The Ideal Laboratory Information System

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• ***Context.***—**Laboratory information systems (LIS) are critical components of the operation of clinical laboratories. However, the functionalities of LIS have lagged significantly behind the capacities of current hardware and software technologies, while the complexity of the information produced by clinical laboratories has been increasing over time and will soon undergo rapid expansion with the use of new, high-throughput and high-dimensionality laboratory tests. In the broadest sense, LIS are essential to manage the flow of information between health care providers, patients, and laboratories and should be designed to optimize not only laboratory operations but also personalized clinical care.**

Objective.—**To list suggestions for designing LIS with the goal of optimizing the operation of clinical laboratories while improving clinical care by intelligent management of laboratory information.**

Data Sources.—**Literature review, interviews with laboratory users, and personal experience and opinion.**

Conclusions.—**Laboratory information systems can improve laboratory operations and improve patient care. Specific suggestions for improving the function of LIS are listed under the following sections: (1) Information Security, (2) Test Ordering, (3) Specimen Collection, Accessioning, and Processing, (4) Analytic Phase, (5) Result Entry and Validation, (6) Result Reporting, (7) Notification Management, (8) Data Mining and Cross-sectional Reports, (9) Method Validation, (10) Quality Management, (11) Administrative and Financial Issues, and (12) Other Operational Issues.**

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Since the 1970s, laboratory information systems (LIS) have been critical components of the operation of clinical laboratories. They were initially developed to collect, record, present, organize, and archive laboratory results, often with a focus on generating information for proper financial management of the laboratory. While information technology in general is advancing at an increasingly faster rate, particularly in the hardware domain but also in software development, LIS have not evolved correspondingly. For example, the current LIS make very limited use of artificial intelligence approaches such as neural[1] or Bayesian[2] networks, fuzzy logic,[3] genetic algorithms,[4] and artificial immune recognition systems.[5] Health care systems in general can be characterized as conservative and resistant to change and current health care information systems (HIS) and LIS are a reflection of this conservative approach. Despite the potential benefits in cost-efficiency and patient care improvements possible with well-designed HIS/LIS, most of these systems lag significantly behind the possibilities afforded by current information technology. In fact, some of these systems have deficiencies that most home- and Web-based software have long overcome, such as efficient navigation, rapid response, and spelling correction.

Modern clinical laboratories are purveyors of information, in the form of laboratory results, which may be numbers, text, graphs, or other images, together with interpretative data, to assist health care providers in delivering optimal patient care. The complexity of the information produced by clinical laboratories has been increasing over time, and with the advent of large-scale analytic techniques, such as microarrays and next-generation sequencing, the amount of data produced will rapidly grow by several orders of magnitude. Advanced developments in data management and bioinformatics will need to be incorporated into LIS for these large data sets to become clinically useful. In addition, the ability to query large cross-sectional laboratory databases (data mining) is increasingly used to improve the quality and efficiency of health care delivery. These 2 tendencies mandate an ever-expanding capacity and processing need for LIS and supporting hardware.

Increasingly, the focus of efforts to improve the quality of laboratory operations is shifting from the analytic phase, which currently presents few problems, particularly for those tests performed by highly automated instruments, to preanalytic and postanalytic aspects of laboratory testing.[6] Advanced LIS and associated database and expert systems[7] will be critical to the goal of improving the quality of the extra-analytic aspects of laboratory testing, including the implementation of paradigm-shifting innovative approaches.

The goal of this article is to list ideas for designing or improving a state-of-the-art LIS from the perspective of practicing laboratory professionals, focusing on optimizing

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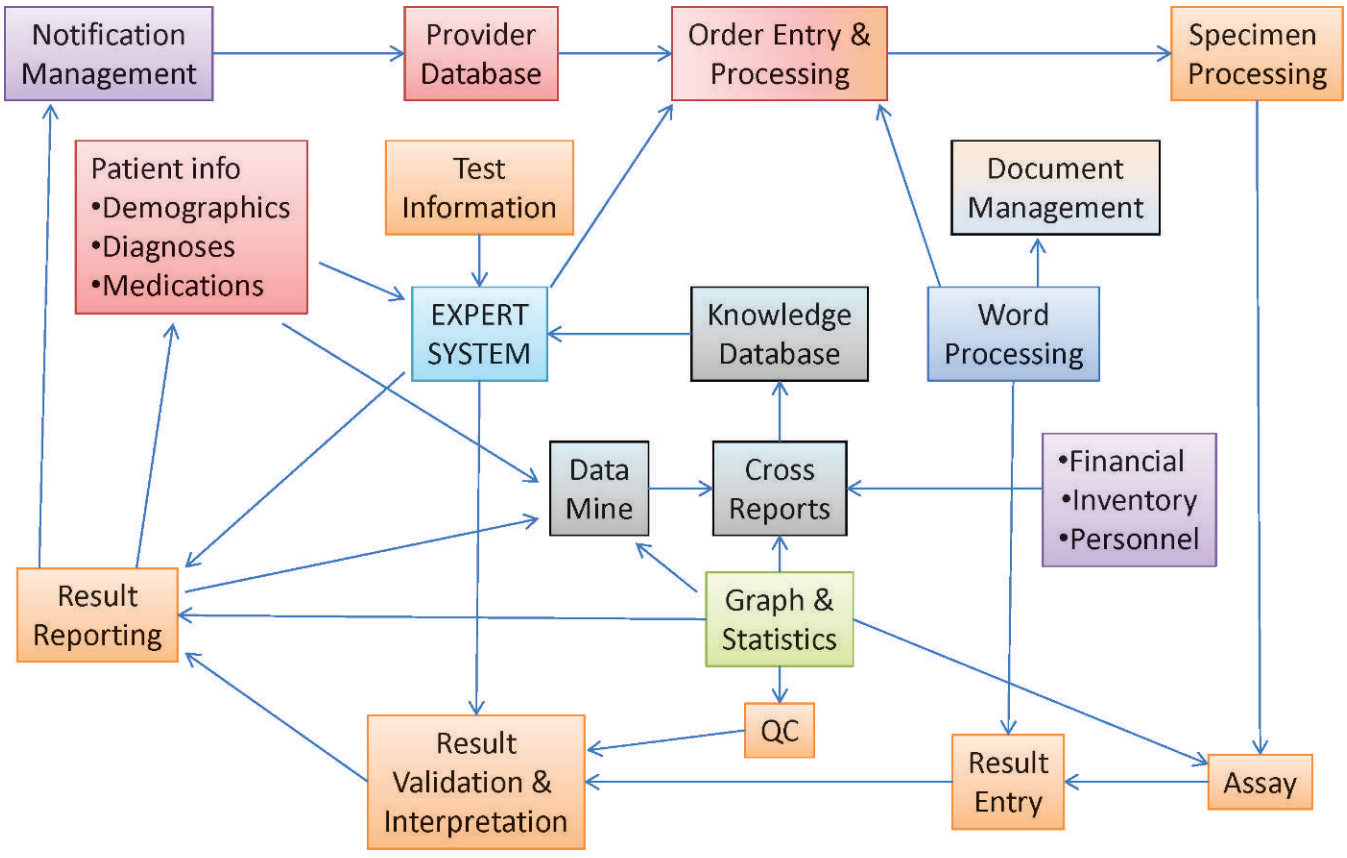

Modules contributing to the ideal laboratory information system.

the operation of the clinical laboratory and on improving clinical care by intelligent management of laboratory information. The focus of this article is to describe desirable LIS functionalities, while the operational and technical details on how to achieve this idealized LIS are beyond the scope of this article. In this work LIS is defined broadly, and some specific functionalities listed might be provided by software modules not strictly considered as LIS. These would include clinical ordering and reporting systems as components of the HIS, analyzer built-in software, specimen processing and management software (often labeled as "middleware"), financial, inventory, and personnel management packages, and others (Figure). In this article we are interested in describing the desired functionalities independently of which particular software package will be responsible for their availability. Although the ideas discussed in this article are mostly applicable to all sections of the clinical laboratory, some specific issues pertaining to anatomic pathology, microbiology, molecular and genomic testing, transfusion medicine, and cell/tissue/blood banking are beyond the scope of this article.

INFORMATION SECURITY

Health care information systems must be secured from unauthorized internal and external access and preserve the confidentiality of health records according to applicable law and regulations without hindering the functionality for legitimate users. For example, health care providers should be able to access all the relevant information for their patients, but not that of other patients unless they are brought in as consultants. Individuals involved in assessing quality of care should have access to certain information on all patients. Different levels of security should be available, and the system should allow users to establish workgroups with user-definable sets of functions and access to data, as exemplified in Table 1.

Secure interfaces to the LIS should include advanced log-in capabilities, for example, by biometric recognition or radiofrequency identification devices (RFIDs), which minimize keystrokes and log-in time, while providing quick automated log-out upon leaving the workstation. In certain secure locations, the system should have the ability to continuously display live reports of laboratory testing (eg, pending "STATs" in the laboratory or patient results in the operating room) without multiple log-in requirements. The system should have the ability for remote log-in and access to ordering and reporting systems, for example, via a secure Web browser, allowing providers and laboratorians to access the LIS from any location and from mobile and handheld devices.[8,9] The system should allow flexible, reliable, and informative electronic signatures for authentication of data and documents.

TEST ORDERING

Test ordering is the step most amenable to intervention in order to improve appropriate use of laboratory resources (laboratory utilization). Test-ordering systems coupled to intelligent decision-support systems have the potential to reduce turnaround times and length of stay, and guide providers toward optimized test utilization,[10,11] and can be a function of either LIS or HIS, sitting at the border between LIS and HIS. Regardless of which system is used, immediate

Table 1. Categories of Laboratory Information Systems (LIS) Users	
Information manager	Full access to all functionalities, including lower-level processes of the system, ability to design scripts and routines to customize functionalities to local needs.
Health care provider	Order tests, attach comments to orders, define alerts, and view results, with the ability of customizing reports and interpretative information according to their needs.
Technical staff	Process orders and specimens, perform tests, record results, attach comments to results, and perform quality and other laboratory management activities.
Manager	Produce and review reports and statistics, personnel management activities, inventory, write and review procedures and other documents.
Laboratory director	Ability to design and review all of the activities in his or her area, including access to patient information, quality management data, document review and management, and cross-sectional reports.
Patient	Depending on institutional policy, the system (LIS or HIS) should provide direct access of laboratory test results, reports, and interpretative comments to patients, eg, through a secure Web-based browser interface.

Abbreviation: HIS, health care information systems.

feedback must be provided to the user. As in other situations at the interface between laboratory and clinical practice, involvement of both clinicians and laboratorians is essential for the development of the policies and rules guiding laboratory utilization. The most useful systems are those that require the health care provider to directly enter the order in the system, therefore affording the possibility of interaction between the system and the provider (computerized provider order entry or CPOE systems). An important consideration for the success of a CPOE system is to properly design it to maximize usability and match routine work processes used by providers.[12] The following is a list of desirable functionalities in a test ordering system.

1. The system should receive inputs from the HIS or from the ordering provider (when the information is unavailable or inaccurate in the HIS) to include the following:
   a. Ordering provider
      i. Name (mandatory).
      ii. Specialty.
      iii. Address (if in a different location). Interfacing with credentialing and privileges databases is desirable to provide the most current provider information.
      iv. Contact media (e-mail address, desk and mobile telephone numbers, pager number, etc) for routine notification (mandatory).
      v. Contact information for critical result notification (pager, cell phone, and surrogate contact for nonbusiness hours), including links to institutional notification cascades/call schedules appropriate to a specific patient (mandatory).
      vi. Additional providers/provider team and other persons legally authorized or desired by care provider to receive results.
      vii. Further notification requests (eg, notify when results are available, or when results exceed reference range, critical limits, or custom threshold limit). Ability to establish notification criteria by institutional, departmental, or other group policy. Ability to select notification media, including HIS overriding alert, HIS alert on patient record, e-mail, short message service (SMS) text message, automated phone call, beeper, telefax, and others. For certain critical areas, for example, operating rooms, new significant results should trigger an audible alert. Certain notifications (eg, of critical results) must include a mechanism that ensures fail-safe notification, returns acknowledgment of receipt of the information, and allows for escalation of unacknowledged notifications according to a preestablished protocol.[13]
   b. Patient information
      i. Patient identification (last and first names and institutional or social security number) or unique coded audit trail if necessary (eg, for research or environmental specimens).
      ii. Patient demographics, including date of birth/age, sex (male, female, transgender), race, ethnicity, and prior names.
      iii. Patient location (permanent address and current location if hospitalized).
      iv. Codified diagnoses (preliminary diagnosis by Diagnostic-Related Groups, International Classification of Diseases (ICD)-9 or ICD-10, where appropriate) and other relevant clinical information ("reason for study").
      v. Codified results of nonlaboratory tests.
      vi. Height, weight, vital signs.
      vii. Medications (with dosing and date/timing of administration).
      viii. Herbal and other supplements.
      ix. Diet and meal times (to determine fasting time).
      x. Medical procedures applied to the patient, including surgical interventions and radiologic procedures.
      xi. Gynecologic and obstetric information.
      xii. Other pertinent clinical information.
   c. Order information
      i. Test(s) requested.
      ii. Source(s) of specimen requested.
      iii. Date/time of order.
      iv. Day/time of requested collection (begin, end).
      v. Repeat frequency (for standing orders, if institutionally permitted).
      vi. Special patient preparation instructions.
      vii. Urgency of the test (categories customizable to institutional needs).
      viii. Collection responsibility (patient mail-in, point-of-care, ward or nursing unit, routine phlebotomy rounds, laboratory collection, etc).
      ix. Other free-text comments and instructions to the laboratory.
2. An expert system uses patient information, previous test results, and clinician input (eg, from a list of

Table 2. Items to Be Included in a Test Catalog Entry

Test name and synonyms
Proper specimen with hyperlinks to collection protocols.
Patient preparation requirements, eg, fasting, diets, medications and herbals to avoid.
Proper timing of collection (time of the day, time relative to meals, drug administration, etc).
Test charge as determined by hospital administration (different levels for different patient types as appropriate).
Performing laboratory section.
Links to test performance characteristics.

probable diagnoses) to suggest appropriate tests, test frequency, and interpretative criteria.
   a. Simpler systems may guide the provider to select from a standardized list of diagnoses and clinical situations and obtain corresponding guidelines and clinical pathways with a mechanism for easily ordering the appropriate tests.[12,14]
3. The system has a user-friendly display of the test catalog (to include testing performed by external reference laboratories), with available alternative groupings, for example, alphabetically, by laboratory discipline, by clinical situation. The menus must be consistent, complete, regularly updated to maintain currency, and with standard nomenclature in all HIS systems interfacing with the LIS. The information for each entry in the test catalog should display different user-selected categories and levels of complexity to include the items shown in Table 2.
4. The system has the ability to restrict ordering permission by location, diagnosis, provider specialty, etc, for certain tests.
5. The system allows definition of tests that require approval, for example, by a clinical or laboratory specialist. The approval system should be integrated with a downstream contact database that automatically notifies the approver and the ordering provider that there are pending tests needing approval.
6. The system has the ability to distinguish research versus patient-care specimens and enable different billing procedures (even for different tests on the same specimen). Research orders should be attached to a research management system, including the availability to link to different protocols and research accounts.
7. An order appropriateness expert system is available with the functionalities outlined in Table 3.
8. The ordering system should have the ability to relay orders to different interfaced systems, for example, another LIS in another institution or reference laboratory, without manual intervention, so that tests ordered in one facility can enable specimens to be collected and accessioned at another location or institution. Ideally, the catalog of the reference laboratory(ies) should be available online to the ordering provider, with implementation of institution-specific restrictions and approval processes for ordering, testing, and reporting. For send-out testing, the system should be able to generate a shipping manifest with sender, receiver, and shipping information.[15]
9. The ordering system should receive real-time feedback from the LIS and notify the ordering providers about the status of the order, including the following steps:
   a. Order acknowledged by laboratory.
   b. Specimen(s) collected.

Table 3. Desirable Functionalities of an Order Appropriateness Expert System

The system displays previous relevant test results (graphically, if required) and pending related orders, with an opportunity for the provider to cancel the order after being made aware of such information.
The system has built-in and customizable medical necessity review and acceptance or rejection criteria, including criteria for maximum frequency of appropriate ordering for different situations, eg, by patient location, clinic, specialist, diagnosis.
The system merges or cancels redundant orders falling within preestablished criteria (institutionally or nationally developed). For example, if 2 providers order thyroid-stimulating hormone tests in the same week, the orders are merged and both providers will receive the results. If a provider orders a hemoglobin A1c test a month after a result is available in the system, the order is cancelled and the provider is notified to call the laboratory if an override is needed.
The system uses available clinical and laboratory inputs to determine appropriateness. For example, if patient sex is female and ordered test is prostate-specific antigen, the order is flagged for cancelling. If patient is receiving rapamycin and cyclosporine treatment, and only cyclosporine is ordered, the system asks the provider if rapamycin measurements are also desired.
The system has the ability to cancel flagged orders with hard stops to prevent inappropriate work-around of the rules, while providing a mechanism for the ordering provider to justify an exception, eg, by asking the provider to call the laboratory for rule overriding. Certain order types, eg, associated with research protocols, should be exempted from appropriateness protocols by policy.
The expert order appropriateness system should be able to halt orders that are not associated with a proper diagnostic code (such as ICD-9 or ICD-10).

Abbreviation: ICD, International Classification of Diseases.

   c. Specimen(s) accessioned.
   d. Accession(s) activated in laboratory.
   e. Analysis completed.
   f. Results verified.
   g. Results reported; order completed.
10. The system has the ability to split laboratory orders, that is, one order may comprise multiple tests requiring multiple specimens and accessions. The system should have the ability to track the progress and report the status of each component separately under 1 order.

SPECIMEN COLLECTION, ACCESSIONING, AND PROCESSING

Appropriate specimen collection and processing is fundamental to the quality of laboratory results, which follow the well-know principle of "garbage in, garbage out." An ideal LIS should have functionalities to optimize specimen collection and processing, including the following:

1. Specimen collection lists as appropriate to institutional operation. For example, for each phlebotomy round to a set of locations, the system produces the appropriate list of patients to be collected, together with preprinted accession labels. The list should indicate the most efficient route to each of the patients, taking into account the desired testing priority.
2. The system guides the specimen collector with an online or printed display of proper specimen collection

Table 4. Information Entered by the Specimen Collector That Can Be Useful for Proper Performance and Interpretation of Certain Laboratory Tests

Specimen number and time of collection for serial specimens.
Specific site of collection.
Fasting or nonfasting, time of last meal.
Last menstrual period for gynecologic and some endocrinology tests.
Date/time/dose of last medication (if not available from the HIS).
Difficulties with specimen collection, eg, prolonged tourniquet, presence of intravenous lines.
Other relevant clinical information (customizable by test and prompted by the system).

Abbreviation: HIS, health care information systems.

instructions, in an easy step-by-step format with links to a full procedure.

3. The system has the ability to present the collector with a list of pending laboratory orders and generate unique bar-coded or RFID labels[16] at the bedside upon scanning the patient identification wristband or other unique physical patient identifiers.[17] The labels generated at the point of collection should include a minimum of 2 patient identifiers, as well as date and time of collection, collector identity, urgency of the order, and as much as possible, the abbreviated names for tests requested. Use of 2-dimensional bar codes or RFID labels allows larger amounts of information to be attached to the specimen. On arrival of the specimen in the laboratory, the system should be able to recognize the specimen upon scanning the labels attached to the specimen container, and initiate testing without further human intervention, if applicable, for example, in a robotic specimen-processing automation line.
4. In addition to automatically recording patient information, location, date and time of collection, and collector identity, the system should allow the collector to enter pertinent information in codified or free-text form that can be useful for proper performance and interpretation of certain laboratory tests, as exemplified in Table 4.
5. The system should be able to support bidirectional interfaces with portable devices for patient identification, specimen accessioning, and point-of-care testing, including the ability to use wireless connections for data transmission. Results from point-of-care testing should be integrated with those from main analyzers while identifying the source of those results.
6. A point-of-care test management system should be available to track instruments, reagents, quality control, and user identity, training, and competency records.
7. The system should separately record accessioning of specimens (ie, matching an order with a physical specimen), specimen receipt in the laboratory, and activation of the specimen for analysis. For example, a phlebotomist scans the patient bar-coded wristband and chooses an appropriate pending order, the system records the collection time and accessions the specimen, and the portable device carried by the phlebotomist prints an accession label. The specimen is collected and the labels are affixed to the specimen container in the presence of the patient. Upon arrival at the laboratory reception desk, the specimen accession labels are scanned to acknowledge receipt by the laboratory, and then transported to the analytic section of the laboratory. When placed in an automated robotic specimen-processing line, the labels are scanned again and the accession is activated for analysis. Alternatively, the last 2 steps are merged and the specimens may be first scanned and activated when placed on a robotic track. In this manner, laboratory turnaround time can be differentiated into time from order to collection to accession to receipt to activation to report. The last component (activation to report) is the analytic time, whereas the previous components are preanalytic. It is important to distinguish the different components of turnaround time because often only the receipt-to-report processes are under complete control of the laboratory. Using these time points, "incomplete lists" can be focused on pending orders, on specimens received in the laboratory, or exclusively on accessions ready for analysis.
8. The system should allow deviations of the sequence of specimen processing described above, according to institutional policy, for example:
   a. Specimens received in the laboratory without an order or accession, but with appropriate patient identifiers. Receipt of these specimens in the laboratory should be acknowledged by the system, pending arrival of an appropriate corresponding order. In defined cases, the laboratory staff should have the ability to enter a paper or verbal order in the system.
   b. Properly identified specimens received in the laboratory with an order, paper or electronic, but without accession labels. The laboratory acknowledges and verifies the appropriateness of the order and of the specimen, and then accessions the specimen and applies appropriate labels or RFID tags.
   c. The system should have the ability to accession and process nonpatient specimens, for example, animal, research, or environmental specimens not associated with a patient, quality control and validation materials, and most importantly, proficiency-testing materials. The system should allow selected personnel to assign proficiency-testing materials to one of many unique virtual patient identities so that the analyst performing the test is unaware that the specimens are proficiency-testing materials.
9. The system should have the ability to de-indentify and codify specimens for research purposes, and include database management capabilities for biobanks and tissue repositories.
10. The LIS should interface with laboratory automation management software to ensure that all the preanalytic requirements stipulated in the ordering process (eg, centrifugation speed, time, number of aliquots, reflexive testing) are transmitting to the specimen-processing system.
11. The system should be able to track the specimen location throughout the preanalytic, analytic, and postanalytic phases, including transportation to various sections of the laboratory or external sites, and management of specimen storage.[18] The latter includes functionalities for easy retrieval of the precise specimen storage location and periodic reports to facilitate batch disposal of specimens.

Table 5. Useful Information Associated With Reagents and Other Test Components

Name of component
Manufacturer
Catalog number
Lot number
Date/time received in laboratory
Date/time opened and put into service
Initial volume/number of assays
Current volume/number of assays left
Expiration date
Storage requirements

12. The system should be able to generate multiple specimen aliquot labels that can be scanned to execute the appropriate testing associated with each aliquot. This capability should include functionalities for tracking and storing multiple aliquots and slides derived from a single specimen.

ANALYTIC PHASE

The analytic phase has been the focus of most technologic developments in clinical laboratory science and is typically associated with the lowest frequency of errors in the clinical laboratory. In addition to interfacing with specimen handling and analytic instrumentation software (often called *middleware*) for streamlined processing of analytic requests—including the ability to direct testing to the appropriate instrument depending on workload, recall specimens for repeated testing, direct specimen dilutions, perform reflexive testing, process add-on requests for additional tests, and record test results and appropriate comments—the LIS should provide the following functionalities:

1. Track and associate with individual testing records all the components necessary for testing, particularly for manual assays and those methods associated with laboratory-developed reagents. Information about reagents and other test components should include the information shown in Table 5.
2. The appropriate standardized operating procedure for each test (particularly for manual assays), managed by a document control system (see below), is easily displayed or printed upon request by the analyst.
3. The testing instrument is recorded with each patient test. The analyzer record should include the information in Table 6 and provide links to online preventive maintenance and service records, with the ability to alert the user for scheduled maintenance and service. If required by the laboratory, the instrument manufacturer should also be automatically notified.
4. The system should produce laboratory-specific workload lists ("worklists") to facilitate batch processing and resulting of both manual and automated tests and to track orders that have not been completed. If additional specimens are received after worklist creation, worklists should be expandable by scanning the bar code or RFID tag of the additional specimens.
5. "Incomplete lists" of tests that have been accessioned but not completed, highlighting those that have exceeded the stated time for the category of the request, should be displayed on demand, as well as on continuous report screens, if so desired. Similarly, lists of incomplete or unfulfilled orders should be available on demand or by schedule with the ability to pinpoint at which point the failure occurred. Incomplete lists should be able to include tests sent to reference laboratories. An example of an incomplete test display with significant clinical impact is the continuous display in a large screen of emergency room orders not completed within a predefined time frame, possible with color coding and/or sorting by age of request, to alert staff to investigate and process orders or specimens at risk of exceeding acceptable turnaround time thresholds.

Table 6. Useful Information Associated With Each Laboratory Analyzer

Name of instrument
Manufacturer
Serial number
Date placed in service
Expected life
Calibration studies (by test)
Maintenance and repair records

RESULT ENTRY AND VALIDATION

The LIS should not only serve as a repository of laboratory results generated by the analytic process, but also guide the analysts into providing high-quality results that are accurate, reproducible, and appropriate to the clinical situation. Desirable functionalities in result entry and validation include the following:

1. Ability to record results in various data formats, including numbers, text with extended characters, and images, with a flexible data storage approach that avoids constraining limits on data size.
2. Automated and manual entry and correction of results of tests performed in interfaced or noninterfaced analyzers as well as manual tests, with appropriate security levels applied. Result entry should include options for individual result entry, batch results entry, batch entry by exception, amended results, appended results, and intermediate and final results. Results can be entered either by individual tests, or by panels, with user-definable panel configuration.
3. The system should allow different levels of result certification, with the ability to withhold release of results until approved by a higher-level user, for example, a supervisor.
4. The system should be able to receive results in a variety of formats such as tables and graphs from other laboratories, including external reference laboratories, through electronic interfaces, for seamless integration of all laboratory results in the electronic record. An example of where such combination of data is highly desirable is for the diagnosis of leukemia, where clinical information together with hematology, hematopathology, molecular, and flow data are often needed to make an accurate diagnosis.
5. The system should be able to use advanced expert decision support for autovalidation of results.[19,20] Autovalidation avoids human intervention in the certification of laboratory results and is a major driver of efficiency improvements in laboratory operations.[21] The more sophisticated the system used to perform autovalidation,

the lower the probability of reporting an erroneous result, and the more time is allowed for a human specialist to examine exceptional results. Inputs used to arrive at an autovalidation decision include the following:

a. Comparison with results of previous tests in the patient record (temporal delta checks).
b. Comparison with results of other related tests in the same or closely related specimens (cross-sectional check). An example is creatinine versus urea.
c. Checking the specimen for predefined limits of hemolysis, lipemia, or icterus.
d. Clinical information, including demographics, location (inpatient versus outpatient, type of clinic), diagnoses, medications, procedures.
e. Results of external and internal quality control.
f. Statistical data on result distribution.[19]

6. The ability to perform temporal delta checks should include analysis of temporal data and calculation of rates of change as well as absolute changes, in reference to preestablished limits that can vary by patient clinical information such as demographics, diagnoses, therapies.[22,23]
7. The expert system should be able to order reflexive testing based on analysis of results and clinical data, definable by institutional or laboratory policy and customizable by the ordering provider, interface with the specimen-processing and analytic systems, and append the appropriate codes or comments to the results.[24]

RESULT REPORTING

The system should be able to provide a variety of reports for use in patient care, including standard and user-definable reports organized by test, test group, date, date range, ordering provider or provider group, clinic or specialty, sequential or tabulated cumulative worksheets, and the following additional capabilities:

1. In addition to the actual value measured, numeric test results should include display of the following (optional or mandatory as appropriate):
   a. Units of measurement.
   b. Reference interval of the appropriate reference population (user-configurable by a variety of clinical inputs, including ambulatory versus recumbent, sex, age, race, body mass, gestational age, menstrual cycle phase).
   c. A measure of individuality[25] should be displayed to guide interpretation of the reference range. For tests with high individuality, where within-subject variability is much lower than between-subject variability, a comment should be appended that the individual-based reference changes are more appropriate than population-based reference intervals. For tests with high individuality and patients with enough recorded data, the system should be able to calculate and display an individual-specific reference range, for example, the central 90% of previous results, with the ability for the user or the expert system to exclude from the calculation results clearly associated with disease.
   d. Confidence interval of the results, based on analytic variability observed at a corresponding level.

Table 7. Useful Flags Associated With Laboratory Test Results

Results outside the reference interval, with indication of multiples of upper or lower reference limits.
Results outside of confidence intervals, with indication of the probability of the change being due to analytic or biologic variability.[25]
Results exceeding various levels of medically relevant thresholds, including multiple tiers of significant and critical results. The latter should be linked to automatic notification of providers.
Dynamic change from a previous result (delta) exceeding user-definable thresholds, eg, exceeding the RCV interval. The flag could be coded to different levels of probability of change, eg, "likely" at $P > .80$, "more likely" at $P > .90$, "very likely" at $P > .95$, and "virtually certain" at $P > .99$.[27]

Abbreviation: RCV, reference change value.

   e. Alternatively, reference change values, that is, the interval around the result that is a consequence of analytic imprecision, within-subject biologic variability, and the number of repeated tests performed.[25–27] The user should be allowed to customize the reference change value interval by selecting a confidence threshold (eg, 95%) and the appropriate Z-value for decisions that involve 1-sided (eg, increase) versus 2-sided (either increase or decrease) changes.
   f. Result-associated flags, listed in Table 7, are available and thresholds can be predefined by the users.
   g. Pertinent comments appended by the analysts.
2. Report generation that is flexible and configurable by users, to include both producers (laboratorians) and recipients (providers, patients) of the test information.
3. Reports should be made available by a variety of options to include user-configurable automated secure faxing, e-mailing, and other electronic text transmission mechanisms.
4. Sophisticated graphing of laboratory results, ideally with integration of other appropriate clinical information such as vital signs, biometrics, medication dose/timing.[28–30] Graphing functionalities should match state-of-the art graphing programs and allow dynamic changes in axis and scales, histograms, conditional formatting, color coding, user-definable formulas for calculated results, and display of multidimensional data. Colored displays are preferable.
5. Ability to incorporate in result comments hyperlinks to pages containing further test information, including analytic parameters, half-life of toxins, drugs, and certain other analytes, calculators, clinical guidelines, suggested follow-up, literature references, and other pertinent data to help providers interpret the results and use the information in clinical care.
6. The system should link pretest and posttest diagnostic information by displaying positive and negative likelihood ratios for selected diagnoses, based either on HIS or user input. Upon selection of a particular clinical condition, the system should display appropriate Bayesian statistics, including sensitivity, specificity, accuracy, positive and negative predictive values, and receiver-operator curves with links to appropriate references.
7. Readily accessible display of all possible significant interferences and causes of abnormal test results,

including diseases, herbal supplements, medications.[31] This information should be flagged if extracted from data available in the HIS, and complete lists should be available for display upon link selection by the user.

8. Intelligent cumulative reports triggered by patient-related events, such as discharge or outpatient visit, to facilitate expeditious clinical care. For example, a decision support to avoid inappropriate discharges due to unidentified or unaddressed clinically significant laboratory results has been described.[32]
9. An expert system should be able to append appropriate interpretative comments on test results,[33–35] taking into consideration not only the result of the test itself, but also other pertinent test and clinical information available in the HIS and a knowledge database updatable with local information, for example, disease prevalence. Temporal patterns should be taken into consideration, particularly for therapeutic drug monitoring and calculation of clinically useful pharmacokinetic parameters such as the area under the concentration curve and estimated elimination half-life.[22,23]

NOTIFICATION MANAGEMENT

Distribution of results to end users should be defined by a combination of institutional policy for certain results (such as "critical results") and user-selected notification mechanisms (eg, printout, fax, e-mail, HIS alert) for routine reports. A rule-based system should be used to select the appropriate mechanism and timing for user notification (see "Test Ordering," above). The notification management system should have the following capabilities:

1. The LIS should have a sophisticated "significant result" notification system. The system should include multiple tiers of urgency for significant result notification. For example, the Massachusetts Coalition for the Prevention of Medical Errors established 3 levels of notification: red, orange, and yellow.[36] "Red" results are those implying immediate danger of mortality or morbidity if not rapidly acted upon. These correspond to the Joint Commission's and College of American Pathologists' (CAP's) definition of "critical test results" and mandate direct notification of a health care provider with the ability to intervene in patient care, within a maximum time frame set by institutional policy (usually 15–60 minutes), and require acknowledgment of the receipt of the information or "read back" process. An example is a potassium level of 2.5 mEq/L (2.5 mmol/L). "Orange" results are highly significant results that must be acknowledged but are not immediately threatening to the patient and can wait several hours (target, 6–8 hours) before notification. "Orange" results include, for example, highly elevated creatinine, amylase, lipase, and aminotransferase levels. Notification of the provider should be made by a high-priority process, for example, by a high-priority HIS alert requiring acknowledgment by the recipient, with a cascading process of surrogate notification if the appropriate provider is unavailable. Finally, "yellow" level results may be associated with significant morbidity or mortality if diagnosis and treatment are not initiated in a timely manner, but are not immediately threatening. Yellow results require notification within 3 days and may include passive methods, such as a HIS alert or chart note, with mandatory acknowledgment and tracking. Examples include a high thyroid stimulating hormone (TSH) or lead level, or a new diagnosis of cancer or human immunodeficiency virus infection.
2. Significant result notification should use artificial intelligence and expert decision-support systems for more relevant identification of true-positive (eg, life-threatening) results, while minimizing false-positive signals (eg, expected results). The expert system should use the various inputs previously described for order entry and autovalidation systems. Even without expert system intervention, dynamic rules should be used to determine whether a result is critical. For example, a single threshold for low hemoglobin level is inappropriate, as chronic anemia is much better tolerated than acute anemia. A dynamic threshold to detect a rapid rate of hemoglobin decline will be more clinically relevant and will identify patients at risk whose condition may not be considered critical when using a fixed threshold.[22,23,36]
3. In addition to the providers and surrogates defined at the order entry step, the system uses rule-based notification of appropriate third parties, such as infection control or public health departments, depending on the laboratory result.
4. Any changes or corrections to laboratory results should be communicated rapidly to providers, and reports on interfaced HIS systems should be accurately and completely updated.
5. The system should provide the ability for end users to inquire about laboratory testing, receipt of specimens, availability of results, with links to appropriate online information and messaging of laboratory staff if further information is needed. Search engines should use state-of-the-art technologies allowing for synonyms, misspellings, and advanced Boolean combinations of search terms.[37] Reports of user activity should be available to laboratory managers for process improvement.

DATA MINING AND CROSS-SECTIONAL REPORTS

The ability to perform queries into the laboratory and clinical databases is paramount to maximize the efficiency and quality of the laboratory operation, provide means of identifying clinical issues affecting a specified population, perform epidemiologic and public health studies, and case finding for clinical or research purposes. Advanced data warehouse and mining capabilities should be available in an advanced LIS. Examples of useful queries and reports include the following:

1. Search functions for combinations of laboratory results and clinical information, such as diagnoses, medications, and treating specialty, using Boolean logic, producing reports with user-customizable display of queried and nonqueried fields such as patient demographics, specimen accession data, and location. Such reports should be exportable to spreadsheet programs for further analysis. Ideally, common statistical functions should be available for aggregate data.
2. Laboratory testing turnaround time reports with the ability to consolidate or split the various components, such as order to collection, collection to receipt in laboratory, receipt to testing, and testing to report, and the capability to group by accession areas, individual test or test groups, hours or shifts, employee, patient location, clinics, providers, etc.

3. Surveillance data online reporting to public health agencies in their required format, using the appropriate standards.
4. Nosocomial infection tracking and antibiograms reporting the frequency distribution of microbial susceptibility to antimicrobial agents. Interfacing with pharmacy records to monitor antimicrobial utilization versus susceptibility.
5. Laboratory utilization reports by provider, provider group, specialty, clinics, wards, patient types, diagnoses and diagnostic groups, ICD-9/10 codes, etc, to include test type, volumes, and costs per case. The system should provide appropriate real-time feedback on utilization data to providers, for example, at the time of patient discharge.
6. Patient outcome analysis using laboratory data-mining capabilities and clinical data extracted from the HIS. Examples of useful parameters to correlate with laboratory testing include mortality, morbidity, hospital length of stay, and cost of care, grouped by diagnostic groups.

METHOD VALIDATION

Method validation is an important step preceding implementation of new assays in the clinical laboratory and is performed periodically in a more summarized mode to ensure the stability of the assay systems and compliance with regulatory and accrediting agencies.

1. The LIS should include a module for method validation with the ability to guide and record the following studies (including calculation and display of the appropriate statistics and graphic displays[38]): assay linearity and calibration verification; assay intra-run and between-run precision; comparison with the established methods or between analyzers; reference range validation; and interference and recovery studies.
2. The system should alert laboratory staff to the need to perform validation procedures (eg, biannual linearity checks and instrument correlations), as appropriate.

QUALITY MANAGEMENT

In the current health care financing environment, institutions are increasingly focusing on improved quality and outcomes of patient care to enhance their financial situation and gain competitive advantages. Quality management for clinical laboratories involves a program to ensure quality throughout all the aspects of laboratory operation. More strictly, quality control (QC) refers to periodic assaying of samples with known reactivity or analyte concentrations to estimate assay accuracy and precision. A modern QC program should aim at improving the accuracy and reliability of laboratory results by maximizing error detection and minimizing false rejections of test runs.[39] The quality management module should support accreditation requirements, including CAP, Clinical Laboratory Improvement Amendments of 1988 (CLIA),[40] and International Organization for Standardization (ISO) 15189:2003 standards,[41] and include the following functionalities:

1. Quality control protocols and alerting mechanisms should use thresholds for acceptability, based on the concept of total acceptable error derived from biological variation[25,42,43] and regulatory requirements. The user should have the capability of customizing the QC protocol, based on built-in databases of biological variability and measured imprecision of the various tests at relevant clinical decision points, based on the specific analyzer used to perform the test.
2. Quality control files for each assay system should record the following:
   a. Information about a particular quality control material (as described for test components, including lot number, expiration date).
   b. Manufacturer or laboratory-assigned control values for each relevant testing system.
   c. Serial quality control test results associated with each control material and each analyzer.
3. Each patient test result should be linked to the relevant quality control result(s) in an easily retrievable record.
4. The system schedules automated running of quality control or alternatively alerts appropriate staff to perform QC tasks.
5. The system should guide the user in QC rule selection taking into consideration the total acceptable error and the analytic performance (precision and bias) of the testing system.[39]
6. Active QC rules and reports should be customizable by test, test group, analyzer type, laboratory location, and working shifts.
7. Sophisticated user-definable display of QC results should include Levey-Jennings plots and interactive display of violations of user-selected rules, such as Westgard rules.
8. Quality control reports including Levey-Jennings plots should be easily interpretable so staff can quickly make critical decisions about test acceptability. Troubleshooting and corrective action guides for QC violations should be available upon user selection.
9. The user should be able to customize date intervals and time scales and aggregate, split, or compare multiple QC levels, QC lot numbers, test groups, reagent cartridge, reagent lot number, analyzers, laboratory sections, and multiple laboratories.
10. Interfaces to third-party vendors for automated upload of QC data and real-time download of peer performance data should be available.
11. The system should provide the ability to document corrective actions resulting from QC failure in real time.
12. The system should be able to remove outliers and erroneous results from QC calculations, based on appropriate statistical parameters as well as user input.
13. For certain test runs, as defined by the user, the system should automatically interrupt analysis or autoverification in case of QC failure and guide staff into appropriate investigation and decision choices.
14. The system should have the capability to batch hold QC results so users do not have to constantly switch screens to verify QC.
15. Peer comparison statistics should include range, mean, median, standard deviations, standard deviation index, coefficient of variation ratio, Youden charts, and time-based plots and histograms. The system should be able to import these parameters from external interlaboratory programs.
16. Alternative means of quality control should be available, including moving averages of normal values, of all results, or by user-defined criteria. If all results are used a median value should be presented. Another valuable

report for quality monitoring is the display of the histogram of results by test and various patient characteristics, with definable flags highlighting deviations from the historical frequency distributions.
17. The system provides user-definable QC summary reports for review by supervisory and management staff with functionality for documentation of review and corrective actions.
18. The system should have functionalities to interface with instrument performance data, temperature-monitoring systems, water quality parameters, environmental measurements, and other data pertinent to good laboratory practice and accreditation requiring periodic documentation.
19. The system should manage proficiency-testing (PT) programs, from inventory control of PT materials to documenting PT results and investigation of PT failures, with available online review and certification of PT results by appropriate management staff. Ideally, interfacing to external PT program providers should allow seamless transmission of PT data.
20. The system manages accreditation requirements online, including preparation of appropriate documents, for example, by incorporating checklists and questionnaires from accrediting agencies in a database allowing for tracking and documentation of answers to checklist questions and inspection findings, containing links to relevant policies, procedures, and other electronic documents as evidence of compliance. The system should be capable of capturing and manipulating all data required for accreditation agencies, such as CAP or ISO 15189.
21. The system should have a user-friendly incident, error, and process improvement tracking mechanism with sophisticated database, querying, and reporting functionalities.[44] The system should allow any user to initiate reporting of errors and incidents in real time with an option of anonymity.

ADMINISTRATIVE AND FINANCIAL ISSUES

Management of a modern laboratory requires access to a variety of data at various levels of consolidation. The LIS should incorporate advanced administrative and financial functionalities, including the following:

1. Ability to generate and transmit the necessary forms and notifications for reimbursement of tests, with the appropriate test codes (Current Procedural Terminology [CPT] Systematized Nomenclature of Medicine [SNOMED], or ICD-9 or ICD-10) selected.
2. Intelligent generation of online and printed regulatory forms associated with laboratory testing, billing, compliance, and accreditation, such as insurance claims in Health Insurance Portability and Accountability Act of 1996 (HIPAA) standard transaction formats, Medicare Waiver/Advance Beneficiary Notice forms, and others, for use at the point-of-care as well as from administrative locations.
3. Tracking of costs of laboratory operation, including consumable, labor, amortization, and other fixed costs.
4. Analysis of pricing, profitability, "make-or-buy" decision tools, and outreach client management capabilities.
5. Workload statistics based on system variables such as time logged in, number of tests verified, and instrument raw test counts, as well as user inputs.
6. Ability to produce periodic reports of laboratory productivity and management efficiency, by using the following:
   a. Aggregate numbers, such as number of total and billable tests and interpretations (and who performed the interpretations), number of full-time employee equivalents (FTEEs, classified as technical, nontechnical, and scientist/pathologist), hours worked, laboratory costs (broken down by section, variable versus fixed, etc), number of patients (outpatient visits, discharges, bed-days, etc), for top-down analyses.
   b. Individual cost and productivity analysis per test and per laboratory workgroup for bottom-up financial and productivity analyses.
   c. User-definable financial and productivity calculations, for example, cost per billable test, costs per FTEE, paid hours per FTEE, number of tests, and costs per patient (different categories), with comparison with benchmarks and the ability to customize granularity (eg, whole laboratory, laboratory section, accession group, or individual test).
7. Inventory and materials management including functionalities for automated ordering from selected suppliers and real-time tracking of budget.
8. A document management system fully integrated in the LIS with readily accessible procedure manuals from testing information menus, and mechanisms for periodic notification, review, and certification by appropriate parties. The document control system should allow scanning and proper linking of pertinent documents, such as reagent and QC package inserts, test requisitions, and reports from outside laboratories.
9. Personnel management capabilities to include interfacing with human resource databases, labor-cost accounting, and tracking of credentials, competency, continuing education training, and performance appraisals. Competency training and credentialing records should be linked to the ability of the user to complete defined tests or test groups, using the LISs. Ideally, the system would provide an interface to online continuing education and role-based competency-training modules.

OTHER OPERATIONAL ISSUES

Other desirable functionalities of an ideal LIS include the following:

1. The system should have enough capacity to record large datasets and interface with legacy systems (in real time or through import functions) to capture historical laboratory data, with the goal of storing lifelong results on each patient. Capabilities for handling large genomic data sets, while providing meaningful reports and "just-in-time" education to clinical providers,[45] will be increasingly necessary in future LIS.
2. The system should capture industry standards for coding, billing, document generation, and interface formats, such as CDC, HL7 CDA1/2, XML, ASC X12, LOINC, SNOMED-CT, ICD-9, or ICD-10, as appropriate for each data type. Mapping dictionaries for interconversion between different standards should be available as appropriate.
3. The user interface and navigation should be intuitive and user friendly.

4. The system should minimize the number of keystrokes required for all activities (use automatic return where possible).
5. The system should have uniformity for similar tasks within the software, for example, using "enter" for all programs rather than clicking "OK" for some and double clicking for others.
6. All screens and reports should be printed and exported in appropriate document text, spreadsheet, or graphic formats.
7. Fully functional text editor in text entry fields with rich text and common word-processing functionalities.
8. Appropriate backup data capture and retention with rapid retrieval in the event of system failure.
9. Auditing capabilities should track changes in all data (results, QC, patient information, etc) made by any user.
10. Interfaces with single or multiple HIS systems should be flexible in data formats and fully functional with appropriate routines available for testing the functionality of the interfaces before use in order to meet end-user expectations.
11. The interface with HIS should allow real-time updating of the LIS with pertinent information, such as patient location and current provider, and conversely, laboratory data should be rapidly available in all interfaced HIS systems. Particular focus should be placed on the interface between the LIS and the pharmacy software for drug and test selection, detection and prevention of drug reactions and drug-laboratory interactions, monitoring of drug levels, etc.[31]
12. The system should integrate instant messaging, forum, online meeting, and social-networking capabilities to enhance communication among laboratorians and with laboratory users.
13. The LIS should be capable of performing multiple functions simultaneously with imperceptible impact on its speed.
14. Where manual activities are involved, these should be accomplished with a minimal number of keystrokes and waste of time and energy, with no degradation of LIS performance regardless of workload.

SUMMARY

In this article we listed a considerable number of features desirable in future LISs, aimed at improving the quality and cost-efficiency of patient care by optimizing the operation of clinical laboratories and most importantly, the interface between health care providers and the clinical laboratories. Laboratory information systems are critical for proper packaging of the information produced by clinical laboratories to be optimally used by clinical providers. We envision the LIS as replacing humans in most activities that allow the option of human error. Humans would interact with the LIS through user-friendly interfaces designed with a lean approach to optimize efficiency and maximize productivity. The ideas listed in this work have been variably implemented in currently available LISs, but considerable effort in incorporating combinations of artificial intelligence, expert systems, advance database, data mining, and other state-of-the-art information technologies must be used to arrive at a comprehensive, fully functional, user-friendly, and clinically useful LIS.

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