LIMS Plate Handling and a High Throughput World

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Introduction

Plate handling and automation are increasingly important and prevalent in biotech organizations. Automation and high throughput needs demand that workflows account for the manipulation of samples in a wide variety of plate formats and configurations. Labs are integrating everything from simple liquid handlers and cherry pickers to highly complex storage and freezer management solutions. LIMS functionality should integrate older ASCII and CSV file transfers as well as modern XML schemes and service oriented architectures. LIMS designed for high throughput environments should contain plate handling functionality out of the box, while remaining flexible in how the system is configured and extended to meet custom needs.

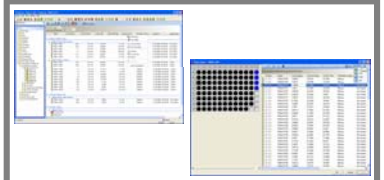
LIMS Essentials

With trends leaning toward increasing data volumes, high throughput environments require information management systems that allow data from automated processes to be modeled and integrated easily. Systems have been developed to meet these needs with configurable functionality available out of the box.

LIMS specific challenges in high throughput environments:

- Intuitive user interface – quickly query and access data
- Configuration tools – easily emulate and modify workflow process.
- Data tracking – track samples, plates, well positions while maintaining hierarchical relationships.
- Storage and location tracking - samples, plates, solutions, reagents, etc.
- Integration with instrumentation and automation equipment.
- Data visualization and dynamic processing – flag hits and create "cherry-picked" plates
- Extensibility - communicate with other applications and custom programs to build integrated solutions

FIGURE 1. Intuitive LIMS interfaces emulating Windows explorer with imbedded .NET functionality for easy query and manipulation of data.



Common Plate Handling Operations:

- Replication – used to make multiple copies of plates. Each replicate, or daughter has the same dimensions and properties as the original
- Splitting – dividing one plate into several other plates. Example: 384 well plate into four 96 well plates.
- Probing – adding another solution to the well positions within a plate.
- Compressing – used to create new plates, each composed of smaller plates. Example: four 96 well plates into one 384 well plate
- Pooling – used to pool the contents of source plates into a new plate or an existing plate. Example: three 96 well plates combined into one 96 well plate.
- Cherry-Picking – Selecting "hits" to be moved from source plates to new destination plates.

Plate Template and Design

Plate design utility must enable:

- Variable dimensions, not just restricted to 96 and 384 well
- Well labeling (Alpha, numeric)
- Common and user-defined fill patterns
- Specific well configurations (inclusion of blanks, standards, QC, dilutions, etc)
- Additional attributes and meta data. (e.g. clients, locations, etc)

Plate Workflows

Informatics solution should provide the ability to:

- Graphically program and emulate dynamic work processes
- Automate creation and track plate hierarchies (mother-daughter)
- Integrate common plate handling operations, such as replication, probing, splitting, and cherry-picking.
- Easy to learn, configure, and update

FIGURE 2. Plate template depicting configurable dimensions and load patterns

FIGURE 3. Graphical workflow allows process to be mapped visually without need for programming

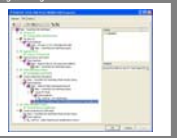


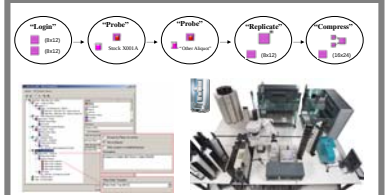
Plate Plans

Automated processes generally involve groups of plates.

System should accommodate:

- Emulate dynamic process involving groups of plates
- Organize workflow activity into steps
- Execute actions on groups of plates at each step in process
- Dynamically define and assign transition at each step (next action)
- Integrate common plate handling operations, such as replication, splitting, probing, and compression.

FIGURE 4. Basic process example with corresponding plate plan built in a graphical workflow utility.



Instrumentation and Automation

Automated workflows and processes involve integration between instruments and robotic equipment. The LIMS should have a flexible set of tools that allow systems to be integrated. This is preferably an inherent configurable utility within the application.

Features include:

- Ability to acquire data from all types of instrumentation, including serial ports and networked instruments.
- Apply specifications and logic to make dynamic decisions based on data.
- Exchange CSV and control files with automation equipment.
- Interface with service oriented architectures and exchange XML messages.

Configuration and Customization

In an ideal world, a LIMS would be able to provide 100% of all necessary functionality straight "out-of-the-box". In the real world, laboratories need the ability to customize the system where appropriate to integrate with other applications or to tweak the system for efficiency. Hence, it is essential that the LIMS provides the ability to extend its functionality via custom hooks and code when necessary.

Extension best practices:

- Never change core code; this could negatively affect future upgrades.
- Use industry standard programming languages. (Long term viability, upgrade, and talent pool)
- Integrate service oriented architecture. (Future proofing and avoid "reinventing the wheel")

FIGURE 5. Example of configurable graphical workflow with the integration of reusable extension written in .NET.

Conclusions

LIMS designed for high throughput informatics contain an abundance of functionality that allows organizations to visualize and manage their processes and still keep up to speed with ever changing needs. With built in plate handling functionality utilizing a service oriented architecture in .NET, Nautilus empowers organizations to maximize their internal talent and not only keep up to speed with science, but remain ahead of the curve.

Thermo Scientific's Nautilus LIMS ensures Scientific Research organizations can keep pace with changes in laboratory techniques, automate processes and manage the increasing data volumes.