Review Article

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Automation in the clinical laboratory: integration of several analytical and intralaboratory pre- and post-analytical systems

Klinik laboratuvar otomasyonu: Çeşitli analitik ve laboratuvar içi pre- ve post-analitik sistemlerin entegrasyonu

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Abstract: Clinical laboratory automation is very important to obtain reliable test results and to provide patient safety. There are some difficulties in implementing total automation to the clinical laboratories because they need a continuous, high quality customer service to keep their high quality serving, a questionable cost-affecting situation. It may be very difficult to keep the balance between the cost and the quality goals, patient safety, and demands. However, clinical laboratory automation may solve the dilemma and be implemented in clinical laboratories provided that it does not result in new bottlenecks in laboratory workflow. It is beyond the dispute that the minimal operator intervention benefited by total lab automation results in increased productivity, intra laboratory traceability of specimens, the decreased turnaround times, improvements in specimen handling, improved laboratory safety, and minimized errors. It has become very difficult, time-consuming, challenging task for the laboratories to decide to automate and which tests must be included in the analytical automation, to decide which one is more appropriate. First of all, a workflow and a workload analysis must be made for the present semi-automated laboratory. It would be focused in the present review that some strategies can be developed for this purpose.

Keywords: Clinical laboratory automation; Bottleneck in lab; Consolidated instruments; Workstation; Workcell.

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Özet: Klinik laboratuvar otomasyonu güvenilir test sonuçları elde etmek ve hasta güvenliğini sağlamak için çok önemlidir. Klinik laboratuvarlarda toplam otomasyon uygulanmasında yüksek kalitede hizmeti sürdürmek için devamlı ve yüksek kalitede müşteri hizmetleri gerektirir gibi maliyeti etkileyen tartışmalı durumlardan dolayı bazı zorluklar vardır. Maliyet ile kalite hedefleri, hasta güvenliği ve talepler arasındaki dengeyi sağlamak çok zor olabilir. Ancak, klinik laboratuvar otomasyonu, bu ikilemi çözelir ve laboratuvar iş akışında yeni dar boğazlara neden olmamak kaydıyla klinik laboratuvarlarda uygulanabilir. Total laboratuvar otomasyonunun sağladığı minimum operatör müdahalesinin artan verimlilik, örneklerin laboratuvar içi izlenebilirliği, azalması turnaround süreleri, numune işlemeye iyileşmeler, laboratuvar güvenliğinin iyileşmesi ve hataların minimize edilmesi gibi faydalar sağlayacağı tartışılmaktadır. Laboratuvar otomasyona ve hangi testlerin analitik otomasyona dahil edilmesi gerektiğiine ve gerektiği olması durumunda ne tür bit laboratuvar otomasyonunun kurulacağına karar vermek zor ve zaman alıcı bir iş haline gelmiştir. Her şeyden önce, mevcut yarı otomatik bir laboratuvar için iş akışı ve iş yükü analizi yapılmalıdır. Bu derlemede bu amaç için geliştirilebilecek bazı stratejilere odaklanacaktır.

Anahtar kelimeler: Klinik laboratuvar otomasyonu; Laboratuvarda dar boşazlar; Konsolide sistemler; Workstation; Workcell.
Introduction

The clinical laboratories need a continuous, high quality customer service in order for them to keep their high quality serving. These requirements are becoming increasingly questionable because of cost apprehensions. It is, thus, very difficult for the clinical laboratories to balance cost with the quality goals, patient safety, and demands. Clinical laboratory automation has been thought to solve the dilemma and has been widely implemented in every modern laboratory with different automation level [1–3].

On the basis of the benefits of automation [4–8], the laboratory directors have changed manual, error-prone laboratory processes to automated ones with minimal operator intervention, resulting in increased productivity, intralaboratory trackability of specimens, the decreased turnaround times, improvements in specimen handling, improved laboratory safety, and minimized errors [9, 10]. All these improvements have provided a positive impact on patient safety, as well. It is to the patient safety that an increased attention has been made by governmental regulations and accrediting organizations [4, 11, 12]. In a recent report [13], a total laboratory automation has been suggested to include the first-line tests with critical impact on the medical decision making, while specialized tests take place on satellite laboratories. Accordingly, automation must not only be present in every modern laboratory but also should be optimized in order to accomplish the efficacy in medical decision making.

It must be decided by each laboratory whether or not automation should be implemented. One should take into consideration both the benefits of automation in clinical laboratory the possible difficulties in implementing automation in laboratory. The needs and resources of each individual clinical laboratory determine the automation type or degree. Clinical laboratory automation can be ranged from automating only a few laboratory processes, partial or local automation, to total laboratory automation, which can include quantitative chemical and microbiological tests together with the majority of preanalytical processes. The total laboratory automation may be designed as core laboratories, combining different automated analytical systems in one location for testing a huge number of samples a day [16].

If an analytical system in clinical laboratory performs many tests with only minimal involvement of the staff in laboratory, the process can be described as operating automatically, a definition of automation which can be applied to the both simple and complex analytical systems. In the presence of automated analyzers, laboratories would have opportunities to process much larger workloads with no increases in staff. In other word, the aim of automation is to save time and to improve performance through the elimination of human error [15].

The automation in the clinical laboratory has evolved together with evolution in the automation-manufacturing industry. During this progression, laboratory testing has grown from a manual process with very narrow, simple test menu to an automatically-processing instrument with very large test menu and high throughput. Similarly, the automated analyzers have evolved from fixed, simple automation to a programmable, versatile, more complex automation. Because of this progression, one can change the old statement “laboratory automation is nice to have” into the new one “the automation must be present in every modern laboratory”. Thanks to the laboratory automation, there has been a reduction in the variability of results and analytic errors, and a significant improvement in the quality of laboratory test results has been caused by the improved reproducibility, which provides the support to clinicians to improve the diagnosis and treatment of patients [16].

Automation in clinical laboratory is used not only to assist the laboratory’s test performance but also to process and transport the specimens, to load the specimens into automated analyzers, to assess the test results obtained, and to store and archive the specimens, which means the automation involves all processes mentioned. To automate these additional functions is of crucial importance with respect to the future prosperity of the clinical laboratory [17].

On the other hand, clinical chemistry or laboratory medicine has combined many different disciplines such as chemistry, immunochemistry, endocrinology, toxicology, informatics, engineering, microbiology, coagulation and hematology etc. In order for laboratory automation to combine these disciplines, a complete integration has occurred, which includes a complex of robotics, computers, liquid handling, and numerous other analytical and non-analytical technologies. However, the most important component of automated systems have been the microprocessor and computer [18].

Historical perspective of laboratory automation

The first phase of the clinical laboratory automation has occurred in analytical instrumentation. Clinical chemistry laboratory gained the first automated analyzer, AutoAnalyzer, in 1956, which could analyze only limited
number of analytes: urea, glucose, and calcium. AutoAnalyzer evolved into Tecnicon single and multichannel continuous flow autoanalyzers in very short time [19]. The throughput of AutoAnalyzer was 150 samples per hour, and repertoire 20 analytes. This multichannel analyzer was a batch and non-selective analyzer. In 1970s, we see a peak point in the autoanalyzer: first, SMA (Sequential Multiple Analyzer) and secondly, SMAC (Sequential Multiple Analyzer with Computer) with a built-in computer [20]. This trend was parallely supported by centrifugal analyzers, in which sequential, discrete, and parallel analyses were being performed, and continued up-to-day with each new generation of instruments that elevated the throughput and increased the assay menu. In early 1980s, the random access, discrete, sequential autoanalyzers were met in market after introduction of the photodiode array for spectrophotometers with grating monochromators and of clinical chemistry ready-to-use assay reagent methodology, with the latter beginning to enter the clinical chemistry field in the 1950s by Sigma Chemical Company in St. Louis [21].

The laboratory information systems (LIS), with other name laboratory information management systems, began to rise in the 1970s together with analytical automation, which made a connection between electronic data management and laboratory instrumentation. Thanks to this coupling, the sample and test throughput of the clinical laboratory dramatically increased. It was after the coupling of instrument and electronic automation by means of LIS that attention was directed to automation of the pre- and post-analytic laboratory work phases. In other words, analytic and electronic automations were followed by pre- and post-analytic automation, being the last phase of clinical laboratory automation. The latter comprises all laboratory work flows such as sample transfer to the laboratory, accepting a clinical specimen into the laboratory, pre-testing processes, testing, and post-testing processes [17].

Progression in analytical automation

It is very interesting that the basic manual laboratory techniques and procedures have generally been adopted in principle to automated, or mechanized, fashion in automated analyzers, while a wide variety of configurations can be observed in modern instrumentation in clinical laboratory. Step-by-step innovations created these ultimate configurations. One can see several approaches to automated instrumentation historically. For instance, multiple samples are tested in a series in batch analyzers. In contrast, in sequential analyzers, the samples are tested sequentially, and the results are reported at that order. Continuous-flow analysis means a form of sequential analysis with a continuous stream. In random-access discrete analyzer, the most common configuration, analyses are performed sequentially on a set of specimens, and each sample can be analyzed for a different test selection. In this type of analysis, an interruption can occur in routine working for spanning a stat sample in-between, permitting measurement of a number of and a variety of analytes in each specimen. Discrete term in this type of analyzers means that each test of a patient (or a sample) is analyzed in a distinct chamber (in a well, cuvette, reaction vessel) [22].

Random-access discrete analyzers are the ultimate, modern-time instrumentations and have much flexibility in their functions. For instance, we can see many different response types or reading modes [22, 23], including (a) one-point end point assay, (b) two-point end point assay, (c) kinetic or rate assay with/without reagent/sample blank, and (d) fixed time.

Unit operations in an analytical process in a modern automated (random-access, discrete selective) analyzer are well defined [23] as follows: specimen identification, specimen delivery, specimen processing, sample introduction and internal transport, sample loading and aspiration, reagent handling and storage, reagent delivery, chemical reaction phase, measurement approaches, signal processing, data handling, and process control, the unloading the waste and the specimens, and storing the specimens.

When one considers the above-mentioned unit operation characteristics, it can easily be seen that the random-access discrete photometric analyzers have dissolved many problems associated with the previous, older continuous flow and centrifugal analyzers. Thus, it will better to summarize some distinctive characteristics of these modern analyzers as follows. The photometric and immunoassay analytical automations can share the majority of these properties and differ in measurement principles and modes.

(a) The modern analyzers use positive displacement pipettes, capable of pipetting of various or fixed volumes of both samples and reagents.

(b) Different kinds of mixing including forceful dispensing, magnetic and mechanical stirring, and ultra-sonication.

(c) Peltier temperature control of reaction medium is achieved by several means: water, air, or oil baths or heating block.
(d) The on-board reagent storage compartments are cooled for longer reagent stabilization.
(e) The reagents and the primary samples are in general identified by barcode labels.
(f) The mix of sample and reagents is the place of reaction called as chemical reaction phase. The determinants of the reaction phase include vessel/cuvette in which the reaction occurs and/or is monitored, the duration of the reaction, transport of reactants and mixing them, and separation of bound and unbound fractions for heterogeneous immunoassay systems.
(g) The reaction vessels of these analytical systems may be glass or plastic, and the plastic ones may of single use or reusable.
(h) In these analyzers, several detector types are used, which include different lamps: tungsten, quartz halogen, mercury, xenon, and lasers. The immunochemical analyzers have different type detectors.
(i) Liquid reagents, which may be provided in the forms of ready to use, concentrated, or usable after reconstitution, are used in the majority of analyzers.
(j) The chemical reaction phase is traditionally evaluated in automated clinical chemistry analyzers by photometers/spectrophotometers. Depending on the response-measuring methodology of the automated analyzer, several different approaches may be made, which includes reflectance photometers, fluorometers, and luminometers; fluorescence, chemiluminescence, and electrochemiluminescence measurements; and electrochemical techniques.
(k) In these analyzers, the signals are processed, the data handled, and process controlled, all of which have been achieved by means of interfacing and integrating the computers into automated analyzers.
(l) They often include an ion specific electrode (ISE) module for electrolyte analysis (Na, K, Cl) [14].
(m) They are designed in such a way that the operator is confident of reliable operation of them and is able to walk away from the instrument for longer periods, since the supplies, or consumables, are of large-size and are enough for large number of testing.
(n) Into some of them can continually be loaded the specimens and all supplies, including reagents.

Development steps in clinical laboratory automation

Several sequential steps may be involved in the development of clinical laboratory automation: (1) analytical automation (workstation), (2) LIS, (3) stand-alone pre-analytical system, (4) instrument consolidation (integrated automation; workcell; instrument clusters), (5) integrated pre- and post-analytical system (modular pre-analytical system; total laboratory automation), and (6) autoverification.

1- Workstations

The laboratory workstation, an instrument or an automated analyzer dedicated to a defined task in modern clinical laboratory, can be placed at the beginning of integrating laboratory automation. The currently-used laboratory instruments are designed for stand-alone operation and are of workstation concept. The workstations are operated independent of other workstations, and the samples are loaded manually by the operator. Specific software is used for controlling all functions by the operator on the vendor-defined basis. If a bidirectional interface with LIS is available in the laboratory, some tasks may become automated [23].

We know that there are a variety of workstations using different analytical techniques in a modern clinical laboratory, including reflectance photometry, electrophoresis, LC-MS/MS, as well as colorimetry/spectrophotometry, potentiometry, and immunoassay [24], which means the richer the analytical techniques, the higher the number of automated analytes in clinical laboratory. Meanwhile, a coupling occurred between clinical chemistry and immunoassay within a single workstation such as Dimension Vista [25].

Homogenous immunoassays either were able to be combined within clinical chemistry workstations as immunoturbidimetric measurements or were designed as immunonephelometric measurements in distinct stand-alone nephelometric analyzers, and the heterogeneous immunoassays were designed within automated immunoassay workstations, with the latter being most important step in automated immunoassay [26]. Many of them are available in our modern clinical laboratories from different vendors: Roche, Siemens, Beckman-Coulter, Abbott, and some others. Some modular designs have been introduced, which can be operated side by side as clinical chemistry plus immunoassay, and the resulting combination means richer analyte menu, higher throughput, and more different methodologies (colorimetry, spectrophotometry, potentiometry, and immunoassays) at the same setting. These instruments may be considered as stand-alone workstations or as integrated workstations [27].

2- LIS

Information technology was partly explained in the heading Historical Perspective of Automation.
As mentioned earlier, informatics is one of the basic elements of laboratory automation [28]. In order for us to define the quality indicators and to evaluate the improvements thanks to the laboratory automation, we should use solid metrics, and it is only with this way that we objectively evaluate the pre- and post-automation performance characteristics and its effectiveness. Laboratory accreditation organizations recommend that each laboratory determine TATs for each test (form both stat and routine analytes) and the number of process failures for a given period, all of which can be followed and evaluated by means of information technology. Middleware, or process-controlling software, laboratory automation and LIS cooperate for many tasks, including reading specimen ID, determination of processing each sample, monitoring the analyzers with respect to predefined algorithms, post-analytical processes such as reruns, dilutions, and others, and quality control. All are associated with information [14].

3- Stand-alone pre-analytical automation (automated specimen processing systems)

As the automated instruments have been evolved, the test throughput of analyzers in the clinical laboratory has increased extensively. Thus, the preanalytical sample processing was not able to step the analytical progression, and the laboratory needed a specimen processing rate greater than what the manual handling could provide. It is in the phase that the attention was directed to the pre- and post-analytic activities of the laboratory work flow after instrument and electronic automations. The main goal of this kind of stand-alone automation was to automate the handling of a clinical specimen for laboratory testing [29].

It has been very difficult to automate the preanalytical activities. At the beginning, several types of stand-alone pre-analytical automation systems were developed, and thanks to these systems, various specimen-processing steps were largely able to be automated in clinical laboratories. Nowadays, many low-to-medium sized laboratories have been using them commonly. In some of these stand-alone systems, several optional modules are also available. Even large-scale laboratories use these more complex, automated specimen processing systems, capable of specimen identification, labeling, decapping/recapping, analysis-scheduling, centrifugation, and sorting to different analyzer racks in laboratory. The sample-filled racks are then transported in any way (manually or by a conveyor device) to respective workstations in the laboratory.

The specimen processing systems have generally been designed in two ways: integrated and modular. A few exceptions may be present such as Tecan. Either approach follows in general the following sequence: sample loading, sample identification and inspection, LIS communication, sorting, centrifugation, decapping, sample aliquoting, labeling, and recapping. Consequently, stand-alone pre- and/or post-analytical systems have become supplementary for automated analyzers in clinical laboratories. This resultant automation can be considered as partial or task-targeted automation [23].

4- Instrument consolidation

Instrument clusters are of significance in combination or integration of analytical systems, which forms a basis for analytical systems to consolidate with pre- and post-analytical activities. Integration of analytical systems provides the advantage of consolidation. For this purpose, several identical analyzers (chemistry + chemistry + chemistry; immunochemistry + immunochemistry; or hematology + hematology + hematology analyzers) are connected to each other by means of a control module (a computer), which is called as a homogenous combination. On the other hand, the combination via a control module may be made with different analyzers as in the case of chemistry plus immunochemistry, a heterogeneous consolidation. In both situations, a single technologist can simultaneously control and monitor the functions of several instruments from the computer. However, for each analyzer in these combinations, sample load, quality control, and maintenance must be made separately by the operator.

Another type of the instrument consolidation is the combination of analyzers, on either homogenous or heterogeneous basis, by means of a control module plus a robotic specimen handling and preparation unit, which has been defined as work cell. The robotic system in this cluster can perform some pre- and post-analytical activities associated with sample preparation: sample level, centrifugation, aliquoting and labeling, transport, and even specimen storage. These extra-analytical processes can be considered as a prototype of preanalytical automation and as an important step to it. The responsibility of introduction of the specimens into the each connected analyzer belongs to the robotic system, which allows the operator to monitor the system and to accomplish such works as reagent replenishment, calibration, quality control, and maintenance. The control module can coordinate both the analyzer and robotic system operations. Such a work cell may be considered as a preliminary laboratory automation.

5- Integrated pre- and post-analytical system

Although there are two approaches to laboratory automation as stand-alone and total laboratory automations
the latter can be used for modern laboratory automation. In these systems, one can see several different types of workstations connected to each other by means of a track or conveyor belt. The introduction of robotics and informatics into the clinical laboratory following analytical automation allowed the laboratory automation to develop [5, 6, 29]. Several advantages of laboratory automation include the standardization of testing, reducing the duration of sample handling steps, improvements in TAT, and eliminating the potential human errors, all of which improve patient care and provide a high-quality service. Consequently, a balance between the cost and analytical quality, patient safety, and service needs has been achieved by laboratory automation in clinical laboratories world-wide. In a wider perspective, the laboratory automation may be associated with improvements in analytical methods, TAT, specimen handling (including centrifugation, retrieval, dilution, and rerun), throughput, cost, middleware, laboratory safety, and instrument downtime and service [14].

The ultimate phase of clinical laboratory automation is the instruction of integrated pre- and post-analytical systems, with the other naming being integrated or modular automation systems and total laboratory automation. Since the total specimen work flow in clinical laboratory accounts for about 60% of the time and effort of the total laboratory processes, the contribution of pre-analytic error to total laboratory error may be caused by the pre-analytic phase alone, which is estimated to range from 30% to 86% [31–33]. Just after understanding the pre-analytic errors have a large impact on the test results, the efforts were directed to the automation of the pre-analytic phase, which meant an extra-analytical automation, and the door was expanded out of the testing phase.

Pre- and post-analytical automation systems have specific process-controlling software which, on one hand, can read the specimen’s bar codes and obtain information about specimen from LIS, and on the other hand, can make a connection between LIS and interfacing analyzers to achieve their maximum effectiveness. The calculation of the number and the volume of aliquots depending on the test request, the direction of the specimens to analyzers, recapping of them, their retrieval, monitoring the analyzers, specimen integrity checking, and the detection of troubleshootings of whole system should be able to be accomplished by this software.

### Integrated, modular preanalytical system components

In integrated, modular preanalytical systems, the following modules or functional parts are present in general [29] (see Figure 1). The functional parts or stations are not written in the order of processes of the preanalytical automation. However, the overall composition of system, its components, and the order of the modules may be different, more or less, from each other depending on the manufacturer and the final composition depends on what the customer really needs. The customer may omit such components as aliquoter and/or storage in the optimized system.

1. **Specimen input area**
   - The system is loaded from this station. In a circular-type automation, this part is localized together with specimen storage and retrieval system. The modularity of the systems allows the customer to include, exclude, or expand any module. Some systems may be open for interfaces to analyzers from other vendors and may be closed and can make interfaces to the vendor’s own analyzers.

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**Figure 1:** The modules or functional parts of any integrated, modular preanalytical system.
output area. In some type of systems, input station has also been designed for sorting the samples.

2. Specimen identification area
   Several bar code readers function here. The behavior of the sample in whole system is determined at this position.

3. Carriage device
   Primary or secondary tubes with conventional sizes (16*100 mm and 13*100 mm) are transported to proper localization by means of this transporter in racks or as individual tubes.

4. Centrifuge
   This part is one of the rate-limiting components. The higher the centrifugation capacity or the higher the number of the centrifuges in the system, the higher the sample throughput of the system. In this area, specimens requiring centrifugation are removed from the belt, introduced into the centrifuge and automatically balanced, then removed from the centrifuge after processing, and placed back on the conveyor. The centrifuges may be refrigerated or non-refrigerated depending on the vendor. The parameters of the centrifugation are generally user-defined.

5. Specimen integrity unit
   The volume of each specimen and its adequacy are sensed by level detection. Some systems can detect the clot and physical property of the specimen (serum indices) here. This property is present in some clinical chemistry analyzers, as well, and is always needed.

6. Decapper
   The specimen caps or stoppers are removed by a device and discarded into a waste.

7. Recapper
   The specimens are automatically recapped in any way by the automated system.

8. Aliquoter
   A part of the automated preanalytical system in which an adequate volume of sample is aspirated from primary sample into secondary specimen containers, and the resultant secondary tubes are barcoded, capped, and transported for sorting to “off-line” analytical workstations. How many aliquots and what volumes are required is determined by the system software.

9. Interface to workstations or automated analyzers
   Depending on the system configuration, the analyzers having direct physical connections are called on-line analyzers, which can make sampling either directly from the conveyor belt or by taking the sample into the analyzer and pipetting it. The closed preanalytical system can make interface only with its own analyzers, and the open ones with different vendors’ analyzers.

10. Sorter
    A kind of sorting mechanism is used in some systems, especially the secondary samples are sorted to the specific racks of certain off-line analyzers or to rack positions.

11. Output unit
    These stations are used for temporary storage of specimens after analysis in some types and for holding the specimens for a defined duration in other types, with the latter being called as stockyard and being used for sample retrieval. These stockyards are refrigerated, and their storage capacity is higher than the temporary storage units.

6- Autoverification
   Autoverification is an important part of automation of informatics, in which the verification of clinical laboratory test results is made by a process using computer-based rules with no manual intervention. Although a few published data about autoverification in clinical laboratory, autoverification can easily be said to greatly decrease the inspection time of the results by the stuff, lessening fatigue. It is by this way that the laboratory staff can concentrate on the problematic test results thanks to the autoverification. On the other hand, autoverification needs a good collaboration between the clinical laboratory and LIS services, and some improper releases of test results resulting in a negative impact on patient safety in the case of inadequate installation of autoverification system [34, 35].

Selecting a laboratory automation
   It has been well documented that laboratory automation provides lot benefits and has a cost [7-9, 12]. However, there are few practice guidelines advising laboratories on how to evaluate, select, and implement the automation. Since each laboratory has its own unique characteristics, the criteria helping select the appropriate automation for all laboratories may not be uniformly applicable or fit, and some generalizable principles and strategies may be given for this purpose.

   One must be realistic in selecting the laboratory automation and know that it is not a prerequisite for laboratory processes. The laboratories should use automation provided that it is only necessary and appropriate. The daily workload of the laboratory is very critical and determinant
Table 1: Workload analysis of a semi-automated clinical laboratory.

| A. General information                  | Tube number | Tube size and vendor |
|----------------------------------------|-------------|---------------------|
| Primary tube number per day            |             |                     |
| Mean test requirements per tube        |             |                     |
| Barcoding type                         |             |                     |
| Common sample type (serum/plasma)      |             |                     |
| Other sample types                     |             |                     |
| Daily out-patient number               |             |                     |
| Maximal in-patient number              |             |                     |
| Tube type commonly used                |             |                     |
| Partition of the sample?               |             |                     |
| A. Clinical chemistry                  |             |                     |
| B. Hematology                          |             |                     |
| C. Immunochemistry                     |             |                     |
| D. Coagulation                         |             |                     |
| E. Urine                               |             |                     |
| F. Others                              |             |                     |

| B. Specimen flow                       |             |                     |
| Daily specimen kinetics                | Hours of day |                     |
| Total sample number                    |             |                     |
| The sample number to be centrifuged    |             |                     |
| Coagulation sample number              |             |                     |
| Emergency samples                      |             |                     |
| 08–10                                  |             |                     |
| 10–12                                  |             |                     |
| 12–14                                  |             |                     |
| 14–16                                  |             |                     |
| 16–18                                  |             |                     |
| 18–20                                  |             |                     |
| 20–22                                  |             |                     |
| 22–24                                  |             |                     |
| 00–02                                  |             |                     |
| 02–04                                  |             |                     |
| 04–06                                  |             |                     |
| 06–08                                  |             |                     |

| C. Specimen sorting                    |             |                     |
| Do you need specimen sorting upon receiving? |             |                     |
| – Do you need specimen sorting for archiving? |             |                     |
| – Do you need specimen sorting for individual analyzers? |             |                     |
| – Do you need specimen sorting for any purpose? |             |                     |
| What is the number of sorting address? |             |                     |
| Which analyzer racks do you want to sort for? |             |                     |

| D. Sample archiving                    |             |                     |
| Current sample archiving               |             |                     |
| – Primary tube archiving? if yes, how long? |             |                     |
| – Secondary tube archiving? if yes, how long? |             |                     |
| – Do you want recap the archived tubes? |             |                     |

| E. Specimen aliquoting                 |             |                     |
| Do you make aliquoting?                |             |                     |
| – If yes, why and where?               |             |                     |
| – Number of aliquots per day           |             |                     |
| Hours of day                           |             |                     |
| Aliquoted primary tube number          |             |                     |
| Secondary tube number                  |             |                     |
| 08–10                                  |             |                     |
| 10–12                                  |             |                     |
| 12–14                                  |             |                     |
| 14–16                                  |             |                     |
| 16–18                                  |             |                     |
in this issue. There are different suggestions for daily sample capacity in order for a laboratory to move from semi-automated system to laboratory automation. For instance, a laboratory with workloads lower than 1000 specimen tubes/day should not have these complex systems. Armbruster et al. [30] advised a laboratory with daily workloads of 500–2000 samples to have a stand-alone preanalytical system. However, it has been suggested that the laboratories with workloads of 1000–10,000 specimens per day design the complex laboratory systems, which involves a track for connecting the analyzers [28]. In determining the capacitive configuration, the laboratory should well match the analytical and non-analytical modules of the system to the need.

In order to evaluate the cost effectiveness of the laboratory automation implementation, it has been suggested that a commitment to automate be formed from technologists, supervisors, information services, and hospital and department administration [14]. Some top-level vendors of the systems can be included in this committee for the purposes of selecting the common, competitive features and of gaining the detailed technical properties of the systems. First of all, this committee can also discuss in detail the need to automate and potential benefits of automation.

Before attempting to construct laboratory automation, the current laboratory processes should be analyzed thoroughly and in detail with respect to both laboratory workflow and workloads as a first task [6, 36] (See Table 1). The workflow analysis will clear the strengths and weaknesses, or the bottleneck(s), of the current system, so that an informed decision will be able to be made as to whether automation will provide some improvements in laboratory processes. All phases of laboratory automation (preanalytical, analytical, and post-analytical phases) will be completely illuminated and audited by such a workflow analysis. The laboratory automation may improve or eliminate the impaired steps, and a conveniently-chosen laboratory automation system is to handle the laboratory workload at a ratio of at least 80%. A clinical laboratory may have several, multiple automated systems, and moving from the present situation to the laboratory automation is generally difficult task [14]. As mentioned by the previous reports [6, 14], if we do not properly analyze the needs

| Table 1 (continued) |
|---------------------|
| 18–20               |
| 20–22               |
| 22–24               |
| – Minimal aliquot volume (microliter) |
| – Maximal aliquot volume (microliter) |
| – Aliquot volume constant or variable? |
| – Current secondary tube type and size? |
| – Is the secondary tube capped? |
| – Is the secondary tube barcoded? |
| – What is written on barcodes? |
| F. Stat             |
| Do you need STAT testing? |
| G. Analyzers       |
| Do you have analyzers to be interfaced to the preanalytical system? |
| How many, what kind, and which order? |
| H. LIS              |
| The current LIS?   |
| Processor of LIS?  |
| Current semi-automated systems? |
| Supported protocols by LIS?? |
| LIS compatible to TCP/IP? |
| I. Specimen acceptance |
| How do you accept the specimen? |
| The number of staff in this section? |
| Who is sampling? How are the samples transferred to the lab? |
| Are the specimens confirmed by LIS at arrival? |
| Is the test order by barcode or manual? |
| J. Other           |
| What is expectation from laboratory automation? |
Table 2: Inquirement criteria for selecting the laboratory automation system and related comments.

| Inquisition criteria                     | Comments                                                                                                                                                                                                 |
|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Track design                            | Configuration is a term defining track design, analyzer connections, analyzer orientation (parallel or perpendicular to the track), and size of whole system. The advantages of a circular versus linear design can be discussed. For instance, circular systems need more space but make retrieval easy. Size for rooming the system may be restrictive in smaller laboratories. |
| Analyzer connections                    | The order, the number, and the kind of the analyzers must be well determined by the laboratory depending on the need or capacity. Designing the analyzers makes it easy to access to all facets of the analyzer for maintenance or repair. |
| The mode of sample identification       | The samples are identified by reading the specimen bar code. However, the specimens can repeatedly be identified by one of two options: multiple linear bar code readers and radiofrequency identification. The robust sample identification is very critical. In the case of the radiofrequency identification, manual removal of tubes from the carriers results in loss of the link between bar code and the carrier's identification. Multiple linear bar code readers may be preferred. |
| Aliquoting from the primary sample tubes | How many aliquots can be made from a single primary tube if needed? Does the aliquoting module have a secondary tube-capping, labeling, and sorting capacity for off-line analyzers? Several systems can make aliquots for offline analyzers. However, the aliquot number, aliquot tube type, and label involvement must be considered carefully, which may not be suitable for every laboratory. Some aliquoting modules can detect clot and sense the sample level, which may be important for determining the volume remaining in the tube, and this knowledge is sent to informatics. |
| Specimen carrier                         | In automation systems, single or multiple specimen carriers (or racks) are used for specimen carriage on the belt. The multiple carriers can also be used for centrifuge loading and unloading easily. However, it takes time to refine any sample in rack carriage for retrieval. |
| Primary and secondary tube processing capability | Which sizes can be used? The wider the sizes, the better. Sampling from primary tube by analyzers may be preferable. Systems can process different tube size and type. The versatility of tube size and type may be restricted by centrifuge, decapper, aliquoter, and/or recapper modules. Manual processing must be avoided by the versatility of the tubes used. |
| Centrifugation module                    | Such parameters as the capacity as tube/hour, refrigerated vs. non-refrigerated, user defined adjustment or not, and capability of different tube sizes must be clearly defined. The metrics associated with centrifuge capacity, tube sizes, throughput, auto balancing, and spin temperature may differ from vendor to vendor. The versatility and flexibility are important with this respect. In higher-volume laboratories, an additional centrifuge module may become necessary. |
| Stat handling capability                 | Stat capability must be present both for analytical and pre-analytical components.                                                                                                                        |
| Direct sample loading to analyzers       | In the case of troubleshooting problems in preanalytical system, manual sample loading directly to workstations is of utmost importance.                                                                            |
| Retesting and retrieval capability       | For rerun, dilution, add-on, and reflex testing automatically, this capability is important.                                                                                                               |
| Storage and/or retrieval unit            | The systems generally have rooms accommodating aliquots, primary tubes, or both, which can be refrigerated or not. Their tube capacity may differ depending on the vendor. The workflow of the laboratory can be improved using refrigerated stocky yard with automatic retrieval. At least three major vendors in market offer this unit (See Table 3). The daily primary tube capacity, the area rooming the storage unit, and daily retrieval number determine the need to storage unit depending on the laboratory sample size, which should be carefully considered in the face of the cost-benefit ratio of manual specimen archiving versus refrigerated stocky yards. |
| Decapping/recapping the primary tubes    | Most systems contain a decapper unit. However, not all systems can decap hemograds, rubber stoppers, or screw caps. Plastic caps or heat-sealed metal foil are used specimen recapping for online or offline storage. Some vendors may not have a subsequent decapping for sample retrieval. |
| TAT                                     | TAT should be defined for emergency and routine testing on the basis of each individual test; the shorter the TAT, the better. The throughput of an analyzer dictates in general the overall TAT. |
| Throughput                              | This must be defined for each analytical system separately and for pre-analytical component. The throughputs of analyzers in the system mentioned by the vendor are theoretical and should not be overestimated in the laboratory using typical test mixes. In many cases, the analyzer design and functionality should thus be considered carefully. |
of the laboratory and understand the current state and processes in the laboratory, automation projects will not reach success and match well with initial expectations. On the basis of the present knowledge [6], the possible causes of the failure of laboratory automation have been listed as: incomplete audit of the current laboratory processes, lack of flexibility, throughput limitations, exaggerated or unclear expectations, poor connections of automated and manual processes, unnecessarily complicated configurations, poor technical and/or logistic Support, poor analytical performance, unanticipated costs, and the problems associated with the current process optimization.

In selecting the laboratory automation system, the common criteria should be inquired (see Table 2), which
were related to the whole system including track system and pre-analytical, analytical, and post-analytical components [14]. These criteria, together with our suggestions, can be summarized as: track design, analyzer connections, the mode of sample identification, aliquoting the primary sample tubes (which may be optional if needed), primary and secondary tube processing capability, centrifugation module, stat handling capability, retesting and retrieval capability, storage and/or retrieval unit, decapping/recapping the primary tubes, TAT, throughput, the availability technical service and logistic, test result quality, potential for sample/reagent carryover, clot detection, serum indices, pediatric sampling, open channel availability in analyzers, hands on technologist time, reagent type, quality control, walk-away duration, water consumption, environmental condition, and interface with informatics.

In ultimate decision step, it will be better for the committee to visit a matched, automated laboratory (with similar test volume and workflow to present laboratory) for a better inquirement. The criteria inquired can be listed as questions for site-visit, and the questions can be directed to laboratory workers including administrators, pathologists, supervisors, and technologists. The final comments are evaluated by the committee. Although the discussions with automated laboratories and vendors may show that no system satisfies all expectations or all requirements, one must reach to an optimal situation for installing automation (see Table 3).

### Table 3: The comparison of some modular preanalytical system (including no analyzer).

| Specification                                      | Beckman         | Roche       | Abbott      |
|---------------------------------------------------|-----------------|-------------|-------------|
| Preanalytical system                              | PP              | MPA         | ACC         |
| System design                                     | Circular/linear | Linear      | Circular    |
| Tube carriage                                     | Single tube     | Rack (5-position) | Single tube |
| Tube size (mm)                                    | (13)–(100–75)  | (16–13)–(100–75) | (16–13)–(100–75) |
| Tube identification                               | Barcode         | Barcode     | RFID a      |
| The number of centrifuge                          | 2               | 2           | 2           |
| Decapping                                         | Yes             | Yes         | Yes         |
| Recapping                                         | Yes             | Yes         | Yes         |
| Aliquoter                                         | Yes             | Yes         | Yes         |
| Analyzer interface (sampling from belt vs. inlet sampling) | Robotic arm/inlet sampling | Inlet sampling | Inlet sampling |
| Online stockyard (refrigerated)                   | Yes             | Yes         | Yes         |

aRFID: radiofrequency ID.

Clinical laboratory automation in the future

As mentioned earlier, analytical automation is the fast-developing area of clinical laboratory automation, and new automated analytical platforms are day-to-day being developed such as molecular diagnostic, immunostainer, and microbiological platforms. No doubt will be added the new ones in the future. More analytical platforms will be able to be interfaced on-line with the preanalytical automation. One should take into consideration that the more on-line connected the analytical systems, the more complicated and problematic the total laboratory automation. The other part of the laboratory automation to be developed or improved will be the pre- and post-analytical phases: automated specimen separation, specimen transportation, intra-laboratory specimen transportation, sample labeling [radio-frequency identification (RFID)] and autoverification.

### Conclusion

Laboratory automation is necessary for the laboratories with medium to large capacity, since it is directly associated with patient safety. The manual processes are no longer suitable for emergency and routine testing in clinical laboratories. Although the implementation of laboratory automation is a time-consuming, boring task, the automation is worth to implement to the laboratory, since its advantages are irrefutable. The critical point is that one decides what kind and what extent of automation is suitable for the present capacity of the laboratory. There must be a competition between the vendors at purchasing step, and the vendor claims can be verified by site visits to the laboratories having the intended automation.

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