Agaram TECHNOLOGIES

WHITE PAPER

LIMS for diagnostic & research labs involved in molecular, cytology, histology, NGS, NBS, translational medicine & bio-banking

SPECIALTY DIAGNOSTICS WORLD

Modern specialty diagnostic laboratories need an integrated LIMS that can handle molecular diagnostics, cytology, histopathology, NGS, FLOW, biochemistry, genetic cytology (Cyto / FISH)and microbiology related processes in a single system. Advanced detection of mutations, abnormalities in cells, chromosomes, karyotypes, DNA, gene, enzymes studies and biomarkers are very helpful in identification of potential source of disease and better patient care.

FUNCTIONAL ASPECTS OF AUTOMATING SUCH LABS

Specialty diagnostic labs are a different breed of labs that need a system that can handle multiple workflow processes in a seamless communicative manner. In order to publish a result, samples undergo several pre-processing like aliquoting, isolation, normalization, robotic pipetting, reagent addition including sample preparation and analysis on high throughput devices that are capable of handling different plates& containers. The ultimate goal is to reach to the level of getting the final outcome of a test. Looking at this from a data entry and result publishing perspective it may look very simple which traditional LIMS are quite good at handling. Dynamic workflows with dynamic content capture is one of the key aspects for these types of labs.

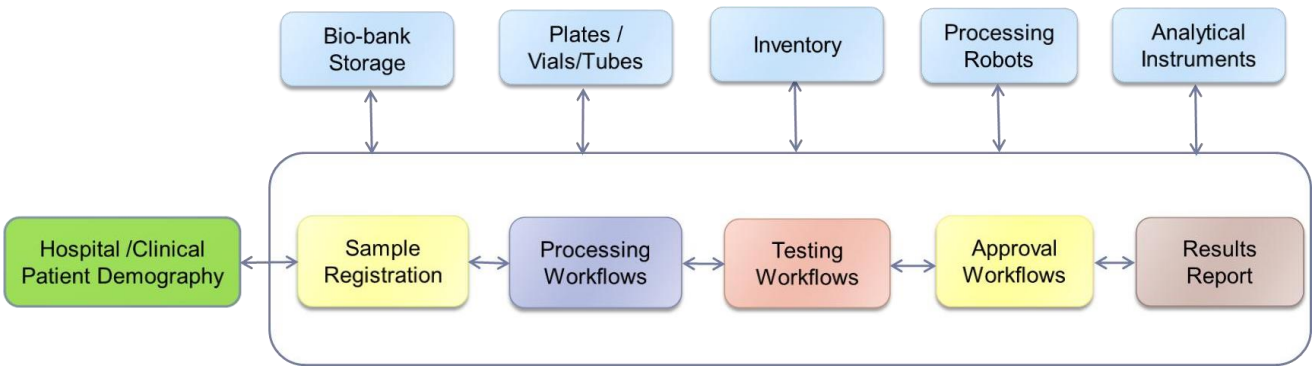

Fig 1: Typical advanced Molecular diagnostics laboratory workflow

PATIENT DEMOGRAPHY

Mostly demographic information comes in as paper based or electronic data exchange can happen between LIMS and external hospital or clinical systems. Middleware system for Electronic Data Interchange (EDI) should be available for bi-directional communication of patient demography, orders and results with healthcare systems. Patient demography could also include hereditary information for advanced research studies based on pedigree.

SAMPLE ACCESSIONING / REGISTRATION & BIO BANK STORAGE

Sample accessioning or registration with patient demographics and appropriate routing of source sample for processing and storage is a critical step for any molecular laboratory. More often the DNA/RNA needs to be isolated within specific time frame after the phlebotomy. Routing of samples to appropriate workflow process becomes important when it comes to following the SOPs and throughput of lab. Bio bank storage involves temporary refrigerators, deep freezers and cryo-storage equipment. Bio bank storage should be really flexible in terms of definition of templates for various types of storage location and destination containers (plates, tube holders). Movement between the bio bank and the processing area is an important process which goes through request and issue of samples based on priority and the process it needs to undergo.

BATCH MANAGEMENT, SAMPLE PROCESSING& TEST WORKFLOWS

Samples can undergo several processing steps like aliquoting, DNA isolation, extraction, normalization which can be done both manually and using advanced robotics. Processed samples undergo testing and analysis in instruments like sequencer, real-time PCR (RT-PCR),MS-MS, next generation sequencers (NGS) and proteomics.

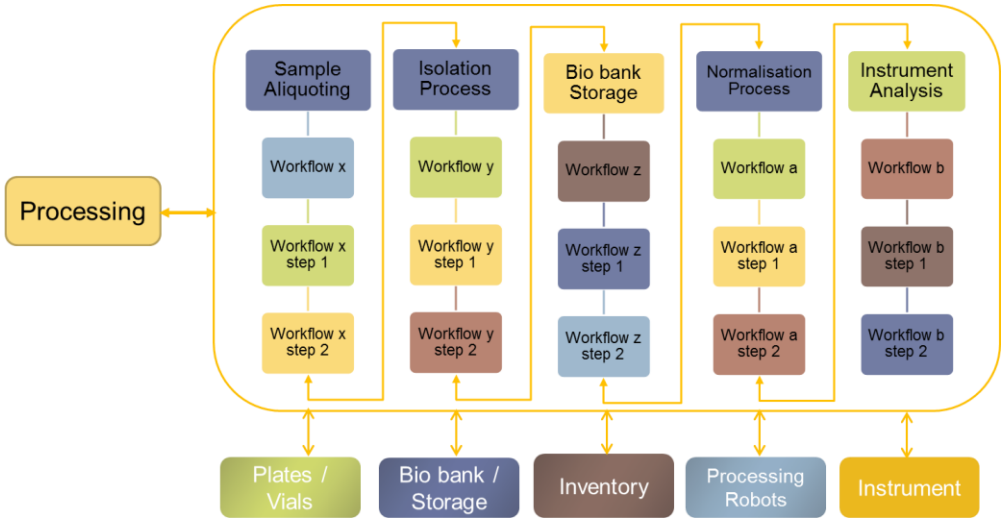

Fig 2: Typical Workflows for processing samples and performing assays

Request and creation of batch for processing or analysis is critical in terms of business rules like identifying the appropriate material, status of material, container etc. Requests received by bio bank needs advance material handling that requires pulling of correct material from storage systems and preparing samples on plates based on the nature of activity for which the request was made. In case of insufficient material the requester should know or the bio bank should be able to place next priority material for processing. The system should be able to identify and prioritize samples issued for processing and have capability to eliminate samples or material which failed during the processing steps.

The most complicated aspect of the workflow in any molecular laboratory is related to material processing and test setup. Although for each sample type there is a standardized sequence of work, a significant number of cases require re-extraction, re-purification, or other adjustments due to variations in sample quality or quantity. Furthermore, due to the increase in retrospective and reflex testing in most laboratories, materials often reenter the sample processing stream at various points. The workflow process should be easy enough to re-route samples and converted material through any process for re-processing. Since several tests works on batches of 96 or more it's always better to have a batch of that size for optimal operation of the lab and hence going back to starting material and reaching the level of other samples is a critical workflow requirement.

SAMPLE PROCESSING & ANALYTICAL TESTING WORKFLOW CAPABILITIES

- ✓ Advanced workflow engine should be available to define sample processing workflow steps, including creation of dynamic checklists for various processing steps
- ✓ Workflows should be possible to be setup by end users. When new methods are available the lab personnel can create such workflows, validate and instantaneously start work through the LIMS.
- ✓ Seamless flow of samples from one process to the next obvious process based on status of samples
- ✓ Advanced positive identification of samples by barcode (1D, 2D) by manual scanning or plate scanners improves throughput and accuracy of sample processing.
- ✓ Rules based (sample type, vial type, test, method of analysis) batch creation for processing of samples for various workflow processes.
- ✓ Dynamic transfer of samples e.g. from one format of plate (96-well) to another plate format (384 well) for specific assays.
- ✓ Active list of samples management based on their status across multi-step workflow. i.e. when you want to eliminate samples from going through next levels of process due to failures.
- ✓ Advanced "Goto" step type of workflows for directing samples passing/failing certain criteria to Goto specific workflow step and continue from that step. (Re-processing or re-routing)
- ✓ Aliquoting of samples, storage in bio bank, transfer from bio bank to temporary refrigerators, centrifuging. Maintaining temperature conditions, PCR equipment start/stop, de-capping/capping of tubes etc.

- ✓ Analytical instrument based control (instrument specific driver), data export (sample list with position) and data import (sample with results)
- ✓ Automated attachment of results raw data generated by instrument for easy review and release of results

CONCLUSION

LIMS for specialty labs should have a generic workflow engine which can beconfigured to meet new sample processing methods and analytical techniques. A rules engine for taking decision and appropriate routing of material would certainly help a lot.

Should have workflow capabilities:

- Actions which involve sample or material movement with traceability (aliquoting, transfer to new container/plate, automated mask based plating)
- Configurable dynamic checklists for user input based on the procedure
- Instrument based dynamic options for input(sending list of material and plat information) and output (receiving results from instruments), control (instrument specific control)
- Movement of samples from one workflow step to another step based on rules or status
- Routing of samples/material to appropriate process based on tests, processes, containers, status, condition etc.
- Safe bio banking of samples and processed material with ease of retrieval.

As a software publisher if we are able to provide new or advanced “workflow steps” without disturbing the existing site installation it will be the best choice for such labs. This will pave way for continuous optimization of processes.

References:

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