



# Implementation of laboratory automation in a CRO environment — from basic steps to advanced solutions —



## A few general considerations

Lab automation is commonly used in clinical routine laboratories for standard demands:

- High sample numbers
- Day-in, day-out the same analysis



In Pharma, in-house analysis is performed with robotic systems, if/since projects are scheduled for long periods and outsourcing is not foreseen

But in CROs, with short to midterm projects, sample numbers/study 100-5000?



## In the beginning... (7 years ago)



Tomtec and Tecan Genesis: Short and simple scripts for liquid transfer, no handling of worklists, no integration of peripheral instruments (only semi-automated)



# Introducing state of the art automation



# What did we want to achieve?





# Take time and care for your user requirements

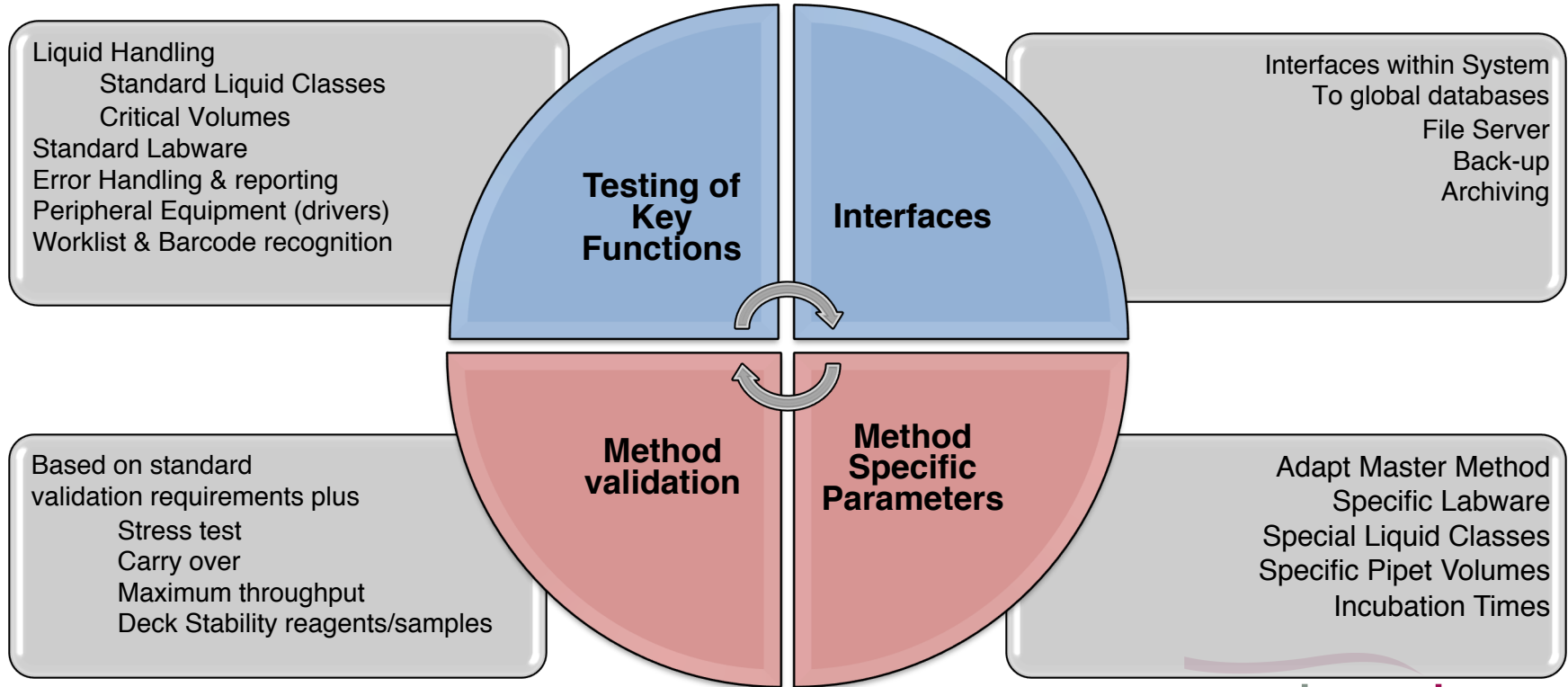
- Software security: 21CFR11 should be standard for any modern lab automation
- Liquid transfer: accuracy & precision, error detection, handling and reporting, stress test under maximum capacity
- Peripheral instruments: drivers/compatibility with robot software
- Throughput (instrument size and capabilities)
- Consider flexibility and user-friendliness

And test it repeatedly !!



# Automation Validation Approach

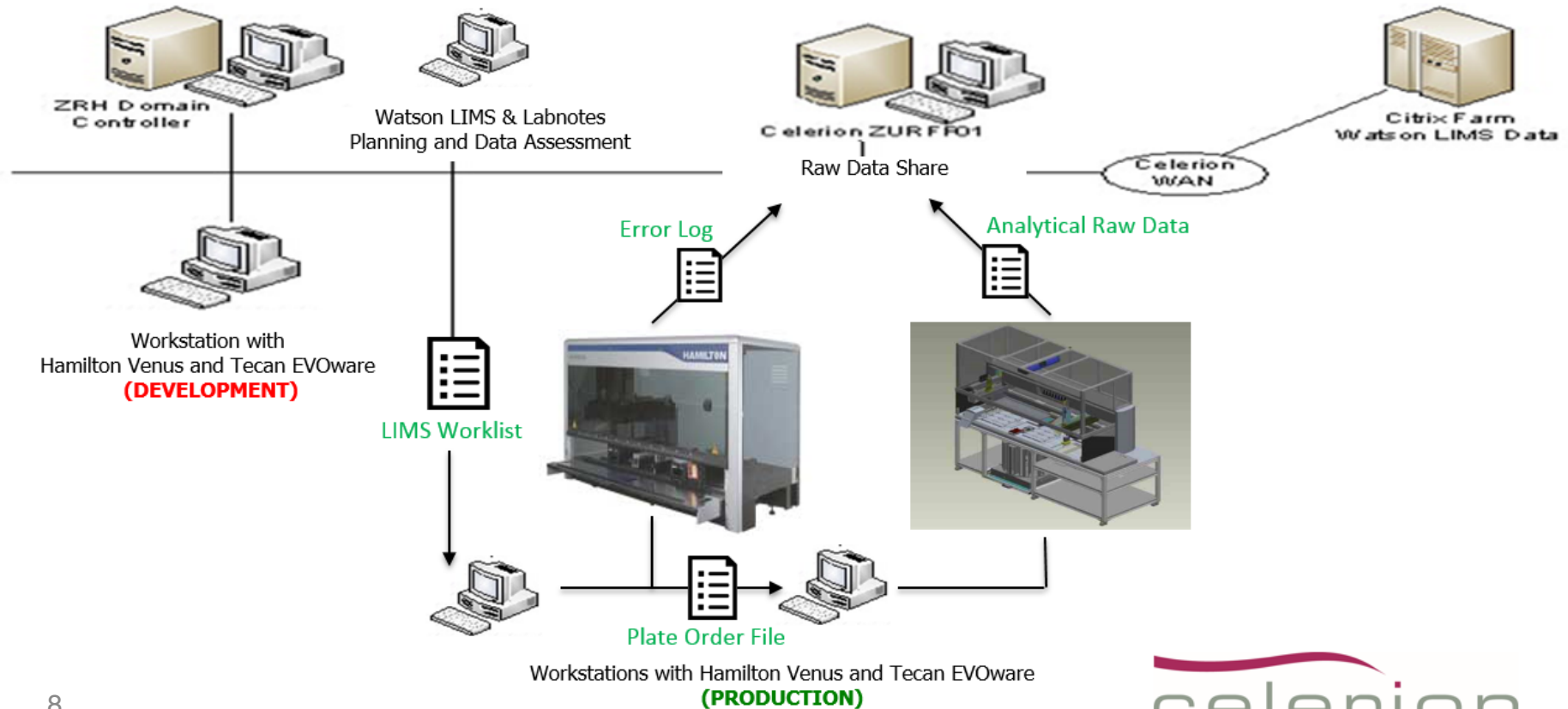
## Prove suitability for intended use





# Data flow within your IT-infrastructure

## Out of the LIMS – Into the LIMS





# Continuous routine checks

What is practical and reflects the purpose of the system

The image displays four overlapping screenshots of the Celerion software interface, specifically the 'Equipment Recurring Task' forms. The forms are designed for recording and managing routine checks for various pieces of laboratory equipment.

- Top Left Screenshot (Tecan Freedom EVO PQ):** Shows the 'Start Up / Shut Down / Daily Maintenance as per SOP Performed Date' section with a date of 13 Sep 2019. It includes fields for 'Microplate Reader', 'Volume 01 (mL)', 'Volume 02 (mL)', 'Weight of Empty Plate (g)', 'Weight of Full Plate with Volume 01 and 02 (g)', 'Accuracy Volume 01 Pass / Fail Status', 'Accuracy Volume 02 Pass / Fail Status', and 'Precision Pass / Fail Status'. The 'PQ Pass / Fail Status' is marked as 'Pass'. The 'Performed by' field is filled with 'CELERION\gabeta01 (13 Sep 2019 05:00:13)'.
- Top Middle Screenshot (EQ-ZRH-PR-1071):** Shows the 'Check Tasks Performed' section with a list of tasks: PM, PQ, NIAP, and NIAP. The 'PQ' task is checked. The 'Describe Details' field is filled with 'PQ'. The 'Equipment / Components Used to Performed Task' field is filled with 'EQ-ZRH-PLATE-1155'.
- Top Right Screenshot (EQ-ZRH-INC-1274):** Shows the 'Check Tasks Performed' section with a list of tasks: PM, PQ, NIAP, and NIAP. The 'PQ' task is checked. The 'Describe Details' field is filled with 'temperature check'. The 'Equipment / Components Used to Performed Task' field is filled with 'EQ-ZRH-THERM-0755'.
- Bottom Screenshot (EQ-ZRH-RLH-1025):** Shows the 'Check Tasks Performed' section with a list of tasks: PM, PQ, NIAP, and NIAP. The 'PQ' task is checked. The 'Describe Details' field is filled with 'Annual PM'. The 'Equipment / Components Used to Performed Task' field is filled with 'Annual PM'. The 'Results' section shows 'Task Pass / Fail Status' as 'Pass'. The 'Results Details' field is filled with 'write down results obtained or refer to supporting documentation (e.g. CO values, service report, calibration certificate, etc.)'. The 'SoftMax Results printed into .pdf file' field is filled with 'Yes'. The 'Location of Supporting Documentation' field is filled with 'Electronic copy saved in se'. The 'Equipment Status' section shows 'Following Recurring Task(s) needs to be Performed' as 'PM'. The 'Equipment Tagged "Out of Service"' field is filled with 'NIAP'. The 'Performed by' field is filled with 'CELERION\gabeta01 (03 Oct 2018 06:42:08)'. The 'Reviewed for Completeness and Correctness by' field is filled with 'CELERION\groesm01 (03 Oct 2018 07:51:43)'.



# Method specific development and qualification

**Liquid Handling Robotic Methods Change Control ( New / Updates )**  
Celerion - T201 SOP 20016-03 Liquid Handling Robotic Method Change Control (Version 03)

ID: **8M6-194\_Screening\_Part1 / LHR Method QC - Released Build 1**  
Computerized System and UIR Type: **CS207 CS219 Tecan Genesis RSP 150**

**Requirements List (Request, Evaluation and Approval)**

\*Request Type: **New** \*Current Build: **0** -- If N/A, please add "0" --

\*Requirements:

Detailed description of how the robotic method needs to perform:

Read input file and write worksheet  
Dispense acidic acid in subsequent wells of DWP (in portrait orientation) according to number of wells from worksheet (200 or less uL)  
Distribute controls and study samples into subsequent wells of DWP according to worksheet (200 or less uL)  
Count timer down for application (15 min)  
Dispense channel in subsequent wells of DWP (in portrait orientation) according to number of wells from worksheet (200 or less uL)  
Mixup for shaking (user prompt)  
Dispense TRIS in subsequent wells of DWP (in portrait orientation) according to number of wells from worksheet (200 or less uL)  
NOTE: Volumes might be scaled down for Screening Assay, if approved by sponsor

\*Approved by: **CEL6160N/bramp01 (02 Aug 2019 01:27:41)**

**-- this section is to be left empty for new methods --**

\*Risk:

\*Risk Assessment:

\*Testing Plan:

\*Approved by:

**Development and Testing**

\*Self Test:  
Document reference to a 3 simulation run (reaction and/or account) with data columns demonstration, placement, mix, run with test materials etc.

\*Run-Through Test:  
Document reference to a successful run with test materials simulating an actual analytical run, e.g. backoutput file.

\*TQA and Stress Test:  
Document reference to successful run, e.g. run 0.

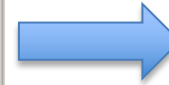
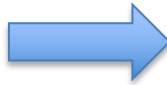
\*Additional Information:  
N/A

\*Programmed by: **CEL6160N/grownd01 (30 Aug 2019 05:44:27)**  
\*Reviewed/ tested by: **CEL6160N/grownd01 (30 Aug 2019 05:44:39)**

**Release**

\*Released Date: **30 Aug 2019** Released Build: **1**  
\*Approved by (RnD): **CEL6160N/bramp01 (30 Aug 2019 05:05:49)**

Request for a new method to be approved by TFM: no/samples, timeframe etc.

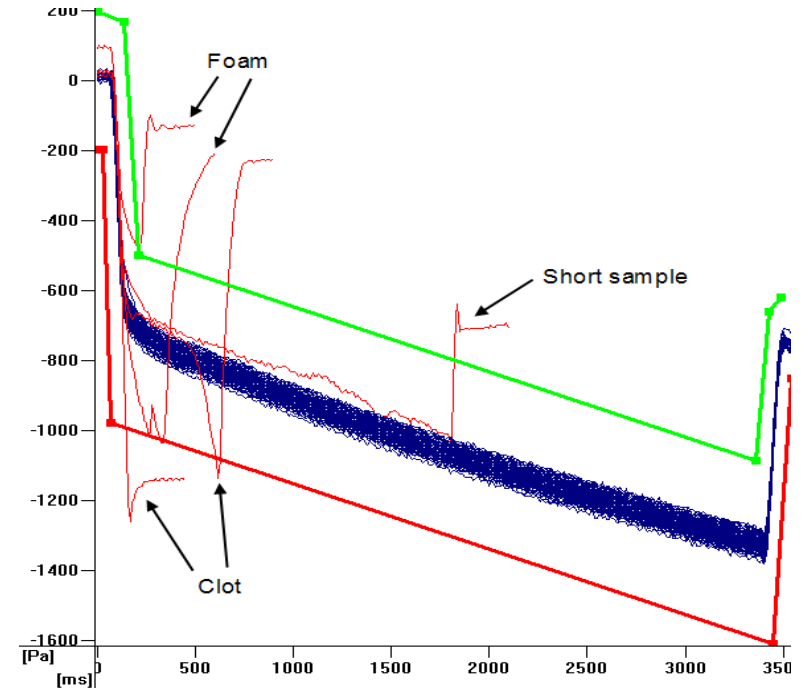
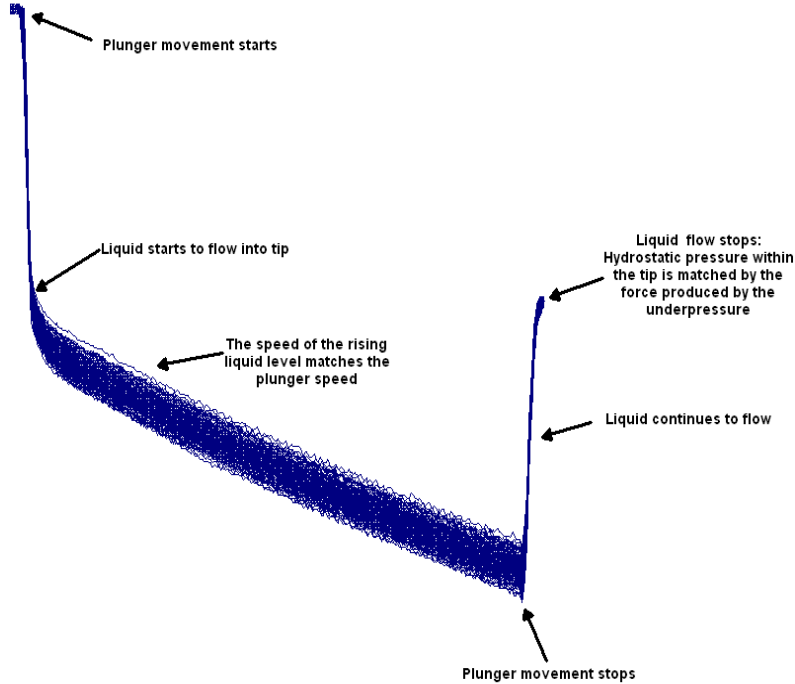


- Approval and Release
- Implementation in SOP
- Validation
- Productive usage



# Liquid Handling and Error recognition

## Total Aspiration and Dispense Monitoring



Recording and monitoring of complete pressure curve during aspiration and dispense  
User defined tolerance band. If measured value leaves the tolerance band, pipetting stops immediately and error handling is executed”  
Requires recording of pressure curves for each liquid class and volume



# Examples



# Current level of Laboratory Automation

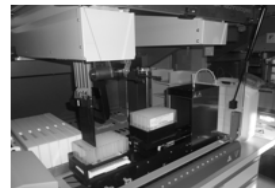
Lead-in (Spiking)

Tube to plate  
reformatting

Plate processing

Read-out

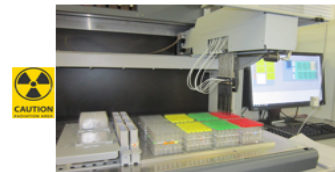
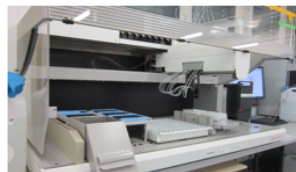
LCMS PK



EIA PK & ADA



RIA PK & ADA





# The biggest challenge.....

... and how to overcome

- Inadequate labels on tubes sent from central labs: limitation of tracability, relabeling might be necessary

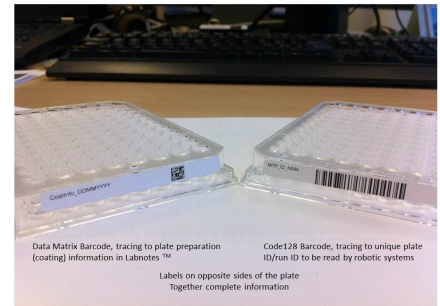
No «white space» for start/end of barcode



Horizontally affixed label – not readable (even not with handheld scanners)

- Different labware used for sample storage within study: leads to false determination of filling status

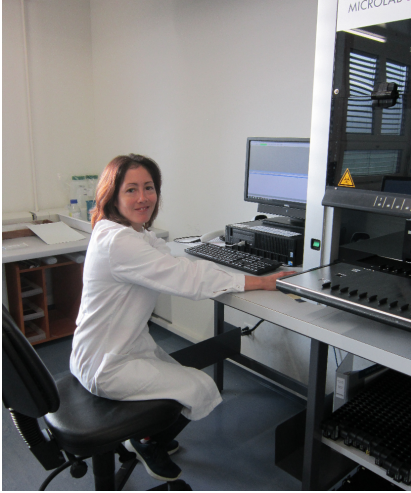
→ Request tester of «kit» (readily labelled sample tube) for central lab/clinic



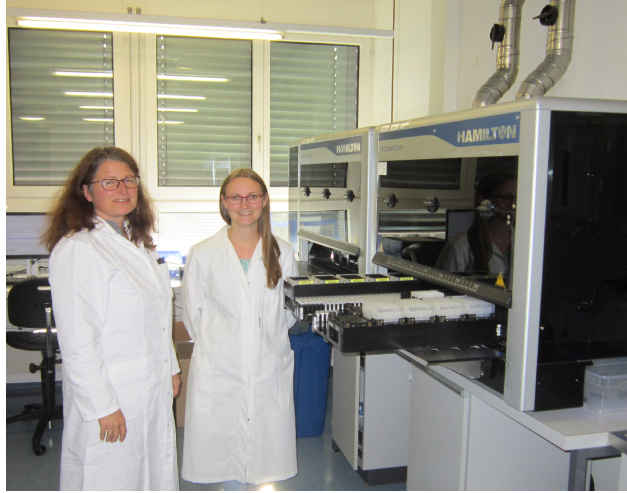


Last but not least

## Build a team of dedicated people



Rebeca  
Robot and Labnotes Programming



Simone  
Beta-User

Anke  
Instrument Responsible  
(Programming and Hardware)



Irene & Frieder  
Instrument Responsibles (Programming and  
Hardware)

→ **Lab staff needs to understand robotics as fellow, not as rival**



# Summarized overview

- No System can accomplish all tasks: define your needs, configure the system and keep it to a dedicated functionality
- CS validation: Cover all basic, standard, daily aspects of the system, also including induced errors
- Depending on the method the output per person increased by a factor 2 to 10
- Have a manual/semi-manual process as back-up in case of system failure or limited system capacity included in the validation
- Increased traceability throughout the process
  - Alerts related system status via light and email
  - Error logs / barcode reading
- Increased batch success rate
- Ensure proper training of employees
  - e.g. Deck layout check, loading of samples and disposables, filling volumes
- Early Communication with internal & external partners regarding container types and volumes, bring everyone on-board early in the process
- Purchasing control for disposables, like for like is not always the case

Reliability of results

Increase throughput

Tracability of data

Reproducibility of results

Assay robustness

Availability of resources



Thank you for your attention