

## *Analytical Survey*

# Laboratory Information Management Systems — Part II. Implementation\*

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**Abstract:** In this, the second of two articles on Laboratory Information Management Systems (LIMS), the stages of the acquisition of a system are discussed. First, the laboratory automation strategy is developed leading to the writing of the requirements specification sent to prospective suppliers. The next step, in conjunction with the chosen supplier, is to write the functional and systems specifications from which the LIMS will be tailored. Once installed the LIMS must be validated and in the event of hardware or software changes, should undergo partial or full re-validation.

The education and training of users, and operational considerations are presented before concluding with possible developments of LIMS in the future.

**Keywords:** *LIMS; laboratory information management; laboratory automation; validation.*

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### Stages in acquiring a LIMS

The first part of this Analytical Survey [1] discussed the concepts of a LIMS. The issues relating to the installation of a LIMS are now presented.

A project of this size and complexity can rarely be accomplished by one individual. In the authors' organisation at SK&F Welwyn, the involvement of the Department of Computer Science and Statistics, throughout the Drug Analysis Department's LIMS project has been essential. A joint project team was formed, comprised of members of both departments to oversee and review the project continually. Positive backing by higher management, coupled with this interdisciplinary approach were the major factors in the success of the project.

There are three stages in acquiring a LIMS: (i) writing the requirements specification; (ii) choosing the supplier of the system; (iii) working with the supplier to produce the functional and systems specifications (from which the LIMS will be built).

#### *The requirements specification*

The requirements specification summarises the overall aims of the LIMS from the laboratories' viewpoint. It does not include any detail of how it is to be achieved. The importance of this document cannot be over emphasised [2], moreover, it is essential that the reader formulates his own ideas before approaching a potential supplier or developer of a system. Substantial planning has to go into this area to evaluate the current as well as the future (2–3 years) requirements of the laboratory. The overall aim should be flexibility to accommodate present and future needs. At the fore-front of all thinking should be the question: what is to be done with the data or information? The purpose of this document is to allow potential suppliers of the LIMS to tender quotes.

In theory, the process of producing the requirements specification should be to step back and review the current working procedures within the laboratory with an open mind [3]. However, the authors geared their LIMS to current work practices within the Department. The list of overall objectives that were decided upon for the LIMS in the authors' laboratory are given in Table 1. Possible requirements have been outlined by Braithwaite [4]. Furthermore, Liscouski [5] recommends the use of pre-set criteria to measure the achievement of each objective. It is important to avoid using any jargon when writing the requirements specification because disciplinary boundaries will be crossed: if necessary define any keywords [2].

The requirements specification should contain the following sections as a minimum: the structure and organisation of the department detailing the type of work, the number

**Table 1**  
Objectives of the proposed Drug Analysis LIMS

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- (1) Increase productivity.
  - (2) Compliance with Good Laboratory Practice regulations.
  - (3) Elimination of calculation and transcription errors.
  - (4) Automated generation of reports and integration with word processing.
  - (5) Help and speed the interpretation of data.
  - (6) Bar code labels for samples and rapid data entry.
  - (7) Verification of data entry.
  - (8) Flexible and expandable system.
  - (9) Sample tracking and scheduling.
  - (10) On-line access to historical analytical data.
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of samples assayed and the analytical instrumentation used. This document must also give an overview of the tasks the LIMS will be required to undertake and if connection to any existing computers is needed.

The plans should be discussed with laboratory personnel; keeping them informed of developments and asking for feedback on proposals is a good way of building enthusiasm for the system. However, care should be exercised to ensure that the expectations of the laboratory staff, regarding the capabilities of the LIMS system and the timing of its delivery, are realistic. The laboratory staff should be made aware that this is the chosen method of approach, but it could vary depending on the systems available. Consultation with other Departments, who either submit samples or process the results, is also essential, both to keep them informed on developments and to consider any forthcoming suggestions.

In producing a requirements specification there are two possible approaches: the first would not radically change the working practices of the laboratory that have been built up over the past years. In essence, this tailors the LIMS to the laboratory. The second method tailors the laboratory to a LIMS and could be used as a way of implementing changes in the working practices. In either case, it is better to aim high and incorporate all the wishes of the laboratory into the specification and then debate with the supplier each point where the product on offer does not match the specification requested. Otherwise, the resulting system may be a disappointment.

The production of a requirements specification can be achieved by senior analytical staff if the information flow in the laboratory is relatively straightforward. Alternatively, computer consultants may be retained. However, they have to be briefed on the function of the laboratory and how it operates before they can begin to analyse the information pathways and make suggestions.

Consultants may offer new ideas and fresh approaches combined with experiences from different installations. This approach may be attractive if there is lack of time or staff within the laboratory to write the requirements specification. Expressing a personal view, the authors consider it better to involve the analysts in preparing the specification as they will be putting the system into operation and they know their own laboratory, regardless of which approach is taken.

When considering a large LIMS one question that may be raised is that of phased implementations. This is when different parts of the system are introduced to the users at different times. Hong [2] suggests that this is not ideal as the users will be faced with several different software systems before the final version is established. Whilst agreeing with this view, the authors would maintain that phased implementation of a

LIMS is possible providing that each new phase is a complete module of the whole system and does not destroy the previous work nor change the overall operation of the system. Indeed, if the LIMS is highly customised then a phased implementation may be highly desirable.

There are two types of philosophy concerning the implementation of a LIMS. The first is a "black box" approach where all data is acquired and processed automatically by the system with little intervention from the analyst; this approach would use extensively the automatic calculations discussed in Part I. The alternative is to think of a LIMS as another analytical instrument to be used and controlled by an analyst whose responsibility is to accept or reject data or any calculations. The type of laboratory, staff available, workload and assays will determine the course of action to take.

In summary, good planning and forethought are essential to lay the basis for overall success and provide for the growth of the system in the future. If an analysis of your laboratory needs indicates a LIM system, proceed to the next section. Some laboratory managers, after this analysis, may find that they do not require a LIM system although the analysis in itself may make them more productive by highlighting inefficiencies. It should be pointed out that a LIMS will probably entail staff working with less flexibility compared with manual systems, however the benefits of such a system should outweigh this disadvantage.

#### *Source of the LIMS*

There are three ways to acquire a LIMS: (i) by in-house development; (ii) from a software house; and (iii) from a commercial supplier. The advantages and disadvantages of each source are discussed.

*In-house development.* If a do-it-yourself approach is adopted, whereby a computer department or other individuals develop the software to the specification, this will mean a huge resource commitment by the site. The easiest method would be to take an existing commercial database and write the requisite routines around it in order to access the information properly. The major disadvantage would be the length of time needed to write the software, together with the resources required, e.g. taking on, or redeploying staff.

The advantage would be that laboratory staff have a system written specifically for their needs, although enhancement of the system could only come from within that laboratory. The huge demands of a LIMS project on computing resources make it doubtful whether any, except the largest companies would choose this route.

Given the status of commercial LIMS software today, this approach seems akin to re-inventing the wheel.

*Software house.* The choice of a software house to provide the LIMS system is a viable alternative; the end result should be exactly what you require but the development costs will be high, especially if the system is unique. The time taken to write the software will depend on the expertise of the supplier and the programming staff employed. If the software company has been well chosen they should have some expertise in this field and should be able to use or adapt existing software in this project and help keep costs down. As in the case of the in-house development, extensions to the system would come from within the laboratory and these would be chargeable if the system were not maintained in-house.

*Commercial supplier.* The last option is to use a commercial supplier. Over recent years analytical instrument companies have seen that information management is a logical extension of their product ranges, so much so that all major manufacturers now offer LIMS in one form or another. These commercially available systems are competitively priced, the development costs are spread over the whole customer base and the systems are sold in competition with other vendors. Competition means the product is under continuous development and is constantly evolving as ideas are incorporated for the benefit of all users [5, 6]. The overall development of the package can take many tens of man years and this will increase throughout the lifetime of the product.

Conventional wisdom favours this option. A survey, cited by Liscouski [7] stated that there was less than one chance in twenty that an in-house system will be, for a brief time, marginally better than any available commercial system. Squirrell [3] advises “do not make if you can buy, but try before you buy”.

When assessing the standard packages from an instrument company it is important to visualise how they would operate in your own laboratory. As the operation of every laboratory tends to be different there will be a certain amount of tailoring of the standard package to your requirements. However, for specific needs, e.g. specialised reporting requirements or graphical presentation of results, custom software will need to be written. How much is required will obviously influence the final price of the system. If there is a suitable computer on site it may be possible to save on some hardware costs just by purchasing the software rather than the whole system. This has been the approach of the authors colleagues in the Quality Control Department, SK&F Laboratories, Welwyn Garden City, UK [8, 9].

In choosing a commercial system, the basis of their operation must be borne in mind: most standard commercial systems are specification driven [10–12]. That is, aimed towards a quality control environment in which small numbers of samples are put through relatively large numbers of tests. After splitting the original sample, ensuing results must be collated to see if they meet a predefined specification. However, the authors' application required a protocol driven system to cope with the reverse situation in that the Department receives a large number of similar, but unique, samples and usually applies a single test. Frequently, individual samples are irreplaceable and of limited volume — being biological in origin. Although individual samples are important, it is the relationship and trends between groups of samples that is sought. The concentrations to be measured result from many pharmaceutical and biological factors and they cannot be compared to any meaningful standard value. This is a vital distinction for laboratories working in the analysis of biological fluids in the pharmaceutical industry.

If a commercial vendor is to be chosen, the best advice is look closely at all the available systems, because the final choice will depend on several factors such as economics, time constraints — both for delivery of the hardware and the writing of the software, including any customisation. It is essential to visit a site that possesses such a system as one is proposing to purchase and to obtain the comments of the people who have used the system. Hong [2] details more advice to prospective purchasers of commercial LIM systems.

Comments on the appearance of the software and how it would operate in the laboratory are relatively easy for analysts. However, appreciation of the computer operation and how the database stores and retrieves data come best from experienced

computer personnel (the advice is much better if they have the laboratory experience to appreciate the problems of analysis). This experience and advice manifests itself in the sizing of the hardware: e.g. considerations of memory and disc size. In the authors' project this worked very well and the advice was always excellent.

### *Choice of supplier*

The choice of supplier depends on a number of factors, the first of which is the ability of the supplier to meet the requirements specification with their standard system. Any potential supplier should indicate in their response what areas they cannot meet. Custom software may be a method of overcoming the problem. Furthermore, detailed discussions should ascertain whether they can fulfil the requirements in practice. All these discussions are time consuming but it is essential to evaluate the potential of each considered supplier of a LIMS. The selection process cannot be hurried.

The cost analysis justification for a LIMS has been presented by Golden [13]; although intended for an American readership it shows how a LIMS could pay for itself in two to three years.

Credibility of the supplier is important. This can be established in several ways; by visiting sites where relevant systems have been installed and obtaining first-hand information concerning the advantages and problems they have had. Meeting users is another good way of finding out how a particular LIMS has developed and learning how much effort is being put into the product [2].

The timing of delivery may be an important factor, for instance if the LIMS needs to be installed within a set time for budgetary or other reasons.

The after sales support and training offered is another area of vital importance. The first 12 months after delivery is when many problems occur, particularly major problems in the software and the users' inexperience in dealing with faults are highlighted. The location of the vendor relative to the site may be an important factor. Once a LIMS has been purchased from a supplier, the user is then linked with that vendor for the life of the system. Enhancements, if not written by the users can be expensive as can software upgrades when the basic system has been extensively customised.

The need to have a clear understanding of the requirements before approaching any potential supplier cannot be overstated.

### *Functional and systems specifications*

*Functional specification.* Once the choice of supplier has been made the hard work begins. The requirements specification produced earlier is used as a basis for producing a further document called the functional specification which defines the functions of the system without detailing the methods by which those will be achieved. (The functional specification can be submitted to a supplier instead of the requirements specification as a basis for tender, this is especially true when computer consultants have been retained to write these documents.)

*Systems specification.* Often a further systems specification is produced that defines the methods to be used to implement the required function of the LIMS. This is the specification which the programmers will use to produce the actual software for the system concerned, and will include such items as the screen layout and the procedural logic for all the tasks that the LIMS will perform.

These documents are drawn up by a systems analyst/programmer working in

conjunction with the senior scientific staff of the laboratory. Close liaison with the programmer is essential as the initial problem to be overcome is the crossing of disciplinary boundaries. The systems analyst, who is drawing up the specification documents must become aware of the intimate workings of the laboratory. Great care is needed to include all working practices to ensure that flexible software is produced. Remember that one is dealing with another discipline where a word can have an entirely different meaning; for instance sample and test can have different meanings to the personnel involved with writing this specification [2].

A note of caution: once the system specification has been agreed between the two parties it becomes the basis for settling any problems in the future. It is therefore in the laboratory's financial interest to see that the exact requirements are specified. If something is found to be missing and it is not included in the specification documents the vendor will be charged.

In practice, it is unlikely that a fully working and functional LIMS can be obtained from the specification documents at the first attempt. The reasons are:

- (i) It is inevitable that some functions that looked attractive on paper will prove to be difficult to use practically;
- (ii) There will be areas that will be underspecified or even omitted;
- (iii) Sections will be wrongly specified.

Analysis of nine US Government software contracts showed that the main causes of failure were vague system and user requirements coupled with an inability to upgrade the software for future requirements. Of software contracts worth \$6.3M only \$0.1M was used as delivered, a further \$0.2M used after modification and \$3.2M was never used. This demonstrates the need to define the system carefully and exactly [14].

In the authors' experience, between 75–90% of the system will work as specified, the remainder will require additional programming and/or enhancement for the reasons above. It is essential that this eventuality is planned for and the cost of further enhancement is allowed.

Source code of the system software is useful if further in house programming is considered; remember that commercial companies differ in their attitudes to this. Some suppliers will release the source code for the whole system provided a non-disclosure agreement has been signed whilst others will only give that relating to any custom software. In all cases care should be taken that any proposed changes to the software do not invalidate the maintenance agreements. Moreover, these should be discussed with the supplier before programming starts to avoid any major problems.

In summary, long-term planning is essential to the success of a LIMS project. Mistakes will be expensive to correct and a badly designed system will be difficult to operate. Good planning will bring the full benefits of laboratory automation.

### **Validation of LIMS computers**

Validation is probably the most neglected area of scientific computing. This is surprising, considering the impact computers have had in recent years and the fact that many industries come under external regulations. Little has been done until recently to incorporate any quality assurance requirements into computerised systems. Although the computer can provide many powerful enhancements in quality assurance for the laboratory with increased data integrity, the use of a computer does not guarantee that a given program is valid [15].

At this point it is useful to define some terms using the work of Chapman [16]: validation, establishing documented evidence that a system does what it purports to do; validation protocol, a prospective experimental plan that, when executed, is intended to produce documented evidence that the system has been validated. The keyword in both these definitions is “documented”.

Initially, validation is aided by good system design (through the various specification documents) and the software quality assurance practices of the supplier [14, 17, 18]. Ideally, the LIMS should be checked thoroughly by the supplier before delivery to ensure that the system works in the manner prescribed. It is essential that the software supplier has a defined test plan and that the results of it are available to the customer. In the authors' experience, the best personnel to validate the LIMS are scientists, because the supplier will not have intimate knowledge of the working methods of the laboratory. Moreover, the FDA considers the final user of the system to be primarily responsible for the validation process [19]. It is therefore imperative that the analysts involved with the validation are allowed sufficient time to undertake these tasks: it is unacceptable to expect them to validate the computer and perform their normal work at the same time.

How does one validate a computer system? The FDA Good Laboratory Practice Regulations (GLP) [20], written before wide spread introduction of computers within analytical laboratories, states:

“Equipment shall be adequately inspected, cleaned and maintained. Equipment used for the generation, measurement, or assessment of data shall be adequately tested, calibrated and/or standardised.”

“Written records shall be maintained of all inspection, maintenance, testing, calibration and/or standardising operations.”

In this instance, the LIMS can be considered as an analytical instrument.

It must be realised from the outset, that computer systems other than the simplest cannot be completely validated [21]. Therefore errors will be discovered later during operation of the system. The US Department of Defence, for example, lays down minimum standards that 100% of the statements in any software component be executed during validation and that 85% of the possible branches be executed. Exhaustive software validation takes place in the avionics and space industries where lives depend on the validity of the software in computer controlled operations. For instance, 44% of the total software budget of Saturn V project was spent on software validation [21]. This amount of effort is excessive in the context of analytical laboratories but does not remove the onus of validation from the user.

It is necessary to restrict validation to some achievable goal that will engender an acceptable level of confidence in the system. The validation protocol is the means of achieving this.

For convenience, the LIMS can be divided into two parts: the computer hardware and the software, of which the latter is further split into the operating system and software modules. Each aspect will be considered in turn.

#### *Validation of computer hardware*

Computer hardware, including the terminals and other peripheral devices, should be considered analogous to an analytical instrument. Preventative maintenance contracts ensure optimum performance of the system. Analog to digital (A to D) converters can be checked using peak simulator modules to monitor their output, recently automatic



validation of these units has been described by Mansfield *et al.* [22]. Effective transmission of the data from an analytical instrument should also be tested by sending the same results on several occasions. Further details of hardware validation are discussed by Motise [19].

#### *Validation of computer software*

The operating system software is such that its validation is too complex for the user to contemplate. Instead, the LIMS software should be tested thoroughly, as it uses the operating system, and these tests should indirectly validate part of the operating system.

There are six stages in the validation of LIMS software. These should be documented in a Standard Operating Procedure (SOP). Note that computer programs *per se* are not considered to be SOPs as changes to software can adversely affect study results [23].

*First stage.* The first stage is to divide the system into tasks that are to be tested and then define each task. (These tasks are usually the components of the system as defined in the functional specification.) Tasks that form the LIMS fall into three areas, each of which have their own particular testing requirements.

- (a) Input related tasks must establish that only the data required for processing or output is accepted and that any other data is rejected. Only data within defined limits is accepted and all unacceptable data is rejected. Examples of this type of task are entry of the 30th February as a date or 59,6 rather than 59.6 as data. Only authorised individuals should be able to enter the system to enter and modify data.
- (b) Output related tasks are to show that only the specified output in format, content and layout is produced and no extraneous data is observed, i.e. information can be archived and retrieved efficiently and reliably or results are reported with no corruption.
- (c) Process related tasks are the most difficult to validate as they occur within the computer and require that the input and output tasks are validated. Here we are concerned with calculations and internal data manipulation: the accuracy and reliability of any calculations used must be checked and formulae documented outside the LIMS. An assessment of data corruption must be made when passing files to and from other computers on site as well as between analytical instruments and the central processor.
- (d) The relationship between the data sets must be validated to ensure that they have the correct logical relationship to each other.

*Second stage.* For each task to be tested the operational limitations and any special test conditions must be defined and documented in the validation protocol.

*Third stage.* Ensure that the purpose of each test is documented, and that suitable test data have been constructed. Detailed written instructions are essential for undertaking any test and the expected results must be recorded.

*Fourth stage.* The test is undertaken as specified within the validation protocol and all the results are recorded and documented.

*Fifth stage.* The test results are reviewed and any deviation from the expected results must be documented and explained.

*Sixth stage.* The test specifications and the reviews of the test results are collected together as documentary evidence of the system validation.

Further reading for validation of computers within the pharmaceutical industry can be found in the articles by Motise [19, 24] and Taylor [23]. Although written about computer validation of process computers and toxicology data they provide useful reading as the authors are officers of the Food and Drug Administration. Herrick [21] presents the validation of computer systems in more detail.

In summary, documentation of validation procedures is all important. State what is to be done. Document what one said one would do. Do it. Document the fact that it was done, record the results and in the case of revalidation compare with the previous results. The majority of deficiencies in FDA inspections concerned the lack of the required SOP or the failure to amend them when necessary [23].

### *Re-validation of LIMS computers*

The definition of a re-validation protocol according to Chapman [15] is

“repetition of the validation process or a specific portion of it, once the system is in a state of control.”

Thus, enhancements and new revisions to any part of the software will require re-validation. Re-validation tests are to enable the user to check if the LIMS is functioning correctly.

Hardware when it is repaired is returned to its original state, however, software after an error has been corrected is changed into a new state. Re-validation is a matter of judgement: should a complete re-validation protocol be run to test a simple error correction or just the affected module around the problem. Even if there has been no change in the system it is strongly suggested that periodic re-validation of the software should take place [24].

In short software change must trigger re-validation.

### **Operational considerations**

Once operational, a great deal of reliance is placed upon a LIMS installation, therefore, it is vital that the system itself is highly reliable [12]. In addition to the computer hardware and software, some other aspects to ensure the smooth operation of LIMS will now be discussed.

#### *System manager*

It is imperative that the first consideration with a LIMS is the appointment of a system manager, to be responsible for the running and operation of the system. Ideally this person should be involved with the project from the start: from writing of the specification through to the acceptance testing and validation. The system manager is instrumental in ensuring the success of the system and the authors feel that the following attributes are important and worthy of mention. The position should be full-time, with a deputy who can stand in for the manager either in their absence or help during periods of heavy demand. It is essential that the manager has a technical understanding of the computer and the operating system but should also be a scientist, with a feel for the user's requirements. They will need to converse with a wide range of people. To be

effective they should have good interpersonal skills, on one hand being firm with the vendor yet on the other understanding the users.

Current legislation may require registration of the LIMS under the data protection laws, the system manager should determine whether this is the case by liaison with the Computer Department or the local registration authority.

#### *Audit trail*

Regulated industries are required to monitor any changes to data and have access to these over many years. In the context of a LIMS installation an audit trail is required. Audit trail is a file linked to specific data sets, e.g. sample, analysis and result, and every change made to any entry is written in a separate file; this file is a sequential record corresponding to a single event that will be automatically identified with time, date and user ID to comply with regulatory requirements. All revisions and alterations to the dataset are logged in this file. This can be accessed at regular intervals and a printed report obtained [6, 11]. Maintaining an audit file across a distributed database may be a problem in the full implementation of a LIMS on microcomputers. Further information on general aspects of computer auditing can be obtained in the book by Chambers [25].

#### *Database backup*

Database backup has two aspects for consideration, the first is the routine backup for security purposes in case of disaster and the second is the archival of data that is not required on-line but must be retained for regulatory or historical reasons.

Security backup must be undertaken on a regular basis as the database can often be considered as raw data [23]. If possible this task should be run by the site computer department as they will have the staff and expertise to do this. Backup of large discs used to contain the database can be tedious especially with an 800 or 1600 bytes per inch (bpi) tape drive. The use of 6250 bpi speed helps enormously as the data is compressed into a smaller number of tapes which also aids storage. Furthermore, the use of a transaction log can reduce the number of full backups required, this file records all the changes to the database from which it can be reconstructed in the event of a major problem. In this event the database can be rebuilt by loading the last full backup onto disc followed by successive transaction logs. Transaction logs must not be confused with an audit trail as a transaction log will only record the last change to any record and will not satisfy any regulatory authority guidelines.

Archival and retrieval of data is a specialised job that should be left to the system manager, scientists should be contacted at regular intervals to ascertain if there is any data to be archived. This practice removes unwanted data from the database to prevent it from becoming full of unused material and helps speed up searches. The resulting tapes should be stored separately from routine backup tapes to prevent any confusion.

#### *Maintenance*

Equipment maintenance is an important consideration as the GLP regulations require that all instrumentation used to support pre-clinical studies should be adequately inspected and maintained. Computing equipment is usually covered by a short warranty period of 90 days as it is considered by the vendors that any major component will fail within that time. Therefore, maintenance agreements must be purchased to cover breakdown and preventative maintenance visits. All computer vendors offer this service, the service agreement best suited will depend again on the configuration of your system

and need to restore it to working order. For a laboratory with centralised data processing, i.e. one which acquires data on-line, the need to get the computer functioning again is far greater than is the case with a distributed system.

The hardware agreements are based on a maximum call out time. For the centralised system above a 4 h call out would be justified, this is the time by which the computer company would guarantee a service engineer being present on the site. With respect to the distributed LIMS the call out could be 8 h or the next day. It is the authors' experience that the computer hardware is usually extremely reliable but the major reason for time lost on the system is due to software problems.

#### *Notification of problems*

There should be a coordinated procedure for notification of system problems. In the authors' laboratories, a standard form is available for staff to notify the system manager of any problems with the LIMS (Fig. 1). The form ensures that the problem is documented and this makes it easy to identify faults and remedy them. When any problem is passed to the vendor for solution, there is an additional form which is used to check the problem has been successfully remedied. In this way a complete appraisal documenting the history of the problem is available for inspection.

#### *Security*

The security of the system should also be considered, there are two main types, the class and the hierarchical systems. In the hierarchical system, the users and the software modules are assigned a numerical security value. A user can access any module with a value less than or equal to their own but not any software with higher values. Care must therefore be taken when assigning the security values. In contrast, the class approach is more sophisticated as individual users are only allowed to access specific software modules defined by the system manager. In either case modifications to the security can be made on-line.

Terminals left logged on whilst data acquisition is taking place and the use of direct phone lines are both areas that are open to abuse. With the increasing incidence of computer fraud, more sophisticated procedures are needed to protect computer systems especially via an external line which should be password protected. If the password became known it would become a serious security problem. To overcome this, it is possible for incoming calls to be intercepted and the user's name and password checked. After verification the caller is told to hang up and the unit calls back on a pre-defined telephone number. Thus, to gain unauthorised access to the LIMS the intruder must know the account number, password and break into the premises of the authorised user and use their telephone.

#### *Education of staff*

Initial impressions of a LIMS system are very important as staff may well be daunted by the prospect of using the new technology. Education starts at the writing of the requirements specification and continues throughout the lifetime of the system. It is therefore imperative that the "users" are not exposed to an "unready" system. The authors recommend that the system is not used for general use until it has undergone a validation procedure and the major bugs have been removed. Where necessary, a scheme to avoid problems already encountered should have been devised, pending enhancements to solve the situation.



Software bugs will be found (this is more so in custom than standard software) and sometimes enhancements will be necessary to solve particular problems. However, with a system for notification available these problems can be remedied efficiently.

Like all computer systems, the best way to learn how to use a LIMS is with “hands on experience”. Small rather than large groups of people should be trained, this allows individual tuition if required. The use of a user friendly screen format is essential at this stage. The best person to do LIMS training is the system manager.

Training should take place at an allotted time, not fitted in around the routine work. This is essential as otherwise it places the analytical staff in a position of learning new technology whilst still being expected to produce work on time.

### *Documentation*

As an adjunct to training, documentation for the users which is readable, self-contained and in a standard format must be available. The intention is that it can be referred to when appropriate, be understood and useful. Documentation improves efficiency by allowing users to understand the system with which they are working and to overcome any fears of the LIMS. It should be aimed at the first time user in tutorial format. A useful guide to the writing of computer documentation has recently been published [26].

As the LIMS expands or new software upgrades become available then retraining or updating staff will be necessary. Additionally, the LIMS documentation should also be updated at the same time.

### *User group*

The establishment of a Departmental LIMS user group allows a formal method of channeling feedback from the system manager to the user and vice versa. Decisions affecting the development of the software can be made with the confidence that the users' needs and comments have been taken into account. All users can be informed of potential problems and new procedures can be easily highlighted.

Similar benefits are found with a user group affiliated to one company's product. This is the route to the long term development and enhancement of the LIMS, together with fruitful discussions between users.

### **Benefits of a LIMS**

The revolution in analytical instrumentation promises high productivity providing that the analysts involved are correctly educated and trained [27]. Once this is achieved the benefits of a LIMS can be realised.

There is little in the scientific literature written by users concerning the benefits of LIMS, reflecting that these are early days in the development of this type of laboratory automation. Four articles by users have been published on the applications of LIMS [28–31]. These discuss the installation of LIMS within two laboratories with an overview of the software and a little insight to the benefits. Benefits can be difficult to assess and quantify as each laboratory has its individual requirements. However, generalisations can be made.

Major benefits are realised by laboratories that have successfully installed LIMS systems. These are data storage, ease of data manipulation, and data integrity, which together produce increases in productivity. Each area will be examined in turn.

### *Data storage*

Data storage is the fundamental basis from which all other benefits of LIMS are based. The database facilities searching of on-line analytical data; thus, efficient sample tracking to ascertain the status of a particular analysis is easily accomplished. Additionally, previous results can be searched on-line, this is very useful when compiling year-end figures for a particular project or reporting results [29].

### *Data integrity*

Compliance with regulatory agency guidelines is crucial to the acceptance of studies supporting the registration of a new drug or agrochemical. Here LIMS can be of great value. All changes to the database are monitored by the audit trail which ensures that any modification is recorded. Furthermore, the use of validated programs ensures adherence to any procedures laid down in the relevant SOP. Although the benefits in this area are difficult to quantify, their importance should not be understated. As the majority of scientists appreciate, the checking of analytical data is a very tedious task where mistakes are easily made. The benefit of computerisation will be to avoid transcription checking.

Verification of data entry, using either cross-reference to datasets or via bar codes, is a very powerful method of ensuring data integrity, as well as building confidence in the system and the results produced. Automatic calculations can also be performed to avoid repetitive calculations and transcription errors through manual data entry.

### *Data manipulation*

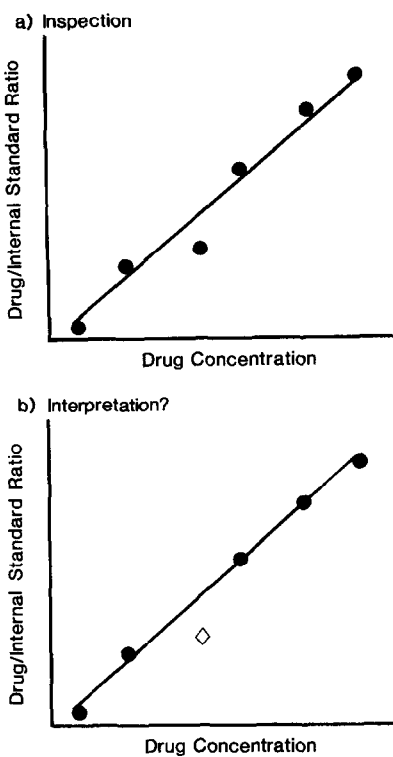
Data manipulation allows the user to transform data into information efficiently and without error. For example automatic calculation, collation and reporting of results are areas where LIMS excels. When using validated computer programs the required information can be extracted from the database and rapidly included in reports.

The acceptance and validation of large numbers of plasma samples from clinical and preclinical studies in drug development can cause long delays before the emergence of the final report. In the authors' laboratories this process was speeded up by plotting each set of subject samples on the screen together with the calibrated curve, if required. Moreover, to aid the process, colour was used to display the data [32] and make interpretation easier.

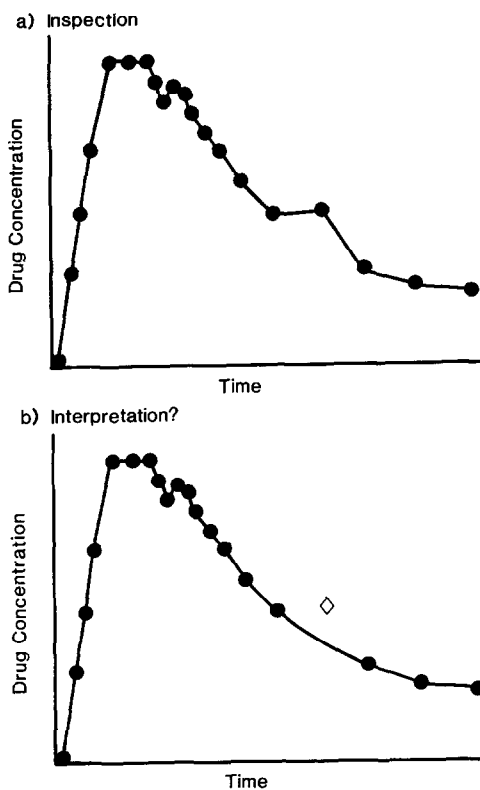
This facility displays the calibrated curve in the form of a graph of the drug/internal standard ratio versus drug concentration with the slope, intercept, correlation coefficient of the line calculated from a regression (Fig. 2a). A prompt asks the analyst if all the points are acceptable, if not a table showing the individual points is displayed and the operator can change the status of any standard to "unacceptable". If this is done, when the graph is next displayed (Fig. 2b) the unacceptable point is shown in a different colour and symbol; note that any points deemed unacceptable cannot be removed from the display and indeed they can be reinstated during this process if required. With each new display the intercept, correlation coefficient etc. are recalculated and shown on the side of the screen. When it is acceptable the calibrated curve is then used to calculate the concentration of drug in the subject samples. The profile of the drug in the subject samples (drug concentration versus time) is then displayed on the screen, shown in Fig. 3a.

Here the analyst can view the profile and accept the results. If, on visual inspection one or more points appear wrong then a table similar to that for the standard samples

**Figure 2**  
Evaluation of standard curves (a) inspection; (b) interpretation?



**Figure 3**  
Evaluation of sample concentration versus time plots (a) inspection; (b) interpretation?





appears. Here the operator can enter not only changes to the volume of the sample, but also change the status of any sample from “acceptable” to either “unacceptable” or “reassay”. A point can be removed from the profile, as shown in Fig. 3b. The concept of this module is to give the computing power of the system to the analyst in an interactive form so that, if required, many combinations of the data can be viewed and evaluated rapidly and the best fit chosen. Again, colour graphics aid and enhance this process.

### *Productivity*

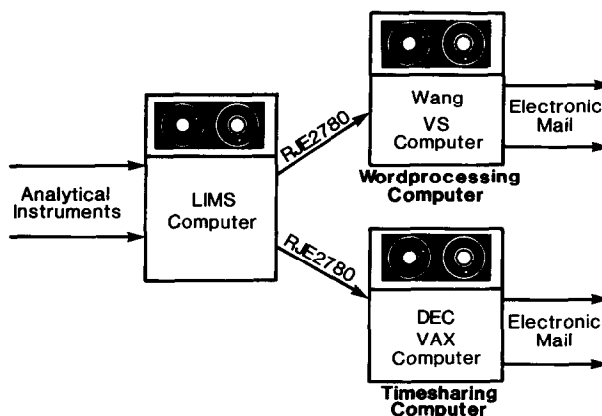
Productivity increases will be dependent on the aims and configuration of the system, however, it is an area where the gains from manipulation, integrity and storage of data are apparent.

No definitive study has been performed to assess the overall benefits of LIMS. Increases in productivity of 10–20% is the average estimate made by most laboratory managers who have installed such systems [33]. A similar figure is given by Golden [13] who assessed the impact of LIMS in both R&D and QC environments. In the former instance, increases in productivity are the main benefit by removing the transcription and checking of data brought about by automatic data capture. This productivity is manifested by the speed at which a product can be perfected and brought to the market place. The rationale for LIMS here is not only the improvement in productivity or in the speed at which specific analyses are completed but lies in the laboratories’ ability to complete entire projects quicker.

LIMS in a QC environment has the ability to quickly accept or reject raw material lots or manufactured goods, thus smaller raw material stocks can be held and finished goods marketed quicker. These are areas of benefit in addition to the increases in productivity.

The use of bar coded labels generated from the authors’ system has saved staff in many departments from writing the labels by hand, enabling us to have uniformly labelled tubes and a speedy method for data entry into the computer.

An aspect of LIMS [34] included the integration of the system with word processing, this can be achieved by installing a word processing package within LIMS. However, in the authors’ laboratory the LIMS had to be integrated with an existing corporate word processing system (Wang), the approach was therefore as shown in Fig. 4. The LIMS can



**Figure 4**  
Data transfer from analytical instruments to corporate computers.

generate reports in predefined formats by writing data files to disc. These files are then transferred to the Wang word processing system by a second program via an IBM communications protocol (RJE 2780) for inclusion into the final report. Once the analytical portion of the final report is within the word processing system it is easily transferred via electronic mail to any part of our organisation. Thus, speed, reliability and the ability to have the results in a suitable format for distribution are prime benefits of a LIMS.

Reporting is much more efficient: the time taken by the old method to prepare the report was about two weeks depending on the workload of the typist. This can now be reduced to a day or less using the LIMS. The time saved allows the analyst to do more productive tasks rather than checking manuscripts for typographical errors.

### **Future developments**

The present commercial LIMS packages are the first generation systems available to the laboratory and as such they are still evolving. However, there is scope for improvement in various areas which will now be considered.

#### *Computer equipment*

Advances with computer hardware will produce faster, physically smaller and relatively less expensive instrumentation. This, will be in contrast to the software which will tend to cost the same or more, reflecting the rise in cost of the human resource required to write it. Fibre optic links available now, will enable faster and more reliable communication over longer distances but at cheaper cost.

#### *Communication*

A major problem with LIMS is the connection to analytical instruments within the laboratory. This manifests itself in the lack of an agreed standards for (i) constructing a local area network with analytical instruments and (ii) transfer of the data to the LIMS. Fulfilment of this requirement would result in a fully integrated data capture LIMS network.

No instrument vendor has offered a complete solution to this problem, nor is any mandated to at present [35]. Introduction of a universal neutral data format [34, 36], and a range of analytical instruments that utilise it, or the ability of instruments from different vendors to be truly compatible (both at the hardware and software levels) is essential. Such standards will become a high priority among instrument vendors only when buyers demand them [36]. In the authors' opinion, what is required is the ability to plug any manufacturer's equipment into a LIMS with the certain knowledge that data transferred between the two can be accessed immediately and manipulated.

#### *Control of instrumentation*

Effective networking in the laboratory will see the emergence of the electronic laboratory [34] where from one terminal the analyst will be able to control instruments, write reports with a word processor, access various databases for information and reporting experimental results (processing power will still be distributed as the networking will make the individual components of the network invisible to the user).

Analytical instrument vendors are already offering robotics systems that have the ability to be controlled by LIMS computers. The collection of analytical data from such

systems is a valid consideration in designing a LIMS, however, the control should be local to enable the database to function effectively. This is temporary expedient for the present, but effective networking will enable robots and other intelligent instruments to be controlled from a terminal rather than the LIMS.

#### *Management functions: the expert system*

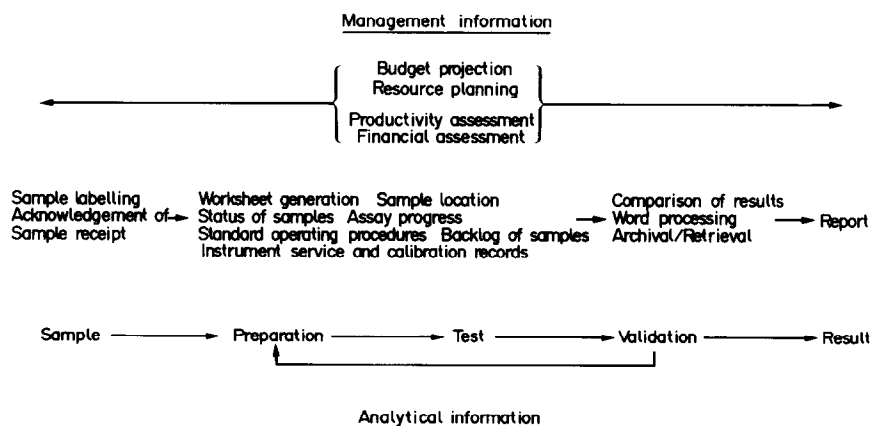
The future development will continue to see the LIMS as the central hub of the laboratory, developing as seen by Braithwaite [4] into an expert system able to help make decisions based on the current status of the laboratory. Managers would be able to plan effectively by interrogating the LIMS, what if a new project were to be added to the workload, what would be the effect within the Department?

The present LIMS are able to undertake retrospective searches and manipulate data effectively, however, prospective evaluation is almost non-existent. The question posed above is the very question the present systems cannot answer. They function very well at the analytical and lower managerial levels of information (Fig. 5), but extensive development is essential before the information contained in the highest management levels can be effectively accessed and utilised.

At present it is possible to search the database and pass the resultant file to a microcomputer for further processing by a spreadsheet program such as Lotus 1, 2, 3 [37]. This involves the purchase of a PC when an expensive LIMS has already been installed, but may be the only practical means of gaining some limited higher management information.

#### *Voice input*

Voice input will be a better method of data entry, especially when working in wet areas, with hazardous or biological samples. Instead of using a keyboard the chemist would enter data by speaking to the computer. The technical details of the process are presented elsewhere [38], but a practical illustration of the technique is the use of voice recognition devices to record the results of microscopic analysis of rat urine [32]. Here, the efficiency of reporting the results was improved by 80% even though the detected error rate by the new method was as high as 5% (compared with the manual rate of 1%).



**Figure 5**  
Information flows within the laboratory.

It was found that the voice entry error was more blatant (lee instead of three) and therefore easier to spot and rectify when compared to a typographical error.

### *And finally?*

A full electronic laboratory, where all data including the scientists notebooks are stored on once-write laser discs will be available in the near future — the question is how will it be accepted? And is it desirable?

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