{ WHITE PAPER }

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Integration Strategies for Digitising your Lab:

Part 2: Automated Stores and Other Processes

Roger Martin, Titian Software Ltd

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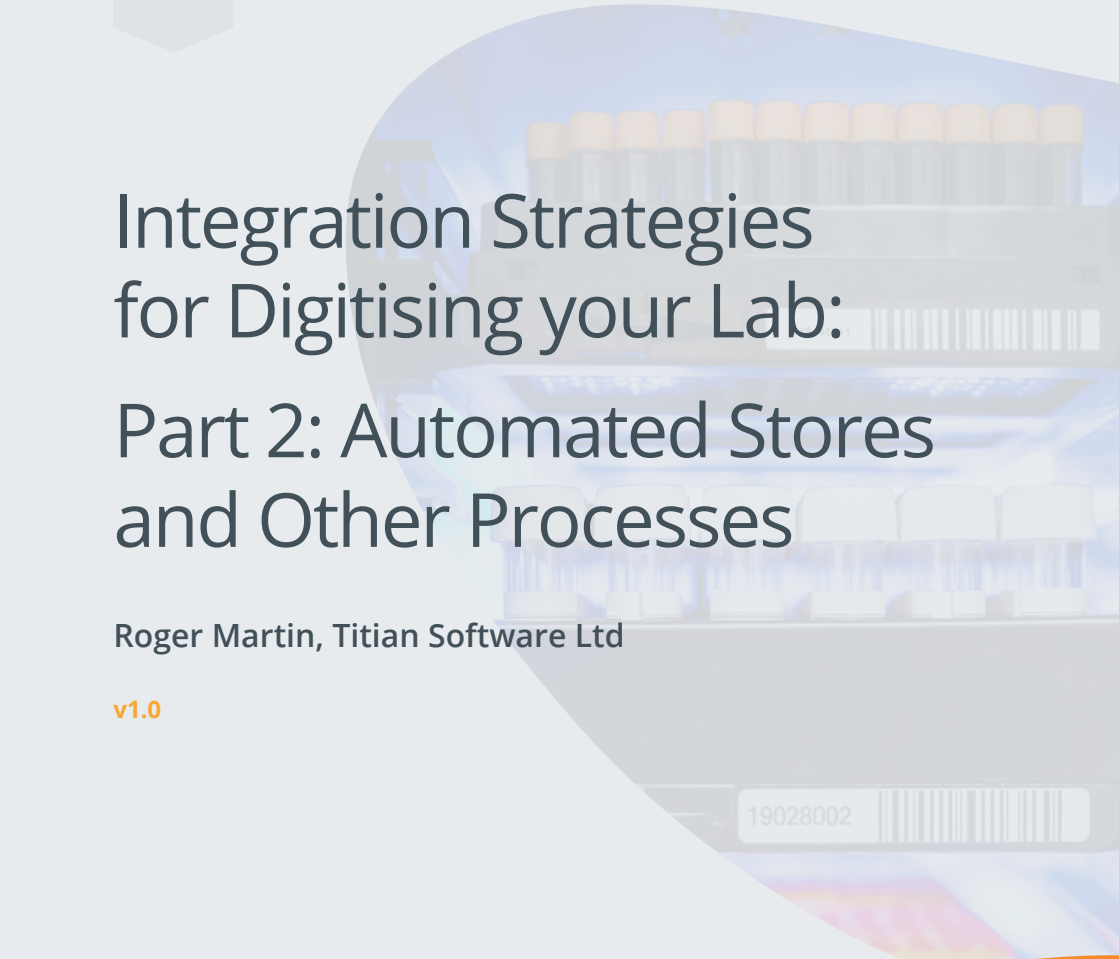

ABOUT THIS WHITE PAPER

This white paper draws on Titian Software's long running partnerships with multiple vendors of laboratory automation and its extensive experience of implementing sample management systems for organisations of all sizes, plus the author's 40 years' experience in the pharmaceutical and software industries.

The principles of good sample management hold for any life sciences laboratory: from a small academic laboratory using manual storage methods with human tissue samples, to large multiuser enterprise environments with multiple complex instruments to manage and supply millions of small molecules.

Cover image courtesy of Brooks Life Sciences

INTRODUCTION

Integrating your lab equipment with your lab information management system (LIMS) is a powerful step towards digitising your lab, as it provides an error-free data flow which can then be delivered to whichever part of your drug discovery process needs it. However, each lab has a different set up and equipment, so it's integration needs will differ.

Part 1 of this white paper discussed the different levels of integration available and how these apply to liquid handlers. This section of the white paper explores how these different levels of integration apply to both automated stores and to manual processes.

The discussion of these examples of different levels of integration aims to help you determine your specific requirements and review the tightness of integration needed for your workflows, whatever your scale of operation, or equipment type.

To recap, we classified the levels of integration as follows:

Scenario 1: Simple integration using file import. This is the most common type of integration. Here, work protocols are manually set up by operators. Once finished, a simple file import process is used to update your LIMS inventory using pre-defined file formats. However, these files have the potential to introduce errors if not imported carefully. It is essential that file data is **verified** before any changes to your inventory are made. File import is the loosest level of integration and thus fastest to achieve at lowest cost, but the most operator intensive. We advise that you specify **verified file import** as a minimum for this type of integration.

Scenario 2: Workflow-led integration by verified file exchange. When your LIMS has a workflow, this allows for a two-way communication integration where operators get guidance from the LIMS of what is required in clear workflow steps. They write the protocols for instrumentation and a verified file exchange process, which is frequently automated, creates pick list files for the protocols and imports verified data into your LIMS to update the inventory.

Scenario 3: Driven instrument integration. A tightly integrated or driven integration is where your LIMS 'drives' instrumentation directly through the equipment's Application Programming Interface (API) and creates the protocols required. The two-way data transfers are automatically managed and verified to update inventory and audit trail in real time. This level of integration is highly efficient but complex, effectively bringing equipment from different automation vendors into one seamlessly managed system. For this reason, it costs more and takes longer to deploy, but it brings swift returns on investment for busy labs through error reduction as well as efficiency.

CHAPTER 3: INTEGRATING AUTOMATED STORES

Automated stores provide high throughput sample access, greater space efficiency and improved sample integrity when compared to manual freezers. Automated stores have simpler inventory management requirements than liquid handlers and so the integration options are simplified to:

- Simple integration using file import, which is the most common type of integration
- Driven instrument integration, where your LIMS drives store processes and inventory is updated in real time

Scenario One: Simple Integration Using Manual File Import

In this simplest case of integration, the placing of labware into a store could be tracked manually by importing a file containing a list of barcodes for all the items added to the store plus their new locations. The process would entail:

- Physically loading the labware into the store
- Recovering the store's log file containing the labware barcodes read as the samples were loaded plus their new locations in the store
- Manually copying the barcode and location information into a spreadsheet format compatible with your inventory
- Updating your inventory with the new file

To physically pick samples from a store, all the store needs is a file containing a list of barcodes to pick. A LIMS system can easily provide this from a sample request.

However, the data file needed to update your LIMS inventory after picking is more complex. In addition to the tube barcodes, your inventory needs to know the rack barcode and the location of each tube within it.

Using manually created files to update your inventory is problematic for two reasons:

- It is easy to introduce errors
- It means inventory updates are not carried out in real time

Inventory updates that are not done in real time have potentially serious consequences:

- They cannot be used in fully audited environments, as these require events to be accurately time stamped
- If updates to inventory lag behind store operations, other operators may try to track down inventory that is already returned to the store or request samples already picked for use elsewhere

Scenario Two: Driven Instrument Integration

It is possible to run an automated store, particularly a low throughput one, using the manual file import method but it is not often logistically effective to do so. Having a driven integration smooths your workflow and brings with it several advantages:

- Real time updates to inventory and audit trail mean that samples cannot be moved without your LIMS knowing about it
- Placing samples into storage is simplified. Operators can simply feed containers into the store and they are automatically put away and the LIMS inventory locations updated

- Pick lists can be created automatically from a scientist's order. The LIMS will convert the sample identifiers used by the scientist into the labware barcodes required by the store. In many cases driven integrations can also pick the request automatically once it has been accepted
- LIMS often include prioritisation to automatically deal with many simultaneous requests. This means orders will be run based on priority or efficiency rules. For example, processing a large High Throughput Screening pick overnight to allow smaller project picks to be carried out during the day
- If your LIMS uses workflows, stored samples can be picked with knowledge of later workflow steps. For instance, if samples picked from the store will be replicated downstream with a block head liquid handler, then tubes can be placed in racks automatically leaving a column free to be used for control addition when replicated into plates

A fully driven automated store integration should also improve the robustness of your operation. A good integration is designed to handle a wide range of errors and aid their rapid diagnosis and resolution with a minimal amount of user input. Most common problems arise from human error. For example, when loading racks of tubes into store, a LIMS can automatically cross check that tubes are present in the racks and inform operators if something unexpected is found, such as unregistered labware. For 'non-blocking' errors like this example, the LIMS can instruct the store to park the rack causing the error and continue placing other racks. The operator can then connect to the store (usually remotely) to resolve the issue and finish the process.

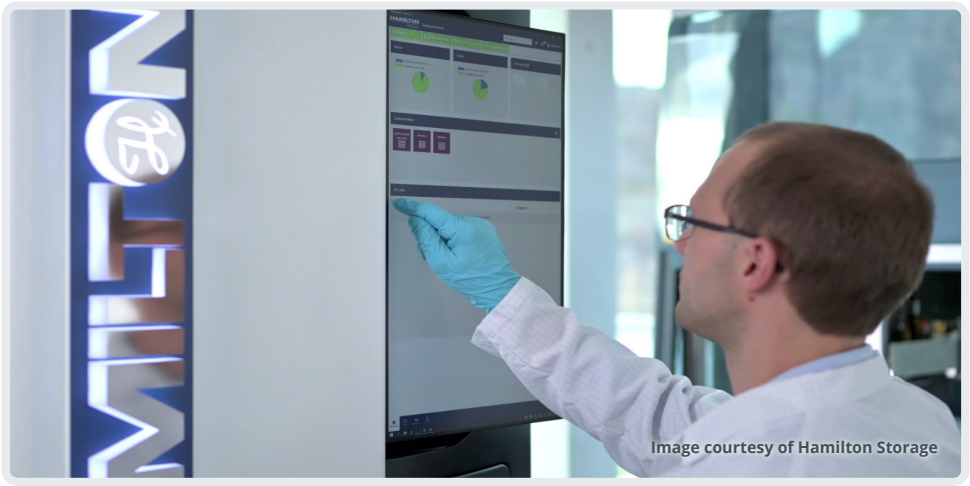

Image courtesy of Hamilton Storage

Questions to consider when considering manual file import versus driven integration for an automated store are:

- Are you likely to be working in an audited environment that needs to accurately track how long items have been out of a store?
- How many people are accessing the store? Many operators manually importing files is much more likely to create problems with inventory lagging behind store operations.
- What verification processes are used on the files imported manually?
- How much automation do you use or are you likely to use in other process steps? The lag from manually uploading inventory updates is more likely to be problematic alongside other digitalised workflows.

CHAPTER 4: INTEGRATING MANUAL PROCESSES

The push to digitalise and track all the pieces of the laboratory process means that manual processes need to be included in integration plans for labs. It is already quite common for some tasks: for instance, manual pipetting can be done following guidance from your LIMS user interface, which gives position information and automatically calculates volumes to minimise human error.

Other processes requiring the operator to manually perform a task can also directly involve the use of laboratory equipment, such as weighing with analytical balances, checking tube positions with rack scanners, or placing and retrieving samples from manual stores.

These manual processes are usually simple compared to the multi-step workflows carried out on automated liquid handling platforms. However, achieving an integration that guides the operator in such a way that it removes human error still requires a degree of effort that should not be underestimated.

Integrating Analytical Balances

Weighing is predominantly done as a manual process with an operator sitting in front of an analytical balance. The process is usually viewed as extremely simple, with the operator just needing to know how much to dispense. So why does this process need integration? There are several strong reasons:

- Even a simple weighing process needs each operator to make a range of decisions, which will introduce many variations unless a reliable process is consistently followed
- Manual data entry is tedious for the operator and a well-recognised source of error
- Automatically capturing accurate information, such as the exact amount dispensed, ensures subsequent steps and calculations are more precise
- It can help ensure company Standard Operating Procedures (SOPs) are followed
- Keyboards need to be meticulously cleaned after manual data entry to avoid cross-contamination

A simple integration using verified file import can be used to update your inventory with balance information, tare and gross weights while avoiding unnecessary contamination of surfaces. However, it does not address process consistency.

A driven integration between your LIMS and analytical balance will directly transfer accurate readings to your inventory in real time but also provide:

- Increased data quality as quantities and volumes in subsequent process steps are calculated based on exact readings
- Automatic calculation of dispense amounts to avoid human error
- Operator guidance from the LIMS to avoid process variations, such as a clear graphical display of range amounts for each weigh and dispense to be performed

- Handling for unexpected events. For example, tracked options on how the operator should proceed if the sample to be weighed is a gum as opposed to a free-flowing powder, or the source bottle is damaged[1]
- Recording and enforcement of SOP processes, such as taring labware or check weighing after a defined number of dispenses
- A 21 CFR Part 11 compliant audit trail of dispenses for every vial
- Label printing to deliver human readable information to the recipient

Questions to ask yourself when considering a file import integration versus a driven one include:

- How important is process consistency to you?
- How many operators use the balance? The more operators, the greater the likelihood of process variations.
- Do you need to record or enforce SOPs?

Integrating Rack Scanners

Rack scanners provide a quick way of tracking tubes by scanning racks of 2D barcoded tubes and providing a list of their positions and barcodes to your LIMS, usually as a CSV file. Scanners are mainly used to introduce new inventory quickly, track manual movements of tubes or to recover after a rack is dropped.

A validated file import integration means that the scanned tube locations can be updated in your inventory, but this is all.

A driven integration between a rack scanner and your LIMS allows the LIMS to provide guidance and alerts when action is needed. For instance, it can highlight:

- Tubes that are **unknown to inventory** and ask if you want to add them as racks of new empty tubes
- Tubes that are known to inventory **but not in their expected locations** - perhaps because the rack was dropped, or tubes from several racks were consolidated, or even that the rack has simply been put on the scanner the wrong way around. The operator can investigate the cause and choose to update the inventory
- A tube in the rack that has an **additional workflow step** against it

The guidance for operators that comes with a driven integration can be invaluable for reducing human error. For instance, if a rack has been scanned 180° wrong, in a file

import integration, the inventory would be updated with incorrect location information. If this rack was then sent to a liquid handler, the robot will try to pick from H12 to get the sample in A1. A driven rack scanner integration would flag the inconsistency to the operator.

Integrating Manual Stores

A critical task for sample management LIMS software is to create an accurate digital twin representing the hierarchy of your manual laboratory storage units: cupboards, fridges and freezers. This allows users to quickly search and locate stock as well as finding free space for placing new samples. Maintaining the accuracy of this inventory and providing an audit trail of who did what requires some level of integration.

The manual process involves the operator using the LIMS user interface to create a list of what samples are needed (maybe on a piece of paper), then collecting or returning them, and finally updating their locations in the inventory. These updates do not happen in real time and it is a common problem to have items returned to the wrong place or the user forget to register the new location.

New technologies enable a driven integration between a LIMS and manual stores by enhancing the LIMS user interface using either:

- A **Mobile** device
- An **Augmented Reality** device

Both devices bring together real time labware barcode verification and context-specific operator guidance from the LIMS. This offers the following benefits:

- Confirms the correct labware has been picked/placed
- Identifies the operator performing the task
- Updates the inventory and audit trail automatically
- Displays warnings if items have hazards associated, which is important when manually processing samples
- Provides informed guidance on where to place items, so that substances that should be stored at -80°C are not placed in a -20°C store

These new technologies also offer efficient processing as operators are immediately directed to the next task, without needing to return to a computer.

Questions to consider when reviewing integration options for manual stores include:

- Are you likely to be working in an audited environment and need real time updates?
- How many people access the stores? The more operators, the greater the need for real time updates.
- What verification processes are used to check manual updates?
- How much automation do you use or are you likely to use in other sample management steps? The lag from manually updating inventory updates is more likely to problematic alongside other digitalised workflows.

Summary of Integration Types

PROS	CONS
Automated Store – File Import	
☑ Easiest implementation	☒ Data exchange is not in real time, meaning inventory information may lag events ☒ More room for human error ☒ Inefficient ☒ Not suitable for an audited environment
Automated Store – Driven Integration	
☑ Eliminates human error ☑ Real time updates ☑ Improves efficiency and robustness of operation ☑ Improves error recovery	☒ More complex deployment
Integrating Manual Processes by Manual Updates to LIMS	
☑ Easiest implementation	☒ Data exchange is not in real time, meaning inventory information may lag events ☒ More room for human error ☒ Inefficient and time-consuming ☒ Not suitable for an audited environment
Driven Integration of Manual Processes	
☑ Generally very cost-effective ☑ Audit trail updates of who did what and when ☑ Reduces human error ☑ Real time updates ☑ Provides options guidance when something unexpected happens ☑ Improves reliability ☑ Hazard guidance in real time	☒ More complex deployment

Other Factors to Consider

So far this white paper has mainly discussed technical and functional aspects of digitising sample management processes to integrate with your LIMS, but there are other considerations too.

Ask about **support** and consider how the integration may evolve as your company grows or processes change. If an integration is entirely custom to you, then it will require unique support, which is more expensive in the long run. If it is an existing product, or based on one, then it is often supported globally at reduced cost and is likely to be kept up to date. There should be an upgrade route to allow for new versions of software, or to upgrade instruments. Will you have a team to support your integration in the future, or is it dependent on one person who may leave the company? Is support local or worldwide, and which matters most to you?

Consider **deployment**. While a driven integrated system requires more setup than a verified file exchange system, some work may be required by you even for verified file exchange integrations. The key is being able to pass files of information smoothly between your systems. In a few cases, data can be used directly by both the instrument and LIMS. When this is not the case, many LIMS offer a generic export/import file format which can be used as the basis for integration. If the LIMS file format does not fully fit your needs, there are options to adjust it without requiring a completely bespoke approach. Various file manipulation software options are available, including vendors who will create custom file manipulations to meet your exact requirements. If bespoke development is your route, then ask to work in a SCRUM way with regular reviews of progress, so you are aware of how easy the system is to work with.

It is important to consider **change management** when implementing levels of automation and integration. Staff may be concerned that their roles will no longer be interesting or valued and thus be resistant to new processes.

Integrations of manual processes can be a useful first step to further automation integration, because they can help staff to accept the value of changes. Often, these manual processes are tedious as well as error prone. Integrations that make these tasks easier for staff, as well as speeding them up and removing errors, will improve user satisfaction.

Introducing more complex integrations will affect your automation expert, who is likely to be central to keeping your current processes running smoothly. Their understanding and expertise is ideal for reviewing new technologies that can help drive further improvements.

CONCLUSION

All the types of integration discussed in this white paper have their uses in capturing data, but each provides a different level of functionality. When discussing your integration needs – with vendors or inside your company – it is important to be clear about what level of integration you are offered. You should have in mind what functionality is important to you and make sure that you fully understand whether this is covered.

When considering integration options for each process, think carefully about how varied the process is rather than the number of samples handled:

- If your process constantly repeats the same steps, such as a testing lab following a validated process with no changes to automation protocols or how samples are received, then file exchange integration is likely to provide exactly what you need
- If your processes are highly variable, perhaps because your company or customers are continually developing experiments to support multiple innovative scientific projects, then a flexible driven integration will be more suitable as it ensures information is up to date across your processes and includes operator guidance

Integrating manual processes with your LIMS brings significant benefits because it brings reliability and traceability to processes that can be prone to errors. For instance, driven instrument integration with analytical balances or rack scanners is likely to be a cost-effective way of improving data quality, irrespective of your overall level of integration.

Considering the human element of integrations is also important to ensure that staff are happy and productive. Digitised processes need to be streamlined and easy to use so that operators recognise the gains from integration. Ask for demonstrations to both operators and lab managers to see how some examples of your processes could be handled. If development is required ask for regular SCRUM demonstrations of progress.

Providing a robust integration to suit your needs will require a partnership between your laboratory, your sample management team, the automation vendor and the integration experts – whether internal or external. The requirements of both lab and sample management teams need to be addressed, as well as the capabilities of the automation. All parties need to be committed to working together, to ensure that information flows smoothly and you can meet the timescale and budget you expect.

Reference

1. https://www.titian.co.uk/news-landing/news/why-the-sample-weighing-process-is-hard-to-manage

AUTHOR

ROGER MARTIN:

Roger worked for GlaxoSmithKline for 33 years. Originally a medicinal chemist working as a research chemist, he later transitioned to cheminformatics and then R&D IT, specialising in compound management software. He joined Titian Software in 2012 where he is a technical application consultant.

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info@titian.co.uk

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UK Tel:
+44 20 7367 6869

USA Tel:
+1 508 366 2234