

# Quality 4.0 – The Future of Quality in Pharma

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McKinsey's Hamburg office



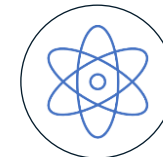
Lead two digital transformations to WEF lighthouse sites



Passionate about Advanced Analytics in Pharma Operations



Background in automotive operations and academic physics



# Digitization is transforming our world...

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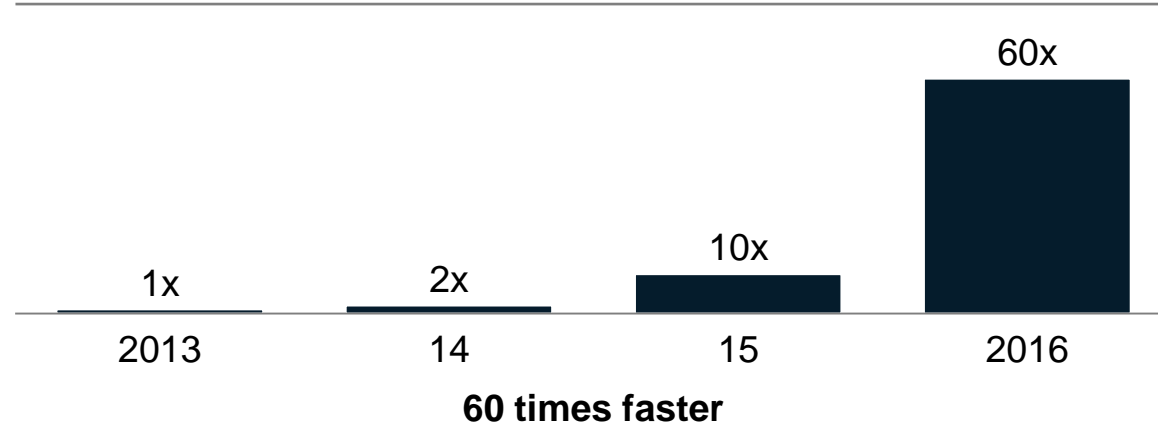
By 2020, there will be **21 billion** connected devices in a global Internet of Things, producing an ever-increasing amount of data

**90%** of the world's data today has been created in the last 2 years only

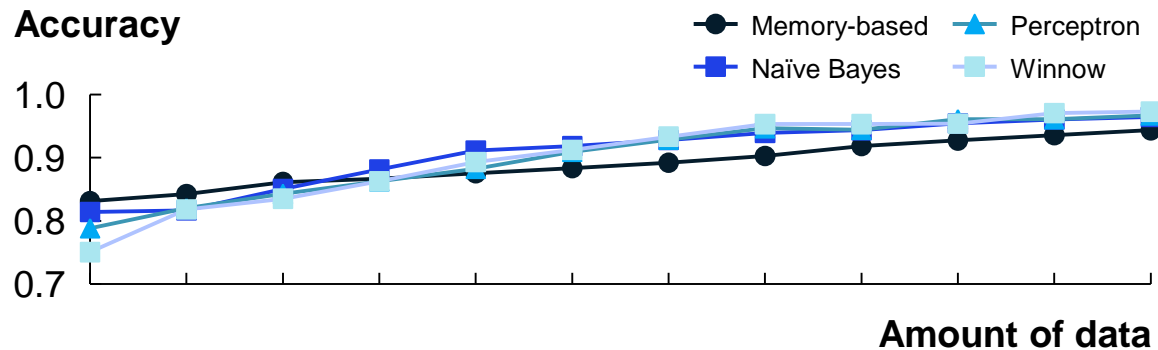
Each day we create **2,500,000,000,000,000,000** (2.5 quintillion) bytes of data. This would fill 10 million Blu-ray discs, the height of which, stacked, would equal the height of 4 Eiffel towers

# The limits of what's possible are continuously moving

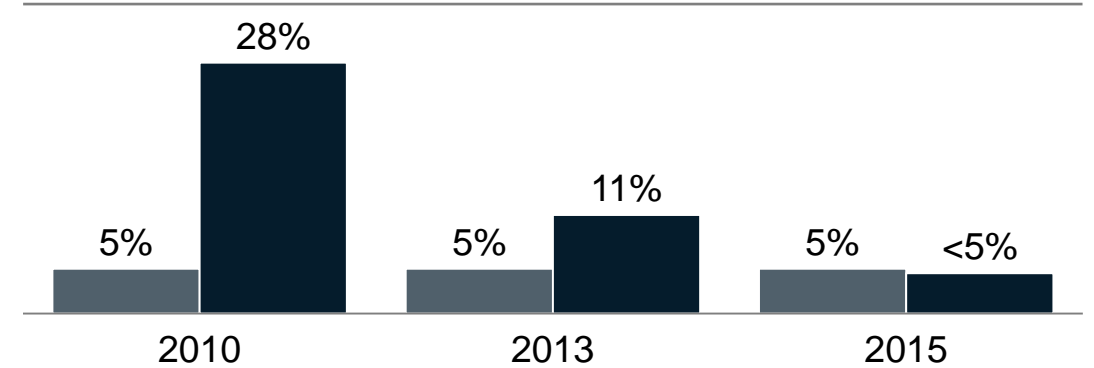
## GPU Image/second training speed



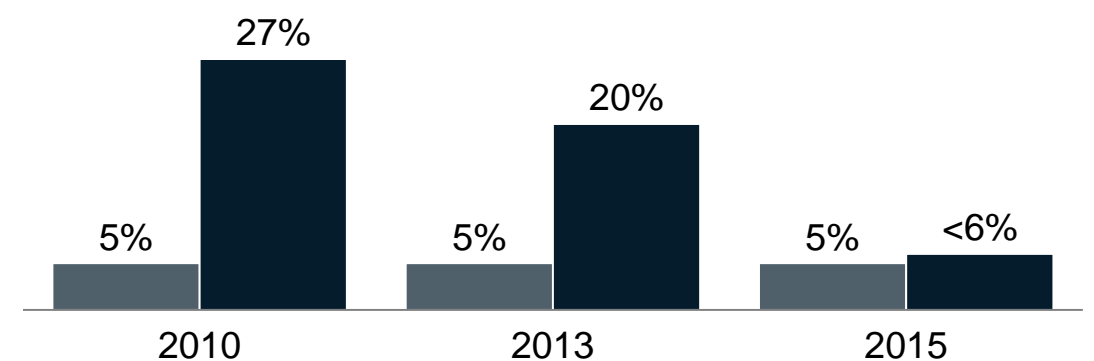
## Accuracy of various Machine Learning algorithms



## Image Recognition Error Rate



## Speech Recognition Error Rate



# The vision

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Video to be added

**How would Amazon redefine pharma quality operations?**

# Digital & Analytics will drive a paradigm shift in Quality towards real-time release



**Digitally enabled  
quality operations**

Quality control operations supported by advanced 4.0 tools

**"Efficient testing"**



**AA based  
product mastery**

Deep understanding of product quality behavior based on process data

**"Reduced testing"**



**Real-time release**

Quality outcome prediction through real-time batch data-fingerprint monitoring

**"No testing"**

# Digitally enabled quality operations

## Examples

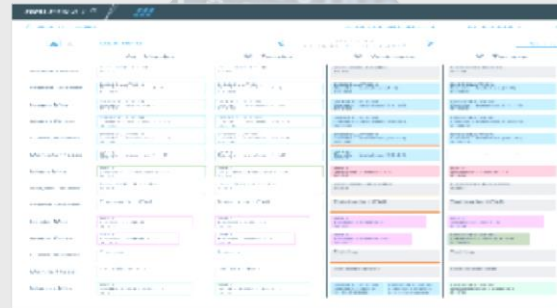


**Digitally enabled quality operations**

Quality control operations supported by advanced 4.0 tools

**"Efficient testing"**

### Digital twin QC scheduling



### Digital twin QC scheduling



### IOT-enabled data transcription



### Automation & robotics



# Many innovative technologies also emerge in quality operations

## New technologies in Pharma Quality (QA and QC)



**Sample preparation automation**



**Enabling Paperless**



**Instantaneous Microbial detection**



**Automation of microbial analysis**

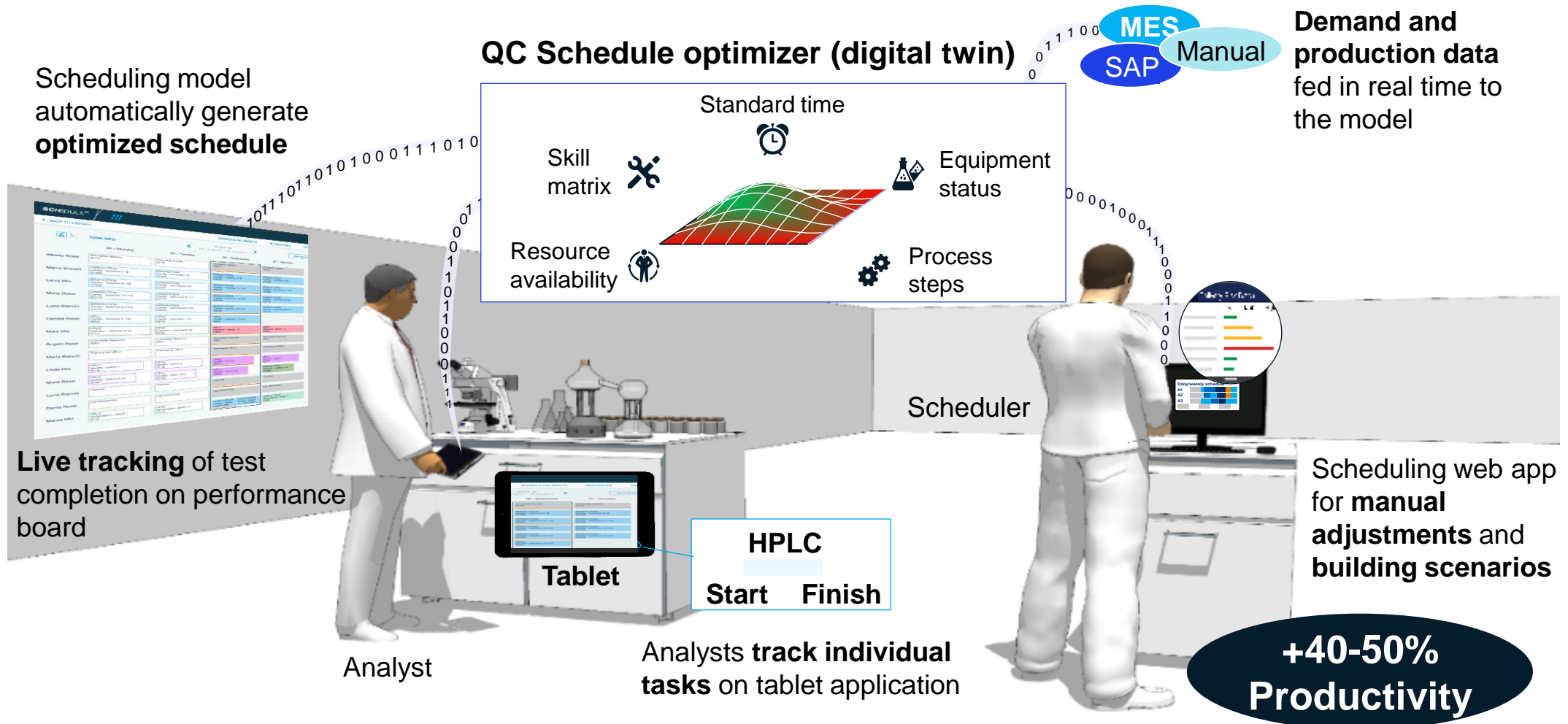


**Automating intangible workflows**





# Digital twin scheduling enables a step change in Quality control productivity



Video to be added

BACK TO LIBRARY

SCHEDULING INPUTS

RESOU

Mod. 1 - DRAFT

WEEK 42  
15.10.2018 - 21.10.2018

Save as new draft

Publish

	15 - MONDAY	16 - TUESDAY	17 - WEDNESDAY	18 - THURSDAY	19 - FRIDAY
Beverly H.	Omnecil 0,5 MG Disso S153	Omnecil 0,5 MG Disso_machine, Disso S1078, S153	Omnecil 0,5 MG Disso_machine, Disso S1089, S153	Omnecil 0,5 MG Disso_machine, Disso S1078, S153	Omnecil 0,5 MG Disso_machine, Disso S1089, S153
Debra R.	Validation S1065				
Howard B.	Validation S1070	Caryxrun 1MG HPLC - PD S261	C Tracilgan 0,2G H Disso S S1068	Caryxrun 1MG HPLC - PD S170	C Caryxrun 1MG H Disso S S176
Kevin H.		Caryxrun 1MG Disso S178	Caryxrun 1MG Disso S178	Training S1011	Training S1011
Amy L.	Sageneilt 500 MG HPLC/Assay S128	Sageneilt 500 MG HPLC/Assay S128	Tracilgan 0,2G HPLC/Assay S128	Tracilgan 0,2G HPLC/Assay S128	Tracilgan 0,2G HPLC/Assay S128
Keith C.	Sageneilt 500 MG TI - FE TI-FE	Sageneilt 500 MG TI - FE TI-FE	Sageneilt 500 MG TI - FE TI-FE	Sageneilt 500 MG TI - FE TI-FE	Tracilgan 0,2G Disso S1067
Catherine P.					Validation S1011
Henry K.	Validation S178	Caryxrun 1MG Disso S176	Caryxrun 1MG Disso S176	Caryxrun 1MG Disso S178	Caryxrun 1MG Disso S178
Lawrence G.	Sageneilt 500 MG Disso S1067	Sageneilt 500 MG Disso S1067	Exodricy 10 MG Disso S1065	Exodricy 10 MG Disso S1065	
Angela R.	Omnecil 0,5 MG HPLC/Assay	Omnecil 0,5 MG HPLC/Assay	Caryxrun 1MG Disso	Caryxrun 1MG HPLC - PD	C H

Unscheduled steps

Evovinavi 1, Omnicil 0,5 -  
Disso\_machine step 1  
Deadline: 20.04.2018

Unscheduled batches

Exodricy 10 MG - Production  
Quantity: 5  
Test types: HPLC/Assay

Omnecil 0,5 MG - Production  
Quantity: 3  
Test types: HPLC/Assay

Caryxrun 1MG - Production  
Quantity: 14  
Test types: HPLC/Assay, Disso\_machine, HPLC - PD

Tracilgan 0,2G - Production  
Quantity: 5  
Test types: Water, TI - FE

Sageneilt 500 MG Caryxrun 1MG Tracilgan 0,2G Exodricy 10 MG Omnicil 0,5 MG

# Augmented/assisted reality is a great tool to optimize standard times, and strengthen process robustness



**-20-30%  
standard time**



**Augmented/assisted reality helps**

Reduce standard times through highly efficient performance dialogs on task level

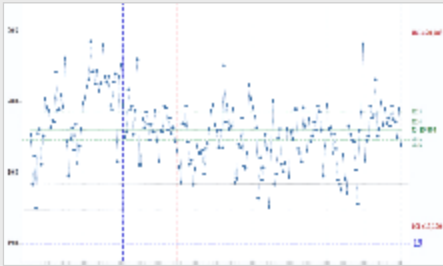
Ensure fast best practice transfer and consistent quality

Train new employees quickly

# Advanced Analytics based Product Mastery

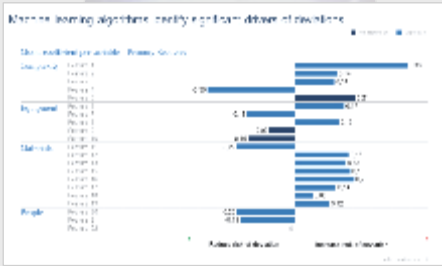
## Examples

### Automated data-trending analysis



### AA based product mastery

### AA enabled Deviation rootcause analysis



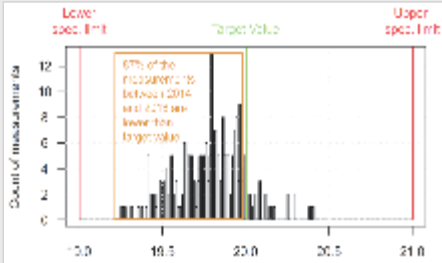
### Quality Bots



Deep understanding of product quality behavior based on process data

**"Reduced testing"**

### Real-time deviation prediction



# Advanced analytics opens new paths to understand and reduce quality deviations

## Approach for pilot

Extracted data from **17+ data sources**

**Modeled 1,000+ variables** including process, data, people, environment, process parameters, etc.

**Generated drivers of deviations** using machine learning algorithms that partly leverage expert hypotheses

Worked **very closely with the SMEs** on **root cause analysis** on drivers of deviations, quantified benefit and developed action plan

## Impact

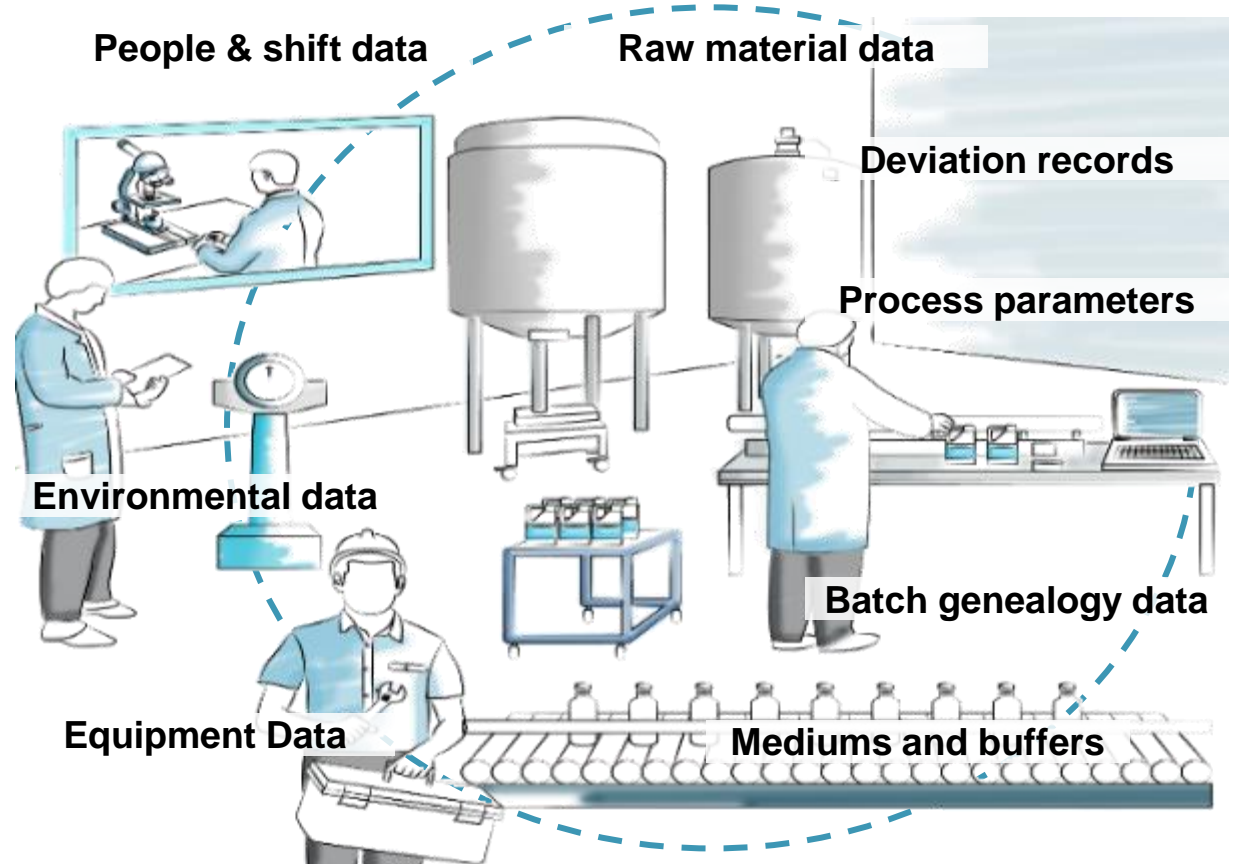
**67%**

Of deviations explained

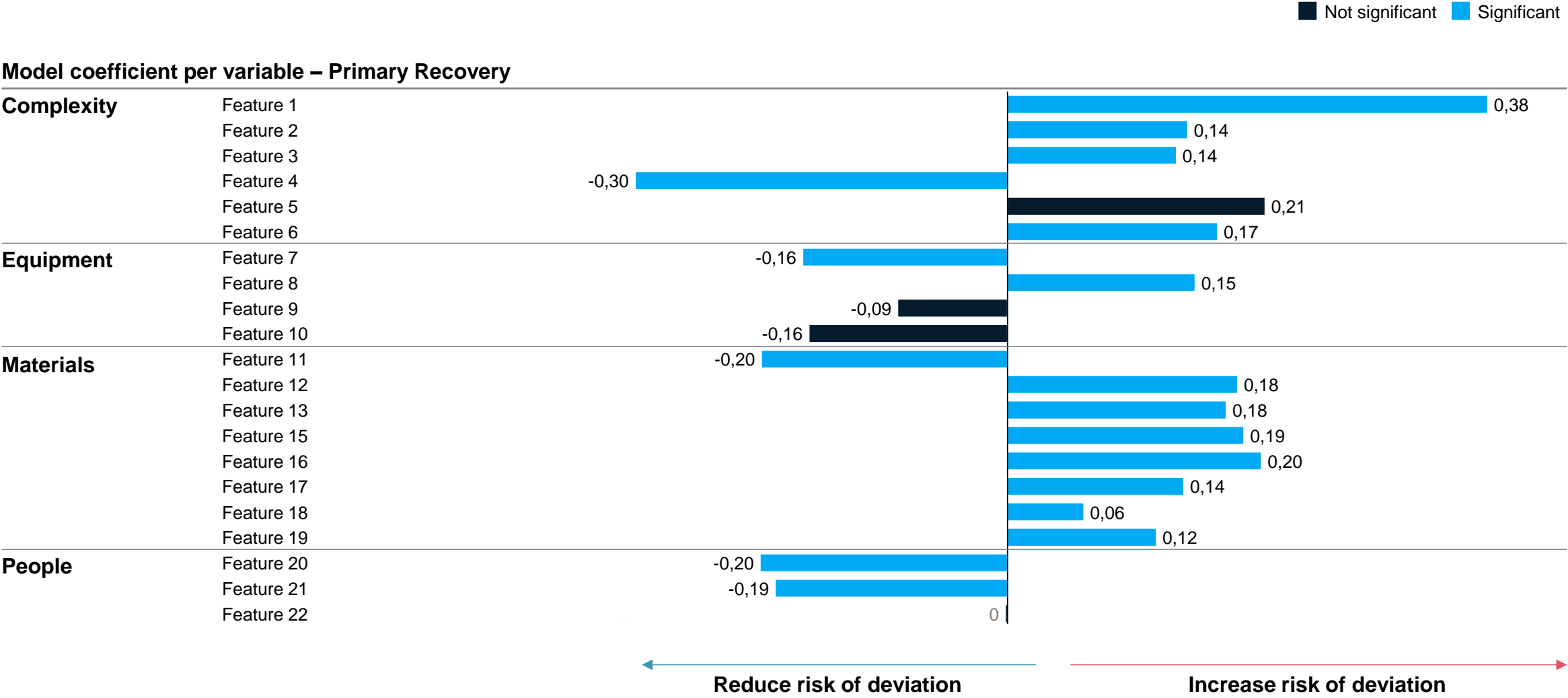
**36%**

Deviation reduction

## Datasets we extracted and analyzed

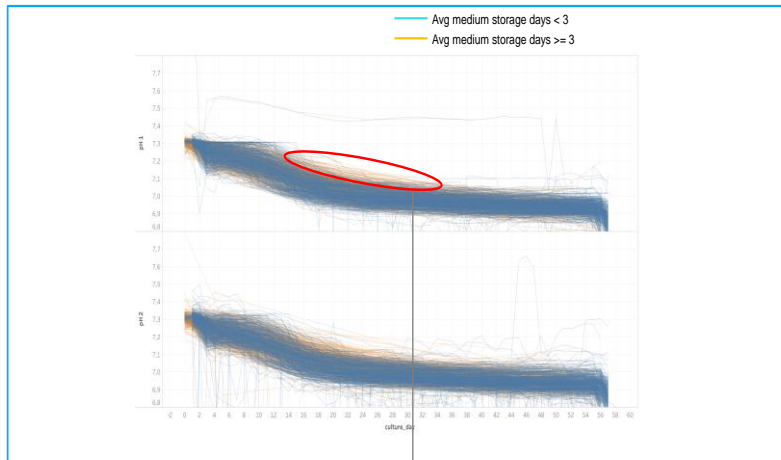


# Machine learning algorithms identify significant drivers of deviations...



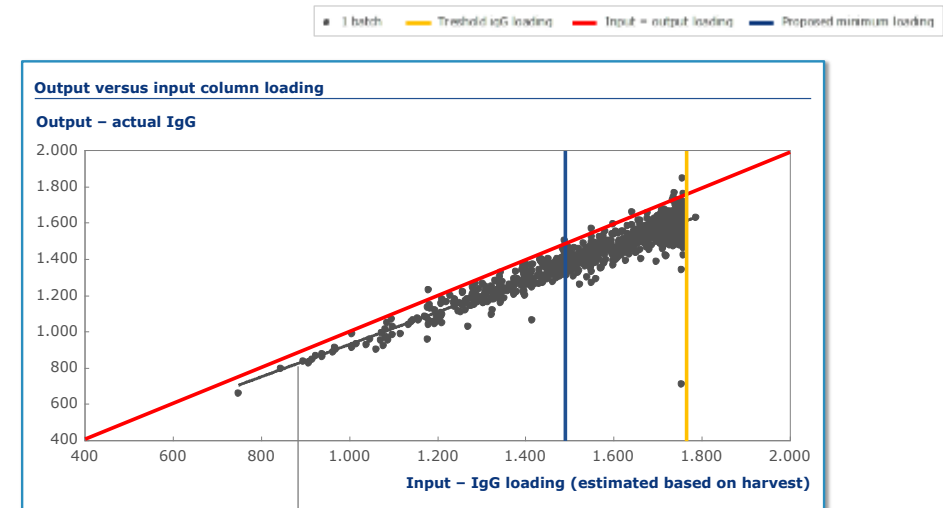
# ... and uncovers previously unknown product and process behaviors

**Insight 1:** Consuming media that has been stored for a shorter period of time (median less than 2 days) leads to more deviations



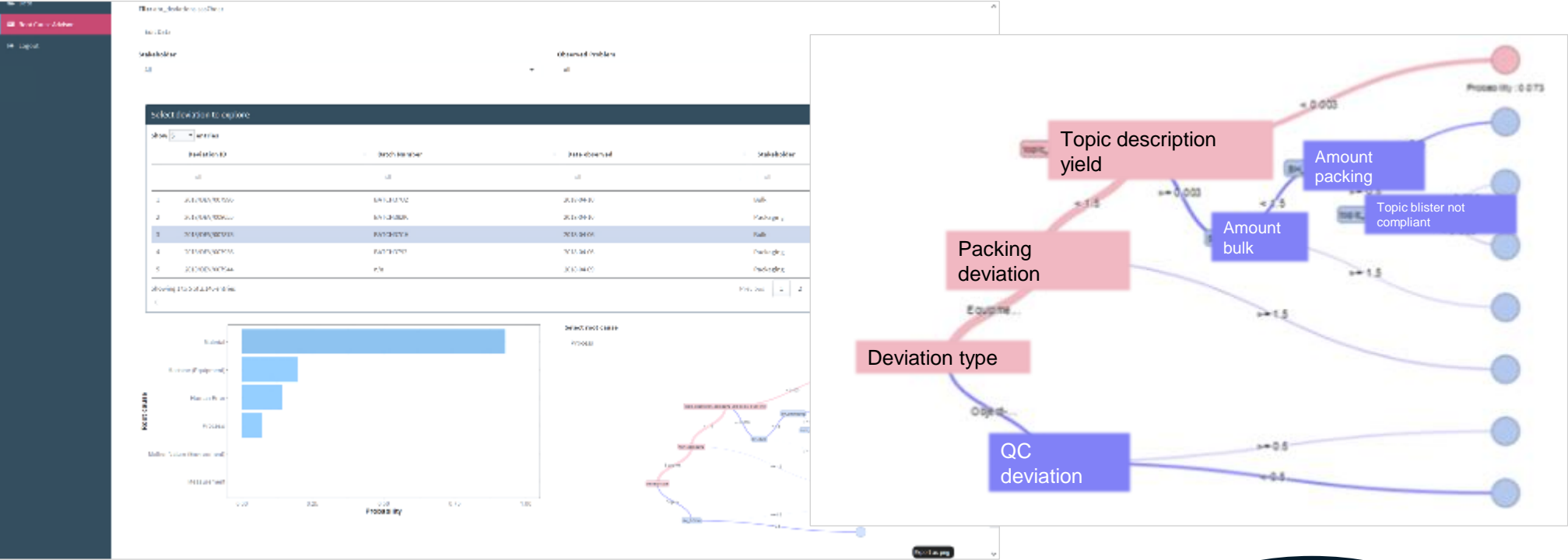
pH decreases more slowly (less risk of deviation), when older media are used.

**Insight 2:** The relative difference between output and input of stage 3 is higher for lower column loading, leading to yield deviations



Currently 20% batches below (85% loading) can be eliminated by adding more harvest

# Automation of deviation investigation process leveraging AI



**-90% QA investigation leadtime**



# Real time release

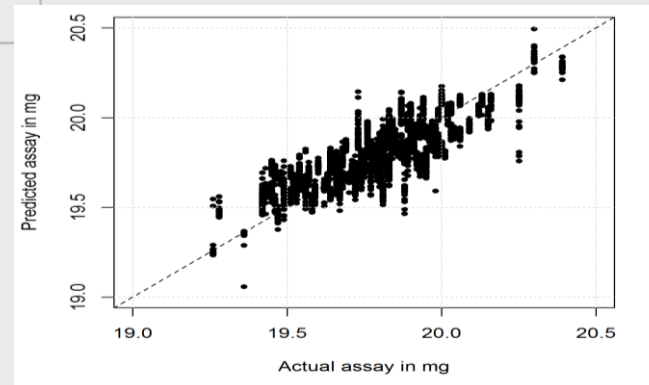
## Examples

### Distributed quality control



Real-time release

### AI based Quality outcome prediction



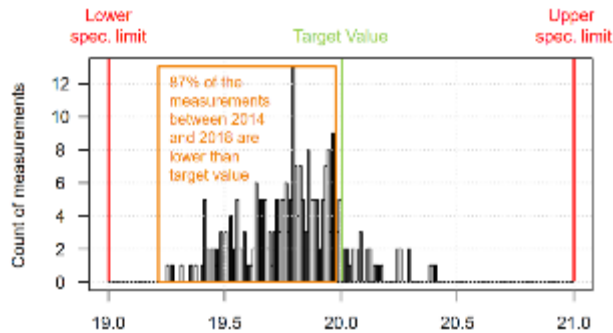
Quality outcome prediction through real-time batch data-fingerprint monitoring

**"No testing"**

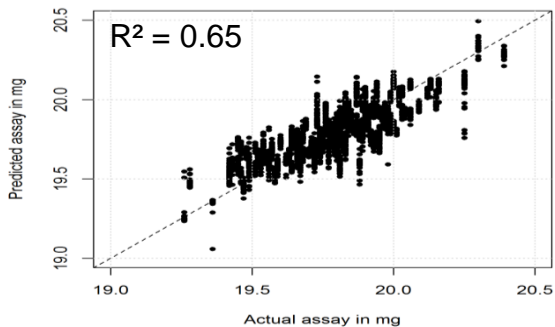
# Quality outcome prediction leveraging Advanced analytics

■ QC test  
 ■ IPC test  
 ■ Environment  
 ■ Process par.  
 ■ Raw material

## QC assay test result



## Advanced predictive modelling of assay results



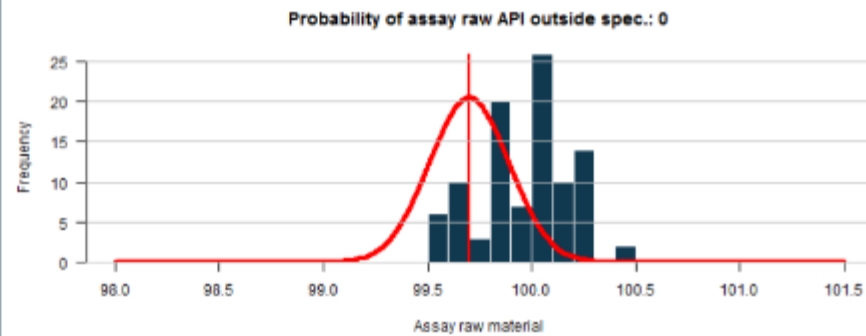
➤ Understanding of key model drivers can be leveraged to increase process capability

### Drivers, relative importance in %

Uniformity of dosage	11
Minimum thickness	10
Dissolution	9
Water content of granules	9
Total time granulation	7
Yield after granulation	7
Assay of raw material API	5
Disintegration	5
Average weight of tablet	5
Yield after compression	4
Weight of raw material	4
...	

Video to be added

Input section

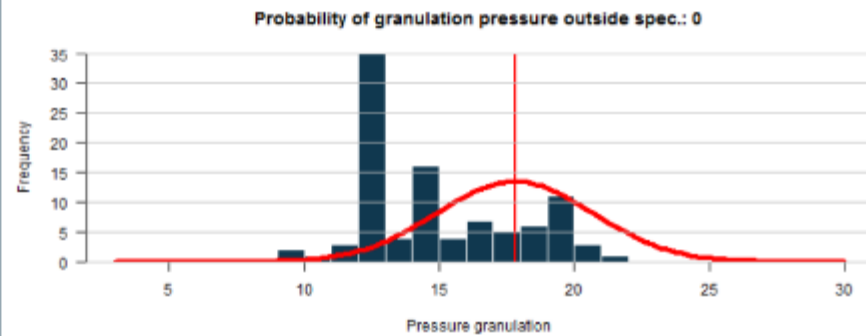


Active

Mean



Std. Dev

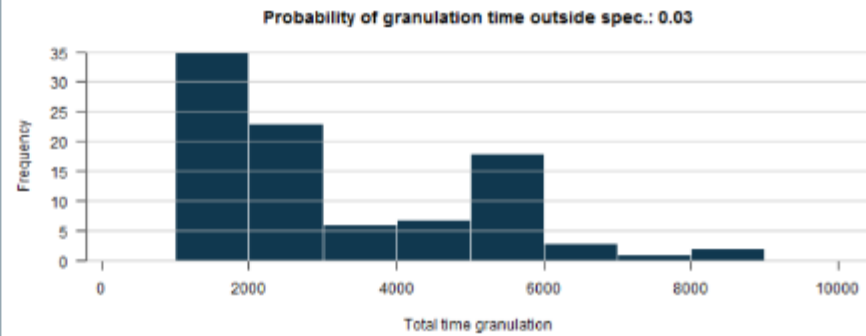


Active

Mean



Std. Dev



Active

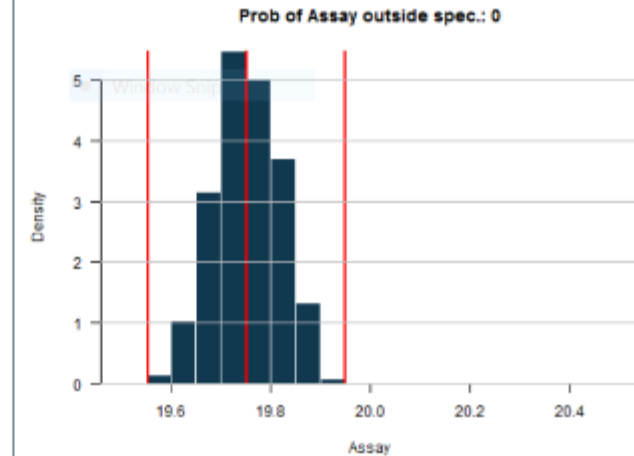


Active

Output section

Start computation

Sample size



# Distributed quality control sets the basis for AI enabled real-time product release

## New Biogen Solothurn API plant

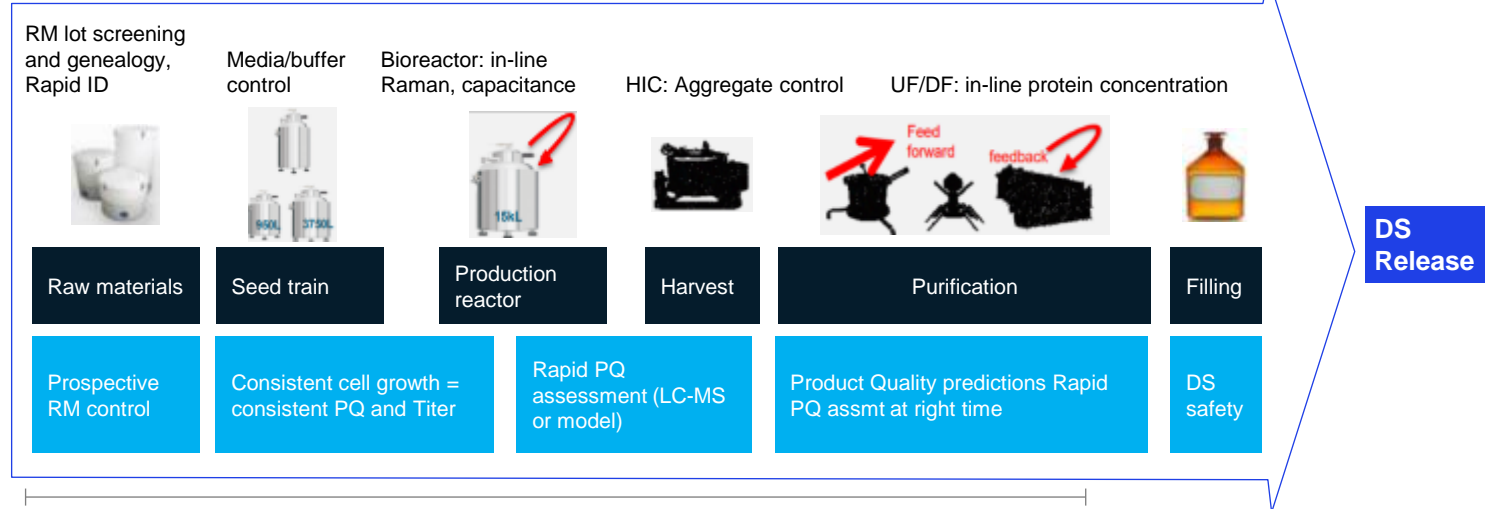


### Foundation

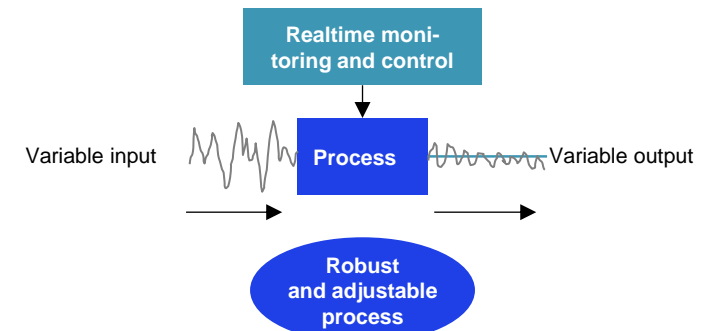
Extensive understanding of raw materials, process, and product characterization

A fully-integrated control system

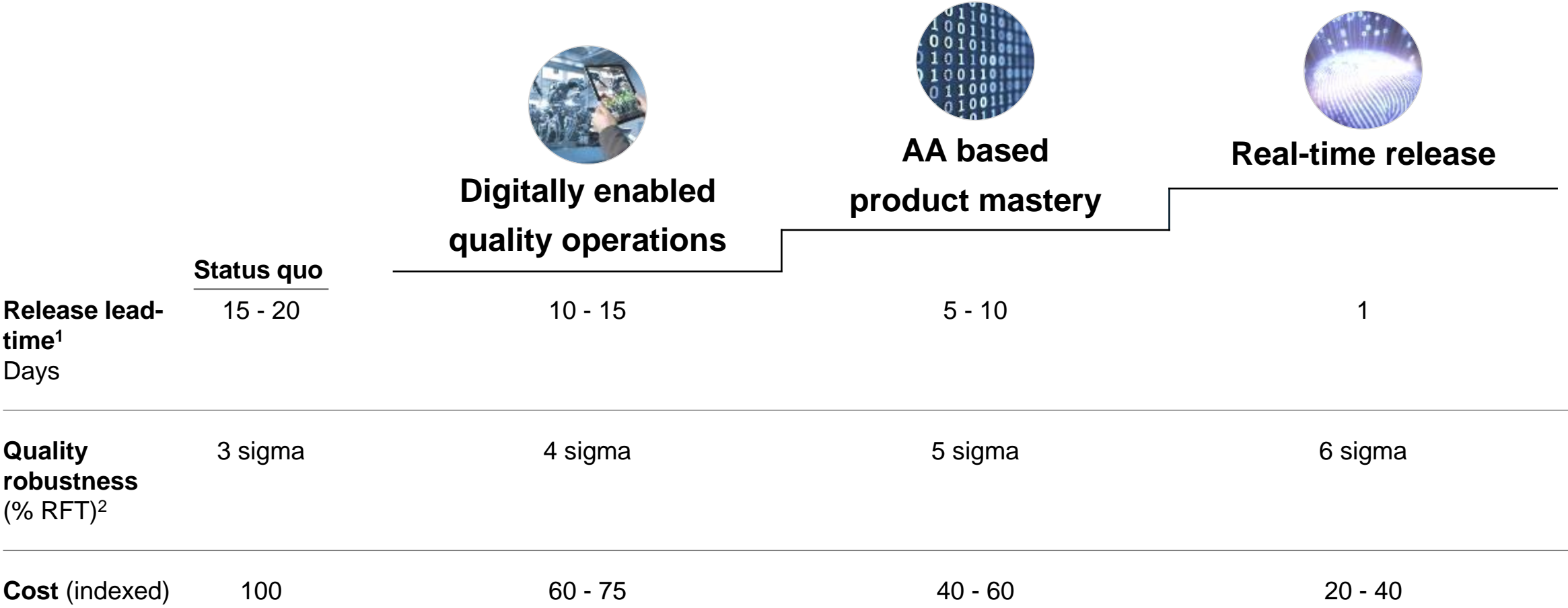
RM Raw Material  
PQ Product Quality  
MA Multiattribute Assay  
DS Drug Substance  
RLS Release



Multivariate analysis for process monitoring and disposition decisions Predictive model for quality and/or feed forward control



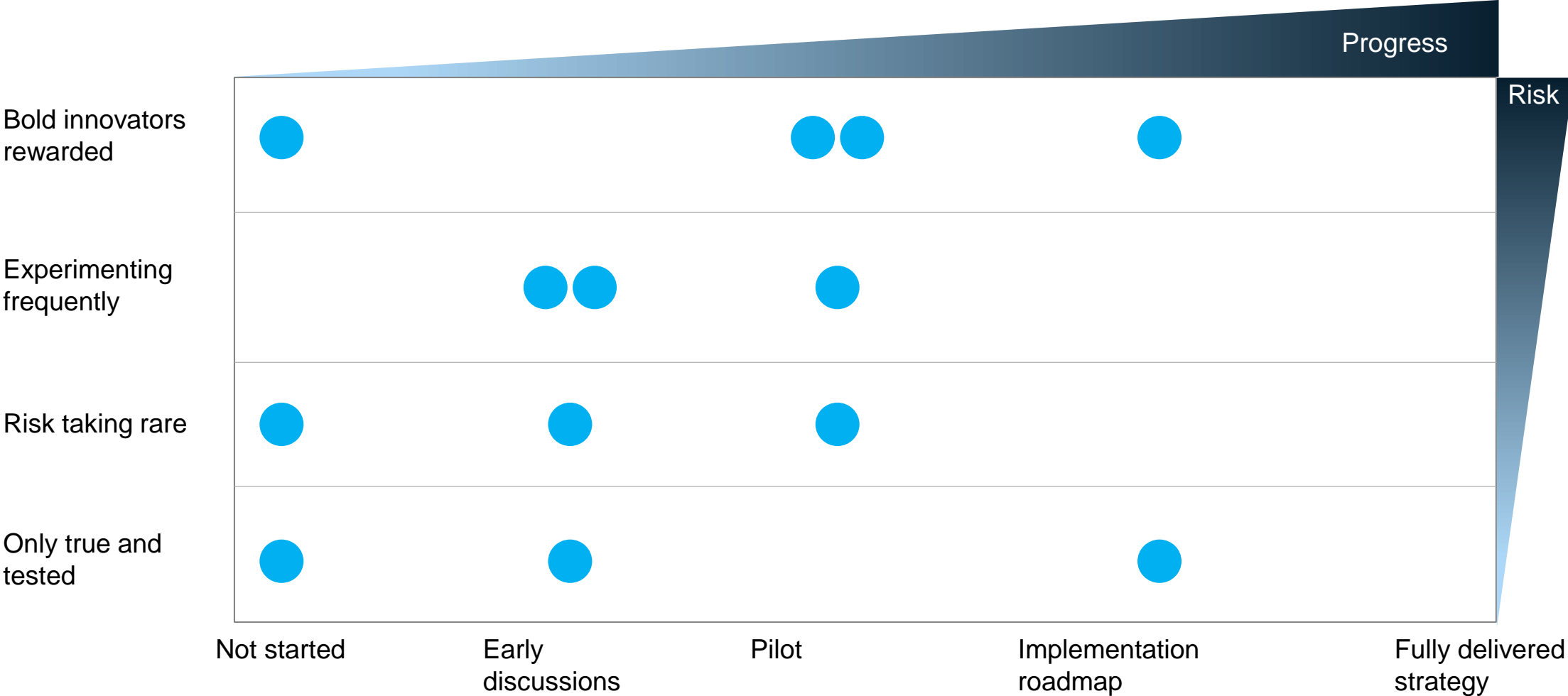
# The opportunity is substantial



1. Bulk release lead MME  
 2. E2E RFT

# More than half of companies have not started pilots yet, and risk tolerance or aversion has not made a difference to progress

Companies, n=13



# How to make this a success

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Make it a business opportunity, not a technology problem. Keep your eye on the **business value**.



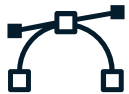
This is an **innovation** project which should have a vision – not just pilots



Give innovation a **home** – lighthouse, CoE



Make Quality digitization strategy a **cross-functional exercise** – lead by quality, but involving R&D, production, IT,...



Build an **IT architecture** strategy, but don't “boil the data lake”...



Understand the '**digital skill and resources**' you need to build over the next years. AND define the new operating model.

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**...and do not forget the change management!**

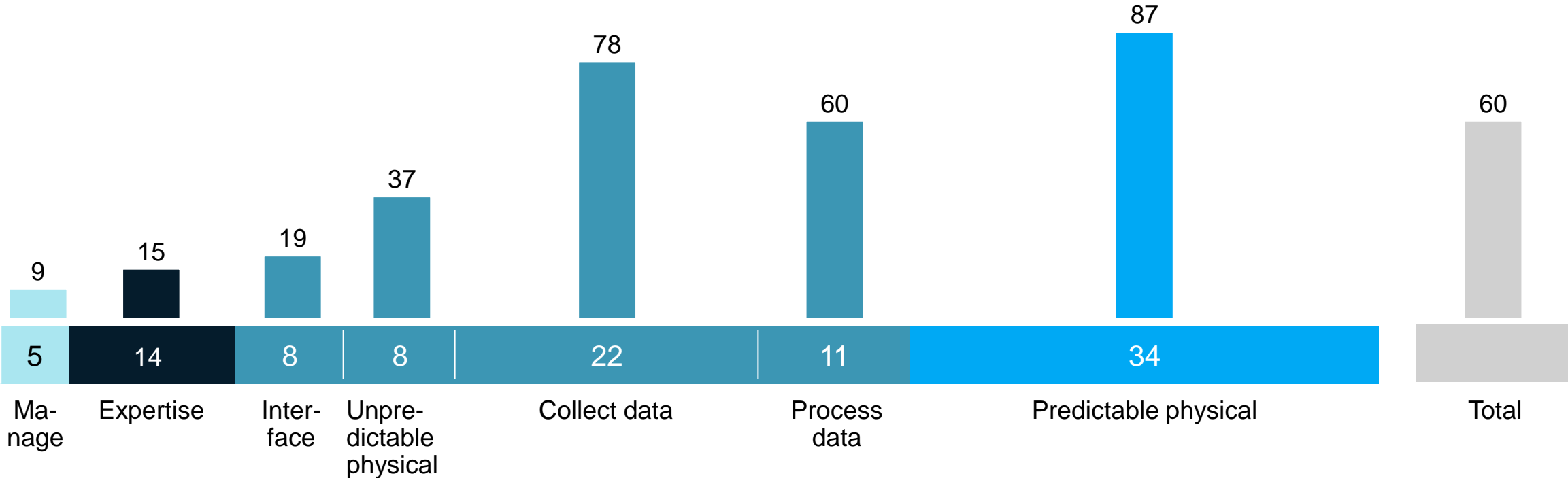
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# BACKUP



# Thanks to digitization and technology advancements, 60% of operational tasks can be automated

Time spent in manufacturing on activities that can be automated by adapting current technology %



**Current automation: 3%**  
(US, Germany, Japan)

# Digitization and automation will transform quality control work in the lab and on shop floor by introducing new ways of working

## Digitally enabled labs

## Automated labs

## Distributed quality control

### NEXT GENERATION PHARMA MANUFACTURING LINE

Parametric real-time release

Connected high accuracy digital sensors

Automated AI / machine learning enabled process and product parameter control

Real-time capture of process and product parameters

Automatic sample preparation & processing

Robotic Process Automation for CoA creation

Automated settle-plate handling

Automated compendial testing

Instantaneous microbial detection for water / air

eQMS  
EMS  
GLIMS  
Cloud/  
data-lake

Digital lab performance management

Advanced analytics enabled lab planning & scheduling

Digitally enabled lab inventory management, digital Kanban

Smart glasses with SOPs & work instructions

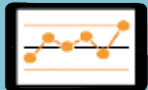
Electronic lab note-books (ELN)



GLIMS interface



Advanced analytics problem solving



Real time trending

Paperless lab direct data transcription

