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Laboratory Information Management Systems in Practice*

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Abstract: To maximize the benefits of a LIMS, the system must be integrated with the analytical instrumentation in the laboratory. This provides on-line data capture or transfer of results for matching with the corresponding sample records held within the database, which reduces transcription error checking and ensures data integrity. Furthermore, the LIMS must be integrated with existing corporate systems to ensure efficient use of resources and to avoid the development of parallel systems.

Keywords: *Laboratory Information Management Systems; LIMS; automated analysis; laboratory automation.*

Introduction

The analytical laboratory has been under pressure to improve efficiency for some years in order to cope with increasing workloads and to contain costs. The solution for many organizations has been laboratory automation. This enables the laboratory to keep pace with the workload and ensures the achievement of good precision and accuracy of analytical procedures at a realistic cost. Automation also frees the scientist to monitor the analysis and its interpretation and develop further automation, rather than carry out mundane tasks such as checking for transcription errors.

Automation in the form of auto-injectors for chromatographs, integrators for calculating the areas of peaks, and computers for the control of equipment are readily available. However, this equipment is concerned with handling the sample or control of the analysis rather than administration of the sample or the laboratory which until recently has been slow and tedious. There are now emerging the tools to drastically reduce this paperwork whilst ensuring data integrity. These are Laboratory Information Management Systems, known as LIMS.

A LIMS is essentially a database that is tailored to a laboratory's organization and working practices. Within the database all the information pertinent to that laboratory is stored; this can range from the types and source of the samples submitted and the tests to be performed, which are common to many laboratories, to the unique requirements for a

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single organization. The main function of a LIMS is to integrate the information from samples with the results from the instruments processing the samples. A LIMS is intended to be flexible in that it can be customized or tailored to an individual laboratory's needs. Further background information can be obtained from reviews [1–4].

The integration of a LIMS into a laboratory

The key to the success of a LIMS is integration, since a system should not exist in isolation. Specifically, a LIMS should integrate in three key areas: laboratory automation, word processing and corporate computing. Failure to achieve this will result in the development of separate and duplicated facilities [5].

Integration of laboratory equipment and automated systems is achieved firstly by transferring results from the equipment electronically via serial data lines to the LIMS. This eliminates transcription error checking and is faster and more efficient than entering results at a terminal. Once results have been entered, they are matched with the corresponding sample information and are available immediately for review and reporting.

The second area is that of word processing. Once results are available they should be passed to a word processing package to produce a final report. This package can run on the same computer as the LIMS or it can be a separate system; regardless of which approach is taken there must be a means of transferring the information or report files from the LIMS to the WP package.

The final area for integration is with existing computer systems within an organization since results from an analytical laboratory often undergo further interpretation or statistical analysis. If a LIMS is introduced into a laboratory without the means of electronic communication to the existing computers and software packages which undertake this function, it will not be used efficiently. As will be shown later, these computer systems need not be on the same site as the LIMS.

Support requirements for a LIMS

The support needs of a computer system, such as a LIMS, are not always realized by the scientists involved in the project nor their senior management. To ensure efficient operation, a system manager (and possibly a deputy) is essential [7, 8]. This person will be involved in validating the system, documenting its operation, training the users, and troubleshooting any problems once the computer is operational. The post is a key factor in the success of any LIMS installation and once established together with the availability of all other support needs, the benefits of a LIMS can be realized.

Benefits of a LIMS

The benefits provided by a LIMS [3, 9] can be defined as: data storage; data integrity; data manipulation; productivity. Each of these areas will be examined in turn.

Data storage

Data storage is the fundamental basis from which all other benefits of LIMS are derived. The logical relationship between the stored data makes it relatively easy to search the database for results or information that would be impossible or very tedious to

find with a manual system. When data are stored within a computer system they are available to many more users than when a comparable manual procedure is in use. Collation and reporting of results are areas where a LIMS excels, the required information can be extracted from the database and rapidly included in reports. The user does not need to wait for a secretary to type the report, but can insert the required field in a series of menus for the search routine in the report writer and the information is retrieved rapidly from the database. Limits can be set on the results for particular assays and the system programmed to highlight spurious results for the attention of an analyst to verify or retest.

Data integrity

The integrity of data is fundamental to any scientific discipline, but this need is often reinforced by regulatory agency guidelines. Verification of data entry by using references within the database is a very powerful, yet simple method of ensuring data integrity. This facility should be used at every opportunity as the data or entries can be rigorously checked and this builds confidence in the system and the results produced. The integrity benefits of a LIMS are at their greatest with regard to the reduction of both errors and transcription error checking. Sample information is stored within the database and automatically updated by the software modules that access it; results can be transferred to the database from analytical instruments and incorporated in the records for the appropriate sample. This automatic transfer means that little transcription checking needs to be done if the programs have been validated and a final report concerning any sample will be a true representation of the data and any calculations performed within the database.

Where results have been typed into the computer, then there is no alternative to checking all results manually before issuing the report in order to avoid errors entered during typing. Thus, the best performance of a LIMS occurs when it is directly linked to analytical instruments for automatic transfer of results.

Data manipulation

Data manipulation allows the user to transform or reduce data efficiently and without error. This can take two main forms: automatic calculation and graphical manipulation.

Automatic calculation of data and results has been shown to be a feature of data integrity benefits. Data can be transformed or manipulated easily and speedily, without human intervention and without error by the system. A LIMS should therefore be designed to take advantage of this benefit whenever possible. An instance of the use of automatic calculations is the on-line capture of chromatographic data which can be reduced, interpreted, and passed to a LIMS database automatically.

If required, the data can also be presented graphically in a number of ways to show the reproducibility of chromatography, integration and interpretation. An example in our laboratories is where the time versus drug concentration profiles from subjects who have ingested a drug are displayed graphically. Here, the analyst can enlarge any portion of the display to investigate the absorption phase or, via a log/linear plot, the elimination phase of the profile [10].

Productivity

The productivity increases attributable to a LIMS are simply the sum of the data storage, integrity and manipulation benefits. This will be shown in many areas depending

on how the LIMS has been designed; the major realizations will be time saving and the faster reporting of results as shown below.

LIMS in practice

In this section it will be demonstrated how the four benefit and areas of a LIMS are realized in a bioanalytical laboratory of a major pharmaceutical corporation, where a well-designed LIMS integrates laboratory automation, word processing and corporate computing.

Before a study takes place, the expected samples are entered into the system and labels are produced for the submitter to use on the sample tubes. On these labels are printed unique laboratory numbers together with a bar code generated by the LIMS.

When the in-line phase of the study has been completed, the samples are received in the laboratory and are logged into the computer via the bar coded labels. Where the actual sample details differ from those anticipated there is provision to alter them at this stage. At the end of this process an acknowledgement of receipt form is printed by the computer for the customer.

Samples are then prepared for analysis in batches and for this purpose a worksheet is printed by the LIMS for the analyst to use in the laboratory. As mentioned earlier, the greatest benefits of a LIMS are obtained when instruments are interfaced to the system allowing direct transfer of results to the database. Figure 1 shows a fully automated sample preparation unit coupled to an HPLC chromatograph with an AASP (Analytichem Automated Sample Processor) LC module [11–13]. The sample preparation is automated with a Gilson 222 autosampler which transfers the sample and the various solvents to activate and wash the solid phase cartridge in the AASP. This allows the analyst to present centrifuged plasma samples to the instrument in the same order as on

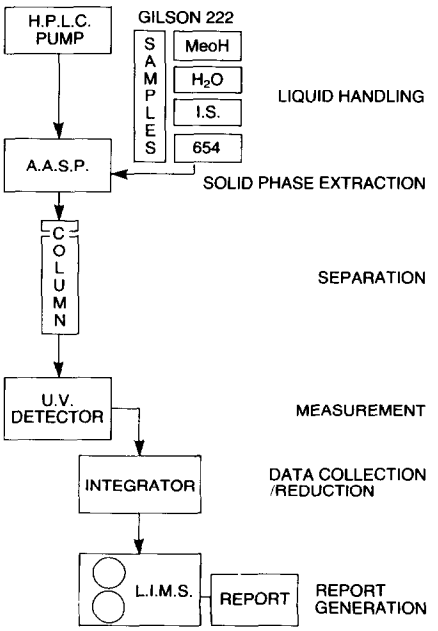

Figure 1
The integration of laboratory automation (sample preparation and HPLC) with a LIMS for data processing.

the worksheet; the addition of internal standard and the preparation of the standard curve is carried out automatically by the combined sample preparation/chromatography unit.

The detector output of the chromatograph is fed into an integrator that has the facility to store raw data on floppy disk. The laboratory numbers for the samples to be assayed are entered into the integrator from the worksheet. This allows the LIMS sample number to be appended to the appropriate chromatographic run. When all the samples have been assayed, the chromatography is checked for quality and any samples can be re-injected if necessary. If peaks are wrongly identified by the integrator, re-injection or re-integration is not required as the LIMS is used to interpret the integrator report.

When the analyst is satisfied that the chromatography is acceptable, the results, but not the raw data, are transferred to the LIMS for further calculation. The analyst reviews each integrator report on the screen, checking that the peaks have been correctly identified and correcting where necessary.

Electronic transfer of results means that the peak height measurements do not have to be checked for transcription errors, likewise the calculation of drug/internal ratios can be used in confidence as these programs have been validated [13–14] by the system manager. A standard curve that has been interpreted previously and stored in the LIMS, or one that has been carried through the procedure with the sample is used to calculate the analyte concentration. This is carried out automatically and the results are entered into the database; after validation of the results, an interim report can be issued by printing the results locally.

Pharmacokinetic analysis and detailed graphical display of the results are achieved by transferring the results file to VAX computers with RS/E, these computers are located in either SK&F Research facilities in Welwyn (U.K.) or Philadelphia (U.S.A.).

For a final report, the results file is transferred to a Wang word processing computer, and once within this system distribution within the SK&F organization worldwide is simple. The Mailway facility enables the report to be distributed to the customer, either locally or overseas.

A comparison of the time taken to perform the tasks for 300 samples by the LIMS, compared with the partially computerized system that it replaced is shown in Table 1. The old methods involved the use of a series of computer programs which undertook particular portions of the study, e.g. receipt of samples, printing worksheets etc. However, there was little integration between the programs and as the system was developed on an *ad hoc* basis, often the output from one program was re-entered into the computer for further manipulation. It can be seen that this was an inefficient method and required much transcription error checking before a report was issued.

Table 1 shows that for the LIMS sample administration includes a slight overhead to enter the study into the system, but this is easily offset by time saved in labelling the specimen tubes and logging the samples into the LIMS. During analysis of the samples there is no difference in time between the two systems; LIMS has no effect on the actual analytical procedures within the laboratory.

In contrast, the benefits of a LIMS begin to become more pronounced with the calculation of the results. Automatic transfer of analytical data from the instruments to the database eliminates numerical transcription error checking and is faster than abstracting the data from metres of chart paper and typing it into the old program to calculate sample concentration. The burden of work for the analyst using a LIMS moves from detailed checking to interpretation of the report which is faster and easier.

Table 1
The evaluation of LIMS productivity

Task	Time taken Old method	LIMS
Sample administration		
1. Define protocol	NA	0.5 h
2. Label tubes	4.0 h	2.0 h
3. Sample log-in	2.0 h	2.0 h
Analysis		
4. Print worksheets	0.5 h	0.5 h
5. Analysis of samples	5 D	5 D
Calculation of results		
6. Interpretation of chromatograms	4.0 h	1.0 h
7. Transfer of peak area ratio to computer	4.0 h	1.5 h
8. Interpretation and calculation	NA	2.0 h
9. Transcription checking	8.0 h	NA
Report results		
10. Preparation of analytical report	2.0 D	2.0 h
11. Typing manuscript	2–10 D	NA
12. Transfer to word processing system	NA	1.0 h
13. Transcription checking	1–2 D	0.5 h

NA = Not applicable.
Assumes 7 h working day.

The benefits of reporting the results from the LIMS are even more conclusive. As outlined earlier the task is under the control of the analyst who fills in menus in the system. Transfer to the word processor (Wang VS 100) is effected by another program under the control of the analyst. In the preparation of the report by the LIMS, the analyst does not need to wait for a third party and there is no competition for secretarial resources.

Conclusions

The clear advantages of a LIMS outlined in this paper must be tempered by the planning, hard work and support that must be undertaken to achieve them. It is not a simple task to be accomplished on the whim of management or the users, but must satisfy a perceived need to improve the efficiency of a laboratory.

References

[1] R. E. Dessy, *Analyt. Chem.* **55**, 70A–79A (1983).
[2] R. D. McDowall, J. C. Pearce and G. S. Murkitt, *J. Pharm. Biomed. Anal.* **6**, 339–359 (1988).
[3] R. D. McDowall, J. C. Pearce and G. S. Murkitt, *J. Pharm. Biomed. Anal.* **6**, 361–381 (1988).
[4] R. D. McDowall, in *Laboratory Information Management Systems, Concepts, Integration and Implementation* (R. D. McDowall, Ed.), pp. 1–16. Sigma Press, Wilmslow (1987).
[5] R. E. Dessy, *Analyt. Chem.* **56**, 725A–731A (1984).
[6] F. W. McLafferty, *Science* **226**, 251–253 (1984).
[7] R. D. McDowall, J. C. Pearce and G. S. Murkitt, in *Chemometrics and Intelligent Laboratory Systems.* (in press).
[8] G. S. Murkitt, in *Laboratory Information Management Systems, Concepts, Integration and Implementation* (R. D. McDowall, Ed.), pp. 57–66. Sigma Press, Wilmslow (1987).

[9] R. D. McDowall, in *Laboratory Information Management Systems, Concepts, Integration and Implementation* (R. D. McDowall, Ed.), pp. 49–68. Sigma Press, Wilmslow (1987).
[10] R. D. McDowall, *Chem. Brit.* **23**, 1079–1082 (1987).
[11] G. S. Murkitt, J. C. Pearce and R. D. McDowall, *Chromatographia*. (in press).
[12] R. D. McDowall and J. C. Pearce, in *Proceedings of the International Conference on Analytical Methods in*
the Pharmaceutical, Biomedical and Forensic Sciences (G. Piemonte *et al.*, Eds). Plenum Press, New York. (in press).
[13] R. D. McDowall, J. C. Pearce and G. S. Murkitt, *J. Pharm. Biomed. Anal.* **4**, 3–21 (1986).
[14] A. Hampshire, in *Laboratory Information Management Systems, Concepts, Integration and Implementation* (R. D. McDowall, Ed.), pp. 320–331. Sigma Press, Wilmslow (1987).

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