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Applied Translational Medicine

Integrating Automated Systems for Regulated Bioanalysis

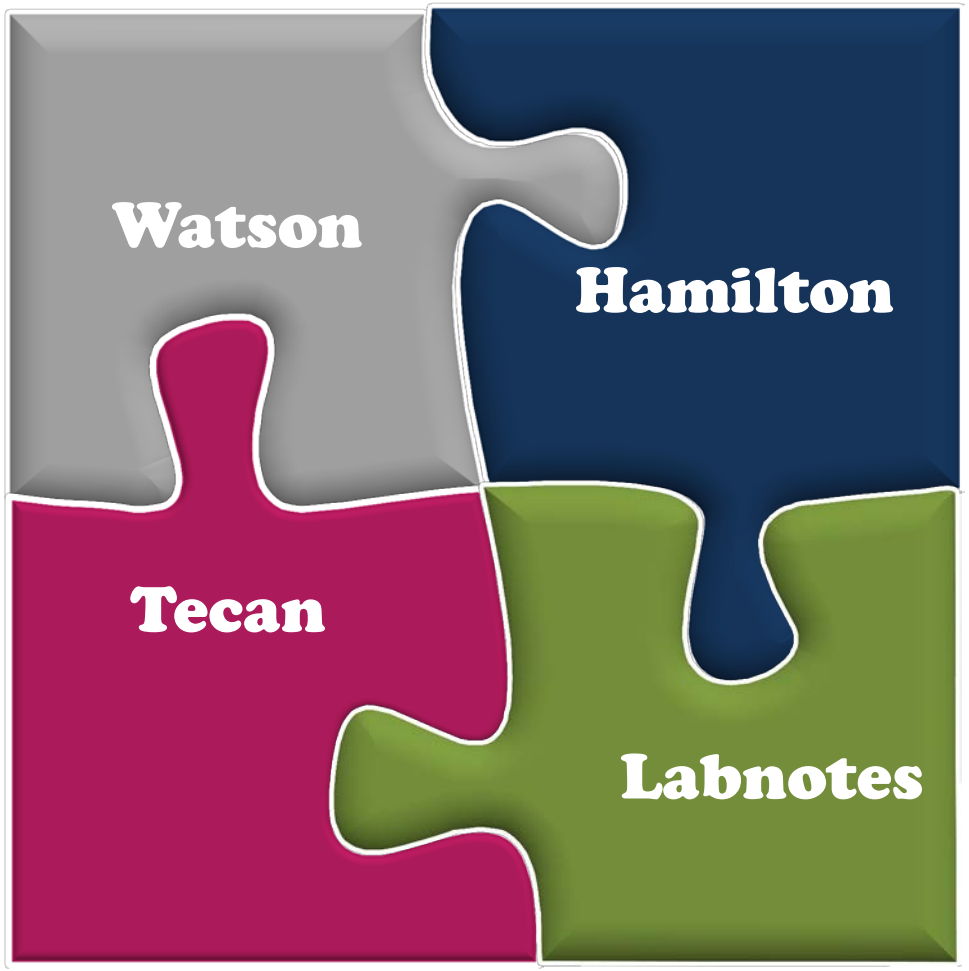
Farmen, R.H., Struwe, P. and Groeschl, M.

EBF Meeting Nov 2014

Implementation Challenges

- Integration of robotic systems into existing bioanalytical workflow
- Interfacing with global databases including management of increased data volume due to increased throughput
- Selecting the correct Robotic System Validation Approach
- Standardization of internal and external processes, i.e. sample tube size and labelling

Interaction of Databases and Equipment



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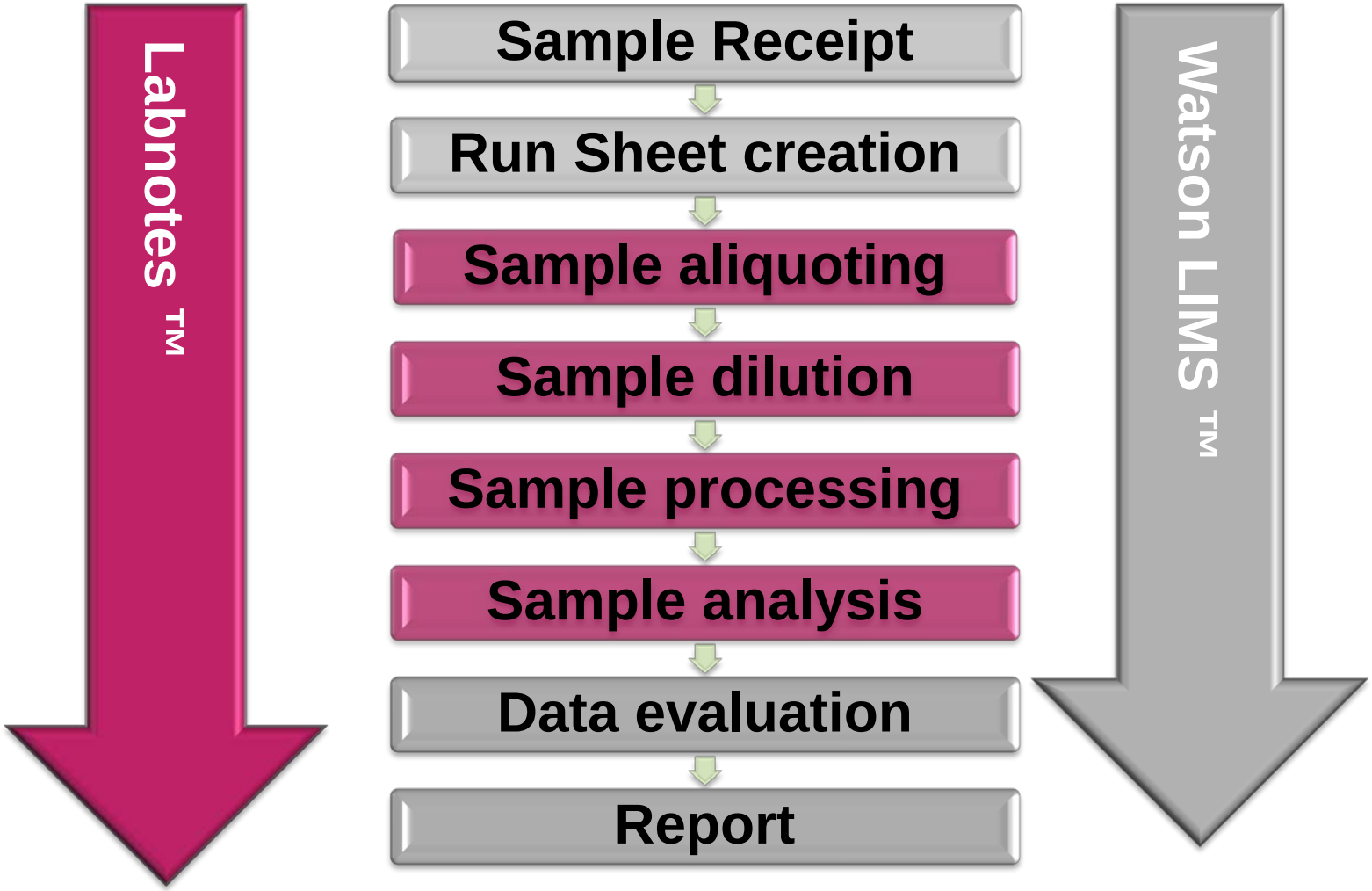
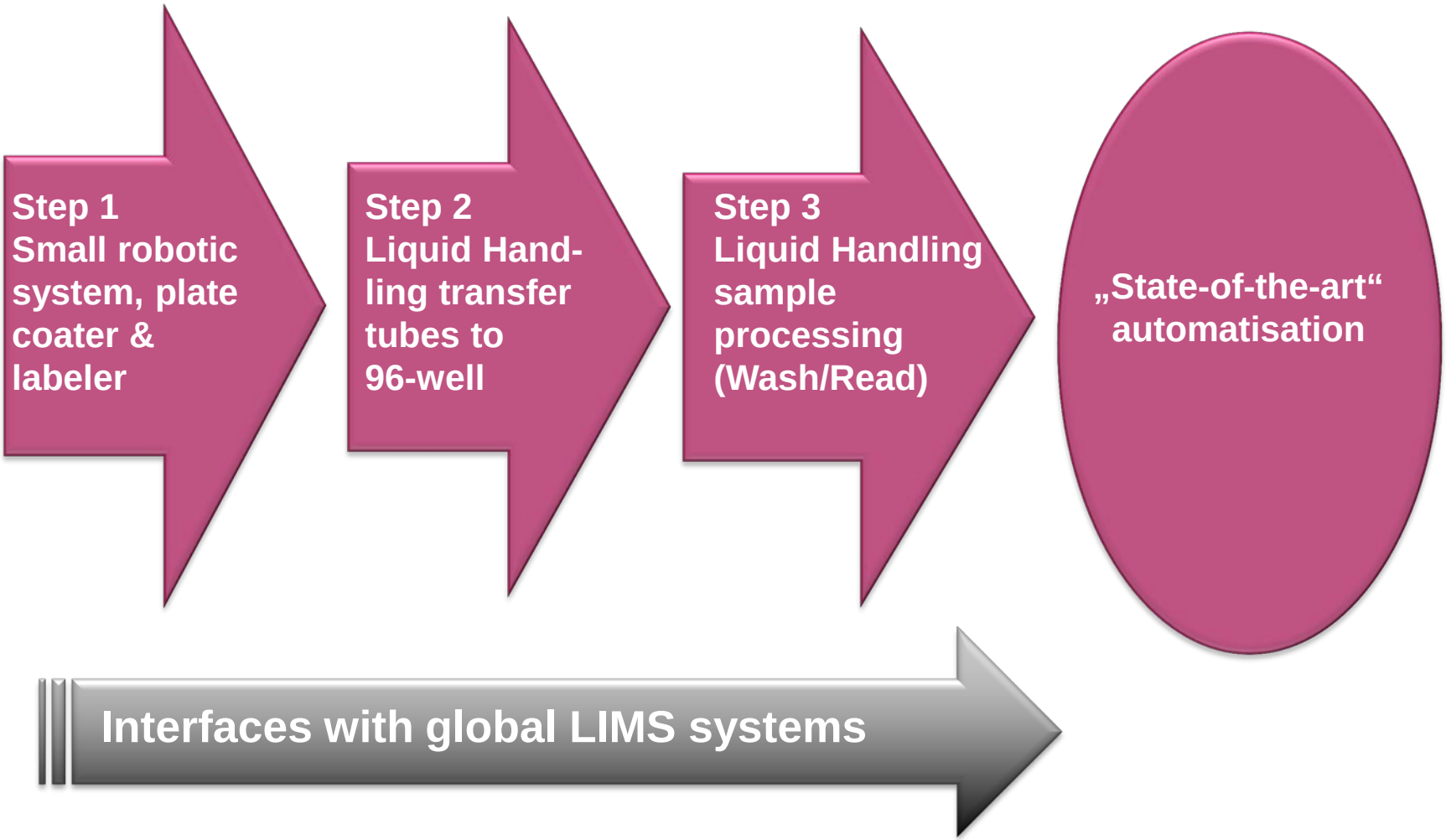
Process Flow of typical ELISA Assay



Stepwise Implementation of Automatisation



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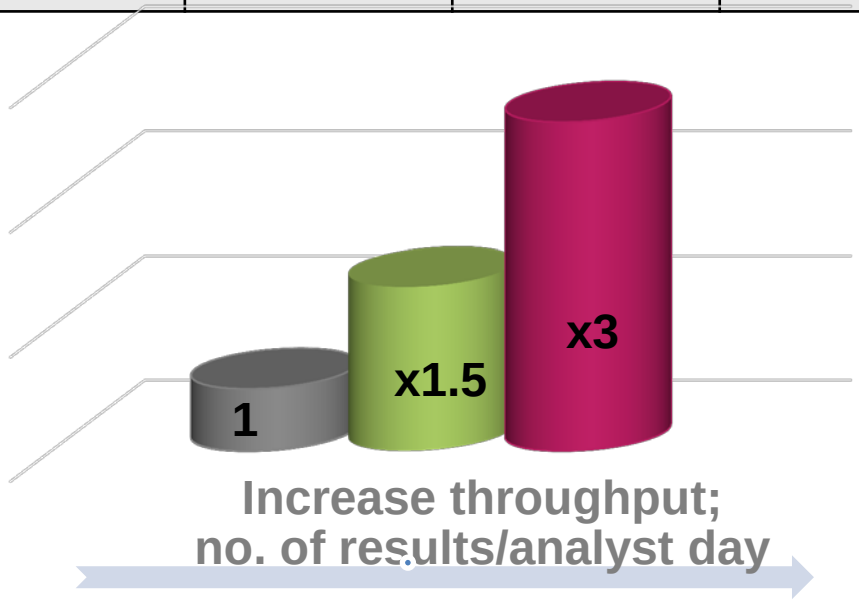
Throughput increase using automation

Lead-in	Sample Aliquoting	Sample Dilution	Sample Processing	Sample Analysis	Data Evaluation
Manual Approach	Manual	Manual	Manual	Manual	Manual	Manual
Semi Automated	Manual & Robotic	Robotic	Robotic	Manual	Manual	Manual
Fully Automated	Manual & Robotic	Robotic	Robotic	Robotic	Robotic	Manual



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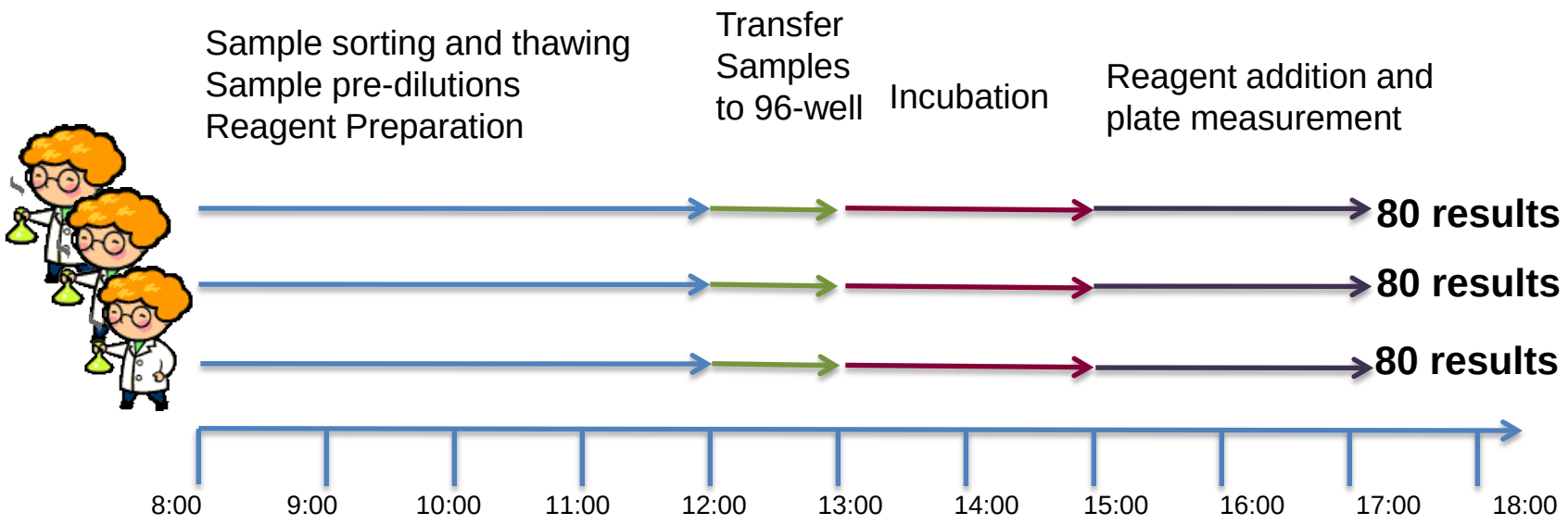
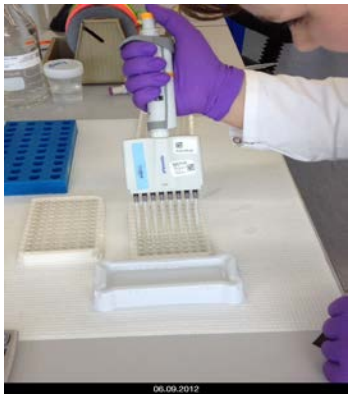
Manual Approach Standard EIA in Human Serum

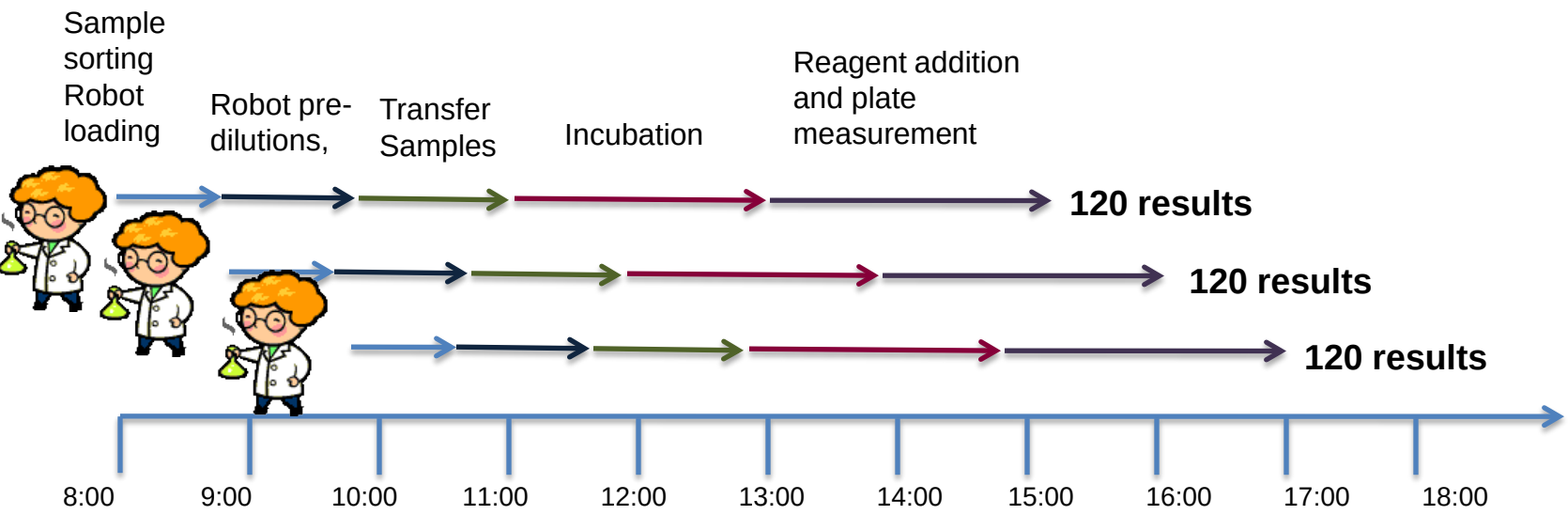
4 plates per Analyst → **12 plates per day (approx. 240 results)**

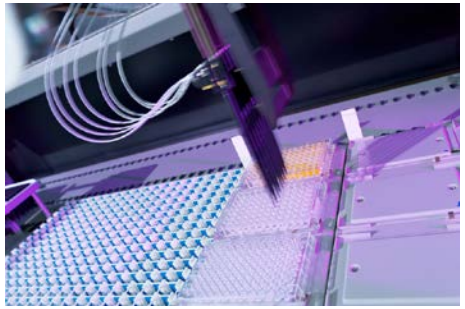




Semi automated approach Standard EIA in Human Serum

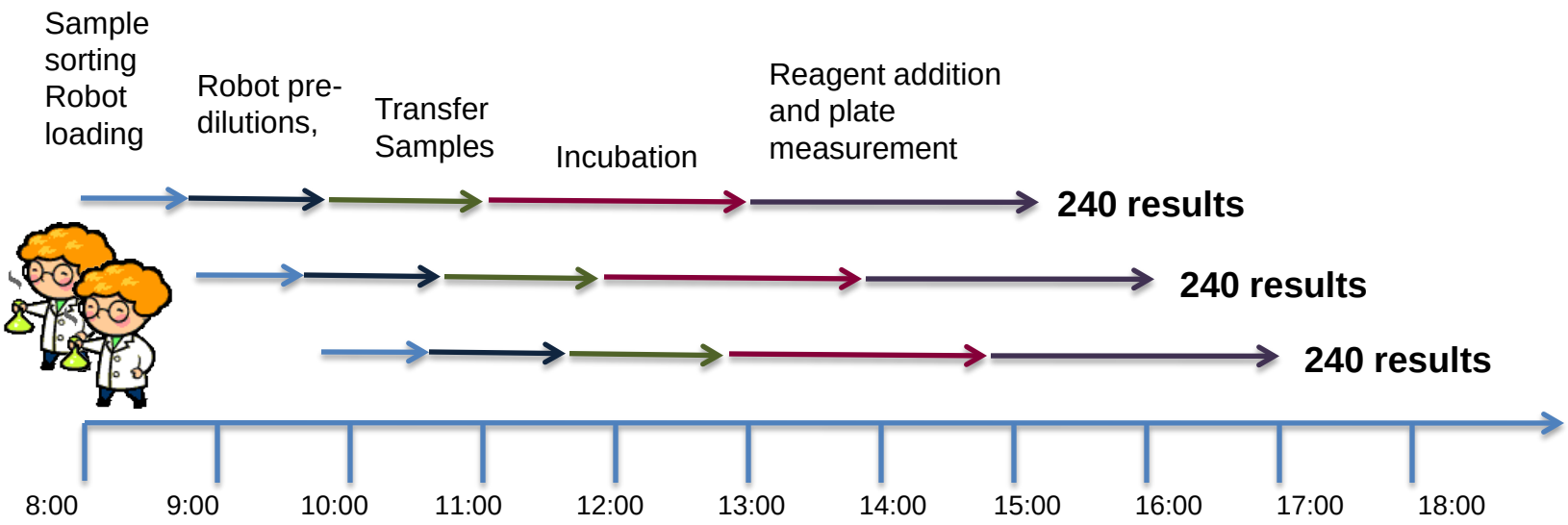
6 plates per Analyst ⟹ 18 plates per day (approx. 360 results)

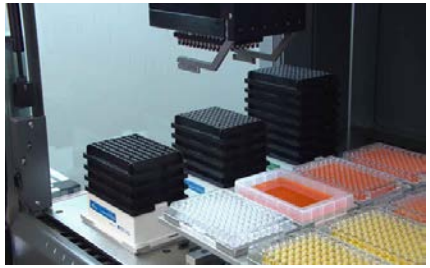




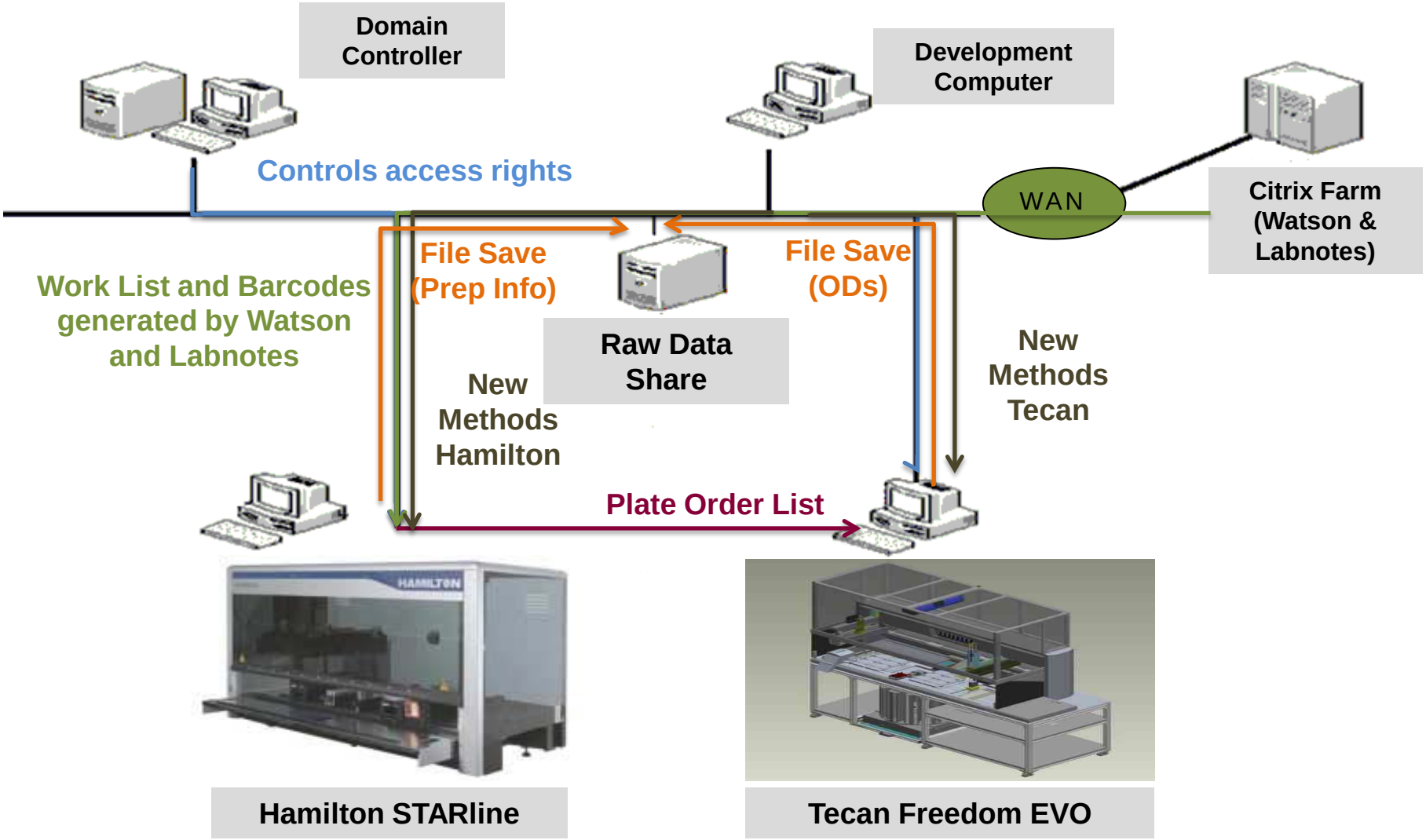
Fully automated approach Standard EIA in Human Serum

36 plates per Robot → **36 plates per day (approx. 720 results)**





System Diagram of typical ELISA workflow



Challenges during implementation

- Overcoming barcode differences between Watson™ and Labnotes™
  - Two barcodes on same label

- Standardizing plate labeling

- Import and export sample lists and results files directly from and to Watson™

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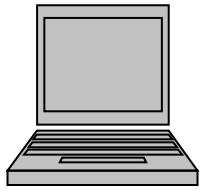
Automation Validation Approaches

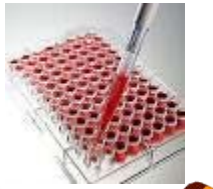


Global databases

Objective:
prove suitability of intended use

Robotic System Validation(s)

Analytical Method Validation



System Suitability Tests

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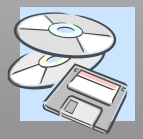
Automation Validation Approach Type 1

All sample process steps and all critical parameters included in original robotic system validation include:

- Liquid Handling
  - (including all possible container types, volumes and potential matrices)
- Peripheral Equipment (i.e. plate coater, washer, reader)
- Barcode Scanner
- Interfaces within the system as well as with global data bases
- Up-Scaling for increased sample throughput

Automation Validation Approach Type 1



Global databases

Objective:
prove suitability of intended use

Robotic System Validation

Analytical Method Validation

System Suitability Tests

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Automation Validation Approach Type 1

Advantages:

- Minimizes individual method validation effort
  - all of the parameters impacted by the robotic system set-up are already included in the original system validation
- Majority of work done before robotic systems are released for method validation

Disadvantage:

- Significantly more time is required for system validation before automation can be used productively because all critical parameters are included in the robotic system validation
- Associated methods have to based on parameters included in the original robotic system validation which limits its flexibility

Automation Validation Approach Type 2

During the original robotic system validation the general handling and processing tests are limited to the following critical parameters:

- Liquid Handling
  - General testing for P&A based on standard container types, volumes and test matrices
- Peripherial Equipment (i.e. plate coater, washer, reader)
- Barcode Scanner
- Interfaces within the system as well as with global data bases

- Method specific container types, pipet volumns and liquid handling classes (if required) are optimized during method development and included in the method validation.
- Up-Scaling for increased sample throughput is tested during method validation

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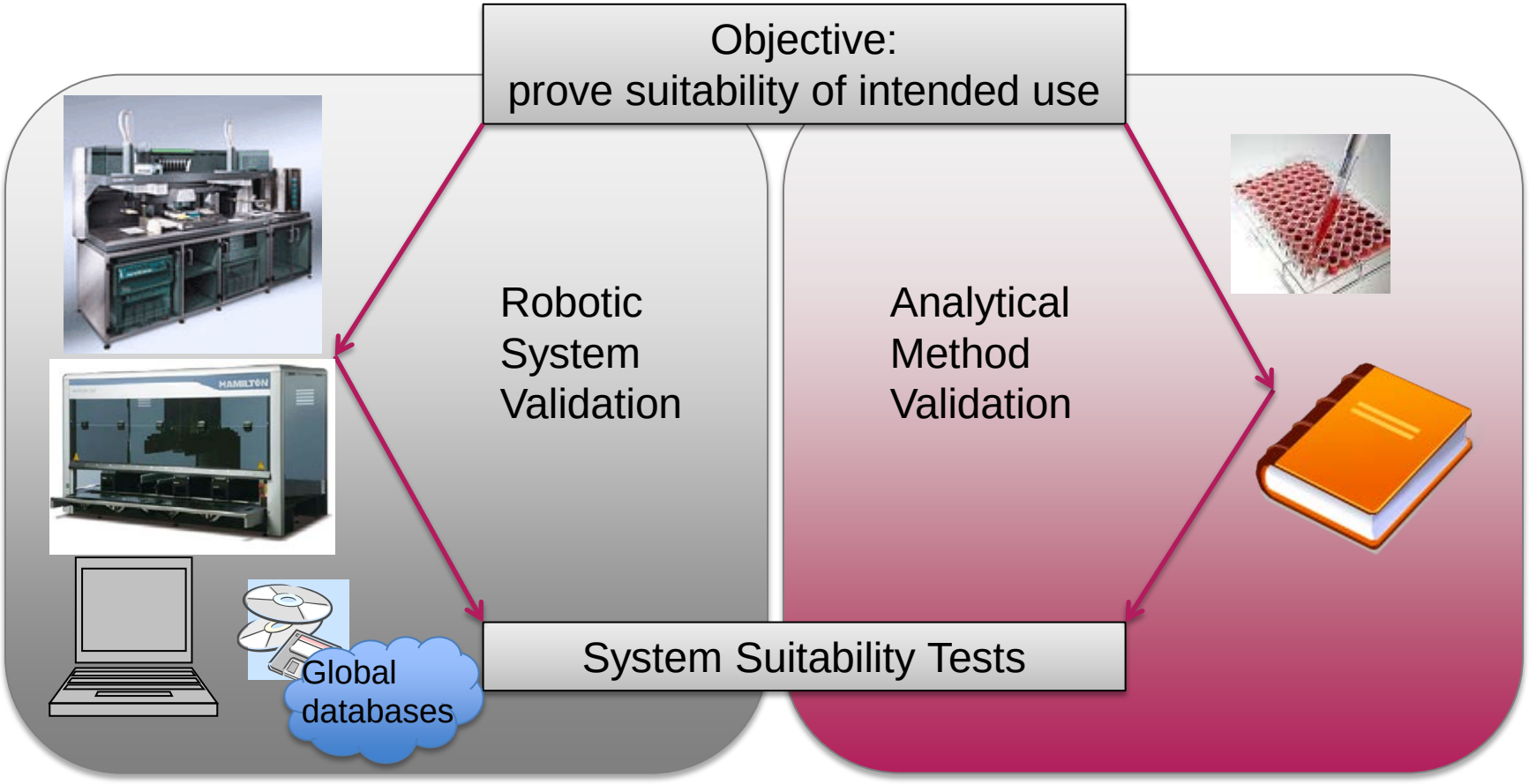
Automation Validation Approach Type 2



Automation Validation Approach Type 2

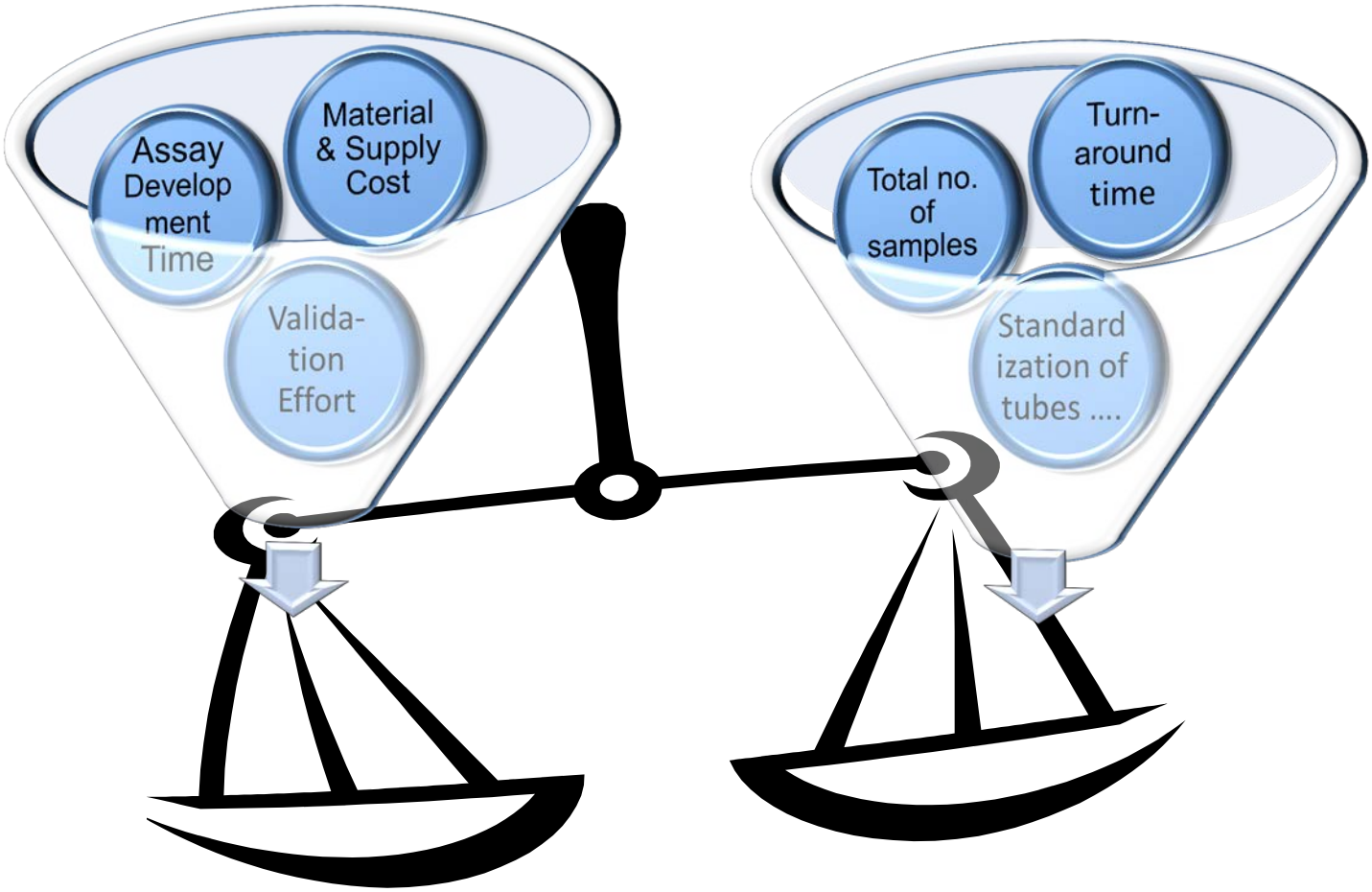
Advantage:

- Reduced effort during the robotic system implementation before released into GxP environment
- Early access to the robotic systems to test its suitability during standard bioanalytical work flow
- High flexibility to adopt to business needs

Disadvantage:

- Increased method development and validation effort to cover method specific parameters
- Increased lead-in time per method

When and how to automate?



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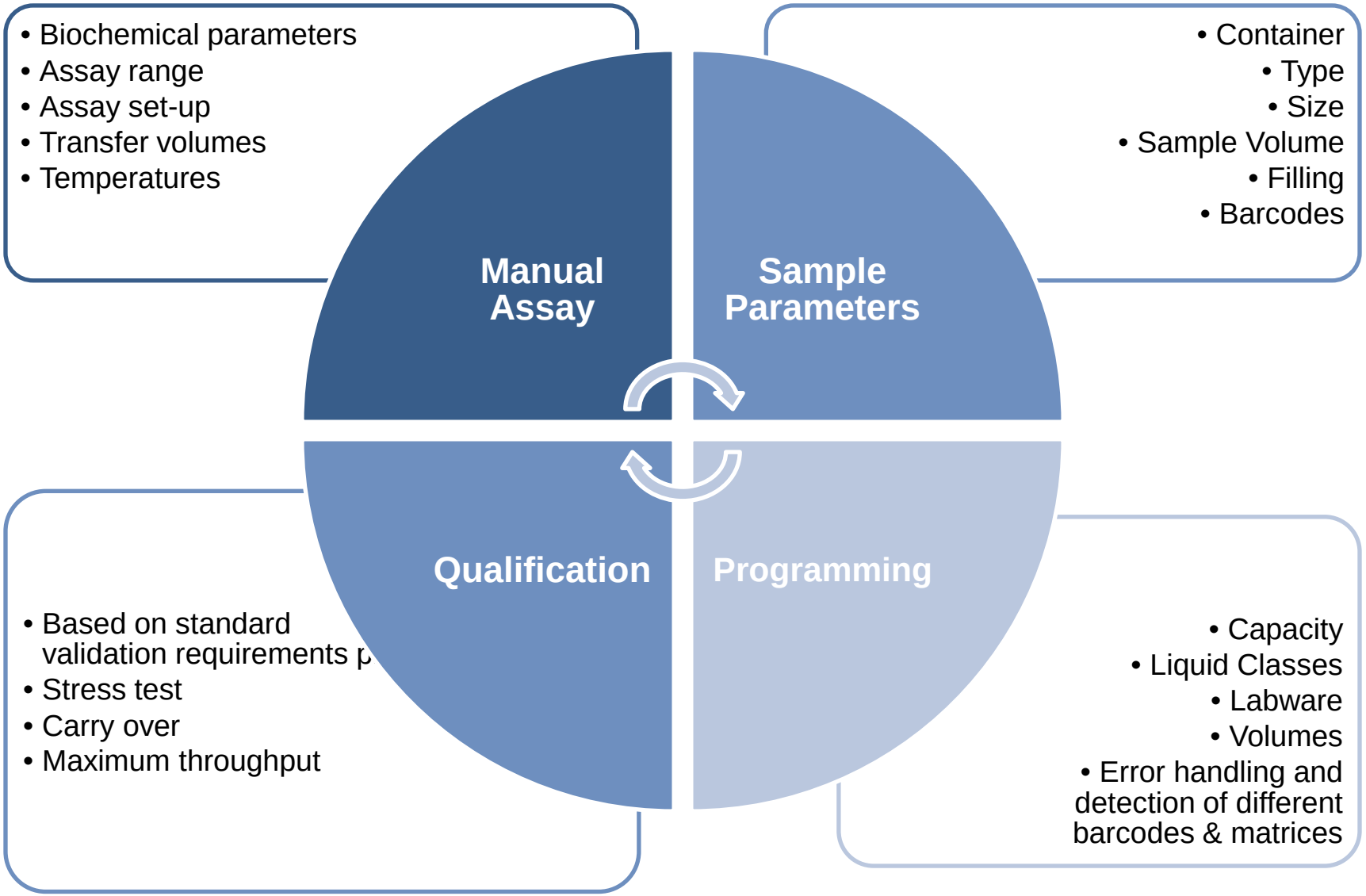
Process Flow Method Development for Automation



Manual Assay Validation

- Specificity (Cross-reactivity)
- Selectivity
- Calibration Curve (Response function)
- Precision and Accuracy
- Dilution Integrity/Dilution Linearity
- Parallelism
- Matrix Selection/Minimum Required Dilution
- Stability

Automated Assay Validation

- Specificity (Cross-reactivity)
- Selectivity
- Calibration Curve (Response function)
- Precision and Accuracy
- Dilution Integrity/Dilution Linearity
- Parallelism
- Matrix Selection/Minimum Required Dilution
- Stability
- Carry-over / Stress Test
- Maximum throughput including associated stability assessments for samples and reagents on deck

Training

System related training

- Software usage (Access rights)
- General usage (Maintenance)
- Security aspects
- Data flow
- Documentation aspects

Method related training

- Process usage (User interfaces/User prompts)
- Specific usage (e.g. Deck layout check, loading of samples and disposables, filling volumes)
- Storage locations input and output files
- Emergency/Error handling
- Purchasing control for disposables (What, Where, How much)

Challenges – Lessons learned

- Early Communication with internal & external partners regarding container types and volumes, bring everyone on-board early in the process

- «Expect the unexpected», reminder automation does not mean everything will be faster! Therefore, allow sufficient time for lead-in.

- Develop flexible systems that will have multiple uses over time.

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Conclusion

- Automation results in significant increases in traceability and reproducibility due to audit trails and standardized input/output files using Watson™ LIMS
- Automation results in online QC of sample container order and identity
  - via Labnotes™ online QC of used reagents and materials
- Automation allows managers to shift personnel lab duties since manual pipetting is largely eliminated
- Important to keep the balance between what you're required to do versus what would be nice to do.

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