# Automation in a regulated bioanalytical lab

## Experience from a five-year journey from a manual to a 100% automated workflow

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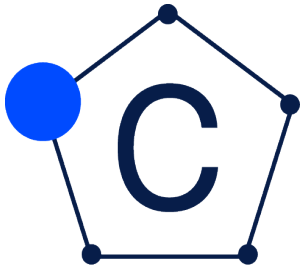
# The story of lab automation @AbbVie

1. Why automation?
2. Designing a workflow
3. System Design
4. It’s all about logistics
5. Total Automation
6. Qualification Strategy
7. Pitfalls
8. Lessons Learned

# Why Automation




Make
Possibilities
Real

- Regulated Bioanalysis @AbbVie Ludwigshafen:

  Responsible for all large molecule BA activities at AbbVie (GLP/GCP)
- Support for PK, Biomarkers, ADA and neutralizing ADA
- IT-infrastructure: Electronic-Lab-Notebook, electronic archival routines etc.
- Working horse: Ligand-Binding-Assays (95% electrochemiluminescence)

**Challenge in 2014 – How it started:**

- Dramatic workload increase but flat headcount

  (35.000 samples within 5 months but capacity for only 12.000 samples)
- Only option to cope with increased demand was to boost efficiency

  → Starting point for lab-automation initiative in reg BA @AbbVie

# Design New Workflow – Pain Points

Sample Receiving:

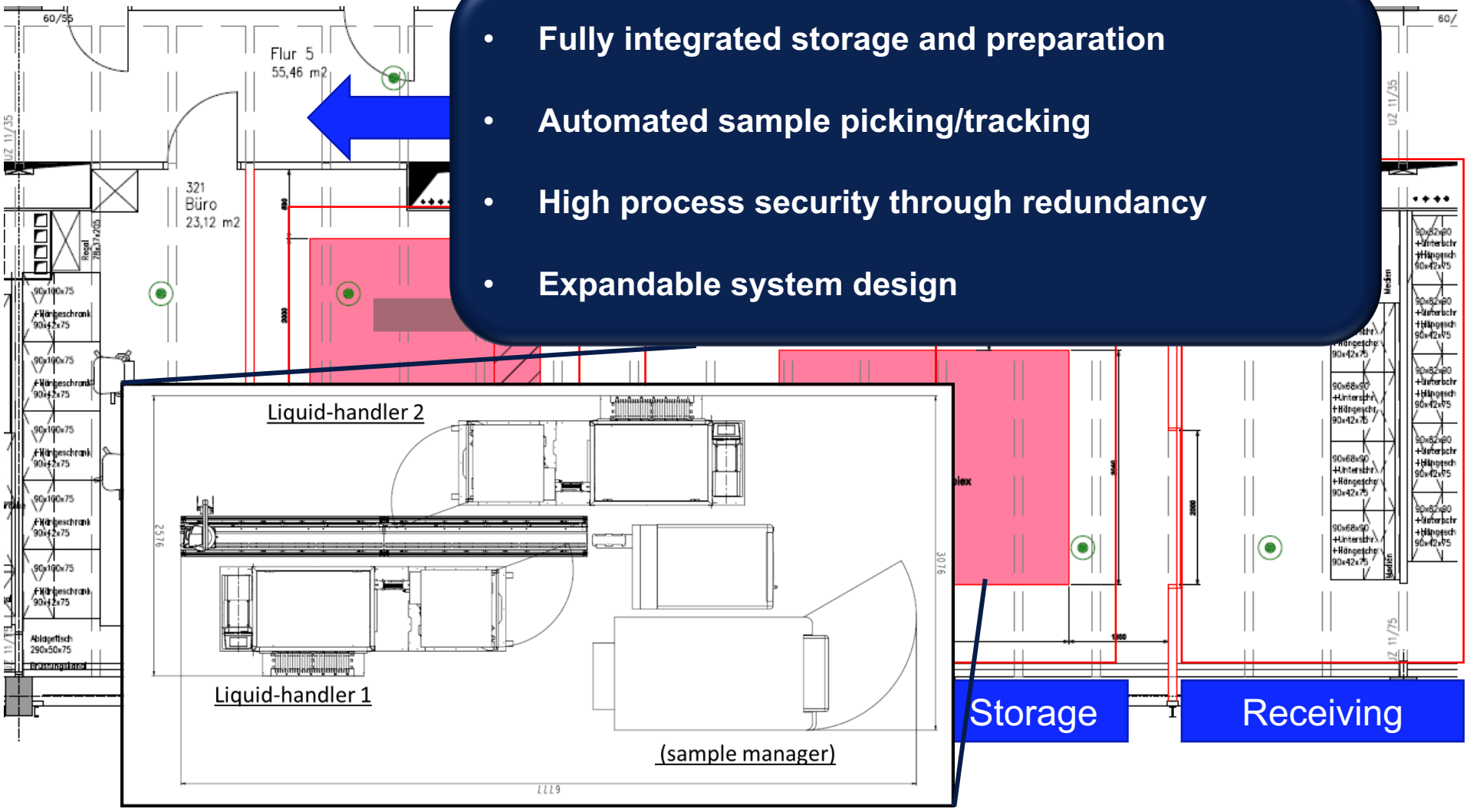
1. Setting up LIMS error prone 
2. Receiving samples slow and error prone 
3. Storage logistics difficult and sample picking labor-intensive 

Sample Analysis:

1. Time from request to samples available long due to picking 
2. Individually diluting samples to 96 well plate difficult, slow and error prone 
3. Preparation of STDs and QCs cumbersome and analyst error introduced 
4. Picking of STDs and QCs cumbersome and inventory hard to maintain for multiple projects 
5. Assay execution long and gaps due to incubation steps hard to fill 
6. Running multiple assays in parallel almost impossible due to logistics 
7. Reassay difficult as samples need to be picked 
8. Return to sample receiving requires scanning of all samples for tracking 

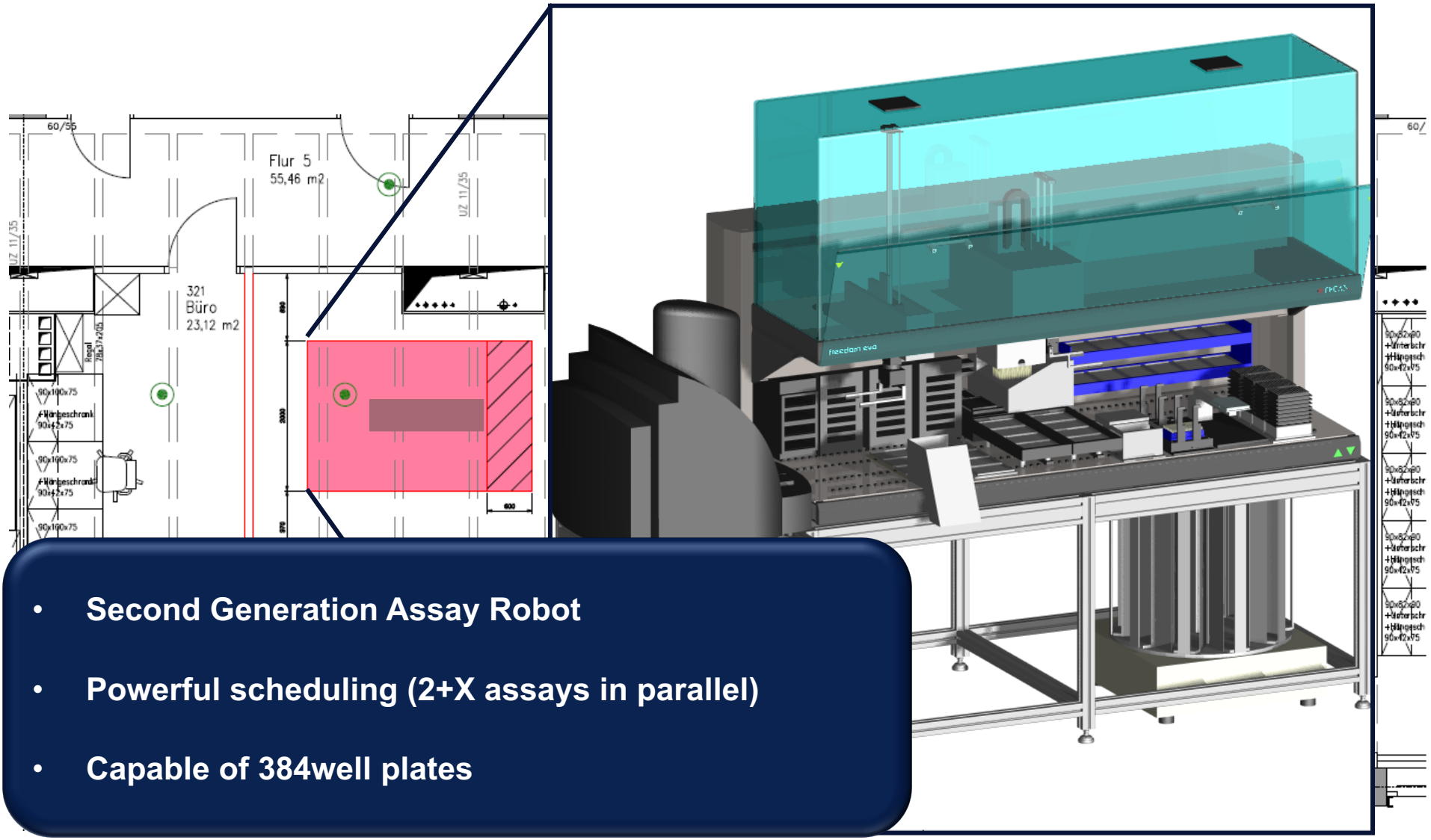
# Assembly Line vs. Island Approach

- Fully integrated storage and preparation
- Automated sample picking/tracking
- High process security through redundancy
- Expandable system design




→ Laboratory layout optimally adapted to process needs

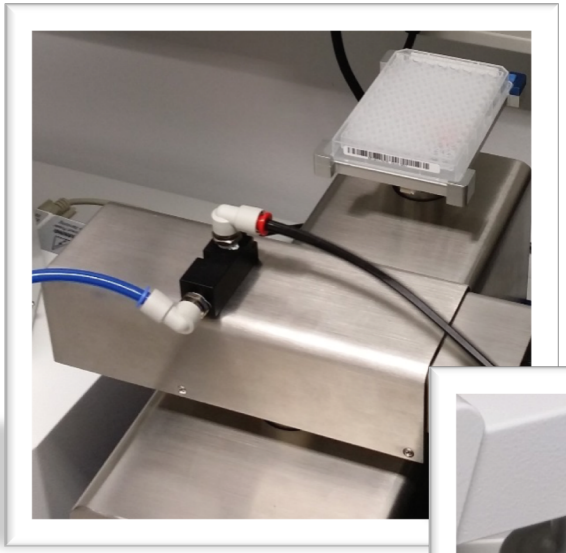
# Assembly Line vs. Island Approach

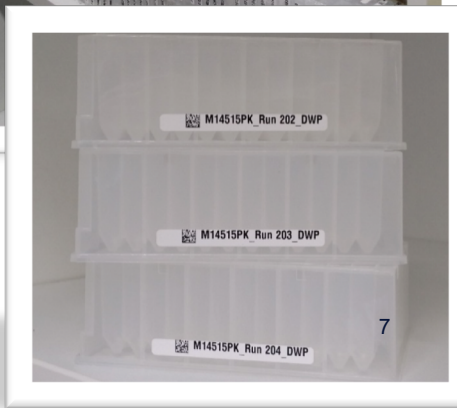



- Second Generation Assay Robot
- Powerful scheduling (2+X assays in parallel)
- Capable of 384well plates

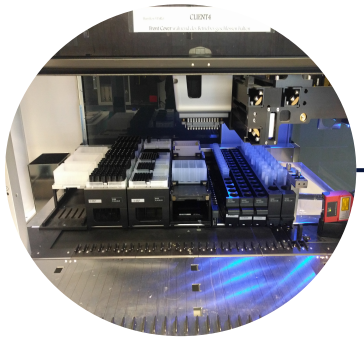
# It’s all about logistics - The little things

With the introduction of automation sample flow traceability becomes an underestimated challenge
→ fully barcode controlled workflow
→ necessity to pre-label thousands of MTPs and tubes!!



# Total Automation: It's not only BA-Operations



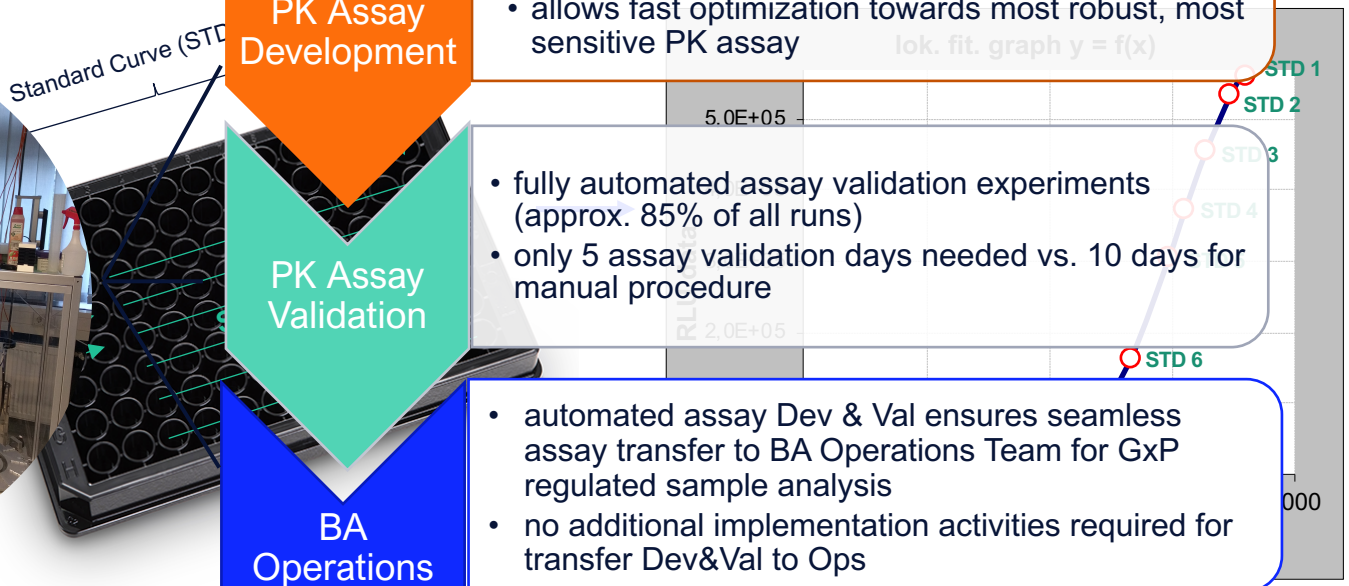
**Automated STD/QC Preparation**

- Standard (STD) Calibration and Quality Control (QC) Samples
- less variability between different preps
- increased process efficiency through less rework

-> high quality data

**PK Assay Development**

- DoE-like setup
- 100% increased thoughput vs. manual handling
- allows multiparametric data evaluation
- allows fast optimization towards most robust, most sensitive PK assay




**PK Assay Validation**

- fully automated assay validation experiments (approx. 85% of all runs)
- only 5 assay validation days needed vs. 10 days for manual procedure

**BA Operations**

- automated assay Dev & Val ensures seamless assay transfer to BA Operations Team for GxP regulated sample analysis
- no additional implementation activities required for transfer Dev&Val to Ops



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# Benefits

- The automated sample analysis went from 0 % percent in 2013 to almost 90% of all PK samples in 2018 and >50 % of all ADA samples (from 0% in 2016)
- The throughput per person tripled for PK and ADA assays when executed using robotics
- Flexible system and process design allowed to cope with fluctuating demand

Pipeline evolution and it‘s impact on operational processes

2014: Primarily late stage pipeline

→ automation and logistics focused on large batches

2016: Strong shift towards early stage clinical development, minimal late stage

→ automation/processes were redesigned for smaller batches

2019: Balanced mixture of early and late stage trials

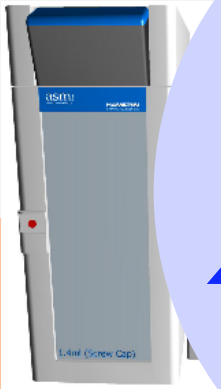
→ automation enables to easily switch between small and large batches

# Pitfalls: Things we've learned the hard way

## Operational Perspective

Sample tubes/barcodes automation friendly???

Chain of Custody? (rather an asset than a challenge!!)



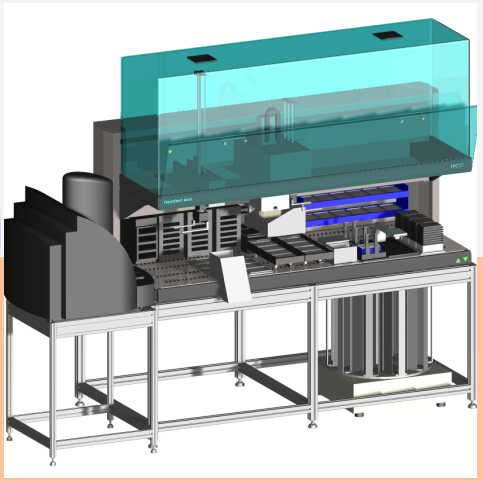
Need for procedures on "How to handle error messages"

Integ… …k

Continious Improvements

…act key information from log-files

System redundancy to backup down-times



Additional stability and robustness testing during assay validation

## Regulatory Perspective

# Qualification Strategy - Things we focused on the most

Analytical performance
- Accurate and identical handling of all steps, liquid transfers → for all analytical plates

User management
- Access for authorized staff only
- Different layers of user rights: User vs. SME vs. Admin
- Impact on operational processes: E.g. overnight runs, access for emergency interactions

Raw data integrity and data flow
- How is the system embedded into the local IT infrastructure
- How are raw data maintained → user friendly archival process
- What exactly are you‘re raw data?

Tracing of expected and unexpected events
- Is it convenient to retrieve error messages from log files → understandable for non-SMEs?

Error handling
- Clear understanding of error handling capabilities → huge impact on system design and qualification but also on operational performance

**Vendor input is absolutely critical to avoid pitfalls and to achieve maximum performance**

# Lessons learned along the way Part 1

- Process scalability without addition of new resources:
  a) Well designed automation is allowing easier coping with fluctuations in the pipeline
  b) The impact of e.g. large phase III studies is minimal in a well designed setup
- Improving the quality of the analytical data:
  a) Due to automation run to run variability is extremely small and variations are mostly explained by e.g. failing parts
  b) Highly standardized raw data documentation
- Increased traceability of the analytical workflow
  a) The trace files available after each analytical run and 100% barcode based workflow allow a perfect traceability of every sample
- Improved scheduling and demand vs. capacity forecasting for accurate planning
  a) The performance of the systems can be predicted “easily”

# Lessons learned along the way Part 2

- Have an ability to back-up automated processes semi-automated or manually
- Consider higher initial downtimes and refinement periods optimizing the solution
- Involve IT early in discussions making sure that e.g. antivirus software, updates and network infrastructure don’t interfere with routine workflow
- Define error handling early with vendors making sure that downtime is minimized and things such as e-mail notification, camera surveillance, remote access etc. aren’t an issue
- If possible, separate workflows in smaller pieces and don’t go to an assembly line like model, as one error in the line will reduce productivity to 0 and combinations of manual and automated execution are not possible
- Identify people in your team that can work as seeds with a strong interest in innovation
- Refine working model with e.g. possibilities to monitor systems remotely and working in shifts
- Make sure that your **vendor** wants to be your **partner** and build a close relationship understanding capabilities and limits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