500	$12,500	$310,500

Table 3
ROI for an automated microbiology specimen processor

Annual labor savings	$77,923.50
Five-year costs	$310,500.00
Payback period	3.98 y

time in a more detailed justification (Zynmark Corporation, unpublished data, 1988). An EJI of greater than 1 (meaning less than 1 year for ROI) most likely occurs in large-volume laboratories where the business case is more justifiable. The cost of TLA could potentially lend itself to more laboratory consolidation due to economies of scale. As a rule of thumb, companies like to see an ROI with a payback period of less than 4 years, but this may vary given what a company uses for expected lifetime of instrumentation.

For the most part, a stronger EJI is more compelling than a stronger SJI for the simple reason of being able to tangibly quantify a business case. If the EJI and SJI value of a project is low (ie, 0.25), this equates to only marginal justification, whereas an SJI and EJI value of 0.75–1 equates to a more compelling justification (see **Fig. 19**). In the end, these calculations provide a simple tool for determining if a project is worth the more detailed organization specific analysis while providing technical staff a means to communicate to nontechnical staff the justification of laboratory needs.

The total cost of ownership is another way to quantify the financial impact of deploying a new technology over the expected lifetime of the system. The gains quantified in annual payback can quickly disappear as equipment becomes degraded and less state of the art. There are costs to annually maintaining and upgrading equipment; although these costs are difficult to predict, they are beneficial to include in the planning process of automation.

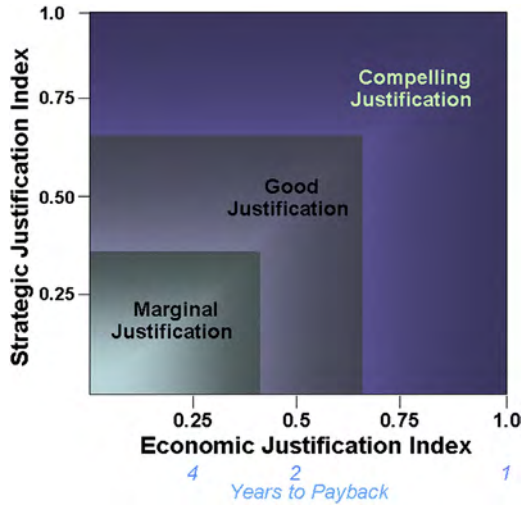

Fig. 19. Justification of automation. (*From* Hamilton SD. Justifying laboratory automation. SLA invited article. 2011. Available at: www.labautopedia.org/mw/index.php/justifying_laboratory_automation. This content is available under GNU free documentation License 1.2. Accessed January 2013.)

The cost of automation can vary greatly depending on the extent of automation. The most logical place to start with automation is the preanalytical instrumentation. Preanalytical automated microbiology processors costs range from $125,000 to $350,000, depending on manufacturer and instrument features. TLA costs are significantly higher and can run in the millions of dollars. Again, the cost of TLA will be laboratory dependent and vary by size of laboratory, specimen volume, and desired features of automation. Although the price tag seems high, the long-term the benefits are much larger. Laboratories in Europe have claimed increases in productivity by as much as 2.5-fold to 4-fold in a short time (Kiestra Lab Automation, unpublished data, 2012).[16]

Laboratories can use the tools discussed in this article to leverage the use of hospital resources to beat the odds and turn an expected administrative response from no to yes. The key to a successful business case is knowing how to present future value to an organization and quantify the gains. With any new technology, there are limitations to assessing costs beyond laboratory costs, particularly when there is a lack of published clinical impact studies. Automation will bring improvements in the quality of results and patient care. Those ROI studies will have to wait until the literature catches up and quality-improvement studies are in place. As Bob Dylan famously sang, "the times they are a-changing"; the face of clinical microbiology is in the midst of a metamorphis.

REFERENCES

1. 2007 Tuberculosis scare [Online Source]. 2013. 2-4-2013.
2. Best M. Strategic laboratory workforce planning—you can not afford not to do it [Magazine Article]. ASCP Laboratory Medicine 2004.
3. American Academy of Microbiology. Clinical micrbiology in the 21st century keeping the pace [Report]. American Academy of Microbiology. Washington, DC: ASM Press; 2008.
4. California Hospital Association. Critical roles: california allied healthcare workforce survey, report of key findings [Report]. Sacramento, CA: California Hospital Association; 2011.
5. The Lewin Group. Laboratory medicine: a National Status Report [Report]. Falls Church, VA: The Lewin Group; 2008.
6. Trotman-Grant A, Raney T, Dien BJ. Evaluation of optimal storage temperature, time, and transport medium for detection of group B Streptococcus in StrepB carrot broth. J Clin Microbiol 2012;50(7):2446–9.
7. Van Horn KG, Audette CD, Sebeck D, et al. Comparison of the Copan ESwab system with two Amies agar swab transport systems for maintenance of microorganism viability. J Clin Microbiol 2008;46(5):1655–8.
8. Van Horn KG, Audette CD, Tucker KA, et al. Comparison of 3 swab transport systems for direct release and recovery of aerobic and anaerobic bacteria. Diagn Microbiol Infect Dis 2008;62(4):471–3.
9. Greub G, Prod'hom G. Automation in clinical bacteriology: what system to choose? Clin Microbiol Infect 2011;17(5):655–60.
10. Bourbeau PP, Swartz BL. First evaluation of the WASP, a new automated microbiology plating instrument. J Clin Microbiol 2009;47(4):1101–6.
11. Mischnik A, Mieth M, Busch CJ, et al. First evaluation of automated specimen inoculation for wound swab samples by use of the Previ Isola system compared to manual inoculation in a routine laboratory: finding a cost-effective and accurate approach. J Clin Microbiol 2012;50(8):2732–6.

12. Centers for medicare and medicaid services OoANHSG [Report]. National Health Care Expeditures Data; 2012.
13. Young DS. Laboratory automation: smart strategies and practical applications. Clin Chem 2000;46(5):740–5.
14. Hamilton SD. Justifying laboratory automation. SLAS [Electronic Citation]. 11-30-2011.
15. Hamilton SD, Kramer GW, Russo MF. An Introduction to laboratory automation. 2011.
16. Matthews S, Deutekom J. The future of diagnostic bacteriology. Clin Microbiol Infect 2011;17(5):651–4.