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LABORATORY INFORMATION MANAGEMENT SYSTEMS IN THE WORK OF THE ANALYTIC LABORATORY

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Laboratory information management systems belong to the class of application software intended for storage and management of information obtained in the course of the work of the laboratory. The systems are used to control and manage samples, standards, test results, reports, laboratory staff, instruments, and work flow automation. Integration of laboratory information management systems with the enterprise's information systems will make it possible to promptly transmit required data to the laboratory and the enterprise administration.

Key words: *information measurement systems, information management systems, laboratory information management systems, functionality of laboratory information management systems.*

The basic objectives and tasks of industrial enterprises comprise the production of products of appropriate quality and achieving increased efficiency of the production process with least costs.

Modern analytic laboratories that are part of enterprises (or are independent entities) constitute complex structures that perform their activities in accordance with standard documents from the quality control system (All-Russia State Standard series GOST R ISO 9000), the principles of the appropriate laboratory (GLP, Good Laboratory Practice) and industrial (GMP, Good Manufacturing Practice) practice and requirements imposed on testing laboratories [1–3]. The efficient activity of a laboratory not only requires that the laboratory be equipped with modern physicochemical instruments, but also that it adopt automation principles to perform analytic studies.

Analytic laboratories carry out a host of functions, including quality control of raw material, intermediate products, and finished products; metrological certification of measurement techniques; ecological management; routine inspection of measurement instruments; external and internal laboratory auditing; and many other functions.

When considering the structure and functions of analytic laboratories, it becomes obvious that successful implementation of such multifaceted activity requires the use of information measurement and information management systems.

An information management system when used in an analytic laboratory constitutes a complex of hardware and software components intended for collection and metrological processing of measurement data obtained as a result of tests of

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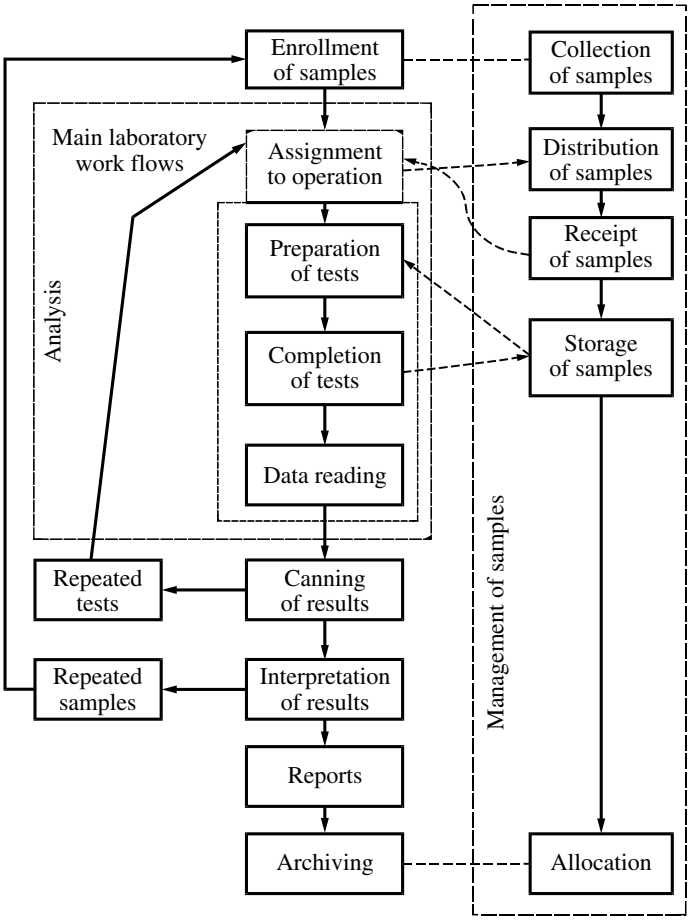

Fig. 1. Basic work flows of a laboratory information management systems [7].

samples for analysis [1–3]. An information management system is a complex of hardware and software components that support the management of collection, processing, storage, distribution, and information representation procedures used with information that has been obtained as a result of laboratory activities. The creation of these types of systems is based on efforts aimed at automation of the laboratory process to produce an increase in the efficiency and productivity of the laboratory in processing a multitude of analytic objects, improve the quality control system, etc.

The class of information management systems includes laboratory information management systems, the development of which has extended for more than 30 years. The first such systems were chromatography data systems, developed and introduced by major manufacturers of analytic equipment, such as Hewlett Packard, Perkin Elmer, and Beckman Instruments [4, 5]. The process was promoted by the appearance in the late 1970s and early 1980s of computer technologies. Subsequently, the technology of laboratory information management systems developed from in-house software products or software produced to order for the solution of narrowly specialized problems to commercial products that generate multifunctional solutions.

There is now a significant number of firms around the world (more than 100) that produce these types of software products. These firms all utilize a number of specification documents and documents that regulate their activity, including a standard for laboratory information management systems [6] which lies at the basis of the Russian national standard [7].

A laboratory information management system is a computer-based application software product that is used in the laboratory to manage analysis and standard samples, test results, laboratory staff, and analytic equipment, as well as for the purpose of generating commercial reports and other functions. Thus, the functions of laboratory information management

systems encompass the management of the work flows of the laboratory, the information obtained in the laboratory, as well as integration with devices and other manufacturing computer systems.

In the present article we will consider questions related to the practical application of a laboratory information management system. A flow chart of the working processes of analytic laboratories is presented in Fig. 1 [7].

As usual, of greatest interest to the staff of a laboratory is whether it is possible to avoid having to undertake the laborious process of maintaining a laboratory log. This, in turn, relates to the need for enrollment of samples, input of data and results of an analysis, and the compilation of reports. The use of a laboratory information management system in this area makes it possible to reduce the number of errors caused by the "human factor" and eliminate confusion with samples and results through the implementation of the basic function of a laboratory information management systems in the trackability of a sample. Through the implementation of this function it becomes possible to track the passage of a sample possessing an identifiable designator through different departments of a laboratory, though at the same time it is essential to preserve information about the sample. A new laboratory information management system product, called the electronic laboratory notebook (ELN), is currently under active review for possible implementation. ELN is an electronic version of the traditional hardcopy laboratory journal used to document studies, experiments, and procedures that have been performed in the laboratory.

The functions of a laboratory information management system may be provisionally divided into the following five basic stages:

The *first stage* comprises enrollment of samples which have been received in the laboratory. By enrollment is understood, besides the assignment of a unique identifier (enrollment number, line code), writing of specific information to the laboratory information management system; this information comprises data on the customer, description of the sample, security information and information on the storage conditions for the sample; what tests must be performed; required costs, etc. Enrollment of the sample may be performed either manually or in automatic mode, and to facilitate information input this step may be performed with the use of specific templates. It should not be necessary to repeat entry of an already enrolled sample, and enrollment of scheduled and unscheduled samples must be monitored.

On the *second stage* (assignment of sample to analysis), analytic work is distributed among the laboratory staff. The system displays a list of all tests that must be performed in accordance with the requirements of the normative documents, information on the quantity of material necessary for each test, as well as on where the samples are to be sent for the analysis, i.e., to a work site in the laboratory or to an outside organization. In this case, the function of the laboratory information management system may be distinguished on the basis of a graph that describes the implementation of the laboratory analyses. The graph will include the following functions: monitoring the execution of assigned analyses (which analyses have been performed, and which have not yet been performed at a given time), tracking the time spent on the analysis of the sample; and reminders to the laboratory staff that a particular analysis must be performed and whether it is possible to specify a time limit for completion of an analysis. The function of distribution of the samples also assists in determining when the sample will be made available for analysis at different laboratory work sites and enables the laboratory management to determine the capacity, the status of the sample, and different reasons for delays in execution of an analysis.

The *third stage* – the process of analysis proper – comprises a host of subjects and actions. These comprise preparation of the sample, carrying out measurements, including those that involve the use of samples for quality control and the generation and collection of information. In certain cases repeated tests must be performed or a repeated selection of samples made (Fig. 1). A laboratory information management system may be used to assure management of the process of preparing samples, at the stages of preliminary processing, as well as for automatic inclusion in the sequence of operations of unknown, standard, and dummy samples necessary for calibration, or operations designed for verification of the method of preparation. All these samples must also be assigned unique identifier numbers to be logged by the laboratory information management system. Following preparation of the samples, they may be input into the system in the order in which they are measured, moreover, the system implements trackability functions on these operations. Once the tests have been completed, data such as the adjustment parameters of the analytic device, information about additional standard samples, observed defects, and difficulties and unusual behavior of the system are input into the laboratory information management system. This information may be of assistance in documenting the performed procedures and serve to explain unusual results. The laboratory information management system implements compilation of current monitoring reports; in this case several

dialog windows may be opened once the tests are completed, thanks to which the system is able to perform current control over the execution of analyses and keep track of the time spent in accordance with the complexity of the tests.

At this stage, the functions of the laboratory information management system are used to manage the use of reagents, equipment, and laboratory personnel. These functions make it possible to track purchases and the use of supplies in the laboratory, manage batch lots and order numbers, usage time periods, costs, and deliveries, and control the inventory of chemicals and reagents. By means of these functions it becomes possible to track the calibration of equipment and execute repair activities, as well as conduct training and confirmation of the skill level of laboratory personnel. Functions that enable the system to store in unalterated form in the database active documents that define how tests are to be performed are also integrated into the laboratory information management system. Of no little importance is the fact that it is possible to create an interface with the laboratory equipment to enable the transmission of results directly from a device to the laboratory information management system (thus reducing the probability of errors in data collection).

The *fourth stage* involves input of results of measurements into the laboratory information management system. Following execution of an analysis of a sample, the results obtained are input into the system manually or in automatic mode. In order to implement automatic input of results from a device directly into an electronic table or report, the system must be integrated with the laboratory equipment. By means of a management function a record is generated that certifies that the results of an analysis have been created; statistical processing may then be performed in automatic mode, and, in addition, an audit of the obtained data may be made in accordance with established standards and the input data checked against the range of permissible values in accordance with the standards documents. Unusual results or results that fall outside the range may be marked for more careful study. A laboratory information management system may also be used to track the location of an ultimate sample and remove unneeded residues. To avoid loss of data, procedures for creating back-up copies and emergency recovery are built into a laboratory information management system.

The *fifth stage* comprises inspection of the test results and compilation of reports. Functions to scan results and approve them (verification and validation procedures) must be built into a laboratory information management system. For this purpose, functions to confirm authorization for decision making, approval, or rejection of test results and quality indicators must be incorporated in the system. Standard operating procedures may be assigned in the system. According to the requirements of these procedures, the reviewer and the test analyst must not be the same person. Measurements and results that have been previously input into the system must be subjected to an audit, in particular, factors on the basis of which adjustments have been introduced or corrections implemented must be presented here. Audit trails are created in a laboratory information management system. Such trails will contain new data and the modification time, an indication as to individual responsible for a particular change and on what basis the change was made. If a test of a sample was incorporated into a graph for repeated testing but it was not possible to perform the test, the result may be simply marked as invalid. Intermediate and concluding results of tests of samples may be generated with the use of a laboratory information management system in hardcopy or in electronic form.

One of the most important functions of a laboratory information management system is the generation of report forms of all types, including quality certificates, test protocols, and analysis certificates; the function of adapting reports to a particular user is also implemented here. For the user's convenience, it is essential that the system support the use of standard software products for report generation (the most widely used product is Crystal Reports) in either a manual or automatic mode through the use of different user programs (for example, a graphical user interface must be present in order to construct graphs), and also make it possible to standardize the report forms. Most often, the capability to implement an electronic signature, in particular, in the form of a graphics file, is integrated into a laboratory information management system. The system must also be capable of printing out reports for authorized specialists as well as transmitting reports by electronic mail.

At the same time, both external (for the customer) and internal reports that incorporate summaries of analytic studies for the laboratory management are generated in a laboratory information management system. Data may be prepared on the number of samples that have been treated at each automatic work site together with the exact length and day of the week, on the basis of collected statistical data and time stamps at different points of the process. The resulting data may be used in constructing a graph of analytic studies, for estimating the rate of consumption of reagents and supplies of reagents, providing information on calibration of analytic devices and their maintenance, and monitoring the work of laboratory personnel.

It is extraordinarily important that functions basic to quality assurance and quality control be built into a laboratory information management system. In this case, the normative documentation (in the necessary volume) in accordance with which the tests are to be performed must be embedded in the system database. There is also the possibility of tracking the conformity to the requirements of QA/QC (quality assurance/quality control), support the production of control cards, perform inspection of analysis graphs, track the degree of observance of the quality requirements of the actual tests, and, finally, confirm the skill levels of laboratory staff responsible for performing the tests.

The database tables of a laboratory information management system that are employed by users are divided into the following classes:

1) static database tables, in which may be found descriptive information (profiles, tests, computations, specifications, and related information);

2) dynamic tables in which are stored information stating how to log in samples and how to input results.

The terms, "static" and "dynamic," provide an idea of a general characterization of the data tables of a laboratory information management system that reflects the frequency of alterations in the data. One of the more significant characteristics of the system is a function that assures the "flexibility" of the database, making it possible to introduce necessary changes, for example, updated versions of normative documents (updating process). The storage periods of all the information, normative documents, and additions and changes to documents must conform to established time intervals. To make it easier to work with databases, a laboratory information management system must be provided with archiving data retrieval functions. Verification of data integrity is a constant problem.

All the functional and work flows exert an effect on the status of information in a laboratory information management system. Thus, the system is capable of retaining information relative to the status of samples, tests, and the comparison of results in accordance with specifications, verification of results, approval of samples, and much else. Information concerning the status is updated whenever there is a transaction in the system. The following may serve as examples of the status of a sample: unavailable, available, obtained in the laboratory, obtained in the course of a test, halted, completed, accepted, and anamolous.

A function designed to protect against unauthorized access by means of password-protected logon and division of authority, i.e., according to which each user must possess his or her own password that identifies their location in the system, must be built into the system to maintain the security of applications in a laboratory information management system. Permission to execute only those operations which are supported by the particular user's functions in the system must be assigned to each user. Any action executed by a user that is implemented in the system leaves a unique label indicating the execution of this action and may be monitored by a more senior manager.

Maintenance of information about business processes in the laboratory necessary for its effective operation is achieved by means of the laboratory information management system. The system contains data that reflects not only the current state of laboratory activity, but also historical information concerning past operations and events. This type of information, which is under the control of the laboratory information management system, may be stored in hardcopy or in electronic form (large-format tables, specialized databases). Whenever a laboratory information management system that is in use is replaced by a new product, it should be possible to migrate data from the initial system to a newly installed system.

An analytic laboratory is a component of an enterprise and does not function "on its own." In order to assure the laboratory's effective activity, data that are obtained in the laboratory, especially data related to the quality of output, must be promptly transmitted to higher management. For this purpose, integration of a laboratory information management system with Manufacturing Execution System (MES) and Enterprise Resource Planning (ERP) information systems is implemented (Fig. 2). Interfaces with the firmware information systems are created or direct integration (for example, with SAP) is implemented for this purpose [8]. Through the use of this function of a laboratory information management system (LIMS) it becomes possible to obtain information about output in a required format. This information may subsequently be used for the management and analysis of an active quality control system.

In particular, this relates to the part of the operations where the results are acknowledged to represent conflicting requirements as well as to pre-certification of laboratory personnel and any similar situation that requires corrective actions. Moreover, with the use of local and global networks it becomes possible to create in the laboratory an interface between LIMS

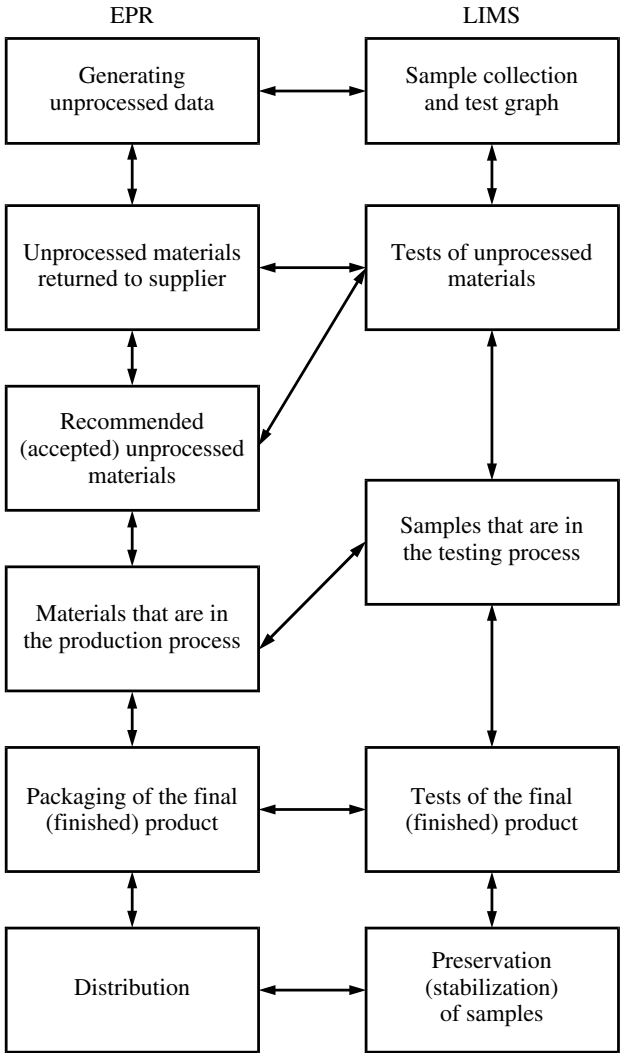

Fig. 2. Possible points of transfer of data between an Enterprise Resource Planning (ERP) System and a Laboratory Information Management System (LIMS) [7].

and the Web client and support work on the Internet. It is also very important that there exist compatibility with the client's information platform, as this is necessary for the creation of an interface with the work station. With such an embedded function, it also becomes possible to achieve optimization of information flows within the laboratory, in particular, paperless document flow.

The LIMS function that makes it possible to compile commercial documentation and manage commercial and financial activity, including the customer database, costs, reports, etc., represents a separate module.

The standards of the R ISO 9000 series devote special attention to auditing activity involved in evaluating the degree of conformity of output to normative documents as well as evaluating the technical expertise of a testing laboratory in accordance with international rules. The audit management module built into LIMS supports management of all actions and changes introduced into the system by authorized specialists while maintaining these actions as well as information on the date and time changes were introduced. Audit records must be encoded and may not be altered.

It should be kept in mind that an LIMS product must enable the user to work with the system in the user's customary Windows, Microsoft Office, or Microsoft Excel environment, using well-known software products for accessing Microsoft Access, SQL, Oracle, etc. databases.

Thus, LIMS must conform to user requirements as regards data identification, acquisition, indexing, access, systematization, and storage and maintain the confidentiality of all logged data. To protect against unauthorized access to the system, password-protected logon and authority sharing functions must be provided in the system.

When installing a laboratory information management system in a laboratory, it is essential to bear in mind the requirements imposed on the computer hardware, which are based above all on the volume of memory, speed of data transfer, and the capacity of the archive. Estimation of the actual vendor requirements includes a review of the following parameters:

- number of competing (functioning simultaneously) users;
- annual number of enrolled documents (for samples and analysis results);
- number of logged documents that will be served in on-line mode;
- archive requirements;
- required type of report; and
- external load on system from applications that are not related to the laboratory information management system.

In order for the computer software to better meet the objectives of the laboratory, it is necessary to take into account the possibility that the nature of the laboratory's activity may change, leading to either an expansion or contraction of functions. Thus, a version of a laboratory information management system that is capable of scaling, whether to a larger, more complex system as well to a smaller, simpler system that could be easily modified in accordance with the appearance of new requirements imposed on the laboratory, would appear to be the most appropriate. In many cases, configuring and adjustment of a laboratory information management system to enable it to satisfy the requirements of a particular vendor as closely as possible must be carried out.

Most systems are installed in a client-server configuration in which database tables are permanently on the server, whereas the user graphical interface is present in the client hardware. The advantage of this type of configuration is that data processing occurs on the server. However, there is now increased interest in the SaaS (Software-as-a-Service) software version of LIMS. The SaaS system is a solution based on Web applications that have been placed on the Internet by the LIMS vendor and executed on demand. The principal characteristic of SaaS LIMS is the absence of software and hardware as well as any infrastructure for the purchase, installation, or maintenance of software. All the components of the product are provided by the SaaS vendor, except for a personal computer linked to the Internet and, possibly, a laptop computer or bar code reader, depending on the applications specified for the laboratory.

In conclusion, we would like to present information based on the results of a survey of LIMS users regarding the most important functional characteristics of an LIMS product [9]:

- input of data and results;
- enrollment of samples;
- tracking samples;
- report generation;
- simplicity of use and training;
- security of applications;
- reviewing of results and their verification (validation);
- customization of reports;
- flexibility and adaptability; and
- conformity to normative documents.

Thus, a laboratory information management system is an optimal, flexible, and multifunctional tool for management and for increasing the efficiency and quality of analytic studies in laboratories that operate in different areas of activity. The use of laboratory information management systems provides analytic laboratories with confirmation of their capabilities.

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