Review Article

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Automation of extra-analytical phase for clinical laboratory

Klinik laboratuvar için ekstra analitik fazın otomasyonu

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published online January 20, 2021**Abstract**

Extra-analytical automation is of critical importance in patient safety with respect to accurate, fast test result reporting. Through the previous decades, significant improvements in laboratory errors have been achieved by technological facilities, which have become a substantial part of the reduction of preventable diagnostic errors. In clinical laboratory practice, the total testing process (TTP) is under the effect of error sources: preanalytical, analytical, and post-analytical variables. Since many extra-analytical processes within and outside the clinical laboratory may be automated, management of the extra-analytical phase can prevent errors, resulting in the total quality of laboratory diagnostics and customer satisfaction. The automation technologies have added a serious impact on the proficiency of clinical laboratories. To improve standardization, organization, efficiency, and quality of TTP, many manual tasks have now been partially or entirely automated by labor-saving instrumentations. The implementation of extra-analytical automation in the laboratory processes has recently made them standardized and manageable. Depending on the workload and workflow of the clinical laboratory, it is of

critical importance to implement adequate systems, providing standardization of the TTP and resulting in high-quality test results.

Keywords: automation; extra-analytical automation; laboratory automation; preanalytical phase; specimen handling.

Özet

Ekstra analitik otomasyon, doğru, hızlı test sonucu raporlaması açısından hasta güvenliğinde kritik önem taşır. Son otuz-kırk yıldır, teknolojik imkânlarla laboratuvar hatalarında önemli iyileşmeler sağlanmıştır. Bu teknolojiler önlenabilir teşhis hatalarının azaltılmasının önemli bir parçası haline gelmiştir. Klinik laboratuvar uygulamasında, toplam test süreci (TTP) şu hata kaynaklarının etkisi altındadır: Preanalitik, analitik ve postanalitik değişkenler. Klinik laboratuvar içinde ve dışında birçok işlem otomatize edilebildiğinden, ekstra-analitik aşamanın yönetimi, hataları önleyebilir; bu da laboratuvar teşhisinde toplam kaliteyi ve müşteri memnuniyetini sağlar. Otomasyon teknolojileri, klinik laboratuvarların yeterliliği üzerinde ciddi bir etki yaratmıştır. TTP'nin standardizasyonunu, organizasyonunu, verimliliğini ve kalitesini iyileştirmek için, birçok manuel işlem, iş gücünden tasarruf sağlayan cihazlarla artık kısmen veya tamamen otomatize edilmiştir. Laboratuvar süreçlerinde ekstra-analitik otomasyon uygulaması, son zamanlarda bunları standardize ve yönetilebilir hale getirmiştir. Klinik laboratuvarın iş yüküne ve iş akışına bağlı olarak, uygun sistemlerin kurulması, kritik öneme sahiptir. Bu da TTP'nin standardizasyonunu ve yüksek kaliteli test sonuçlarını sağlar.

Anahtar kelimeler: extraanalitik otomasyon; laboratuvar otomasyonu; numune işlenmesi; otomasyon; preanalitik faz.

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Introduction

Automation, in general, means a process with minimal or no human intervention. The currently used definitions associated with clinical laboratory automation and related fields are summarized and subclassified in Table 1. Automation in the clinical laboratory comprises extra-analytical as well as analytical phases, with the latter being developed earlier than the former [1]. The diagnostic area has changed consistently by a powerful catalyst “automation” in clinical laboratories. However, the lack of management of the pre-analytical phase exerts unfavorable influences on test results, which wastes healthcare resources and negatively affects patient outcomes. Extra-analytical and analytical automation has assisted the improvements in such laboratory processes as specimen labeling, sorting, transport, processing, loading on the analyzers, storage, and archiving as well as in the laboratory’s test performance [2]. Despite the asynchronous development of analytical and extra-analytical automation, clinical laboratory performances have dramatically changed today [3]. The automation technologies have added a serious impact on the proficiency of clinical laboratories. To improve standardization, organization, efficiency, and quality of TTP, many

manual tasks have now been partially or completely automated by labor-saving instrumentations, and the cost of the investment will possibly return on a long-term basis [4, 5].

Five or more decades earlier, the term automation was used to describe the test processes in clinical chemistry analyzers. However, during the past two decades, the automation has also covered extra-analytical processes, which have become substantial for the efficiency of clinical laboratories [1, 6, 7]. A high-quality test result means it must be correct and be reported as soon as possible, i.e., short turnaround time (TAT). The value of extra-analytical technologies besides the automated analytical devices can be appreciated, and extra-analytical automation will become crucial for improving clinical laboratory performance and patient’s sample safety [8]. Extra-analytical automation continues to grow as it is widely recognized as a principal means of eliminating errors, improving the quality, and reducing the labor, costs, and TAT [3]. The preanalytical phase is an essential component of total laboratory test quality. The preanalytical phase covers specimen collection, handling, and processing before analysis, all of which have potential variables affecting the TTP. Laboratory diagnostics implies the total testing process. Preanalytical errors

Table 1: The frequently used terms in clinical laboratory automation.

Term	Definition
Laboratory automation	General term used for automated clinical laboratory (instrumentation + LIS/HIS).
Total laboratory automation, TLA	Laboratory automation composed of heterogeneous, physically-integrated analytical and extra-analytical systems (many analyzers performing different types of tests on different sample matrices).
Analytical automation	Automated analytical systems or workstations.
Extra- or extra-analytical automation	Part of laboratory automation other than analyzers; pre- and post-analytical automation.
Intra-laboratory extra-analytical automation	Pre-analytical automation within the clinical laboratory (pre- and post-analytical phase automation).
Extra-laboratory extra-analytical automation	Pre-analytical automation outside the clinical laboratory (prepre-analytical phase).
On-line analyzer	An analyzer interfacing the integrated laboratory automation system.
Off-line analyzer	An analyzer extra-interfacing the integrated laboratory automation system; stand-alone analyzer.
Integrated/modular laboratory automation	An automation composed of pre-analytical, analytical and post-analytical component linked by a conveyor.
Modular analytical system	An analyzer designed as modules; module addition or exclusion possibility depending on the need.
Modular extra-analytical system	An extra-analytical system designed as modules; module addition or omission possibility depending on the need.
Stand-alone pre-analytical system	A pre-analytical specimen processor interfacing no analyzer.
Turnaround time, TAT	The duration in which the laboratory reports the test result.
Analytical TAT	Testing duration beginning with sample load to analyzer and ending with readout.
Intra-laboratory TAT	Reporting duration beginning with sample submission by laboratory and ending with report verification.
Total TAT	Reporting duration beginning with either test ordering or specimen collection and ending with report verification.

constitute more than 70% of all errors that occurred, especially in this phase's manually intensive processes [9].

Extra-analytical automation in the clinical laboratory has recently progressed to a point where extra-analytical and analytical components have been integrated or interfaced constructing fully integrated modular laboratory automation. There have been some phases in extra-analytical technologies based on their development, as shown in Table 2 [1, 3, 10]. The following part will illuminate these phases. First, the preanalytical processes can be considered as intra-laboratory (preanalytical) and extra-laboratory (prepre-analytical), with the former comprising the specimen processing within the laboratory, and the latter covering at least the following steps: out-of-laboratory

test order, automated specimen container preparation (vacutainer selection and labeling specific for each patient), sampling, and transporting. Consequently, the preanalytical phase begins with the test order and ends with the analyzer entrance of the processed samples. All the processes spanning test order to result reporting are recognized as TTP in routine laboratory work and are interconnected to each other. On the other hand, the post-analytical section of the extra-analytical automation covers auto-verification, recapping, automated specimens archiving, retrieval, decapping in the case of a rerun, and secondary specimen sorting for off-line analyzers [1, 3].

The diagnostic area has changed consistently by a powerful catalyst “automation” in clinical laboratories.

Table 2: Technological and bioinformatic advances helping automate some steps of extra-analytical phase (with modifications).

Automation	Details
(1) Computerized physician order entry	
(2) Positive patient identification by	– Bar coding technology – Optical character recognition – Magnetic stripe recognition – Magnetic ink character recognition – Voice identification devices – Radiofrequency identification (RFID) – Touch screens – Light pens – Hand print tablets – Optical mark readers – Smart cards
(3) Transport systems	– Active tubes (chip-integrated containers) – Pneumatic tubes system (PTS) – Robots – Transportation monitoring systems
(4) Instrumentation	– Automated sampling devices – Devices to find the vein (real time digital imager) for sampling – Tube labeler and preparer – Automated specimen sorter – Automated specimen submission to laboratory – Query-host communication – Primary tube processing – Volume/clotting/bubbles sensors – Serum indices – Automated centrifugation – Decapper, aliquoter, barcode labeler, recapper – Automated specimen storage and retrieval – Secondary tube sorter
(5) Informatics	– Query-host communication – Automated verification – Expert systems – Delta check technology – Error-recording software – Process-controlling software

However, the lack of management of the preanalytical phase exerts unfavorable influences on test results, which wastes healthcare resources and negatively affects patient outcome. The study has been intended mainly for laboratory professionals, managers or directors. It will help them select and implement this kind of automation for their clinical laboratories. Based on current workload and future demands, laboratory directors or professionals should consider theoretical advantages and limitations of extra-analytical automation as guidance to configure the suitable local solutions (see Table 3). Extra-analytical error types and their improvements by extra-analytical automation are also summarized in Table 4. During the implementation of extra-analytical automation in this phase, laboratory professionals should also appreciate

the error-improvement matches mentioned in Table 4. By this mode of action, they will be able to find an opportunity to establish some new quality indicators and to measure the laboratory performances, which will render TTP measurable and under control.

Extra-analytical automation systems

Figure 1 shows the schematic representation of the sub-classification of clinical laboratory automation, which contains two major components: **analytical** automation and **extra-analytical** or extra-analytical automation. The

Table 3: The advantages and limitations of extra-analytical automation for clinical laboratories.

Advantages	Limitations
Lower biological risk for staff and lower labor costs	Cost of maintenance, energy, and others
Prevention of sample waste	Space requirement/constraints
Improved sample management (rerun, reflex and add-on)	Increased costs for supplies/consumables
Improved efficiency and traceability	Higher costs on the short term
Decreased congestion in the laboratory	Inappropriateness for low-workload labs.
Extra-analytical variability governance	
Lower costs on the long term	
Providing standardization for accreditation/certification	
Tests results integration	
Prevention of potential bottlenecks	
Workflow and bottleneck analysis in extra-analytical phase	
Much more quality indicator selection possibility	
Appropriateness for high-workload laboratories	

Table 4: Extra-analytical error types and improving extra-analytical automation.

Extra-analytical error types	Improving extra-analytical automation
Wrong/missing identification	Positive patient identification
<i>In vitro</i> hemolysis	Usage of an adaptor, automated venous sampling system, and real-time digital vein imager
Wrong container	The tube labeler and preparer
Inadequate label alignment on the specimen tubes	
The low-resolution print quality of the bar-code label	
Insufficient sample	Usage of an adaptor and the containers with a pre-determined vacuum volume
Inappropriate blood to anticoagulant ratio	
Inappropriate transport and storage conditions	Pneumatic tube system
Inappropriate centrifugation conditions	Automated centrifugation
Inappropriate storage condition in the posttest phase	Automated specimen storage and retrieval system
Delayed submission and inefficient specimen traceability	Automatic tube loader and sorter
Errors from inadequate sample integrity	Volume/clotting/bubble-controller
Impairment in secondary sample traceability	Secondary tube sorter
Delayed test reporting	Automatic verification
The deceleration in integrated automation	Process-controlling software

The improvements are generally associated with shortened TAT, high-quality test result, and patient and staff safety.

detail of extra-analytical automation will be illuminated below. Extra-analytical processes can be divided into two groups: **intra-laboratory** extra-analytical processes (pre-analytical) and **extra-laboratory** extra-analytical processes (prepre-analytical).

Stand-alone preanalytical systems

Single-function, stand-alone preanalytical systems [1, 3] (Figure 2)

Because of the complexity of the intra-laboratory (pre-analytical) specimens processing, the single task stand-alone preanalytical systems, also called task-targeted, can even be implemented to the low to the medium-sized

Figure 1: Schematic representation of subclassification of clinical laboratory automation.

Figure 2: A single-function extra-analytical automated workstation. [Yaskawa Motoman AutoSorter 1200, which has sorting speeds of up to 2,000 specimens per hour, several different options for deck configurations, and the possibility of different analyzer-specific output racks. <http://www.motoman.com/labauto>].

clinical laboratories to automate the TTP and to yield efficient test result quality and improved TAT. This type of workstations can execute sorting, centrifugation, decapping, aliquotting, and recapping of the specimens, which has been the first step in developing the preanalytical automation in the clinical laboratory.

Multifunctional, stand-alone preanalytical systems [1, 3] (Figure 3)

The medium-sized laboratories with daily workload less than 1,500 tubes can plan to use these systems. The second phase in developing the preanalytical automation is multifunctional, independent preanalytical systems. These self-contained systems are more complex than the single-function ones and called automated specimen processors. Specimen-processing automation has been the most challenging area of the clinical laboratory workflow. These systems execute submission, inspection, logging, presorting, centrifugation, decapping, aliquotting, recapping, sorting, and labeling functions.

Some laboratories with higher daily volumes may implement multiples of a stand-alone specimen-processing system, either single-function or multifunction, and may automate post-analytical specimen processing as well. Each vendor in the market offers its specimen-processing workstations. Despite some variations in the functions included, the typical configuration of these systems includes interfacing the LIS, LIS-based specimen submission, sorting, decapping, aliquotting, and bar code-labeling the aliquoted specimen containers. Automated centrifugation, sorting into instrument-specific racks for analyzers, and post-analytical sample storage may be optional in these systems.

Automatic stand-alone preanalytical systems can also be called as automated specimen-processing systems. From a historical perspective, the vendors developed these stand-alone systems to keep pace with the fascinating, high throughput analytical workstations. The other two additional requirements for that kind of automation were the fact (a) that the specimen processing in clinical laboratory accounts for about 60% activity of the total laboratory workload and (b) that the total laboratory error is estimated to be caused by pre-analytic factors of at a ratio of about 80% [11–13]. The integrated or modular stand-alone automation would not only automate the specimen handling [14, 15] but also lessen the extra-analytical errors, mostly. The independent preanalytical systems can be configured to the need (task-targeted). They may be composed of various functional units mentioned above and additionally secondary specimen sorting to different analyzer racks,

Figure 3: A multifunction extra-analytical automated workstation. [Roche Cobas 612 system with automated centrifugation, decapping and recapping, aliquoting, and bar code labeling of secondary tubes, including sample quality inspection, <http://www.cobas.com>].

analysis-scheduling, secondary tube labeling, etc. This type of device may be designed as modules depending on the laboratory need: some modules can be included, excluded, or expanded [1, 3].

Integrated extra-analytical systems

This type of extra-analytical system is integrated with on-line analyzers in the configuration of integrated modular laboratory automation, with the other name being total integrated, modular laboratory automation systems. They can execute the preanalytical functions similar to those of stand-alone preanalytical devices mentioned above. However, these systems include interface analytical tools and post-analytical components, all of which are

linked by a conveyor system [14, 16, 17]. A sophisticated process-controlling software, modularity depending on the laboratory's need, minimal or no human intervention, and specimen storage and retrieval are characteristic for these systems. Open design permits interface with the analyzers of different vendors, but the closed system does not. The advantages of extra-analytical automation include standardization of and reduction in specimen handling steps, improvements in TAT, potential human error elimination, laboratory and staff safety, and reduction in analytical workstation downtime [18]. There may be several options in the design of integrated modular laboratory automation. A specific process-controlling software (middleware) makes all automated components operate. This software considers the integrated system as a whole device and mediates between the laboratory information system and

Table 5: Extra-analytical part of integrated/modular laboratory automation systems and their functions.

Component	Function
Process-controlling software and LIS interface	Controls the system and links it to LIS
Specimen input	Loads labeled specimens into the system
Bar code reader	Logs the specimens for routing along with the system
Transport conveyor	Moves the samples to their targets
Specimen sorter	Directs the samples based on processing requirements: centrifugation or no-centrifugation, omitting it
Centrifuge module	Automates the centrifugation process, removes the specimens from the conveyor belt, puts into a centrifuge, balances automatically, removes after centrifugation, and returns them to the conveyor belt
Specimen integrity-controlling unit	Detects the level of the specimen, evaluates its adequacy, and inspects serum indices, which is present in a few vendors' pre-analytical configurations
Destopper	Removes the hemogard tube caps and wastes them
Aliquotter	Sips sample aliquot from the primary tube based on the control software, sticks a bar-code to a secondary tube, and transfers the volume into it
Interface the automated analyzers	Makes a physical connection between automated analyzers and conveyor belt
Decapper	Caps the primary and secondary tubes
Storage and retrieval	Stores the primary tubes in a kind of storage bin for the rerun, dilution, or add-on testing upon retrieval
Sorter	Sorts the secondary specimens for off-line analyzers into separate racks
Second decapper	Decaps the retrieved samples from stockyard for reprocessing

the cluster of automated machines (1). The high-volume laboratories (>1,000 specimens per day) can plan to implement this type of extra-analytical – analytical configuration. The components of extra-analytical part of integrated modular laboratory automation systems and the functions of these components are shortly outlined in Table 5 [1, 3, 19]. Both pre- and post-analytical processes are closely associated with the TTP in the laboratory and with laboratory performance.

Extra-analytical automated processes

As mentioned above, extra-analytical processes are composed of intra-laboratory (preanalytical) and extra-laboratory (prepre-analytical) processes. In this subsection, the processes, which can be automated (partly or completely) outside and within the clinical laboratory, will be detailed as follows. Table 6 shows the extra-analytical automation outside and within the clinical laboratory and their impacts on TTP.

Venous blood sampling

Automated venous sampling systems [20] have been developed (Figure 4). They are **less painful** because of ultrasound-activated topical anesthetic patch; **friendly** due to open device design and the needle is hidden from

patient view; **more stable** due to quick, steady placement, no needle overshoot, and no needle motion tremor (e.g., during tube changing); **safer** thanks to automated needle handling and no contact with used sharps and **comfortable** because of the ergonomic armrest. Devices to find the veins, or real-time digital imagers, for sampling help access the veins easily (Figure 5) [21]. All tools mentioned above are closely associated with both patient and healthcare staff safety and prevent hemolysis, adding an impact value to TTP and providing high-quality testing.

Figure 4: Automated venous blood sampling device (VenousPlus from VascuLogic).

Table 6: Extra analytical automations outside and within the clinical laboratory and their impacts.

Extra-analytical automation	Impact
Processes outside the clinical laboratory	
Venous blood sampling	Patient safety, staff safety, hemolysis prevention, TTP, high-quality test
Specimen identification	Specimen traceability, TTP, primary tube usability, worklist elimination, correct tube feeding to analyzers, specimen identification error decline
Tube labeling and preparing	Efficiency, fast accessioning, intelligent preanalytical solutions, specimen safety, time saving, staff safety, error prevention, traceability, cost-saving
Specimen delivery	Efficiency, fast, specimen safety, improved TAT
Processes within the clinical laboratory	
Tube loading and sorting	Efficiency, traceability, fast, widening the bottlenecks
Specimen preparation	Improved TAT, safety, TTP
Whole blood sampling	Improved TAT, emergent sample detection
Processes in integrated extra-analytical automation	TTP action
Process–controlling software	Intelligent, fast control, troubleshooting detection, specimen integrity, auto-verification, test and sample traceability, system operation detection
Specimen storage and retrieval	Specimen safety, resampling prevention

TP, total testing process; TAT, turnaround time.

Figure 5: Real-time digital imager (Accuvein av500 from Accuvein).

Specimen identification

The sample must be clearly and accurately labeled throughout the total laboratory process and traceable to the patient's data. Different kinds of technologies achieve automatic identification and data collection. The bar code labeling for automatic identification is a commonly used technology in a clinical laboratory [3]. Labeling is a vital specimen identification tool. An electronic test order for an individual patient, either outpatients or inpatients, by the clinician using LIS is entered, and a single label is generated, which contains the patient's ID and a unique laboratory accession number. Unless this accession number receives the result(s) of the patient, the record in the bio-informatic system remains incomplete, providing the tracking of the sample. During the sampling, provided that the patient is identified correctly, this matchless label adheres to the specimen container. A standard was published by the Clinical and Laboratory Standards Institute (CLSI) in 2011 on Specimen Labels: Content and Location, Fonts, and Label Orientation [22]. This guideline tried to standardize specimen labels and to reduce patient misidentifications. In the case of bar-coded label usage in the clinical laboratory, for the subsequent total testing process (TTP), it is

critical for a specimen tube to have a properly-aligned label and human-readable content on the label. The laboratory can submit only that kind of labeled specimen. LIS, together with the hospital information system (HIS), can automate the test requisition form, sampling time/date, and phlebotomist ID.

Laboratory acceptance of the specimen is recorded electronically by automated procedure by the accession number mentioned earlier. Then, TTP (analytical and extra-analytical) begins within the laboratory. Some workstations can read primary specimen tubes with accession number on bar code label, and some other analyzers need aliquoted, identified secondary samples generated from the primary specimen tubes. Removal of the sample from the primary (original) tube and secondary tube preparation, to which is affixed a bar-code label identical with the primer specimen, have been able to be automated by several vendors.

Barcoding is a vital sample identification tool in clinical laboratories. CLSI's standard (AUTO02-A) was published in 2000 and updated (AUTO02-A2) in 2003, suggesting only the use of the Code 128B or two-dimensional one for sample labeling [23]. The automatic specimen identification by using the bar-code labels may provide several extra-analytical phase-associated improvements [3] such as elimination of work lists for laboratory procedures, avoidance of mistakes related to the placement of tubes in the analyzer or during sampling, avoidance of the need for analysis of specimens in a defined sequence, and decrease in identification errors. There may occur several errors in specimen identification. The mismatch of specimens and results of the patients may affect total testing processes in the laboratory from the sampling to the analysis. Hand transcription is another considerable risk, which can affect the worklist creation, accessioning, labeling, and relabeling. Transposed digits result in an incorrect accession number, and such a number causes an inaccurate worklist, suggesting a mismatch between the patient and the results.

The automatic bar-code label reading can dramatically decrease the specimen identification errors [from 1/300 characters (manual entrance) to about 1/1 million characters (automated entry)]. However, there may be a few read errors in automatic bar-code reading, including imperfect printing of the bar-codes, insufficient bar-code scanner resolution, or skewed orientation of bar code labels on collection containers [3]. Besides, patient identification errors were reported to be caused by a misreading of one-dimensional bar-codes [24]. This problem was focused on in much detail in another report about the use of linear bar-codes [25]. As a result, the suggestion by the CLSI

standard came as mentioned earlier about the use of two-dimensional bar codes.

Tube labeling and preparing

Accessioning is another area for increased efficiency and speed by using laboratory automation. Many phlebotomists still use currently hand-selected and hand-labeled specimen tubes, which must then be bar-coded at the laboratory. Some laboratories use another approach: they supply their blood collection sites with pre-bar-coded containers, and another method uses chip-contained specimen tube technology. The chip takes-up the patient information so that no matter where that tube goes, the lab can read the patient information directly from the chip.

Recently, several automated products have been introduced (such as BC-ROBO) [26], which automatically prepare the specimen collection supplies for the phlebotomist. These intelligent machines select and bar-code the specific tubes and collection supplies for an individual patient. They link the bar-codes to the patient information, then load the necessary containers and collect supplies for the individual patient into a tray or a bag. Everything the phlebotomist needs for that patient becomes ready to use. If you have a waiting room full of patients, eliminating the need to hand-select and label tubes would significantly speed up the process. That kind of instrument offers clinical laboratorians intelligent pre-analytic solutions and reduces and prevents preanalytical errors. In general, tube labelers and preparer systems reduce errors in pre-analytic processes (tubes with specimen labels attached, specimen labels, alignment of the tube labels, and patient identification labels). They **guarantee** patient, specimen safety, **shorten** preparation times, and **improve** convenience for medical technicians and patients. With the development of the health quality standards, extensive usage of automated eligible pre-analytic devices minimizes errors, and these intelligent machines log operational data for analytic processes. These systems communicate with LIS/HIS and get the data about specimens and patient. They automatically select the proper tubes, labels the patient's information on containers, and transfer the prepared samples to the phlebotomist. The benefits of tube labeler and preparer in short as follows. a) Time-saving: it automates the preanalytical process, so that the tube labeling and preparation duration shortens, with the TAT reducing. b) Safety: it prevents erroneous identification of patient samples, providing sample safety. c) Error prevention: it prevents wrong patient, wrong labeling, crazy tube, and incorrect data errors. d) Traceability: it records all pre-analytical processes from the doctor's request to the tube

sorting. e) Cost-saving: it avoids repetitions in the pre-analytic process by minimizing pre-analytic errors.

Besides stand-alone systems (FututeLab 300) (Figure 6), some types of tube labeler and preparer are designed as mobile or desktop automated systems (FutureLab 200) (Figure 7) [27] to select and label specimen collection tubes by LIS or HIS order. They are intended for hospitals inpatient services and low-capacity hospitals blood collection units because the stand-alone types are generally used for outpatient services. All types of these machines can process and sort all kinds of primary tubes. However, technical specifications may vary depending on the vendor. The device easily handles any cylindrical tube with a length of 76–120 mm and a diameter of 8–19 mm. Because they can be configured as modular, labeling capacity may vary. For instance, there may be multiple printers in design and test tubes kinds, and the drawers also range from 6 to 20. A continuous operation is possible because tubes can be replenished quickly while the system is running. Different types of bar-codes such as Code 93, Code 128A/B/C, 2 of 5, etc. may be available. Similarly, Varying interfaces are also available (TCP/IP, RS232C, Ethernet, RJ45, WI-FI ...). In the market, there are a wide variety of systems with different throughputs or labeling capacity (from 300 to 1,200 tubes/h or more).

Figure 6: Stand-alone tube labeler and preparer (FutureLab 300).

Figure 7: Mobile tube labeler and preparer (FutureLab 200). [The **blower** produces pressure or vacuum. The material is transported by matching **carriers**. The selection of the target and the input of the filled carriers are made at the **stations**. For connecting all stations, a **tubing network** and **diverters** are used. With these diverters, it is possible to transfer a carrier in the network to station X, and at station Y, it will be discharged from the tube-network. For all to work correctly, highly integrated **controllers** are used (Courtesy of <https://aerocom.de/en/pneumatic-tube-systems>)).

Specimen delivery

To get rid of such challenges such as staff shortages, cost-effectiveness, and the increasing size of the facilities and to maintain and improve the level of service and patient care, one does need an escalating reliance on technology instead of manual methods. Automated processes must be used to deliver specimens to the laboratory. Of them, pneumatic tube systems (PTSs) are commonly used in many hospitals. Though PTSs have been around for nearly a century, their sophistication and capabilities have improved dramatically in the last decade. Today, even more, a properly designed PTS can be just the solution to a hospital's growing challenges and need for improved efficiency. In addition to relieving vital staff members of the routine transport of laboratory samples, PTSs deliver these items in a fraction of the time. Perhaps even more important than increased efficiency is the fact that critical samples reach their destination in a few minutes, even in seconds [28]. Adjustable speed for shock-free transport is critically vital

in hospital PTSs. The transport of samples requires special care. The leak-proof protective carriers within which a soft material is lined not to damage the inclusions and individually-adjustable transport velocity are primarily of importance. Blood samples, for example, can be transported gently at a reduced speed [29]. For rapid, safe specimen transport, PTSs are widely used and are reliable when installed properly as point-to-point services. Switching mechanisms used in the system allows carriers (the bullet-shaped containers) to be sent to various locations, which may cause mechanical problems, sample disintegration, and misrouting.

For this reason, attention for PTS design is necessary to prevent hemolysis of the blood specimens. One should avoid sudden accelerations and decelerations. The use of proper soft material inside the carriers keeps the inclusion. The components of PTS include the following [30]. The **blower** produces pressure or vacuum. Carriers transport the content in the carrier. At the **stations**, the target and the input of the filled carriers are selected. For connecting all stations, a **tubing network** and **diverters** must be used. These diverters transfer a carrier in the network from one station to another. For all to work correctly, highly integrated **controllers** are used (Figure 8) [28, 30]. For safe transportation by PTS, a carrier with a high radius (about 160 mm), soft material support within the carrier, low or optimized acceleration and deceleration, extra-sharpened corners, or bending points, in tubing network are of critical importance.

Mobile robots have been adopted successfully to transport laboratory specimens both within a laboratory and outside a central laboratory [31]. However, some limitations to the usage of these robots are present [3].

Figure 8: Principle scheme of PTS (Aerocom).

Tube loading and sorting

Laboratory submission of the specimens and presorting them is a critical and automated step in the preanalytical phase. The tube loader and sorter can submit the specimen containers and their sorting for laboratory devices based on user-defined criteria. Such a system is an automated system to load and sort blood collection tubes by LIS or HIS order. It is very fast (throughput higher than 1,500 samples per hour) and efficient device, improving the workflow in clinical laboratories, particularly in the preanalytical phase in the entrance area of the laboratory and close-by the PTS station in the laboratory. It allows the laboratory staff to make their time more efficient and concentrate on their primary tasks. For instance, the FutureLab Sorter [32] can process and sort all types of primary tubes (Figure 9). The machine easily handles any cylindrical containers with a length of 76–120 mm and a diameter of 8–19 mm. A tube description can be made by user-defined rules based on cap-color, and bar-code information or by LIS-transmitted rules. A conveyor transports the described tubes, and then wipers guide the tubes into target drawers. Unidentified or problematic tubes are collected in a box at the end of the conveyor. On a continuous flow basis works the system with no interruptions. More specimens can be loaded at any time without stopping the device. Some models in the market have a modular structure, with the structure consisting of modules, each containing two drawers. With the addition of modules, the system can be reached to the desired number of drawers, depending on the need. No limitation is present for the number of drawers. Thanks to these devices, fast processing and sorting are achieved, and easily handling widens the bottlenecks that occur, especially during peak hours in the laboratory. Different bar-codes can be processed, and several interfaces are possible.

Specimen preparation

After sorting the specimen tubes, a given time duration is necessary to complete such tasks as clotting of blood in specimen collection tubes, their subsequent centrifugation, and if necessary, secondary tube creation. In the case of manual execution of these steps, the process will result in a delay in the analysis of specimens, and TTP will necessarily be affected. These steps may be shortened or automated, as mentioned below. Using thrombin-accelerated tubes may reduce the clotting time, or plasma vacutainer tubes do not need clotting time. Automated, high-capacity centrifuges and automated aliquoter are

Figure 9: Tube loader and sorter (FutureLab S2500).

process-shorteners. In other words, preanalytical specimen preparation automation considerably reduces the TTP, all of which improve TAT and provide patient safety and satisfaction [1, 3].

Whole blood sampling

The limited number of tests (electrolytes, blood gases, dry chemistry analyses) in the clinical laboratory must necessarily be executed in whole blood specimens. Consequently, waiting for sample clotting is substantially eliminated, resulting in shortened TAT. The modern clinical chemistry analyzers in the market contain an automated ion-selective electrode (ISE) unit measuring ion activity in whole blood. Within a short time, one can obtain the test results after introducing the specimen. A new approach is that plasma vacutainer tubes with lithium heparin and physical barrier, manufactured by BD [33], are being used for sampling for the majority of the clinical chemistry and immunoassay analytes instead of serum separation tubes. Consequently, it is not necessary to wait for clotting, with the result being a shortened TAT. Similarly, extra thrombin-containing serum separation vacutainers also lessen the TAT by reducing the coagulation duration. Both tubes are called “fasting” tubes. They have different color caps from regular serum/plasma separation tubes, which makes these samples accessible by the staff in the laboratory for prompt processing, which is very important for lowering the TAT

in critically-ill patients and improving the TTP for urgent patients. That kind of specific tracing such samples in the laboratory may be considered as a new QI issue. The comparison can be made between these samples and other-tube-using urgent samples concerning intra-laboratory TAT in patients of the emergency room and intensive care unit.

Processes in integrated extra-analytical automation

Several vendors of integrated modular automation systems have been able to combine or connect extra-analytical and analytical components through conveyor belts, which has made the TTP fully-automated. In other words, all pre-analytical sample processing steps mentioned above and post-analytical processes such as specimen storage and retrieval, and secondary tube sorting for off-line analyzers are all included in this system. There are some differences between stand-alone preanalytical automated systems and extra-analytical automation in integrated/modular laboratory automation systems. The latter contains automated transportation by conveyor, analyzer interfaces, specimen storage, retrieval function, and a sophisticated process controller, which operates the whole system as if a single device. These systems may be appropriate, especially for high-volume capacity laboratories with daily blood sample numbers higher than 1,000. Because of the modularity of the extra-analytical automation in integrated/modular laboratory automation systems, a task-targeted choice of the modules by the customer is possible. Some vendors offer open design for interfacing different vendors' analyzers, and some offer closed design to which only their own analyzers interface.

Process-controlling software

The process controller, which is an essential component of integrated modular laboratory automation systems, connects the LIS to the whole system. Through the bar-code reading, all information about the sample, including the specimen procession and its action route, is consequently transferred to the system for maximal effectiveness of the total testing process. For standards about automation communications, one can consult the CLSI (AUTO03-A2) [34]. Accordingly, the process controller of the extra-analytical automation in integrated/modular laboratory automation systems calculates the number of aliquots and

required volumes, makes the route of each sample through the system, recaps the tube after processing, and stores the specimen in the stock area. Besides, the troubleshooting of the whole system is displayed by the process controller. This software's specimen quality and integrity. Auto-verification and auto retrieval are two crucial characteristics of this type of laboratory automation. In the former, test results are verified automatically by rules-based decisions, and in the latter, specimens are returned to the analyzers for a repeat, reflex, and dilution testing. For taking support in designing an auto verification system, CLSI Guideline AUTO10-A may help [35].

Specimen storage and retrieval

Automated specimen storage retrieval is the central part of the post-analytical phase, which functions like a take-out station or storage bin holding specimens at the post-analysis period for test repetition or other purposes. However, the former functions as a refrigerator, hosts thousands of samples for several days away from light in closed containers, and makes retrieval of specimens possible when needed. The storage capacity can be selected depending on the daily workload. There is a robotic system in it by which the containers are loaded and retrieved using sophisticated software of the automation system. An automated specimen discard may be possible in some, and manual removal of the tubes from the storage systems is made in some others. The process-controlling software can manage the functions of the storage bin: storage at an appropriate location, follow-up of the lasting specimen period, removal time, returning-back the retrieved specimen, etc. For the retrieval process, the integrated automation system operator selects the sample using process controller software. The robotics picks up the container and delivers it to the conveyor. The sample is decapped first and then returned to the system for reprocessing.

Conclusion

The automation technologies have added a serious impact on the proficiency of clinical laboratories. To improve standardization, organization, efficiency, and quality of TTP, many manual tasks have now been partially or completely replaced by automated and labor-saving instrumentations, and the cost of the investment will probably return on a long-term basis. Based on current workload needs and

future demands, laboratory directors or professionals should consider theoretical advantages and limitations of extra-analytical automation as guidance to configure the suitable local solutions. Consequently, it is of critical importance to implement extra-analytical automated devices to the laboratory processes. Thus, a risk management strategy can be developed for the systematic analysis of the present laboratory's workflow and bottlenecks. Extra-analytical automation within and outside the clinical laboratory will substantially lessen the effects of the error sources in TTP, resulting in accurate test results and test result reporting as soon as possible.

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