IMPROVING PRODUCTIVITY IN AN ANALYTIAL ENVIRONMENT: IMPLEMENTATION OF A LIMS

S N WALFORD

Sugar Milling Research Institute, University of Natal, Durban, 4041. South Africa
E-mail: swalford@smri.org

Abstract

Increasing demands have been made on the Analytical and Consulting services provided by the SMRI to the industry, leading to an internal drive to improve productivity, particularly with respect to paperwork. Central to this has been the installation, configuring, customisation and implementation of an Oracle based Laboratory Information Management System (LIMS). LabSystems "SampleManager" has been configured to incorporate analytical data calculation and storage, checking of validity of results, report generation, subsequent billing and management costing reports. ISO 17025 laboratory accreditation has been incorporated by inclusion of SQC control charts and audit functions.

Keywords: LIMS, Laboratory Information Management System, Analytical Productivity

Introduction

As the global sugar industry has focused on improving productivity and reducing costs, similar demands have been made on the SMRI. One consequence was the ISO 025 laboratory accreditation, achieved in 1998, recognizing the competency of the Institute as a testing laboratory. Subsequently, increasing demands have been made on the analytical services provided to the Industry. This led to an internal review to improve productivity. A review of our accreditation procedures, showed that an inordinate amount of time was spent entering raw data into calculation spreadsheets, re-entering the calculated results into analysis reports, certificates of analysis and other associated documents. This is followed by manual calculation of the charges due and subsequent manual generation of invoices. At each stage of this process rechecking and signing-off of the data is required to minimise possible errors. Furthermore, no central repository of these results exists, making "data-mining" for possible industry-wide trends a time consuming procedure. Further demands will be made on the Institute's Accreditation staff as the ISO 025 accreditation is replaced with the ISO 17025 system during the coming year.

A proposal to investigate the possibility of installing a Laboratory Information Management System (LIMS) at the Institute to address these issues was made in September 2000 (Walford, 2000). Discussions were held with LIMS vendors between October 2000 and January 2001. Approval to purchase and install a system was given in April 2001. This paper reviews the existing manual system at the SMRI, the overall structure and benefits of a LIMS. It describes the installation and subsequent configuring, customisation and implementation of the SMRI LIMS.

Review

The existing manual system
Both external and internal sources of samples exist at the SMRI (Figure 1). The dotted lines show the source and direction of samples for normal analyses.

Internal samples. These are samples generated within the SMRI. The Processing Division can provide samples for both the Analytical and Chemical Divisions from either internal (research work) or external (factory contract research) sources. Both the Analytical and Chemical Divisions can provide samples for each other both internally (research work).

External samples. These are samples from outside the SMRI and include routine mill and ad hoc samples from both members and non-members. Routine mill samples include both weekly and monthly samples.

Sugar Milling Research Institute
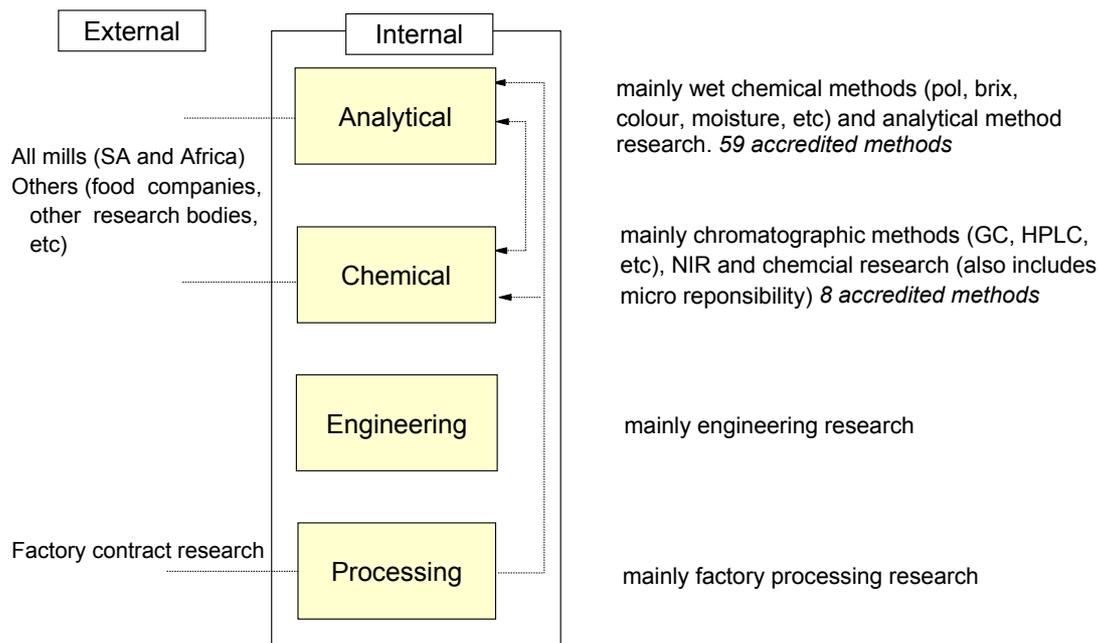### DIvisions and sources of samples

Figure 1. SMRI divisions and flow diagram of sample sources.

The workflows associated with these samples are depicted in Figures 2 and 3 and described below.

Routine weekly or monthly samples. The routine samples constitute a large percentage of all sample analysed. Sample types include raw and refined sugars, mixed juice and molasses. Samples arrive, are manually logged in and an analysis request form completed. They are sub-sampled as necessary and given to each division where the samples are analysed as required.

Divisional processes. In the Chemical Division, after sample preparation and analysis, the chromatographic raw data is entered into spreadsheets via macros and a result sheet generated. This is checked and the data manually transcribed into the existing Paradox database and the Chemical Division Analysis book. In the Analytical Division the samples are analysed, raw data entered into spreadsheets and the results printed and pasted into the analysts book. These are manually transcribed into the Analytical Sample book from where necessary results are again transcribed into the Paradox database or a Corel QuatroPro spreadsheet. The Microbiology Division follows a similar procedure other than results are consolidated with the Analytical Division's. A series of Analytical Report's or Certificates of Analysis (COA's) are manually typed, checked by the analyst and sent for checking and signing by the Divisional Head / Assistant Director. Any errors found require a correction of the report and rechecking. From these reports a series of manually generated invoices are prepared which also require checking for possible errors.
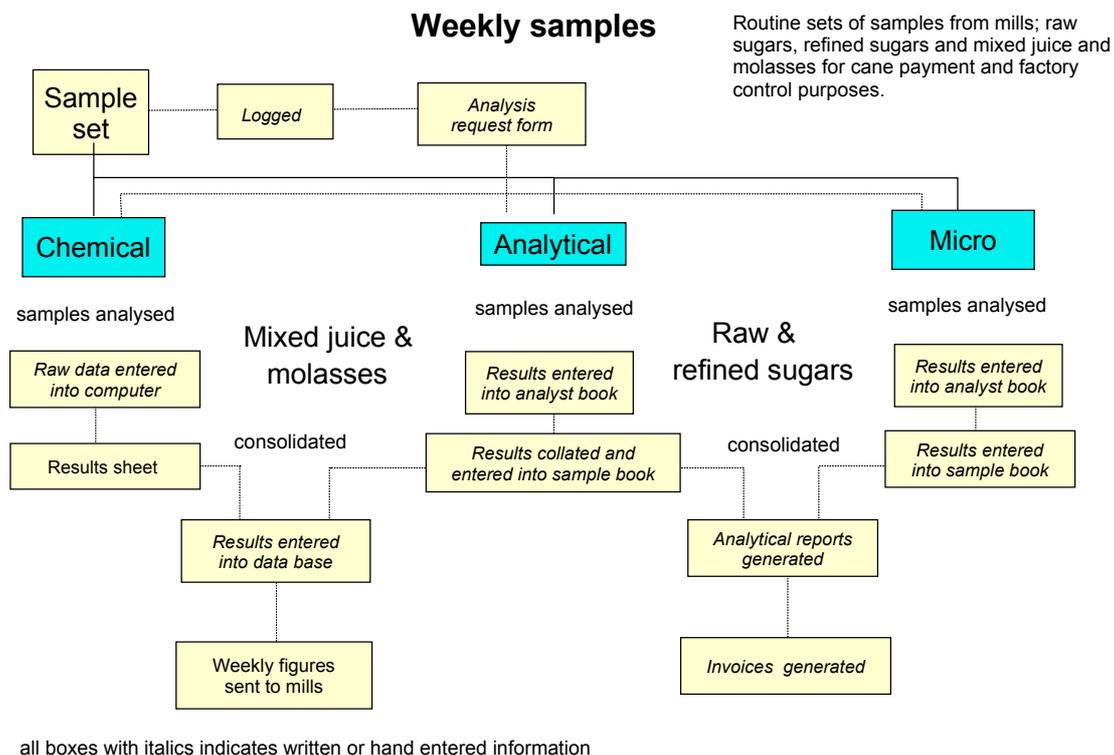
Weekly samples

Routine sets of samples from mills; raw sugars, refined sugars and mixed juice and molasses for cane payment and factory control purposes.

Sample set — Logged — Analysis request form

Chemical — Analytical — Micro

samples analysed

Mixed juice & molasses

Raw data entered into computer → Results sheet

consolidated

Results entered into analyst book

Results collated and entered into sample book

Raw & refined sugars

consolidated

Results entered into analyst book

Results entered into sample book

samples analysed

Results entered into data base

Analytical reports generated

Weekly figures sent to mills

Invoices generated

all boxes with italics indicates written or hand entered information

Figure 2. SMRI work flow sheet: manual procedure for weekly MJ and molasses samples

Ad hoc samples. These are non-routine and include sets of samples from the mills, contract work, external customers, etc. A similar workflow scheme is followed for these samples. The major difference is that each sample (other than Processing) requires consolidation (if necessary) and the generation of an Analytical Report and Invoice. This is checked (by all Divisions if necessary) and signed off. Processing samples are photocopied directly from the Analysis book which are then entered manually into their own spreadsheets.
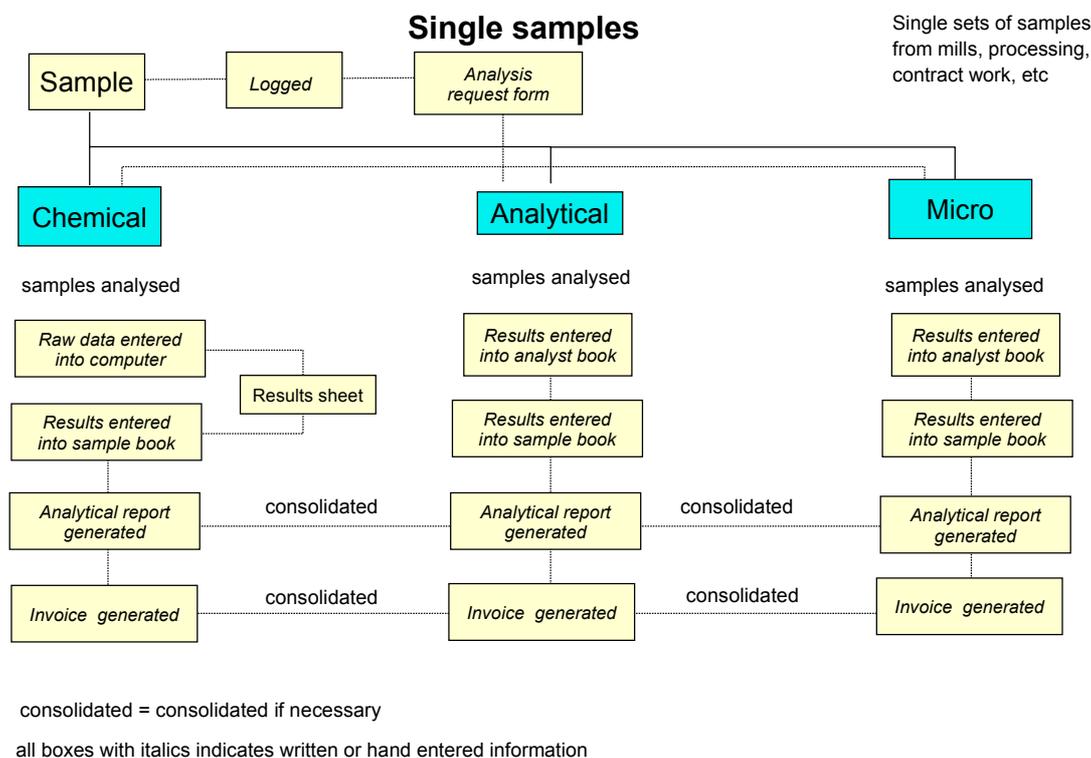
Single samples

Single sets of samples from mills, processing, contract work, etc

Sample — Logged — Analysis request form

Chemical — Analytical — Micro

samples analysed

Raw data entered into computer

Results entered into sample book

Results sheet

Analytical report generated

consolidated

Results entered into analyst book

Results entered into sample book

Analytical report generated

consolidated

Results entered into analyst book

Results entered into sample book

Analytical report generated

Invoice generated

consolidated

Invoice generated

consolidated

Invoice generated

consolidated = consolidated if necessary

all boxes with italics indicates written or hand entered information

Figure 3. SMRI work flow sheet: manual procedure for single samples.

From a study of these flow sheets, it is apparent that an inordinate amount of time is spent either logging samples on arrival or transcribing data into books, reports or invoices and subsequent checking. A cursory examination has shown this to occupy at least half a day of analyst's time. Repetitive and manual entry can result in transcription errors on both reports and invoices leading to a decrease in productivity.

LIMS – an overview

Laboratory Information Systems are applications used to track, manage and report the information used and generated in the laboratory. In a general sense, the term LIMS can refer to a paper based system for maintaining data; however, it is generally used to describe a computer based system. It is a database containing numbers, dates, names, sample and client information organised in a way that lets users extract specific information and compile reports. Since a LIMS cannot produce an arbitrary ad hoc report from a random selection of data, reporting tools are included allowing users to retrieve and review data and generate COA's or Analysis Reports. Commercial LIMS are based on widely available database management software such as Oracle. Since this software cannot be easily used, the LIMS vendor creates interfaces for entering data and generating reports.

This information associated with LIMS includes:
- logging of samples (where they were taken, what kind of sample, any batch or lot number association)
- the tests assigned to the sample (and possibly to whom the test should be assigned)
- tracking the samples through the laboratory and determining their status
- the original data for the test and who entered them
- product specifications (for generation of Certificates of Analysis (COA) or product grading).

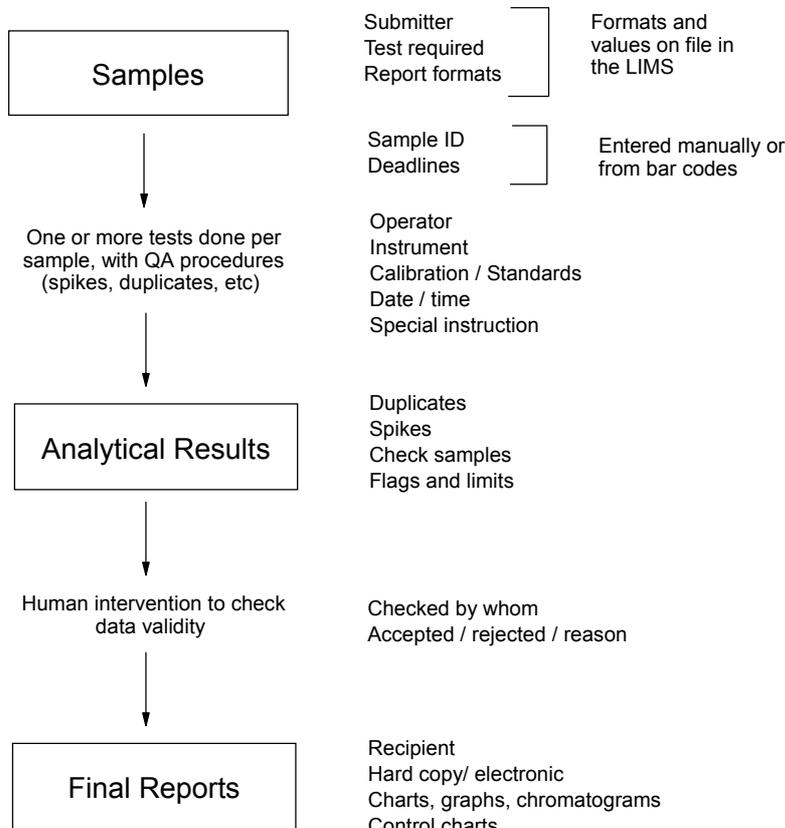Figure 4 shows an example of LIMS data with a typical sample flow.

Figure 4. Example of LIMS data with a typical sample flow.

LIMS – the architecture
LIMS is a combination of hardware and software used to manage the data. The heart of the system is the database (DB), which generally falls into one of three categories:

- Proprietary DB engines. From a software standpoint this type of DB is to be avoided since only the vendor knows the DB structure and the user is dependent on them for continued support.
- PC based DB engines. This second category includes Indexed Sequential Access Method (ISAM) DB engines such as Microsoft Access, Paradox, Dbase and FoxPro. Advantages include ease of configuration and administration, their ability to utilise Windows and being relatively inexpensive.
- UNIX or Windows NT/2000 server based DB engines. The third category uses Open DataBase Connnectivity (ODBC) compliant Structured Query Language (SQL) databases such as Microsoft SQLServer, Oracle and Informix. Scalability of database size, security and their design for multiple users and many transactions are their main advantage. The major disadvantages are that they typically require a Database Administrator and are expensive.

The software application consists of three components or tiers:

- the technology component that handles the presentation and interfacing with the network
- the business-rules component which determines the behaviour of the application in response to different situations
- the database, which is used as the repository.

All three tiers can be packaged together as an inseparable program known as a single-tier application. An example would be an Access based application that runs on a single computer. File server networks allow the separation of the database component from the technology and business rules components. This is known as a two-tier application – the database residing on the server and communicating with the compiled tier (technology and business rules) resident on the workstation, known as file server databases. The part of the application placed on the server is known as the "back-end" whilst the part placed on the client is called the "front-end".

A three-tier application has each component completely separate from a programming/accessibility aspect. This allows the business rules or presentation to change without impacting the data. All three tiers reside on the server with the front-end being loaded onto the client as required. This is a true client/server database with a single server based database engine to perform all database reads and writes. Data is stored in high performance systems such as SQL Server or Oracle which can handle higher volumes of data at much higher speeds than two-tier applications.

All three categories of LIMS require configuring and possibly, customising. When configuring a LIMS the behavior and appearance of the system is controlled without modification of the source code. This is sometimes called "mapping" your existing manual system onto the software package. This will include additional, useful report features with the ability to generate costings, invoice generation based on method costs and operator charge out rates, work lists based on operators and analytical procedures and provision of an audit trail for the entered data and methods (useful in an accredited environment). Customising a LIMS alters the system's behavior and appearance by modifying the source code. The ease with which this can be done decreases with increasing complexity of the system. Thus a Microsoft Access database LIMS can often be both configured and customised by the owner using Visual Basic.

A three-tier application using Oracle will use propriety programme for interfacing between the database and user. A user-interface is added that will only allow configuration changes (e.g. what screens may be accessed by operators versus administrators). Customisation for a specific

application is normally undertaken by the supplier (at extra cost). Most three-tier applications include some high-level programming language that allows routines to be written by the customer for calculations, basic reports or for importing data in the correct form for use in the LIMS (in the Sample Manager LIMS this is known as VGL). Because of these programming constraints, reporting is accomplished using third-party software, such as Crystal Report and InfoMaker which interfaces directly with the database.

Most three-tier, client/server LIMS are designed with extended functionality that can be added for enterprise-wide integration. For example, for the pharmaceutical industry, stability testing functions can be added. SAP3 interfaces can be added for plant level quality management systems and AspenTech plant control interfaces for factory control.

The client/server hardware system requires a Windows NT or UNIX server system to run the Oracle/Windows SQL Server database. Typical configurations of the file server and client server systems are shown in Figure 5.
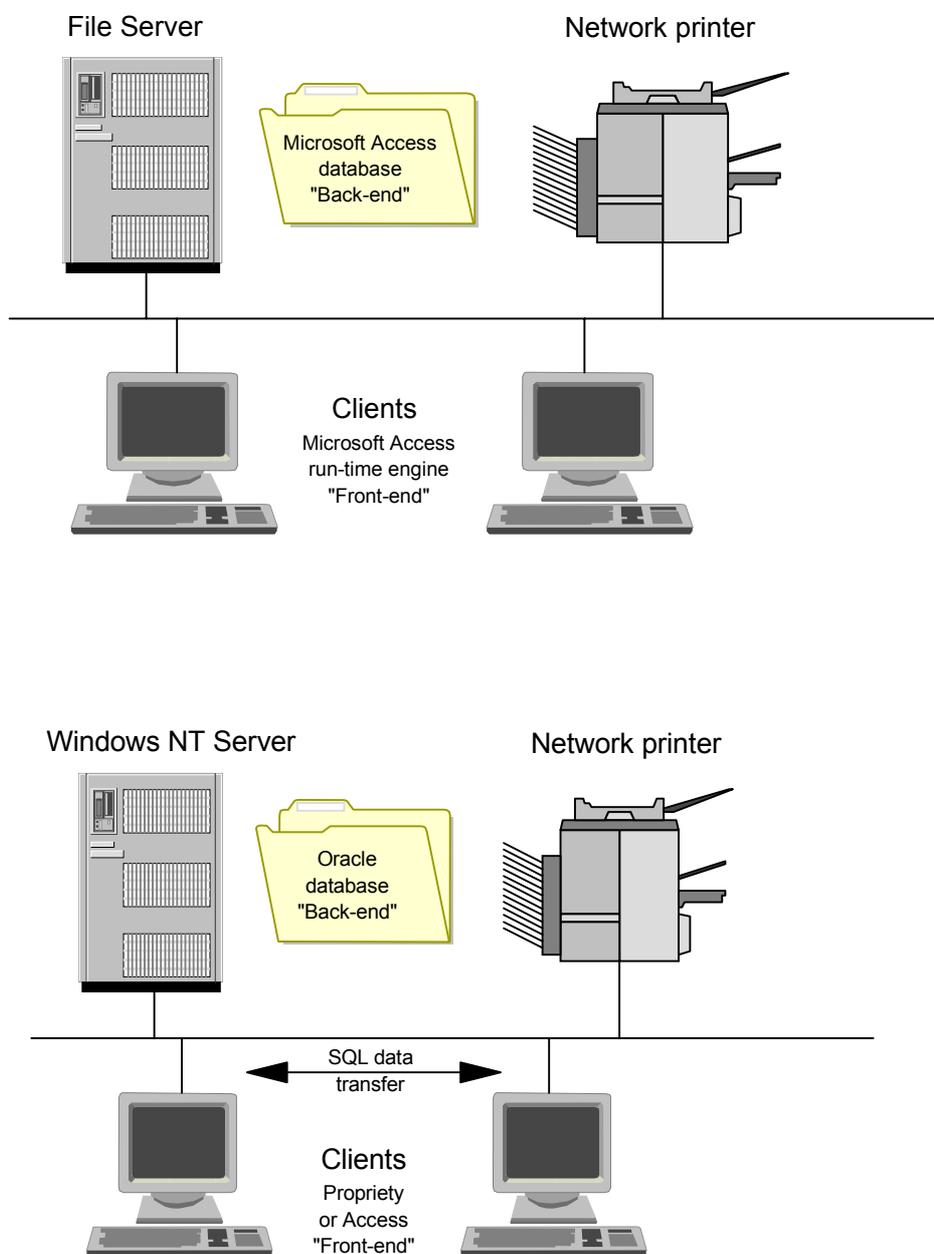

Figure 5. File server (top) and Windows NT server (lower) configurations.

LIMS – the benefits and disadvantages

The benefits that can accrue to a laboratory when using a LIMS include:

- less result entry error
- increased productivity
- better cost control
- faster turnaround time.

Disadvantages include:

- software costs are only a fraction of the expense in installing LIMS
- the need for a LIMS "champion" in the organization
- some form of information technology support
- only structured reports are allowed.

LIMS implementation

Implementation of the LIMS at the SMRI was carried out in the following order:

- Definition of the laboratory dataflow (already described)
- Installation followed by validation of the hardware and operating system software
- Installation followed by validation of the standard LIMS software
- LIMS software configuration (mapping)
- Validation of the total package
- Training.

Installation

The Sample Manager Server and Oracle 8i Enterprise Edition Software were loaded onto a Compaq ML350T (P1000 processor) with 256M RAM, 54 GB disk space and Windows 2000 Server Software. Three instances of the Oracle DB were loaded – one for Training and one each for Development and Production. The training and production instances are kept as identical copies, whilst changes to the system can be tried in the development system with no fear of corruption of the production instance. Sample Manager for Windows (SMW) is installed on client machines as required. A TCP protocol is used for communication between the server and clients. A maximum of five concurrent users, per instance, can be connected simultaneously.

The ISO 17025 standard details the general requirements for the competence of testing and calibration laboratories if they wish to demonstrate that they operate a quality system. These are that the laboratory is technically competent and is able to generate technically valid results. It also requires validation of process in order to achieve and maintain compliance with the standard. Validation is the confirmation by examination and the provision of effective evidence that the particular requirements for a specific intended use are fulfilled. This means that the system does what it is expected it to do and there are documents to prove it. For LIMS, initial validation was performed in two steps using documented, predefined tests supplied by the software supplier to check that installation and operation of the standard software was correct:

- installation testing (installation qualification - IQ) - performed when the system was installed to ensure the correct installation procedures were followed
- operation testing (operational qualification - OQ) - using standard test cases and the standard configuration to give a defined set of results.

Software configuration

Configuring means modifying the operation of the software to meet the requirements of the application, in this case the SMRI laboratory installation. The following items were configured:

- *System Configuration* – each user logging into SampleManager picks up a range of defined configuration items, including which group the user belongs to, which menus they have access to and the role that they have been assigned. For example, an analyst in the Analytical division will not be able to see information pertaining specifically to the Chemical Division.
- *Menus* – separate menus have been created for individuals or groups of users. It is important that users only see options that are relevant to their daily operations and roles, e.g. an analyst will not see the same menu functions granted to a manager who has authorisation rights. Menu items have been added that give access to specific SMRI reports.
- *User Defined Tables* – the definitions of the Oracle database tables can be altered. This can add to or modify the systems' capabilities. For example, a Pol Flask table has been added that stores the SMRI Pol flask identification codes and volume correction factors. The Pol test requires the user to enter the Pol Flask identifier and the relevant correction factor is used in the calculation.
- *Laboratory Table Editor* – this is used in conjunction with the User Defined Tables to set up maintenance screens that allow table entries for new or modified tables to be maintained.
- *Browse facility* – to display database information appropriate to groups of users.
- *Master Templates* – these define which fields are available for inclusion in sample, batch and job templates and consequently for sample login and job creation. They control how each field is used during login by defining settings for information control flags and default data values e.g. for the weekly MJ sample login, a default customer and sample template is used.
- *Sample Login* – templates were created and configured to match the type of samples entering the laboratory, e.g. mixed juice samples, molasses samples, raw and white sugar samples. Unique login names are automatically assigned at login by the login template to make identification easy. Code for the syntax generation was programmed for combinations of sample types, mill names, SASA week numbers, dates, etc.
- *Result Entry* – screens were created to allow logical entry of interactive data. Rules were added as required to ensure results cannot be entered in the wrong sequence, e.g. before a mixed juice pol can be calculated from the saccharimeter readings, a valid brix reading must be entered. The SampleManager LIMS include a high-level programming language (VGL) that allows routines to written for more complex calculations, basic reports or for importing data in the correct form for use in LIMS. Figure 7 shows a sample brix calculation using this language. Most results are entered via a Batch template screen which allows samples which have the same test assigned to be grouped together (see later). The Total number of analyses entered in the system is 183 and 246 calculations have been programmed.
- *Product Checking* – SampleManager has the facility to check results against a Multi Level Product Specification (MLP Spec) containing one or more sets of limits for each component tested. The MLP Spec is used at the SMRI to generate the white and raw sugar Certificate of Analysis specifications. A different MLP Spec is used to check and flag out of specification controls.

A decision was made early in the configuration stage that invoicing would be an integral part of the LIMS. The critical structure to implement this was the use of job templates. Samples would be logged in using a job template and result reports, COAs and invoices would be generated from the authorised job. This required the addition of an analysis charge table to the database, which is associated with the analysis methods. Further tables were added to allow samples that required sub-contracted analyses to be tracked and charged at the relevant rate.

```
{********************************************************

        J_BX
        SNW 28/09/01


 ************************************************************}

 SET COMPILE_OPTION DECLARE

 JOIN LIBRARY $lib_utils
 JOIN LIBRARY $lib_re_formula

 GLOBAL ROUTINE calculation ( current_sample,
                              current_test_number,
                              current_component_name )
 DECLARE RR1, RR2, RR3, Bx_avg

 RR1 = RESULT_VALUE ( current_sample, current_test_number, "Refractometer reading 1" )
 IF RR1 = EMPTY THEN
        RETURN
 ENDIF

 RR2 = RESULT_VALUE ( current_sample, current_test_number, "Refractometer reading 2" )
 IF RR2 = EMPTY THEN
        RETURN
 ENDIF

 RR3 = RESULT_VALUE ( current_sample, current_test_number, "Refractometer reading 3" )
 IF RR3 = EMPTY THEN
        RETURN
 ENDIF

 Bx_avg = (RR1 + RR2 +RR3)/3

 RETURN (Bx_avg)

 ENDROUTINE
```

Figure 7. Example of the use of Sample Manager's high level programming language (VGL), the calculation of average brix.

LIMS – Operation

The basic operation of the LIMS is as follows:

- A sample is logged in as a job and the sample(s) given unique identity numbers. Requested tests for the sample are either automatically assigned (in the case of the weekly MJ, molasses and white sugar COA samples) or manually assigned (Figure 8).
- On a weekly basis, samples that require the same test are *batched* together and necessary standards and controls automatically added to the batch. Results are entered directly into the batch results table where the necessary calculations are performed. The analyst checks the results in the batch and *authorises* them together as a batch. Once all the tests for the particular sample are done, the sample can be checked and authorised, again by the analyst (Figure 9). Batch templates are the key to providing Statistical Quality Control (SQC) Charts. The SMRI makes extensive use of control samples and SQC charts to show trends in the analyses and ensure validity of results. These charts have been maintained manually on paper. The LIMS allows immediate visualisation of the charts for the control sample associated with the batch analyses (Figure 10).
- An **interim** analytical report can be printed at this point showing the entered results. However, this report clearly states that it is an Interim report and that the job has not been authorised. This report does not have the SANAS logo as this can only be printed with results that have been authorised by one of the signatories held with SANAS. At this point, the Head of Department can see the sample is complete and authorised, whereupon he can check the results and authorise the job. This allows printing of an authorised Analytical report, Certificate of Analysis (if required) and an invoice. A copy of the invoice is generated which gives a divisional breakdown of costs associated with the job, a

requirement of the Finance department. Once printed, only a *copy* of the invoice can be generated, to ensure repeat billing for the same work does not occur. Billing routines are coded to bill with or without VAT (for countries other than South Africa) and calculate charges based on membership (Associate, Affiliate, Non-member and internal).
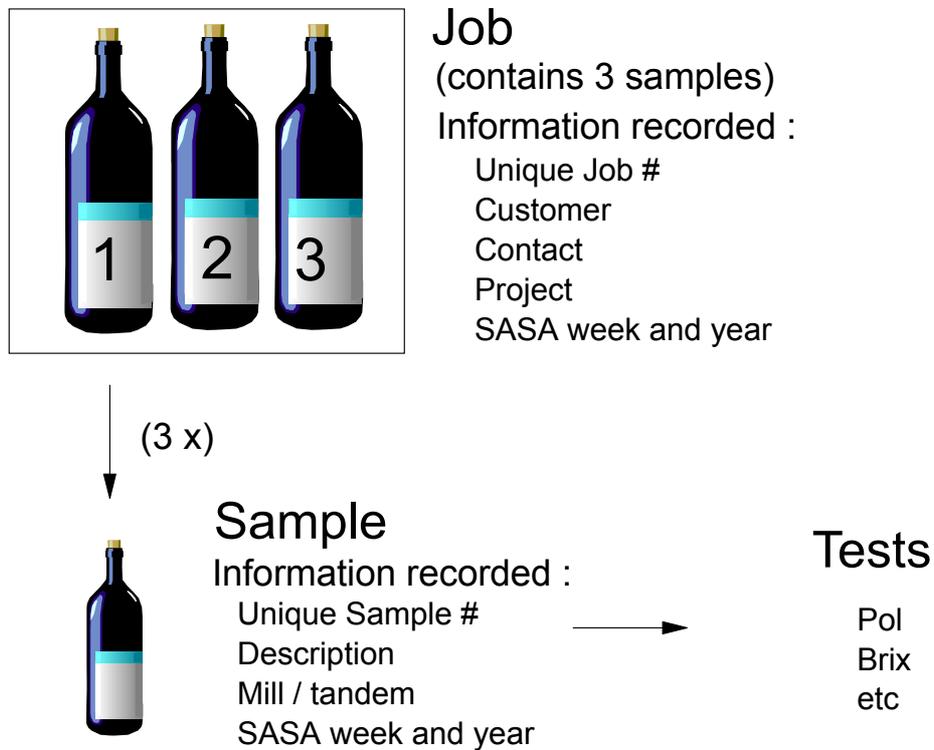
Job

(contains 3 samples)
Information recorded :
- Unique Job #
- Customer
- Contact
- Project
- SASA week and year

(3 x)

Sample

Information recorded :
- Unique Sample #
- Description
- Mill / tandem
- SASA week and year

Tests

Pol
Brix
etc

Figure 8. LIMS login procedure for incoming samples.

Test

Brix
Pol

Brix
Pol

Brix
Pol

Batches

Result entry

	Brix
Control	12
Sample 1	14
Sample 2	13
Sample 3	13

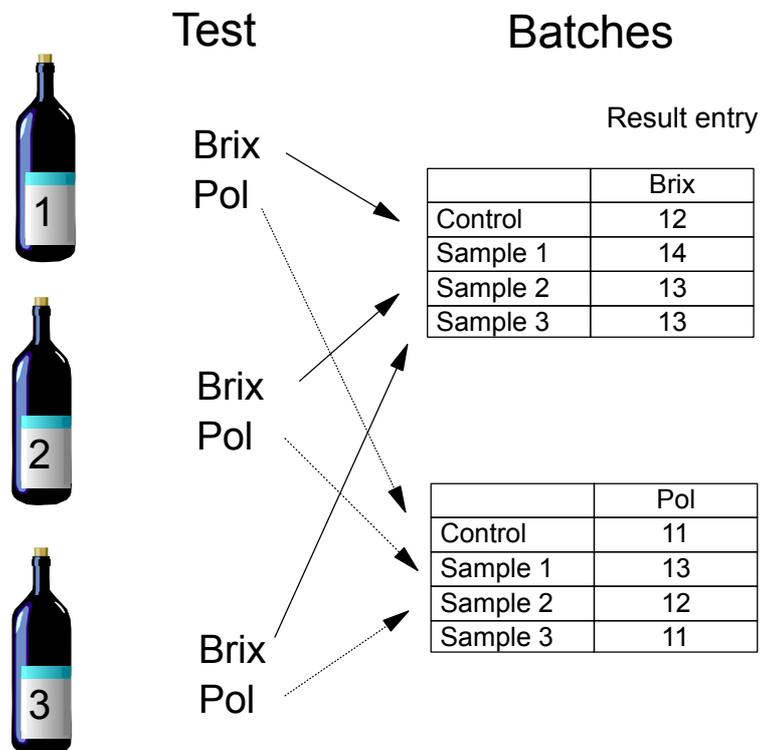|	Pol
Control	11
Sample 1	13
Sample 2	12
Sample 3	11

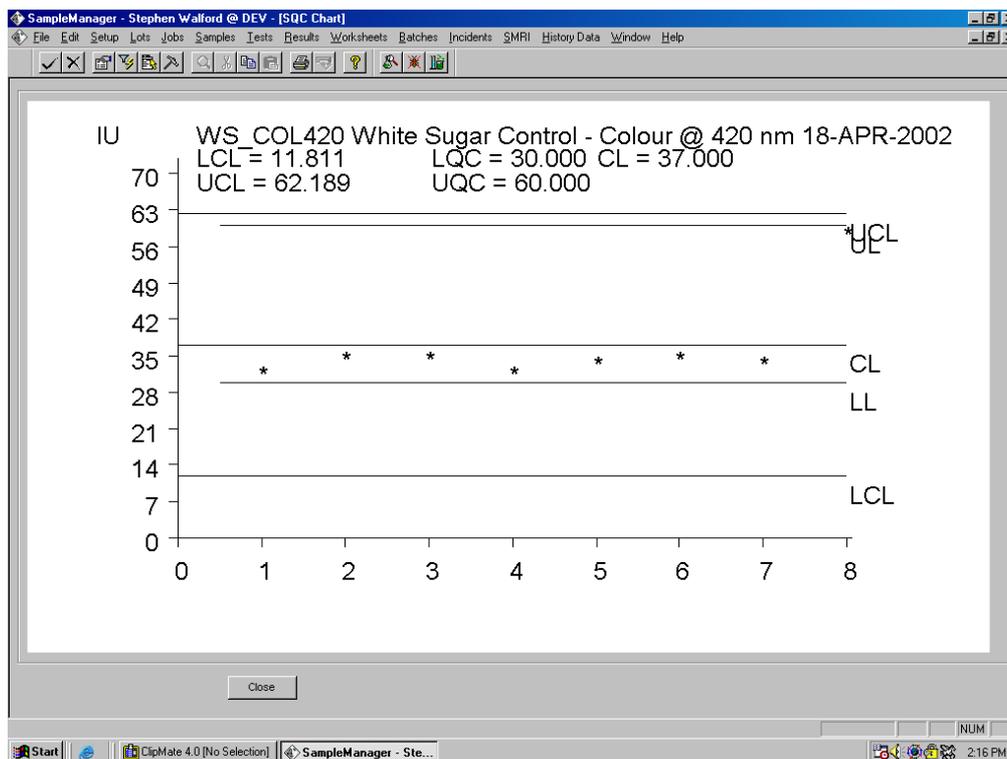**Figure 9. Grouping of sample tests as a batch for result analysis.**

Figure 10. Screen dump of a white sugar colour control SQC chart.

The future

The Institute's ISO 025 accreditation will expire at the end of 2002 and will be re-assessed according to the ISO 17025 Guideline. This guideline outlines the general requirements for competence in a testing laboratory (SABS, 1999). Section 4.12 describes the "Control of Records" and mentions that "all records shall be held secure and in confidence" (4.12.1.3) and "to prevent unauthorized access to or amendment of these records" (4.12.1.4). Furthermore "measures shall be taken to avoid loss or change of original data" (4.12.2.3). Section 5.4.7 describes the "Control of Data" in a similar manner. LIMS covers all of these factors with secure login facilities and subsequent role assignment. Direct database access is generally unavailable and consequently two layers of security are in place – SampleManager login and then SampleManager to Oracle each with different passwords and levels of access. Auditing of all entry, modifications and authorization occurs in the background and can be reviewed at any time.

Inclusion of costing functions in the LIMS allows for the future generation of Divisional cost reports. It is planned to extend this with inclusion of overheads and running costs. The backbone of this system is already configured.

The Chemical Division generates large amounts of chromatographic data which is still manually entered into LIMS. The system has features for automating transfer of this type of data directly from the instrument into the database. This will be investigated in the future with implementation giving improved operator productivity. Possible interfacing with Analytical Division instruments will also be considered.

South African mills are currently installing SampleManager LIMS as part of the CTS and mill lab updating. Information from the mills to SMRI for inclusion in reports will be in a form which is easily transferable into the LIMS. This again will lead to less transcription errors and improved productivity.

Conclusions

The increase in the analytical workload and associated paperwork at the SMRI prompted the purchase of LIMS. Anticipated benefits accruing from installation include reduced paperwork, increase in analysts productive use of time, less transcription errors and better control over accreditation issues. Long term anticipated benefits include better cost management, integration with equipment and mill data, helping improve the overall productivity of the Institute.

REFERENCES

SABS (1999). SABS ISO/IEC 17025. South African Standard. Code of Practice – General requirements for the competence of testing and calibration laboratories. Edition 1. SABS, Pretoria.

Walford, SN (2000). Proposal for a Laboratory Information Management System at the SMRI – Discussion Document. 22 November 2000.