Stand-Alone Automated Solutions Can Enhance Laboratory Operations

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Clinical laboratory automation has developed over the past decade as one means of consolidating testing, reducing costs, and improving the effectiveness of laboratory testing. Most of the developments have been aimed at core clinical laboratory operations, and have primarily addressed preanalytical and analytical processing of traditional specimens arriving in blood collection or similar aliquot tubes. Much less attention has been given to specialized applications such as processing specimens for urine toxicology, and only recently have vendors attacked the problems associated with sorting and maintaining the laboratory’s inventory of specimens. This report highlights selected developments in these areas, describes one approach to cost-effective custom platform development, and discusses the advantages and pitfalls to solving problems with laboratory automation.

Clinical laboratory automation has been evolving over the past 30 years as one means of improving laboratory performance. Analytical equipment has been successfully automated, yielding dramatic improvements in throughput, precision, convenience, and data handling. Automated analyzers now form the backbone of all clinical laboratories, both large and small. Over the past decade, automation has been extended to preanalytical processes as well but has been most often viewed as the large, fully integrated total laboratory automation (TLA) systems that include sample sorting, routing, centrifugation, aliquot preparation, analysis, and sometimes, postanalytical storage and retrieval.

Systems referred to as TLA systems developed first in Japan and began to appear in the United States less than 10 years ago. These total systems included many of the preanalytical functions, such as sorting, centrifugation, and specimen routing as well as analysis and subsequent retesting.

TLA systems offer substantial enhancements in throughput, allowing laboratories to increase capacity severalfold without adding space or personnel. They can be fully integrated, turnkey systems that include most, if not all, of the preanalytical processing, transport systems, and analytical instruments. Because instruments for chemistry, immunoassay, hematology, coagulation, drug screening, and other tests can be included, dramatic gains in consolidation of work and personnel are possible. However, such large systems require substantial financial investment and planning, major architectural work, and far-reaching organizational changes to be effective. Only a few institutions to date have made this commitment in North America and Europe. Additionally, the workload in many laboratories does not justify the initial investment even for the minimum configuration of hardware included in a TLA.

Another disadvantage of some potential TLA systems comes from the fact that they are less than truly turnkey and require the laboratory to select and coordinate equipment from many vendors. For such a system, the tasks associated with interfacing the various instruments, automation components and data systems can be formidable.

Modular systems of laboratory automation have been developed in more recent years as an alternative to TLA. These systems recognize the need to provide cost-effective analyses through continued consolidation of testing, but they provide more flexible alternatives for incorporating automation of preanalytical processing into the laboratory. Modular systems provide either analytical capability or preanalytical processing, which can be selected independently to meet the users individual needs. Notably, the preanalytical platforms can be added to existing laboratories without disrupting the analytical capabilities and efficiencies that may be in place. They may also allow

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more flexible use of space or positioning of functions is existing facilities.

Typically, today’s modular analytical systems provide one or more analyzers for chemistry, immunoassay, hematology, and other testing. The modules are linked by a track or conveyor and resemble the TLA systems from this standpoint. The modular systems are distinguished from the TLA systems in that they can provide a wider variety of test volumes. For example, the Roche/Hitachi Clinical Laboratory Automation System can process up to 300 tubes/h virtually 24 h per day (8000 tubes per day) in its smallest configuration. Modular systems currently being introduced can be tailored to smaller volumes as well as the larger volumes associated with large automation systems.

Modular automation also offers the opportunity for implementation over time because analytical and preanalytical components do not need to be connected. These systems can be installed with a much smaller initial investment. However, these systems may be more difficult to interface with laboratory information systems (LISs) if systems from different vendors are chosen for different functions. They may also be more labor-intensive than the larger, more integrated automation systems.

Modular systems offer the laboratory possibilities for staged selection and installation of equipment and offer management the chance to “wait and see” whether the first components are successful before proceeding with later additions, but this approach can be counterproductive. The potential gains that accrue from comprehensive organizational changes, economies of scale, and workload consolidation might never be seen if the staging is too conservative.

In addition to the modular systems, manufacturers have developed several products to support selected areas of preanalytical processing. Systems, which can be purchased as stand-alone modules, include machines to sort, aliquot, and archive specimens. Some of these include cap removal and may include centrifugation in the future.

Typical of these systems are the task-targeted automation systems (1), including the Roche Diagnostics PSD 1, which can decap, archive, and sort up to 1200 tubes/h. The Roche Diagnostics VS II does similar functions and can make up to three bar coded aliquots per specimen. As of this writing, several of these platforms have been installed in laboratories throughout North America.

The OLA 1500 (Olympus America) is a high-speed device that uncaps and sorts up to 1500 tubes/h into a wide array of destination racks for distribution into the laboratory. Because it is designed for large numbers of samples, this system may be most appropriate for larger laboratories or for those handling large numbers of very hazardous specimens. This system is unique not only for its speed, but also for its ability to decap and sort nearly all of the commercially available blood collection tube sizes and cap styles simultaneously. However, to date, none of these have been installed for use in laboratories; therefore, their effectiveness cannot be determined yet.

Sarstedt AG and Company has also developed a series of platforms for decapping only or decapping and sorting blood collection tubes. A larger system can be configured to decap blood collection tubes, sort to up to 18 analyzer-specific destination racks, and prepare bar code-labeled aliquot tubes. All of these systems process the proprietary S-Monovette blood collection tubes only and cannot be adapted to other types of blood collection tubes at the present time.

Developing Stand-Alone Automation: A Hospital Case Study
During the course of designing and implementing its total core laboratory automation, the Veterans Affairs North Texas Health Care System in Dallas, Texas identified two areas that were not addressed adequately by the systems under review. The first area identified was the preanalytical processing of urine specimens for drug abuse testing, and the second was storage and retrieval of clinical laboratory specimen tubes for retesting. Two novel solutions were developed to address these functions.

The Toxicology Automation Solution
The first area identified for development was the specialized preanalytical processing of urine specimens for drug abuse testing where some of the most repetitive tests occur, specimen volumes are large, repeated handling and aliquoting of specimens is required, and extensive additional chain of custody requirements complicate documentation and reporting. In addition, specimens for urine toxicology are collected in a variety of containers ranging from large test tubes to bottles of various shapes and sizes. When specimens are collected for federally controlled drug testing, two separate samples (designated as A and B) are collected and maintained for possible repeat testing.

Beginning in 1997, the Veterans Affairs North Texas Health Care System established a unique partnership with a group of companies to design and build a compelling automation solution to address preanalytical processing for urine toxicology testing. An additional objective was to design and build all of the necessary expendable and ancillary materials in a relatively short time frame.

In approaching this problem, the designers were aided by a focus group of customers (2) who identified a wide range of problems, issues, and potential targets for automation. Of the many identified, several were considered the most crucial and unique to toxicology testing.

Lack of standardized collection containers prevented implementation of automation because virtually dozens of containers of various sizes, shapes, and materials are in use as primary collection containers for urine collection. In addition, large sample volumes are required for toxicology analysis compared with those encountered in routine clinical chemistry laboratories, with sample volumes ranging from a few to 120 mL. Aliquot volumes
required for drug analysis are also larger (typically 1–2 mL) than volumes usually transferred to analyzers for most chemistry or immunoassay tests.

Multiple samples from the same subject collection are handled and inventoried by SAMHSA-regulated laboratories (two specimens, referred to as A and B specimens, are required), and typically all specimens testing positive in the primary drug screen must be retrieved for subsequent confirmatory testing, in contrast to usual clinical testing where only a small percentage of samples are retested.

Chain of custody requirements different from those encountered for medical testing occur when drug test results are used for legal or employment purposes and must be addressed in the processing of these urine specimens as well.

In addition to addressing the issues outlined above, other elements were identified as required for successful completion of the project in our laboratory and successful commercialization of this equipment.

The system needed to incorporate current urine collection and labeling practices but reduce preanalytical labor requirements. Specimen containers with screw caps that held 60–90 mL and would accept current labels and security seals were required.

The system had to operate at a speed sufficient to provide 300 aliquots/h, the speed of typical large-scale chemistry analyzers performing drug screening. It also needed to accept random, direct loading of primary specimens without intermediate racking. Batch output of samples to maintain current screening practices was also required, as was preparation of initial aliquots for drug screening without the introduction of a sample probe into the primary container to eliminate the possibility of cross-contamination. The system also needed to operate without disposable pipet tips to eliminate the cost of this expendable product.

We also determined that the system should process specimens one at a time to maintain positive identification and further reduce the possibilities for cross-contamination of specimens and include an integrated system suitable for both short- and long-term storage of specimens capable of identifying, sorting, and retrieving specimens while the system was in operation. It also had to include both electronic and paper chain of custody documentation to maintain current laboratory practices and regulatory requirements.

Once the critical performance elements were identified, an automated preanalytical processing system was designed to perform the tasks designated and incorporate the characteristics required. The Specimen Processing System (SPS; CRS Robotics Corporation) consists of a self-contained robotic unit linked to an industrial inventory system for storage and retrieval (Fig. 1). The SPS processing section is built around two articulated robots. One performs labeling and aliquoting steps, and the second performs tube transfer and primary sample storage operations. The processor incorporates a tube feeder, bar code printer, and labeler. The system can process up to 300 specimens/h, performing all of the operations shown in Fig. 2.

The storage system of the SPS uses an elevator mechanism to move large (24 × 36 inch) trays that hold primary urine specimens. The unit has a capacity of 2600 specimens and is controlled by the SPS computer. Retrieval of samples can be accomplished while the system

![Diagram of the CRS Robotics SPS for preanalytical processing of urine toxicology specimens.](image)

*UPS, uninterrupted power source.*
is in operation or during scheduled periods. Individual samples can be located and delivered in <1 min when the system is not in operation.

The SPS utilizes a proprietary robot-compatible container (Starplex Scientific), shown in Fig. 3, that permits aliquoting from the container without the use of sample probes or disposable pipet tips. Because the entire lid is not unscrewed from the container during processing, the screening aliquot can be obtained without breaking the security seal. This is accomplished with a break-away tip that opens a small orifice for dispensing sample into a tube by inverting the container over the tube. The orifice is then resealed using a heated fixture incorporated into the processing hardware. An alternate container design can also incorporate both a 60-mL volume for the A sample and a 20-mL volume for the B sample within the same device, eliminating the need for separate inventories or additional chain of custody documents.

The SPS provides preanalytical processing of urine specimens for drug testing integrated with sample storage, retrieval, and documentation. The system allows continuous loading of primary containers, batch output of aliquot tubes consistent with current practice, and provides all of the chain of custody documentation for each
step in the process cycle. Using off-the-shelf articulated robots and a commercially available storage device, we have developed a system that met its original design goals and retains the flexibility to fit into laboratories of various sizes and configurations.

The sample rack system for aliquot tubes is designed to accept both the 5-place sample racks from Hitachi analyzers and the 10-place racks from the Olympus analyzers, which are the most widely used for drug screening. It can be changed to accept other racks in the future with minor hardware and software modifications. The storage system incorporates relatively standard industrial technology, so handling and disposal of specimens do not require additional equipment. The trays in the storage system are corrugated cardboard trays that fit standard industrial carts and racks and can be recycled.

AUTOMATING STORAGE AND RETRIEVAL OF CLINICAL LABORATORY SPECIMENS

The second problem identified was the need for automated storage and retrieval of blood, serum, or plasma specimens processed in the core automated laboratory, where >1500 blood collection or aliquot tubes are processed each day. Again, working with CRS Robotics Corporation, we designed an automated, refrigerated storage and retrieval system (SRS) that integrated with the processes occurring in the core laboratory but did not require connection to the system. This eliminated the costs of mechanical interfaces and allowed development and installation in <6 months.

The SRS consists of a modular robotic platform that accepts both the Hitachi and Sysmex racks from the automated laboratory, an industrial inventory management structure, on-board inventory control software, a PC controller, robot controller, and an uninterrupted power supply (Fig. 4).

Design goals for this system included the ability to (a) process ~360 specimens/h and accommodate peak work load in the automated laboratory; (b) process all of the tube configurations handled by the automated laboratory line and instruments; (c) store at least 10,000–12,000 specimens at 4 °C; (d) utilize the specimen racks and trays already in the automated core equipment to eliminate or minimize manual transfer of specimens between racks; (e) permit rapid retrieval of individual specimens or small groups of specimens, in random order at any time of day or night; (f) identify the presence of an individual specimen and maintain tracking on that specimen as it is retrieved from the system; and (g) perform automated disposal of outdated tubes and maintain electronic records of storage and retrieval activity.

Like the previous system for processing urine specimens, an off-the-shelf articulated robot formed the core of the unit, and the same industrial storage device was used for sample inventory, except that now it was refrigerated. Much of the software was based on the previous system with adaptations for the unique needs of tube handling and high-speed retrieval of individual or small groups of specimen tubes.

Specimens are manually loaded into the system by transferring entire sample trays containing up to 150 tubes each directly from the laboratory’s automated areas.
or from individual racks to the robotic platform. Tubes are then automatically selected by the robot, inventoried by reading the bar code, and transferred to large-capacity storage trays (696 tubes/tray). When filled, the trays are mechanically transferred into refrigerated storage. The total capacity of the system is 12,000 tubes originating from both automated and manual process areas.

Once stored, specimen tubes can be retrieved for subsequent retesting by keyboard entry or scanning of its printed bar code. Retrieval of a specimen from the tray actively being loaded requires \(<12\) s, whereas retrieval of previously loaded specimens requires \(\sim60\) s. As an additional function, the robot discards expired specimens at off-peak times to maximize system productivity. The system also tracks waste container capacity and alerts operators when containers are full.

The system accepts both 13 \(\times\) 75 and 13 \(\times\) 100 mm plastic blood collection and aliquot tubes processed in the laboratory with a variety of cap configurations. It provides two different inventory query functions that can determine in only a few seconds whether a tube is or has been in the system, and it includes several error-checking routines to ensure integrity of the sample inventory and database. Troubleshooting, the need for maintenance, and software updates can be provided directly from the factory through an on-board modem.

**Discussion**

Although TLA may provide dramatic improvements in productivity and cost containment, other more focused solutions can provide the same benefits in both large and small laboratories. The introduction of task-targeted automation and the development of focused solutions such as the SPS and SRS demonstrate that automation does not need to be fully integrated to be effective. Designs that clearly incorporate automation of a series of related tasks may offer the most beneficial solutions. These islands of automation that perform labor-intensive or hazardous tasks are becoming more prevalent and may solve more clinical laboratory problems in the future.

The successful design of the SPS and SRS also demonstrates that automation does not necessarily have to be mechanically integrated into a TLA system. Stand-alone automation systems that perform labor-intensive or hazardous tasks are becoming more prevalent in the clinical laboratory and may represent cost-effective solutions to more problems in the future.

However, care must be taken in selecting automation solutions to ensure and maximize their effectiveness. A clear understanding of the changes in laboratory operations and procedures is also required. For example, many of the automation systems introduced to date require restrictions on the type and size of blood collection tubes and aliquot tubes that can be used, but this is not peculiar to stand-alone systems. The Roche Diagnostics/Hitachi TLA system at our institution requires the use of only 13-mm diameter tubes with Hemogard (Becton Dickinson Vacutainer Systems) blood collection tubes. The SPS described above was developed to handle only the proprietary containers designed for it.

This limited use of tubes or containers is typical of many stand-alone systems, which often are built to support proprietary products as value-added enhancements to their product line by the expendables vendors. On the other hand, this forced product selection can be beneficial by reducing inventory, reducing the number of suppliers, and in some cases, reducing collection and processing errors.

Task-targeted or stand-alone automation may also require more time and effort to integrate LIS interfaces if required because each must be treated as a single platform. TLA systems or the more recently introduced modular systems usually are connected to the LIS as a single system through a system master controller. Implementation of robust interface standards such as those proposed by the NCCLS (3) might make this task more efficient in the future.

Development of customized or “first up” automation is also not the optimal strategy for many laboratories. Although such projects clearly note the users as innovators and early adopters, such projects carry risks. Development of complex automation systems requires partnership between vendor and developer to ensure success. Untested hardware and software require more surveillance than off-the-shelf products produced by major vendors. Schedules for production and delivery are difficult to predict or maintain during development phases. The payback, however, should be substantial and comes in the form of increased productivity and improved morale when there is an exact match between mission and automation.

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**References**

