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Analytical Survey

Laboratory Information Management Systems — Part I. Concepts

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Abstract: The purpose of this analytical survey is to give a summary of some of the main design features that can be incorporated into a Laboratory Information Management System (LIMS), in the context of the total automation of the laboratory. Additionally it will give potential purchasers of such systems some essential background knowledge and a summary of our experiences. The survey is presented in two parts: the first covers the features and the possible concepts that could be used in a LIMS system. This is followed in the second part by an outline of the stages of acquisition, validation and benefits of such a system. Together the two articles provide the information required to aid the design and installation of a LIMS.

This first section deals with the possible features that a laboratory could include when contemplating the installation of such a system: the basic tools that are required for a LIMS, the database and the computer equipment are discussed. This is followed by the interfacing of analytical instruments and central versus distributed processor philosophy. The various screen formats available and the use of bar codes as a means of identifying samples and for rapid data entry into the computer system are discussed.

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Keywords: *LIMS; laboratory information management; local area networks; laboratory automation; central versus distributed processing; screen format; bar codes.*

Introduction

A trend in analytical instrumentation over the past 10 years has been the widespread introduction of computers and microprocessors [1]. This advance has had the effect of increasing the speed of data production as well as the amount per analysis. The production of data from modern analytical instruments is more sophisticated and comes in larger volumes than from previous generations of equipment: compare the data from a simple titration to that from a modern analytical instrument such as a Fourier transform infra-red spectrometer.

Analytical laboratories are now becoming information and data intensive, and this data has much time and resource devoted to its manipulation, collation and interpretation. The widespread use and availability of microcomputers means that these processes are available to anyone for a nominal cost.

Concomitant with computerisation in the laboratory is a parallel trend towards laboratory automation. This has occurred primarily because of increased staff costs and the requirement to keep pace with ever increasing workloads. There is also a desire on behalf of the analyst to assure the quality of the results emanating from the laboratory. Automation of analytical procedures is one way to keep pace with the workload and ensure the achievement of good precision and accuracy of analytical procedures at a realistic cost. Automation will also free the analyst to monitor the analysis rather than carry out mundane tasks such as the checking for transcription errors. Laboratory automation takes many forms: automated chromatography equipment and integrators have been available for many years, both flexible robotic automation [2–8] and dedicated laboratory automation [9, 10] instruments are becoming more accepted.

The automation of the laboratory is an evolutionary process. It is rare for one to be presented with either sufficient finances or opportunity to build an automated laboratory from first principles [11]. The constraints on the design of the LIMS within the laboratory begins with the purchase of the first item of analytical instrumentation.

The application of databases to laboratory problems brings together a very effective unit for retrieval and dissemination of information inside and outside the laboratory. Databases have been used extensively in business applications during the past decade and are now being applied to scientific tasks for the management and manipulation of analytical data. Thus Laboratory Information Management Systems or LIMS have been developed to provide a central pillar to the laboratory automation strategy: they aim to disseminate analytical information by accessing the database.

The increasing sophistication of equipment now means that analytical chemists must necessarily be acquainted with a working knowledge of some of the aspects of computers in order to understand the workings of LIMS. A good source of introductory material is "AC Interface" published under the editorship of R. Dessy in the A pages of Analytical Chemistry. The introductory articles on LIMS [12, 13] are useful background reading although the individual implementations of LIMS may not reflect accurately the situation as it stands today [13]. The early articles in this series have been published as a book [14].

In a recent survey [15] on British laboratory managers, one finding was that 71% of managers had not yet made an assessment of the costs of installing a LIMS in their laboratories. This finding, the article concluded, was not surprising considering that little

material has been published on LIMS and the relatively short time since LIMS have been commercially available.

The purpose of this analytical survey is to increase awareness of LIMS and to review the essential areas that must be considered before acquiring and installing such a system.

What is a LIMS?

An obvious starting point for this article is "what is a LIMS?". This has been defined previously, in general terms by Gibbon, as a computerised system designed to provide on-line information about the analytical laboratory and the samples assayed within it. This information should include the current location of samples, their corresponding status and the results to be reported to the submitter [16]. Furthermore, a LIMS should integrate three areas: laboratory automation, wordprocessing, and the corporate computing philosophy; otherwise separate, duplicate and incompatible facilities will be developed [17]. Whilst a LIMS installation may be compatible with the first two areas, in the opinion of the authors it may come into conflict with the third, depending on the source of the supplier and the views of the site or computer management. It is essential, however, that the LIMS can communicate the pass data to the appropriate computers already on site.

To answer the question more fully we need to consider the analytical laboratory. Although every laboratory tends to be different, in that its function may be quality control, development or research in widely differing industries, the nature of analysis is such that the basic flow of information follows the same pattern depicted in Fig. 1. Here, the aim of the analysis is to take a sample and produce a set of results. To achieve this the sample may undergo a preparation stage followed by various analytical procedures prior to a result being generated. As shown in the figure, re-analysis may be required if the result does not come within the expected range.

This information flow is representative of the analytical level within the laboratory.

However, the situation shown in Fig. 1 is rather simplistic as laboratories do not assay single samples in isolation. In reality the situation is more complex, as usually many samples are being examined simultaneously and may be at different stages of analysis at a given time. A better scheme of the information flow in the laboratory is shown in Fig. 2; here there are many more stages where internal checks are made before the results are verified and accepted by the analyst. Superimposed are the managerial requirements of a modern laboratory: acknowledgement of samples, checking for transcription errors, answering queries about the progress of assays and ensuring compliance with stated procedures. These will include checking that analytical instruments are properly maintained and calibrated [18], the integrity of data, comparisons of analytical results with previous values and charges to a customer etc. The final form is a report containing the results together with any pertinent observations and the conclusions of the analyst.

At an even higher level of management information there is the need to know details of the workload, i.e. the number of assays of a particular type, in order to use resources

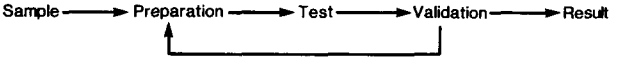

Figure 1
The information flow associated with a sample.

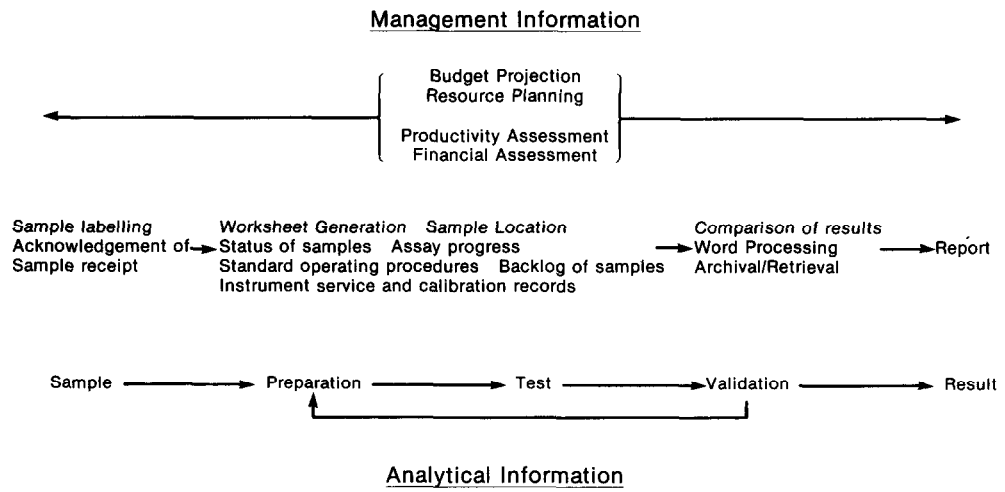

Figure 2
Information flows within the laboratory.

effectively within the laboratory. Scott [19] describes the nature of this information with examples of the type of planning possible: trends in sample load and the services required by each project to give information regarding the efficient deployment of staff and laboratory resources. Activity management (e.g. work schedules, deadlines, project management and updating progress from several different projects) are also areas that can benefit from the power of a LIMS computer system [20]. Table 1 summarises some of the various functions that could be available in a LIMS package at both the analytical and managerial levels. Thus superimposed over the analytical information, there is a complex managerial level of information. The challenge is how to obtain this information easily.

According to Liscouski [21], there are five steps in the acquisition and use of laboratory data:

(1) acquisition, whereby data is captured by a computer;
(2) processing, to obtain the required information;
(3) storage, where either the raw or reduced data is archived for later use;
(4) sharing, where the data may need to be sent elsewhere for further work or dissemination within the organisation;
(5) display of information or data, which can include graphs or histograms.

The flow of information from one step to another need not be confined to a single computer, it can for instance take place amongst several types of computers, intelligent instruments or workstations. However, a LIMS is intended to integrate most, if not all, of the above functions, depending on the configuration in any individual laboratory.

In summary, a LIMS consists of the computer hardware and the necessary software to implement a database management system in the laboratory. The authors define a LIMS as a computer system that should effectively integrate the analytical and management levels of laboratory information by providing, where appropriate, the computational power for the analyst at the bench and sample management information for the manager, from the database. This view is an extension of the definition of a LIMS given by Gibbon [16] above, and will become the more accepted type of package available, especially with the more powerful processor power [22] and sophisticated software that will be available

Table 1
A list of some LIMS functions at the analytical and managerial levels

Analytical level tasks
Automatic sample number generation.
Bar code label generation.
Sample log-in either manually or via bar-codes.
Acknowledgement of sample receipt.
Verification of data format entered into the computer.
Worksheet generation.
Construction and checking of calibrated curves.
Direct data acquisition from chromatographs.
Automatic data collection from analytical instruments.
Entry of instrumental readings via RS232C or IEEE488.
Manual results entry.
Interpretation of calibrated curves and quality control samples.
Interpretation and acceptance of sample data.
Routine automatic calculations.
Plotting routines for visualisation of analytical data.
Managerial level tasks
Backlog investigation.
Sample and status tracking.
Database searches.
Numbers of samples assayed.
Tests utilized.
Numbers of samples analysed per instrument.
Cost per assay.
Customer charges.
Results collation and presentation.
Report generation.
Scheduling and rescheduling of work.
Archival and retrieval of data.
Workload status and the justification of equipment.
Regulatory Agency Compliance:
Audit trail for all database transactions.
Security: Class or Hierarchy.
Instrument records and calibration where appropriate.

Note that not all of these features may be found on every system package.

in the future to encompass both requirements. That is not to say that the computer will be required to collect and store all laboratory data. The prime purpose of a LIMS is to collect data and disseminate information. The difference between data and information will be discussed in the next section.

Information versus data

The analytical process is a means to an end; it is involved in presenting information as an aid to making a decision. For example, the questions posed could be: does a particular batch of tablets meet its specification, or is a new formulation bioequivalent with the standard one, or what is the significance of the concentration of this drug in a patient? The analyst, through the experimental techniques and procedures at his disposal, gains the data, which is processed into information, to answer the questions and help make the decisions.

The information content, as opposed to the data collected from modern analytical instruments, is usually very small. This is shown diagrammatically in Fig. 3: here the

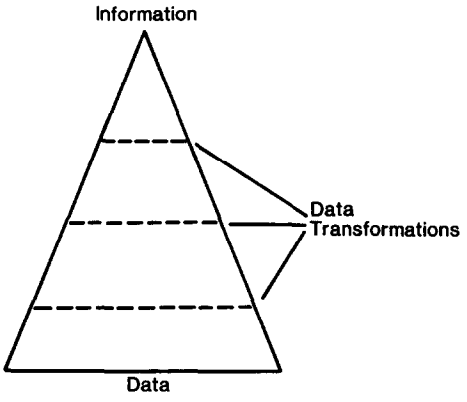

Figure 3
Data versus information.

bottom of the triangle represents the original data which is reduced through successive transformations to provide the requisite information.

An illustration of this process is where chromatography is used to quantify a drug in a bioequivalence study. The base of the triangle is represented by the chromatograms of the sample extracts. The first data transformation occurs when the peak areas or heights corresponding to the drug and the internal standard are abstracted, the remainder of the chromatogram is not used. This data is further reduced, first to a ratio of drug/internal standard peaks and then via a calibration curve to a drug concentration. Areas under the time versus plasma concentration curves (AUC) are calculated to assess the bioequivalence of the new formulation. The end of the data transformation is a simple yes or no to the question "are the formulations bioequivalent?" Thus the information content is small, initially, but increases as the data goes through successive transformations.

In conclusion, there is much data but little information associated with even simple questions that are answered using modern analytical techniques. It is through the control and management of the processes of data reduction and information management that a LIMS achieves its role. In order for the database to work efficiently much thought should be given to if and when data should be transferred to the LIMS database. The amount of laboratory data that should be stored in the database is an issue which is not easily decided [16]. If all laboratory data is transferred then the database becomes very large and could become slow to use. Thus, it is essential to decide when in the analytical process should data be passed to the LIMS for inclusion in the database.

Computer hardware

A typical LIMS installation is shown diagrammatically in Fig. 4, it consists of a central processor unit, memory, disc storage units and a tape drive. The central processor unit (cpu) is usually 16 or 32 bit (although this may change as processor technology develops); typical examples of the computer required to support a LIMS application are DEC Vax, Hewlett–Packard 1000 or Perkin–Elmer 3200 series computers. These very powerful computers are necessary to handle the large amount of data the computer needs to access for this application. A single microcomputer is unlikely to have the processor power required for the large data manipulations of a LIMS system. However, by distributing the database across a number of microcomputers or enlisting the processing power of other machines in a cooperative network, the implementation of a LIMS on microcomputers may be feasible.

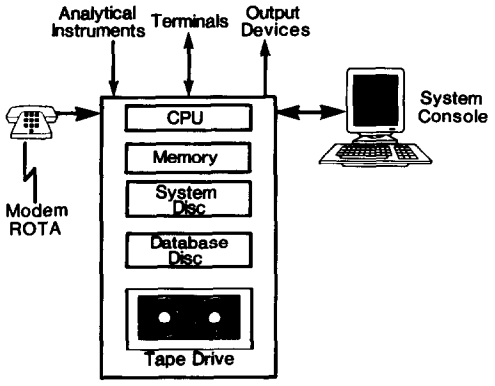

Figure 4
Typical computer hardware required for a LIMS.

Reliability of the computer is very important, as is the fact that it can be upgraded easily if required. The supplier should assume that hardware upgrades will not be required to support new LIMS software revisions.

It is important that enough memory is purchased at the outset to ensure sufficient space to run the programs, otherwise the performance of the system will be slow. Discs are used to store programs and the database; three approaches are possible.

In the first instance, two discs are required as a minimum. The first is termed the system disc and stores, besides the operating system, all the application programs for the LIMS. The second, usually larger, is where the database and the account files will be stored. The system disc can be relatively small (c20–60 Mb) whilst the database is usually larger (c120–800 Mb). If data is going to be left on-line for long periods a large disc will be needed compared to a laboratory that archives all records every month. Again it is essential to ensure that all discs are the appropriate size for the application.

An alternative method, under some operating systems, is to purchase a single large disc and format it into two or more "virtual" volumes which are considered as separate discs by the computer. The effect of either approach is to separate the database from the programs, however, contention of access to the same physical device is likely to degrade the performance of the computer. Where security of the database is of prime concern, a third approach, intended to overcome the problem of a fault with the database disc is possible. Data shadowing or mirroring is a technique where duplicate copies of the database are held on two separate discs. If a fault develops, the alternative disc can be used to keep the LIMS operational until the defective disc is repaired; the operating system then copies all new entries into the original database until there are two exact copies [23].

Archiving and retrieving of data, backups of the database and software updates all require a magnetic tape drive. The speed of the tape drive can be important for they come in 800, 1600 and 6250 bytes per inch, which gives an eight-fold variation in the number of tapes required to back up a large disc.

The computer should be housed in an environment of suitable temperature and humidity; the manufacturer of the hardware will have the requisite information for this task. To negate the effects of power failure the installation of an uninterruptable power supply unit (UPS) should be considered for both the computer and any vital laboratory instrumentation. A system console is used to control the operating system tasks, whilst a link via a modem and the telephone line can allow a supplier to dial in and access the

system to investigate potential hardware and software faults. This is especially useful if the user is very remote from the supplier; it can be very quick and reduce costs on both sides.

Terminals, printers and plotters are a matter for the individual laboratory, the main point to make is that enough terminals of the correct type must be obtained to allow sufficient access to the system.

Databases

The essence of a LIMS is a suite of software programs linked to a database to provide on-line information about the laboratory. A database is a collection of logically related information, usually stored on disc, which in the context of a LIMS is all the pertinent scientific and analytical data that is required by the laboratory. The systematic organisation makes it easier to enter, retrieve, transform and report results with associated information.

Applications programs are responsible for accessing and updating the data in the database. Figure 5 shows an example of the type of programs which interact with the database to achieve this. Data stored within the database can be transformed or manipulated automatically by validated software routines reducing the need to check for transcription errors.

The database for a LIMS can be constructed in one of two general ways. First, the database is divided into a number of data sets or dictionaries with a logical system that reflects the structure of the data to be recorded. Some data sets, such as those pertaining to the samples, analyses and results, will be common to all LIMS systems but others may be unique to an individual laboratory. The data sets are inter-linked by the information flow within that laboratory. Each data set contains a number of entries or records and each entry is then broken down further into a number of data elements e.g. the individual drug or test. Table 2 shows the data record for one of our compounds as an example. Berthrong and Schaeffer [24] and Kipiniak and Finnerty [25] have detailed this type of database.

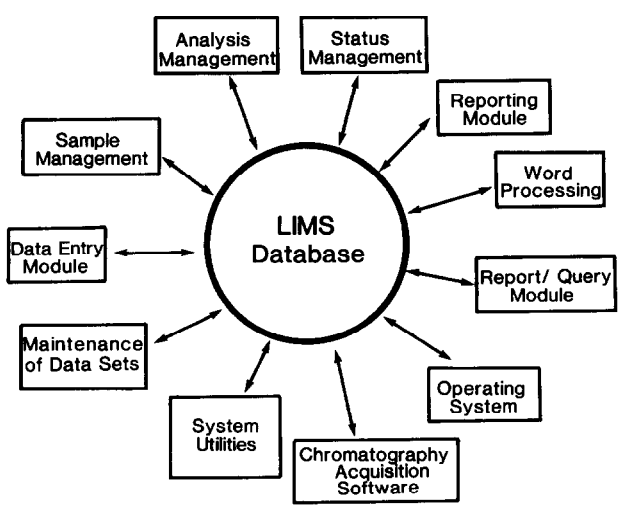

Figure 5
Interactions of the LIMS applications programs with the database.

Table 2
Example of a data set record

Dataset : Drug number	
01 — drug number	: SKF92334
02 — date–time entered	: 17/12/84 13:23:34
03 — date–time modified	: 30/07/85 14:09:26
04 — usage count (chg number)	:
05 — details of drug	: cimetidine
06 — weighting factor	: 1.0000
07 — concentration factor	: 1.000
08 — concentration units	: mg l^{-1}
09 — signoff user id.	: BM

An alternative type of LIMS database has been described by Baumann *et al.* [26]. Here the database is divided according to function into data and sample management. Instruments are interfaced through a data management program into the data management database and the final results are transferred to the sample management database for tracking, reporting and archiving.

In either case the entries in the dataset can be used as a basis for verifying entry and output or for automatic calculations of data. The weighing and concentration factors shown in Table 2 are used for calculations within the authors' LIMS and show the ease of implementation of automated calculations within the database. Further information on the use of automatic calculations is given in the article by Boother [27]. The existence of the data sets provide points of reference for the entries made by the analysts during the operation of the system. By reference to the appropriate data set each entry can be automatically checked and verified to see if it is correct, this avoids misspelt or inappropriate entries. This facility should be used at every opportunity. It bestows on the users and managers of the system the ability to check rigorously and validate data entry. This is a feature offered by computerisation that is not available by manual methods, to the same degree. Moreover, it removes some of the tedium from such a job and allows the analyst to be freed for more productive tasks.

Once the datasets are established, any adjustments or modifications to the database, e.g. the addition of new users or the modification of a users security classification, can easily be made on-line without affecting the applications programs.

Communications

Within this section, the interfacing of analytical instruments to LIMS, the use of distributed or centralised processing and the networking of instruments are discussed.

Interfacing analytical instrumentation

The major constraint on flexibility in laboratory automation is associated with the interfacing of the LIMS computer with laboratory equipment and other computers. When considering the interfacing of analytical instrumentation there are many factors to consider; the case of HPLC and GLC chromatographic data acquisition will be considered in the section on central and distributed processing.

The first question is "Why interface to the central computer and what would you achieve?" The data passed to the LIMS computer must be useful to the laboratory as a

whole. For example in the authors' laboratories there is an automatic microprocessor-controlled thin-layer scanner for the assessment of radiochemical purity of compounds before use in the laboratory. It would be easy to interface this to the LIMS but the data is displayed, evaluated and used by the analyst locally. If the results from the same instrument were used as the basis for further calculations, then interfacing to the LIMS would be justified.

A second factor will be the age of the instruments. If they are more than 5–7 years old, their ability to communicate with the computer will be much less than modern equivalents, so it may be cost effective to replace them.

Having made the decision that interfacing the instrument is beneficial one may still be faced with many technical problems. These have been highlighted in an excellent article by Dessy [28] and further reading on instrument interfacing can be found in two useful books [29, 30].

In the main, communication from analytical instruments is limited to RS232C protocols [28]. Connecting the LIMS computer to analytical instruments using a suitable cable may not necessarily result in successful communications. Compatibility problems may arise because of the rate at which data is sent or confusion as to who is sending and who is receiving. Some of these difficulties are relatively easy to overcome, especially now that sophisticated breakout boxes can be purchased for less than £200 (e.g. Inmac X21). Given that the hardware is now configured correctly the user may still find that the data transmitted cannot be interpreted by the LIMS. This is due to the format in which it is sent. Each instrument may utilise a different format for packaging data prior to transmission. At present it is necessary to write individual programs for use in the LIMS for each type and/or manufacture of instrument. This will be an expensive exercise whether written in-house or out of house.

Manufacturers of LIMS are becoming increasingly aware of this problem and Beckman and Perkin–Elmer, to mention just two, have been developing their own solutions. The latter, with their "Everywhere" approach, has put increased emphasis on the incorporation of standard methods of communication in analytical instruments [31]. In contrast, Beckman's approach to RS232 instrument interfacing is to use their MK5 Digimetry instrument interface coupler. This unit acts as a terminal for the LIMS computer and can also perform real-time data acquisition, sample ID entry via bar codes and instrument control. Compatible data transfer is achieved as follows: a specific program (LIL) is downloaded from the LIMS computer to the MK5. Data is acquired from the instrument and the LIL program strips off any unnecessary information and reformats the data into "packets" which can be transferred to the host. Here, another program (EDLAB) picks up the newly formatted data and inserts the results into the LIMS database (Fig. 6) [23].

The need for a communication standard has been highlighted by Gibbon [16], who recommends that "all computerised analytical equipment should be purchased with both sufficient memory and a suitable operating system to run user-developed programs and an additional terminal input/output port". This would allow programs to be developed that would transmit the required information in a standard format from the instrument to the LIMS.

The need for a "neutral data format" has been highlighted by Dessy [17] and Borman [31]. The initial moves by analytical instrument manufacturers towards standardisation have begun but an agreed standard is essential for the development of successful networks within the laboratory.

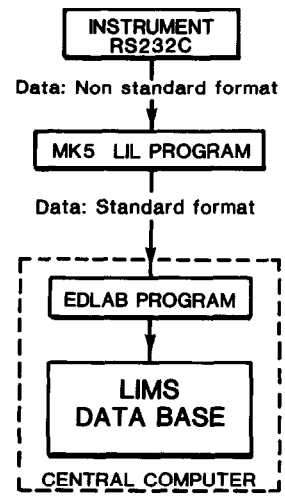

Figure 6
Beckman interfacing strategy.

In summary each laboratory must establish which instruments they wish to interface. The expertise of the LIMS supplier in interfacing these makes of instrument should be established before the purchase of a system. Where compatibility is doubtful consider the following options: (i) replacement with a modern instrument; (ii) not interfacing and entering the results manually; or (iii) specifying custom software to overcome the problem.

Distributed versus centralised processing

Should the LIMS computer be responsible for the collection of laboratory data as well as the database functions? This question gives rise to the concept of centralised and distributed processing. There are advantages and disadvantages of each arrangement which will be outlined below; the ultimate choice for each laboratory will depend on the type of work and how urgently the results are required, personal preferences and available funds. This section is written mainly for data acquisition from gas and liquid chromatographs but the principles involved can be applied to other instrumentation.

Under centralised processing the LIMS computer acquires and processes data from instruments as well as the associated functions of the database. An outline of a central processor system can be seen in Fig. 7. Data is usually acquired from instruments by feeding the analogue signal from the detector into an analogue to digital converter (A/D), this converts the signal from a continuously variable voltage into discrete digital values [32] which are transferred to the central computer for further processing.

The computational power available with such an arrangement allows the use of powerful chromatography software packages in which post-acquisition interpretation is possible — compared to immediate analysis with some integrators. The former approach gives the analyst such facilities as: repositioning of baselines, overlaying of chromatograms where plots can be either directly overlaid or offset vertically to compare any differences.

Subtraction and normalisation of chromatograms are easily achieved and greatly assist the chromatographer [33]. The use of interactive graphics enables a small section of the chromatogram to be enlarged for further inspection.

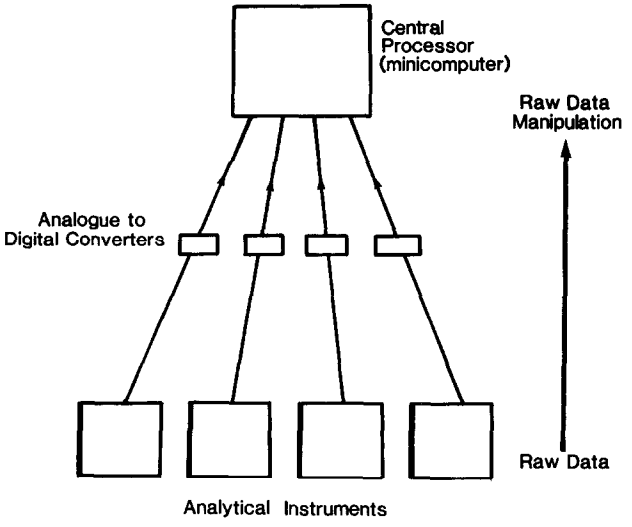

Figure 7
Central processor philosophy.

In a laboratory which must comply with regulatory guidelines, unauthorised change of analytical methods is of concern. The centralised approach ensures that all staff are working with the same and latest versions of any methods and that unauthorised modifications cannot be made. This facility is not normally available on small, single channel integrators. The laboratory's data is contained within the LIMS which means that transfer between the data processing and the database software is simple, straightforward and usually transparent to the user.

The major disadvantage of the central processor arrangement is that the computer is now trying to do two functions: data collection and database manipulation and management. By its nature the former (i.e. real-time data collection) must take precedence over all other tasks; thus, it is possible that a high rate of data acquisition, by a relatively small number of chromatographs, can subvert the database function of the computer, the net result will be a degradation in response time.

A solution to this problem is to have two central processors: one for data acquisition and the second for data management. This will add at least 10% to the overall cost of the LIMS package. The reliance placed on central processor architecture is such that all work (including data acquisition) must stop in the event of routine maintenance let alone a breakdown, however minor. If the average uptime of the system is 98%, this means that there are seven days each year on which it may be unavailable. If 100% uptime is required, then the purchase of a second processor to carry on running if the first develops a fault should be contemplated. Few laboratories can justify the cost of this type of approach, thus managers must resign themselves to the lost productivity when the system is not available, and the wrath of the annoyed users.

An alternative approach is distributed processing. Instead of the central computer receiving all the raw data this task is undertaken by a series of microcomputers linked directly to the instrument and the LIMS as shown in Fig. 8. Data acquisition by a microcomputer is under local control and can be configured enough to do other tasks if required. Raw data is kept at a local level and ensures the independence and resilience of

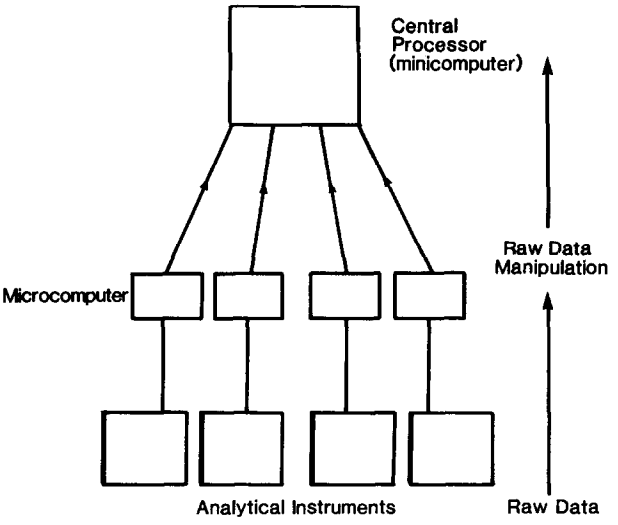

Figure 8
Distributed processor philosophy I.

the analytical system. Only reduced or results data need to be fed into the LIMS software and the computer concentrates on the main task of maintaining the database.

The major advantage is that if a microcomputer fails then only one instrument is temporarily lost, and if the LIMS computer fails for whatever reason then all instrumentation within the laboratory still works. Results can be transmitted to the LIMS when it has been repaired.

A major disadvantage of a distributed system is the lack of computational power for data manipulation, however, this is being overcome as more powerful microcomputers become available at a reasonable price. Other disadvantages are the extra cost, although the price differential is falling with cheaper processor power, and the difficulty of software interfacing the microcomputer to the LIMS so that data can be utilised effectively. Security of software packages running on microcomputers is lower than the central system: it can be difficult to trace changes to analytical methods unless strict procedures are followed; additionally the software packages are not usually password protected.

Experience has indicated that an alternative approach which incorporates the advantages of both configurations is possible. Small reasonably priced benchtop mini/microcomputers running the same chromatography software as the centralised system are now available. These are able to collect data from up to 10 instruments and then send the reduced data to the central computer [34]. The distributed processor system would become that shown in Fig. 9 and this is, in the authors' opinion, probably the best compromise for the future giving flexibility with computational power and a level of security similar to the LIMS itself.

Networks

The basic function of networking is to move information from one location to another, without error [35]. A network consists of a system of links which act as a pathway for the transfer of information to and from the central node and the peripheral nodes of the

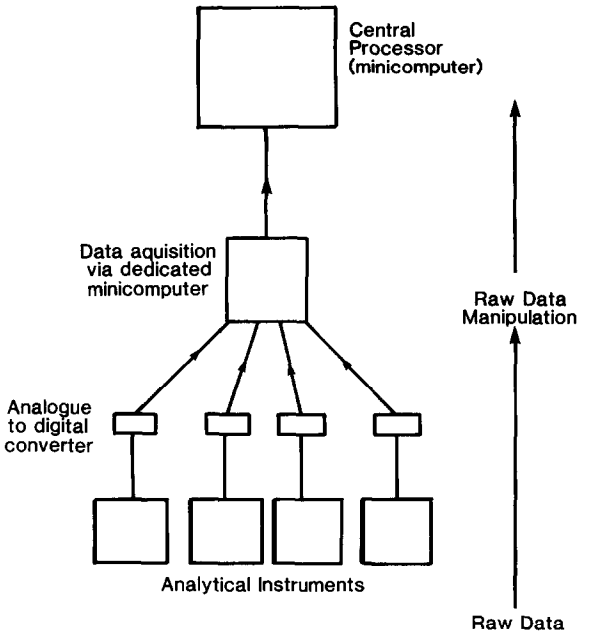

Figure 9
Distributed processor philosophy II.

network [36]. In terms of topology, a node can be defined as an end point to any branch of a network or a junction common to two or more branches. In the case of a laboratory the nodes of a network are the analytical instruments and the LIMS computer.

At present, communication between instruments and the LIMS is usually unidirectional via RS232C protocols; even if the equipment is capable of two way communication (the cost of writing the software to achieve this would probably be prohibitive enough to make it an unattractive proposition). Thus, as a result of the present generation of laboratory equipment the only practical network configuration is the star. Here, the LIMS computer is at the centre of the network and radial connections to the individual analytical instruments (nodes) at the periphery of the laboratory (Fig. 10). An example of this network in a LIMS system is described by Martin [37].

The distinguishing feature of a star is that all nodes are joined at a single point. This was the earliest network configuration to be developed in order to maximise expensive computer resources. However, the central node is a single point of network failure, if it fails so does the entire network.

There are other possible network configurations e.g. ring and bus networks; these are also shown diagrammatically in Fig. 10.

Ring networks consist of nodes connected by point-to-point links, arranged to form an unbroken circular configuration. Each node must be able to recognise its own address in order to accept messages. In addition, each node can serve as an "active repeater", retransmitting messages addressed to other nodes or information can be sent directly to a specific node.

A bus network consists of nodes sharing a single physical channel via cable taps or connectors. Messages placed on the bus are broadcast out to all nodes. The nodes must

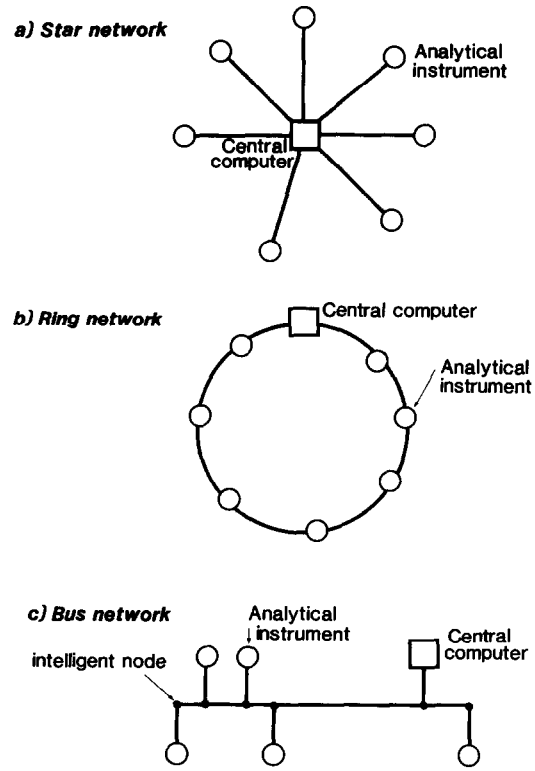

Figure 10
Network topologies.

be able to recognise their own address to receive transmissions. However, unlike ring nodes, they do not have to repeat and forward messages intended for other nodes. This makes them faster and more resistant to failures. This system is also easily configured and expanded in most physical layouts.

However, full implementation of these networks will not be commercially viable within an analytical laboratory for a few years yet, when sophisticated communications e.g. Ethernet with the appropriate software protocols becomes available. For further reading see the articles by Dessy [38, 39] and Braithwaite [40].

Summarising, if instrument interfacing and communication with the LIMS computer appears fraught with problems, a question arises "why bother?" The answer is that once achieved, it removes the problem of incorrect transcription of data, thereby improving consistency of measurement and speed of transfer whilst reducing human error. Data transfer becomes rapid and reliable. As manufacturers begin to incorporate more communications intellegence into analytical instruments (hopefully incorporating standard protocols), then true networks will emerge within the laboratory.

Features

Two main considerations of a LIMS should be the appearance of the system to the user via the screen format and the ease of identifying and entering samples into the computer using bar codes.

Screen format

Consideration must be given at an early stage as to what screen format will be used and how the users will interact with the software. The essential requirement is that it must be "user-friendly". This is a well meaning phrase but has been open to much misuse. There should be no need for the user to call and execute the program (this must be done automatically). Similarly, there should be no need for direct interaction with the operating system. The software should be sufficiently flexible to avoid any need to stop the program when errors are made and to avoid unintelligible error messages appearing on the screen: great emphasis should be placed on the software having error trapping routines. Thus when a mistake has been made, the user should be invited to re-enter the line or perform the task again. Whenever possible, the data entered into the system should be verifiable as to format: what would happen if 59,7 rather than 59.7 or 30th February were entered into the computer? It is essential that the software that you propose to purchase can check for errors of this type.

There are four main methods of screen format, that could be applied to LIMS software either now or in the future, these are: (i) command driven; (ii) menu driven; (iii) graphical methods (WIMP Software standing for Windows, Icons, Mice and Pull down menus); (iv) natural language.

Command driven software. This requires that a series of codes, abbreviations or mnemonics are entered at the terminal to call a particular routine. This has greatest advantage with the experienced user as they can change programs very quickly. However, this approach can be difficult and frustrating for the novice or an infrequent user as there are many codes to learn and the logic of the name of the codes can be rather obscure. Examples of these codes can be seen in the article by Berthrong and Schaffer [24].

Menu driven software. This is the most common interface with LIMS software, and as the name suggests a selection of items is shown on the screen and the user invited to choose by entering a number via the keyboard. An example of such a menu is shown in Fig. 11; once a number has been entered this will lead to a sub-menu display with items of related choices from which a program would be called and executed. Menus are easy for the beginner to explore the system; however, they can slow the more experienced user. There are various methods used by programmers to overcome this disadvantage which have been exploited by commercial systems such as the ability to revert to command language [27] when desired or predefined routines that take the user to a specific place in the nests of menus.

Graphics. Graphics can be used to interface the user to the system software, and can be thought of as an alternative version of menu driven software. There are various methods of achieving this via either a mouse, or cursor control [41]. This is a method of controlling software; however, the main computer applications to date have been in business software (as exemplified by the Apple MacIntosh) but they are gradually emerging in the scientific environment.

A mouse is a means of moving a pointer around the screen display and consists of a movable ball, connected to the PC or terminal. The mouse is moved around the bench until the pointer reaches the required choice on the screen. Located on the top of the

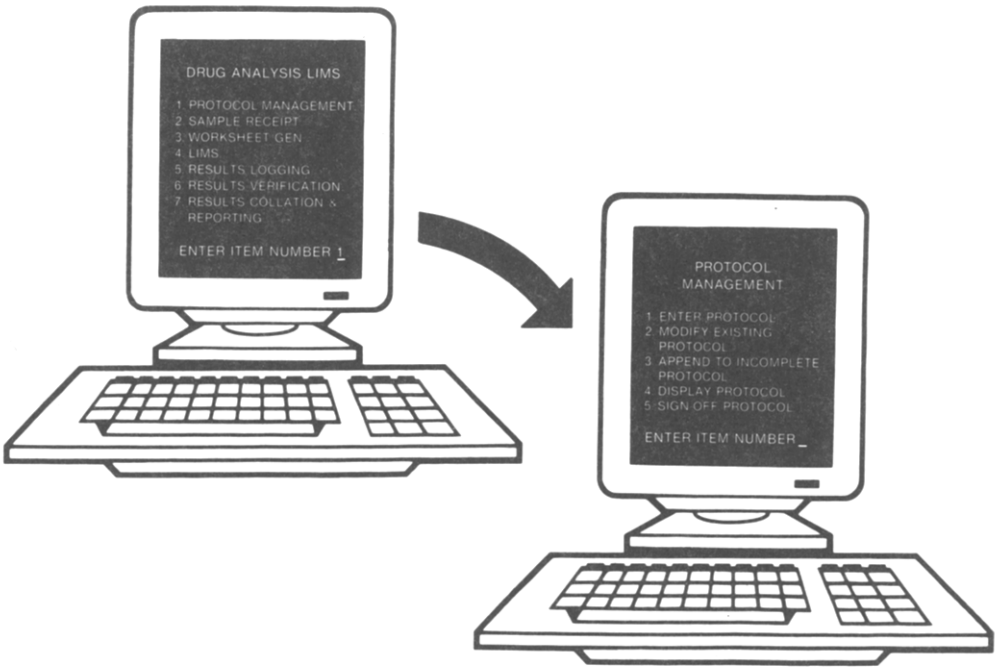

Figure 11
Menu driven LIMS.

mouse housing are two buttons which when used with the mouse can allow the user to rapidly access particular parts of the program and to perform various functions.

Icons are small pictures or graphic elements on the screen which either represent or suggest the operation they perform. Windows allow the screen or terminal to display several functions at the same time. Thus, help menus can be called to enable the user to receive on-line advice about the module they are using. After use the window is removed from the screen without affecting the original display.

This approach can be learnt quickly and the operation of the programs becomes more intuitive, especially if help screens are incorporated into the choices and displayed on the screen if required. However, an experienced user must proceed through all the options, because there are no short cuts that can be taken with this approach. An example of the scientific use of graphics driven software is shown in Fig. 12. This is a chromatography control and data acquisition package that runs on an IBM PC and uses a mouse to select the required options. Graphical selection requires much software development by the programming staff but facilitates easy and rapid acceptance by the users. An example of an icon can be seen as a hand moving the pointer on the flow controller. Interestingly a mouse was not as quick or precise as compared to a keyboard for wordprocessing but was more easily accepted by users according to Freeman [42].

Natural language software. This is an area for future development, whereby ordinary language commands are typed into the computer to carry out the tasks required. Systems using fourth generation languages which could mean that users themselves could configure or change screens (allowing great flexibility) are beginning to appear now.

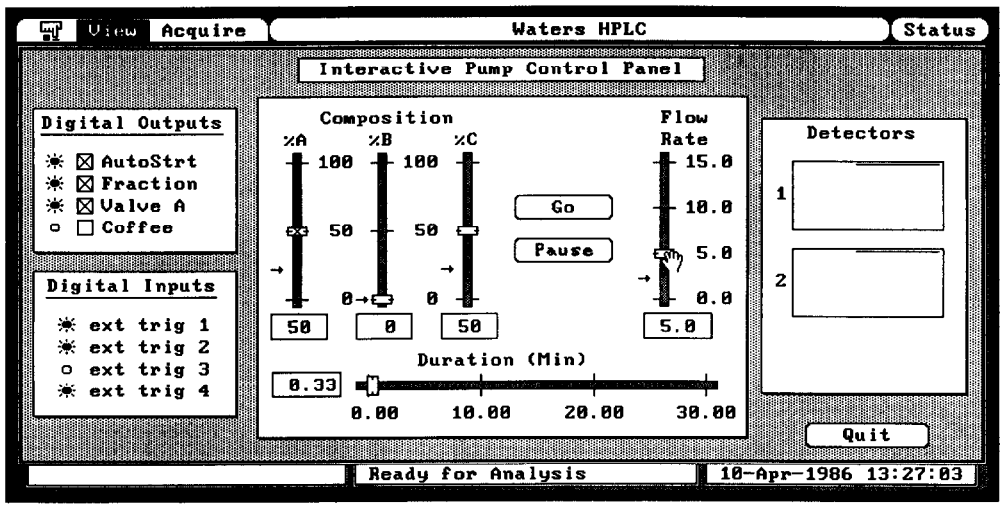

Figure 12
Screen format: using a mouse to control chromatographic equipment. The control of the flow rate of the HPLC pump has been activated represented by the hand. This icon is controlled by movement of a mouse. The actual flow rate is shown digitally at the base of the scale.

The screen format is vitally important as it is the major method of user interaction with the software: bad choice or design will result in the user's frustration. Todays LIMS are limited to either command and/or menu driven systems; time will tell if either commercial pressure or user demands, combined with the appropriate software tools, will mean that software programmers will use the alternatives available.

Bar code labelling

One of the newer methods of labelling samples is with bar codes. These have been used extensively in manufacturing and retail industries over the past ten years and are now being introduced into the laboratory as a rapid method of automated data entry [12] and stock control [43]. Bar codes are a method of encoding numeric or alphanumeric data as a series of thick and thin lines. The method of encoding will depend on exactly what information is to be recorded [44].

An example of a bar coded label used in the authors' laboratories is shown in Fig. 13. The actual size is 1.75 × 1.5 inches and it is designed to fit onto a 5 ml blood tube (although different sized labels could be used as the printer is software programmable). The labels, produced by a thermal printer, can withstand the effects of repeated freezing and thawing, or blood spilt down the sides of the tube and still remain legible. Initially, the labels were prone to "winging" if placed around small tubes and left in a hot

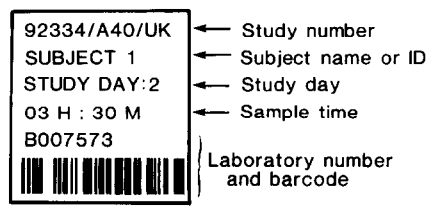

Figure 13
Bar code labels for sample identification.

atmosphere, this was overcome by the use of a high tack adhesive from our label supplier.

Readers for bar codes can take several forms; the most common is a pen with a light source at the tip which is moved by hand across the code. If the code has been successfully decoded the reader will emit a beep to inform the operator. Use of this type of reader is very technique dependent: the success rate is low at the beginning but rises rapidly with practice. Battery powered scanners can be used to read labels off-line prior to transmission to the computer, allowing mobility if required. The utility of bar codes is illustrated in a commercial LIMS where many operations (e.g. sample identification, location and identifying operators or instruments) are represented by a single bar code entry. This approach eliminates the need for many keyboard entries [37, 45].

Fixed beam readers are an alternative to the hand held wands; in this instance it is the bar code (attached to the sample) that is moved past the head. For large numbers of samples automation using laser scanners should be considered, these are high speed devices that can read the label when it crosses the light path at any angle.

If sample continuity is required by the laboratory then bar codes should be considered in the context of a LIMS, as the computer can act as a second analyst comparing the data input to that in the database and ensuring that it is correct.

Full automation using bar codes to identify individual samples is now available within our laboratories (P. A. Mason, personal communication). This operates on radioimmunoassay equipment and is shown schematically in Fig. 14. The sample tube labelled with a bar code is placed in a carousel which offers each sample in turn to a static laser reader to decode each bar code and read the number into a file in an Apricot Xen microcomputer. The microcomputer controls a dispenser diluter which takes an aliquot of the sample and adds the solutions appropriate to the test being undertaken. The sample identity file is transferred to an IBM XT microcomputer that controls a gamma counter; the IBM takes the counts from each head and calculates the drug concentration in each sample. The IBM micro now produces a file that contains the sample identity and drug concentration that is passed to the LIMS computer wherein another program takes each result and enters it in the appropriate record in the database.

From the start of the sequence of events, there is no written transfer of data, which only occurs in automatic electronic form, therefore no transcription errors are made. The

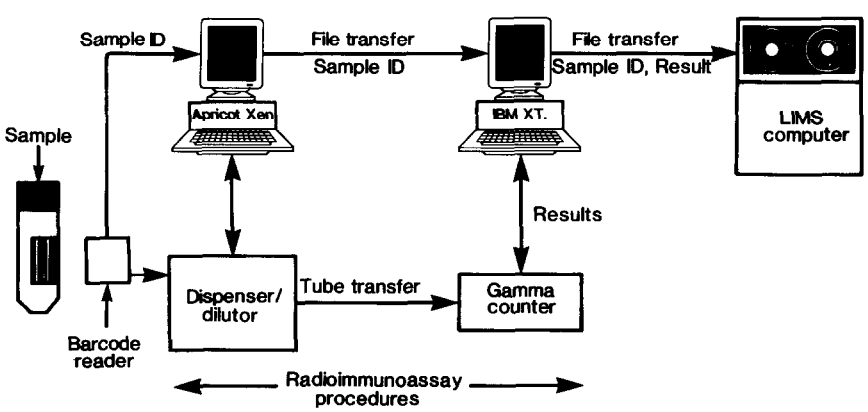

Figure 14
Automated entry of sample and results into the LIMS database using bar coded labels.

only human involvement is in the physical transfer of the samples to and from the dilutor and the gamma counter and the operation of the microcomputers.

Why acquire a LIMS?

The benefits of acquiring a LIMS can best be identified by reviewing the major issues confronting a modern analytical laboratory: increases in sample throughput and compliance with Good Laboratory Practice (GLP).

Considering sample throughput, there is a need to accommodate an ever increasing workload against a background of resource constraint. Initially, the demand can be met by increased productivity and by the introduction of laboratory automation such as autosamplers, integrators and (lately) robotics. However, the resulting increase in sample throughput now leads to bottlenecks in checking, verification and reporting of data. It is in this area that a LIMS will have its greatest impact. Automatic data capture and manipulation leads to more reliable data produced more rapidly.

Industries regulated by Government agencies are experiencing greater demands for data integrity. The emphasis is on the accurate collection, storage/retrieval, calculation and interpretation of analytical data and the information contained within it. In addition, transcription errors, inherent in any system of data transfer from document to document, must be eliminated or at least, greatly reduced. Again LIMS with its database is an ideal solution for this problem with automatic file transfer and avoiding report correction.

These are two major reasons for acquiring a LIMS; there are others whose relevance will depend upon the configuration adopted by an individual laboratory.

The purchase of a LIMS as a tool to overcome these problems is a logical step in the evolution of the automated laboratory. As we shall see, it becomes the hub of the analytical laboratory removing many labour intensive and monotonous tasks in analysis and administration. Staff are thus freed to concentrate on more innovative and productive experimental work.

In addition to the computational power exerted "at the bench", the system also aids the organisation and management of the laboratory. Reports can be generated rapidly from the database to provide useful statistics such as sample status, monthly throughput figures and instrument usage.

The acquisition of a LIMS will therefore meet the requirements for increased productivity in the laboratory, whilst maintaining the quality of the data and ensuring GLP compliance.

The stages involved in the installation and validation of a LIMS will be outlined in the second part of this Analytical Survey.

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