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IPA
Innovation, Quality and Global Reach

Leveraging automation in Pharmaceutical operations for continuous improvement

GANADHISH KAMAT

Global head of Quality,

Dr. Reddy's Limited

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Challenges faced by Pharma industry

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- Pricing pressure due to government initiatives & consolidation of buyers in US
- Large number of approvals on day 1
- High cost of development, high investments & long gestation period for complex generics
- Increased regulatory expectations & scrutiny
- Increasing operating cost (including manpower cost)

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How do we overcome the challenges

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- Continuous improvement
  - First time right (Development / manufacturing)
    - Reducing failures / defect rates
    - Reducing COPQ / COPE
  - Cost competitiveness
    - Doing more with less resources

- One of the important enabler
  - Adoption of new age technologies

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Digital transformation around us

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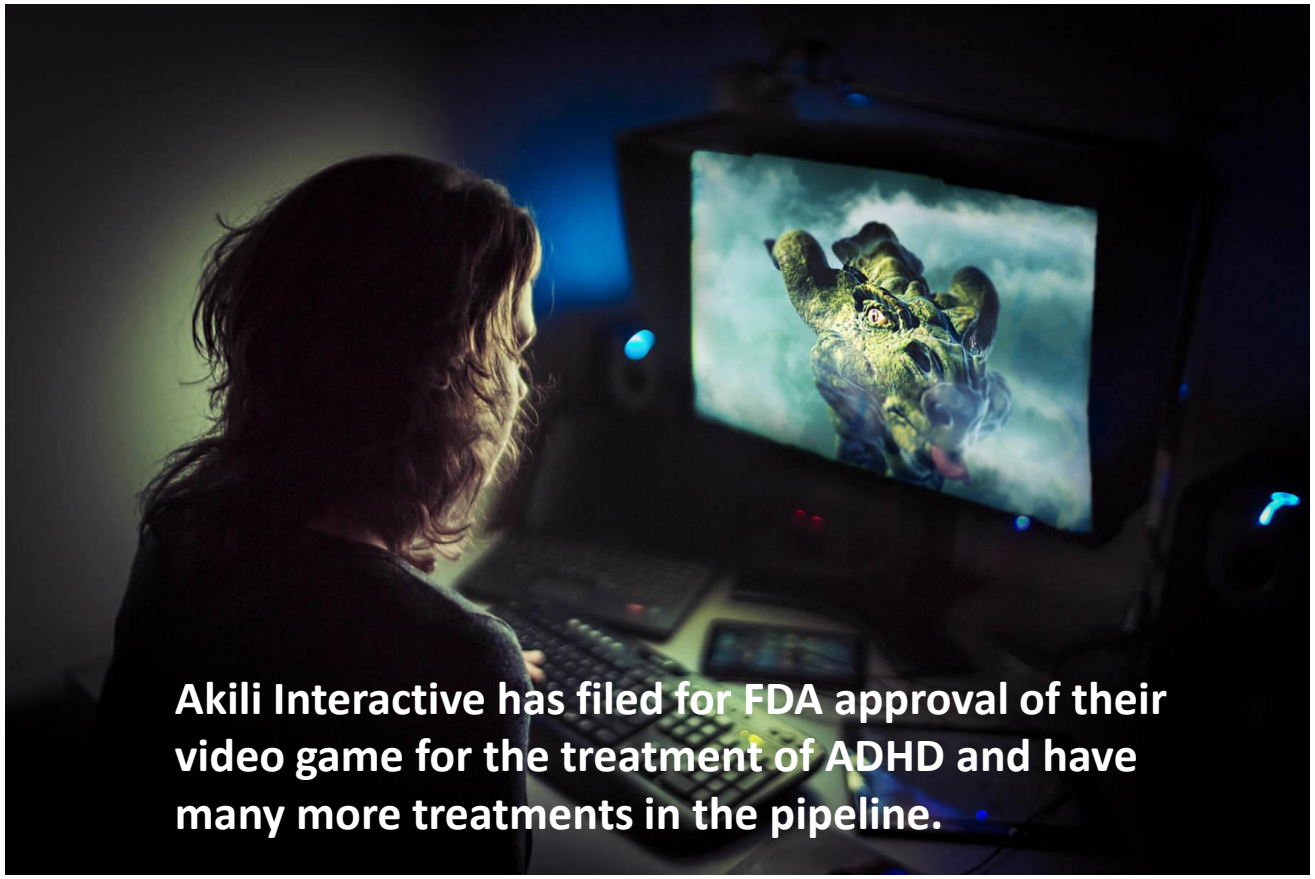
Success stories

- Google
- Amazon
- Uber
- Oyo

Missed opportunities

- Kodak
- Swiss watches
- Blockbuster
- Xerox



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Automation and digitization in Pharmaceutical operations

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Automation / Digitization landscape in Pharmaceuticals

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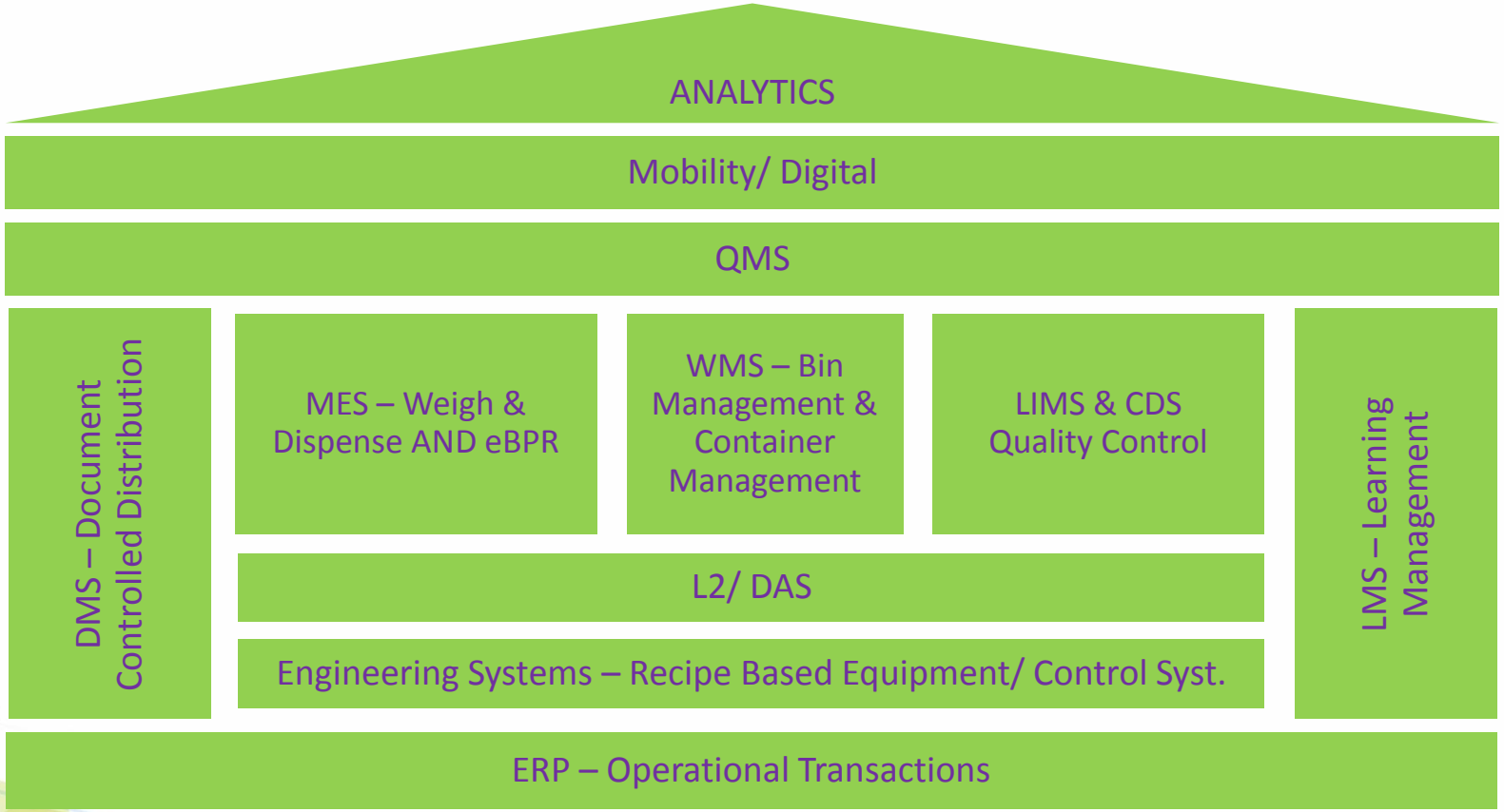

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Mechanization

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Case Packing Bottles

Case Packing Blisters

Shipper Conveyors

Robotic Palletizer

AGV

ASRS

Sachets Packing

RM Drum Cleaning

AHU Filter Cleaning

Solvent Handling

Air Tube Samples transfer

Ampule Blister Packing

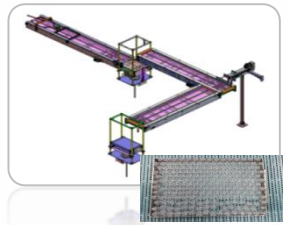
Drum Lifting & Tilting

Carton Bundling

Powder Transfer PTS

FBD – Bowl Spin Flow

Vial Frame Conveying



Benefits - Eliminate muscle work, Fully automated and integrated systems, Improved safety, efficiency and compliance

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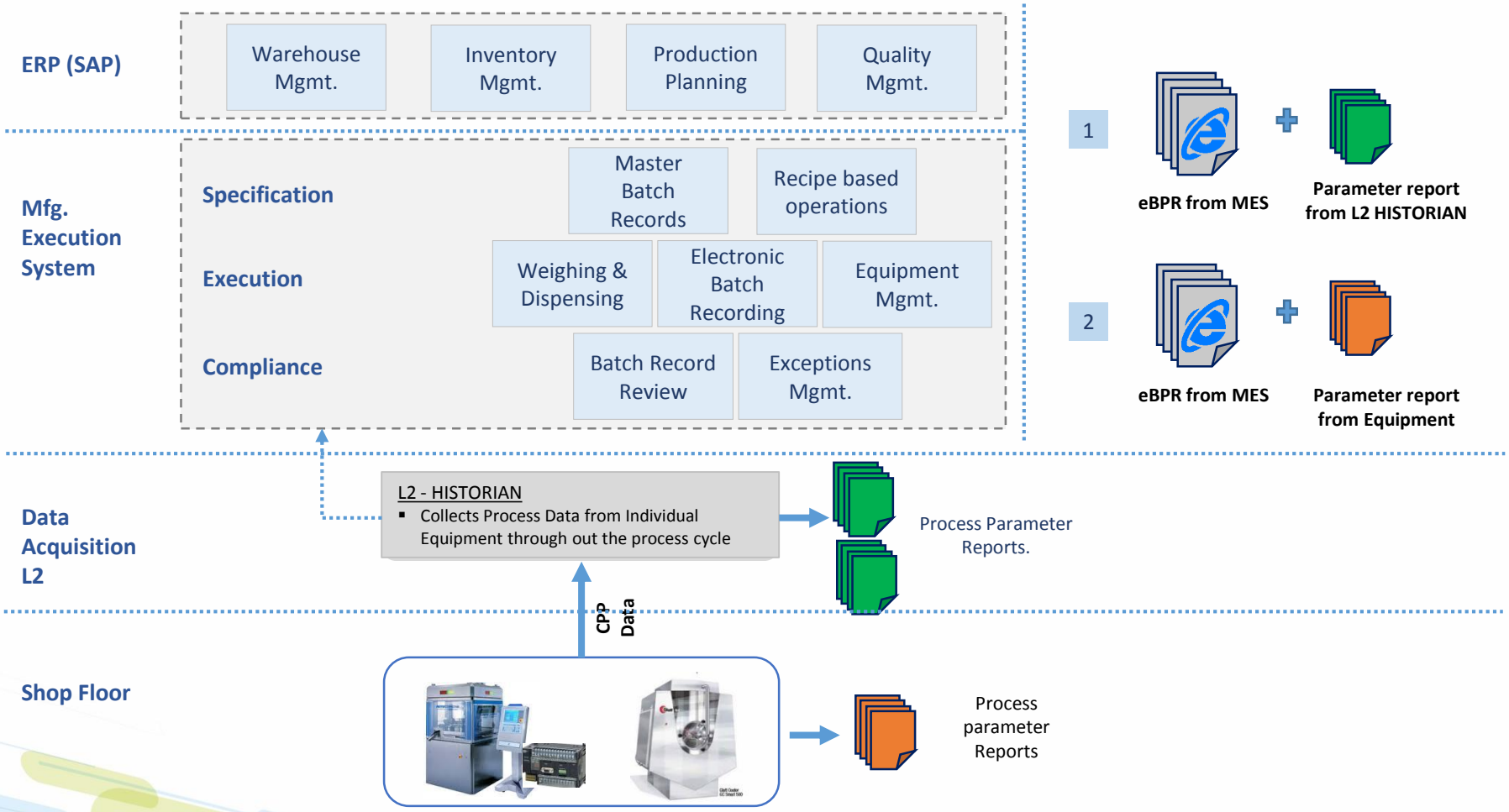
Process Automation & digitization



Benefits : Reduction of manual activities, paper, errors. Easy data retrieval, online trending and status reports. Traceability. Improved compliance

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Digitization of Maintenance

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Preventive Maintenance App

- **Overall Efficiency -** No paper based work
- Almost **real-time** updating leads to increased compliance
- **Authenticity** - better equipment handover through mobile sign-off
- **Ease** of order management
- **Online** record-management for decisions

Mobile Label - Printing

- Mobile label printing directly from the app makes the activity robust and clean

Calibration Maintenance App

- Eliminate duplication, inefficiencies and errors that come with paper management.

QR Code Enablement

- QR code enablement on equipment will allow for evidence of an engineer actually performing the maintenance activity.

Breakdown & Facility Maintenance

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IT Enabled Functionalities in Utilities: SCADA & DAS

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UMS – Utilities Management

PMS – Power Management

Water System Management

BMS & EMS Systems

Central Dashboard

Benefits

Digitization of Log Books
Improved Data Integrity & compliance
Effective tracking on Utilities Consumption
Uninterrupted Power cycles,
Electrical Loads - Control & Distribution
Enhanced Visibility on energy consumption

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Product Traceability through Serialization

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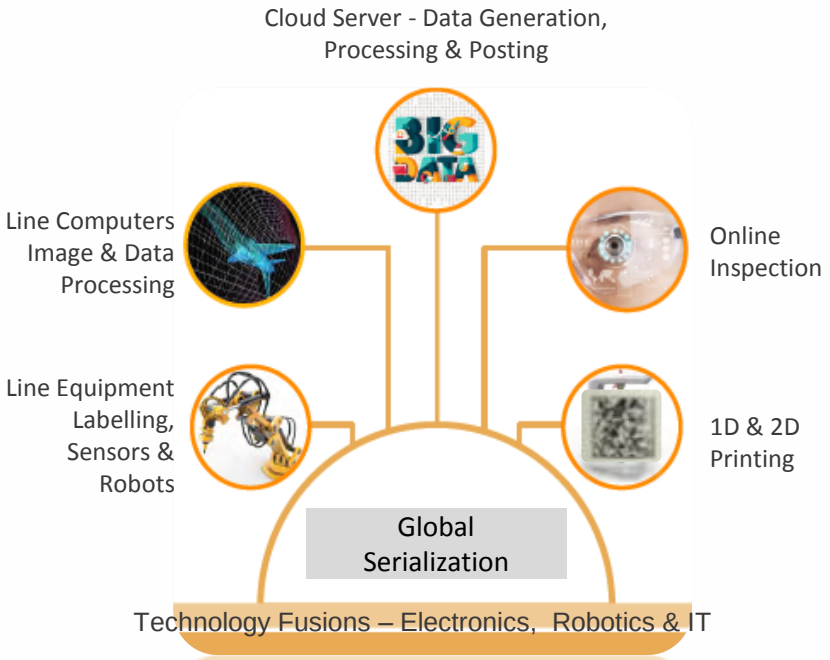

Functionalities

- Serialization - Data Generation & online Printing
- Online inspection – OCR & OCV
- 360 Inspection, Bulk Scanning
- 1D & 2D codes Handling
- Aggregation - Data marriage – bottle to shipper to pallet
- Parent Child Relationship
- Data commissioning & Batch Reporting
- Finished Goods online Report
- Data Posting - Cloud Data

Primary

Secondary

Tertiary -shipper

Tertiary-Pallet Level

Benefits : Supply chain traceability, elimination of counterfeiting

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Laboratory Operations and Quality management

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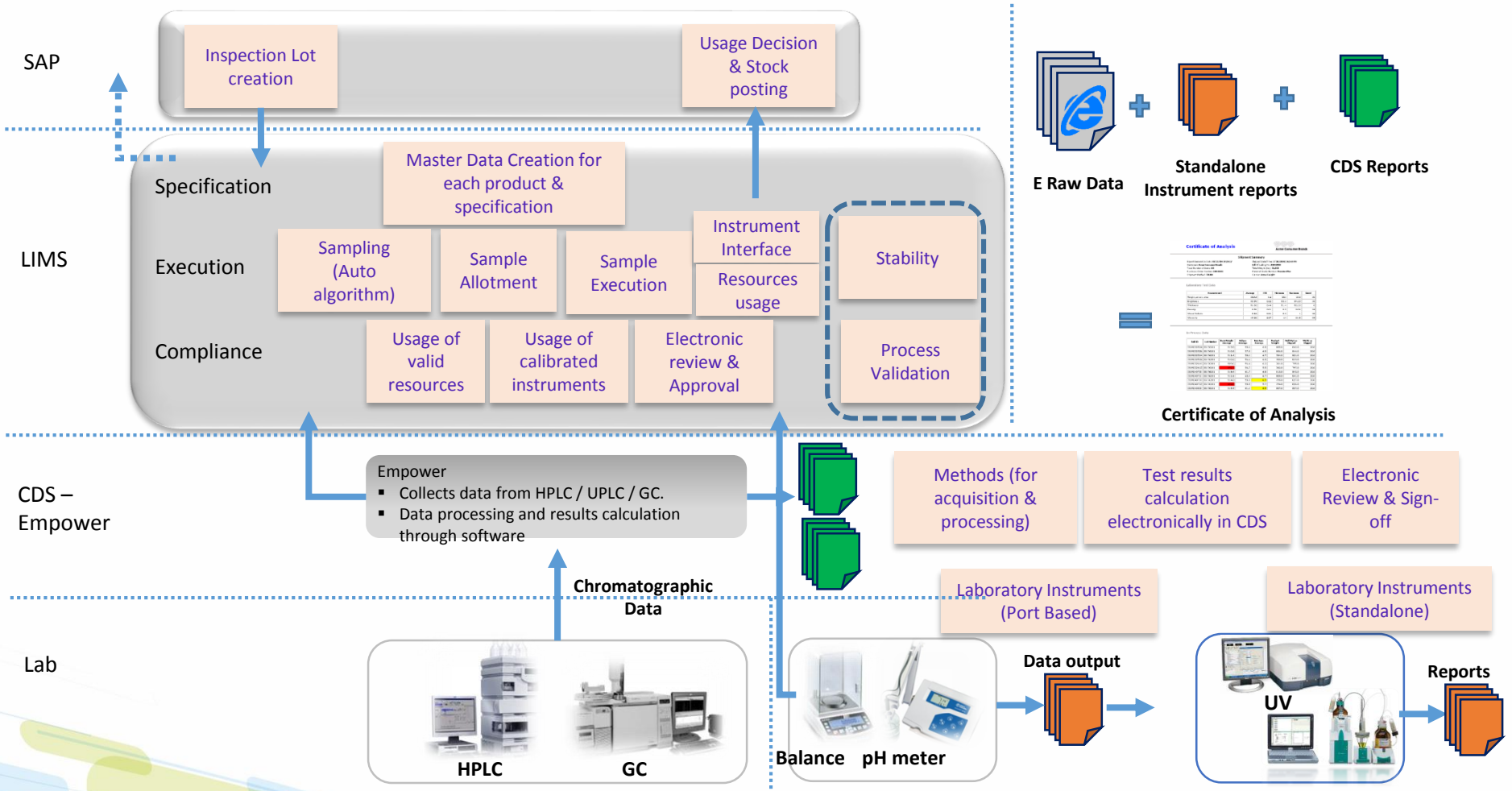
LIMS, CDS & Others



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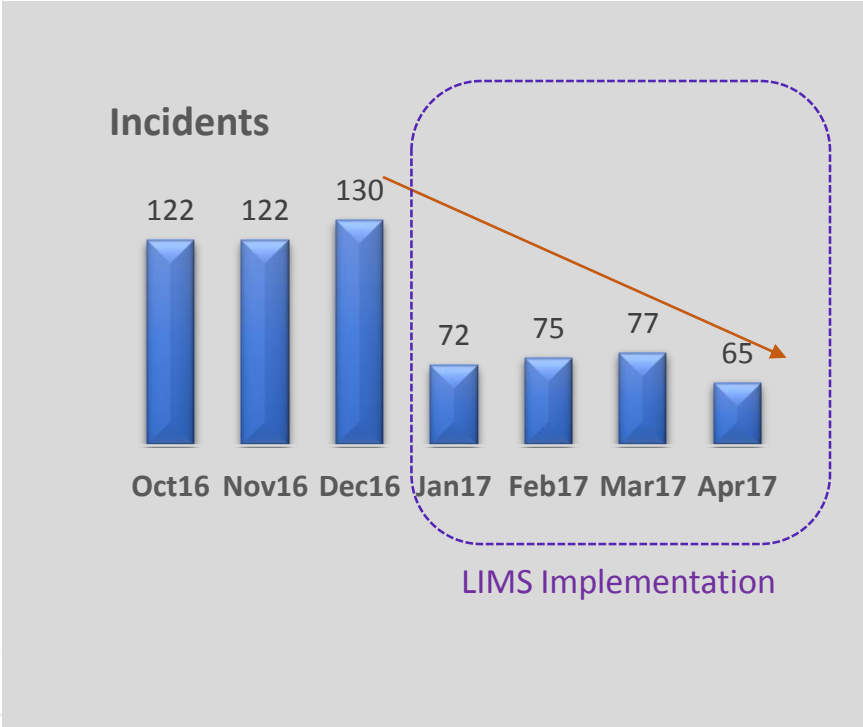
Benefits realization
LIMS (Reduction of incidents)



LIMS Eliminated

- Calculation errors
- Use of non-calibrated instrument
- Stock entry missing
- User not qualified
- Transcription errors

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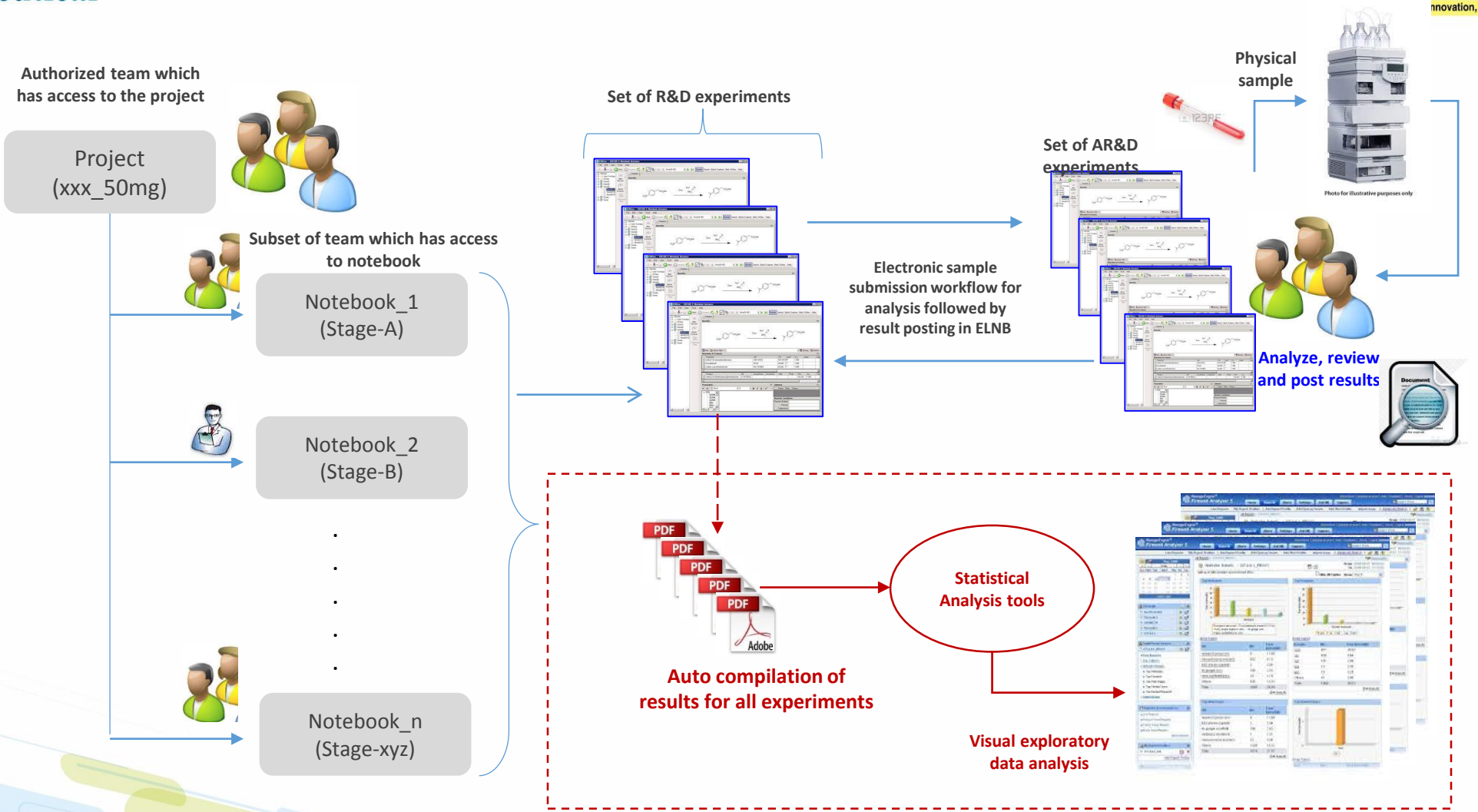
Electronic Lab Note Book



Benefits：Automated calculations, Enhanced data security, Storage space reduction, Interface with other systems, Ease of data retrieval, Improved compliance

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Quality Management System

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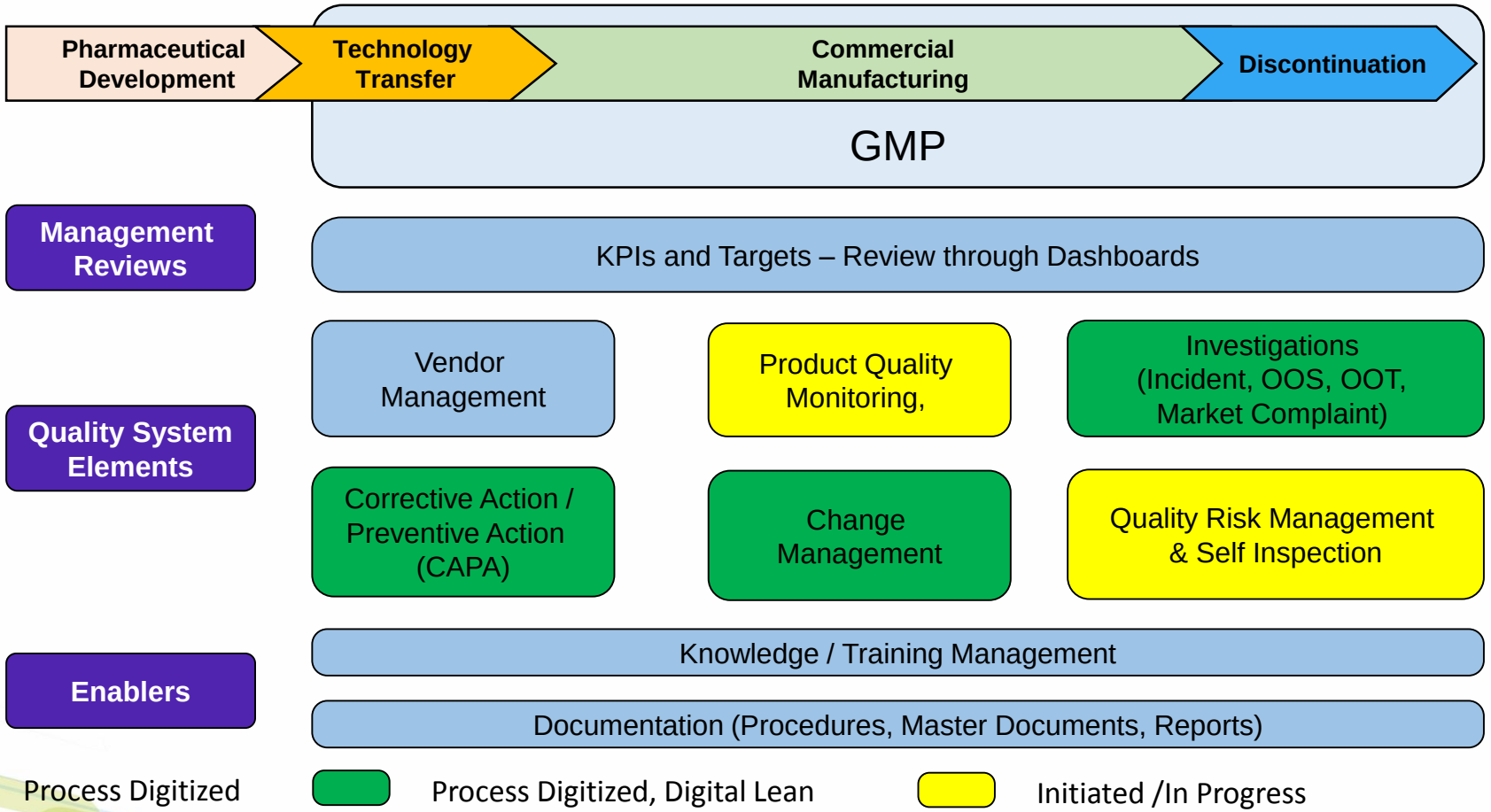

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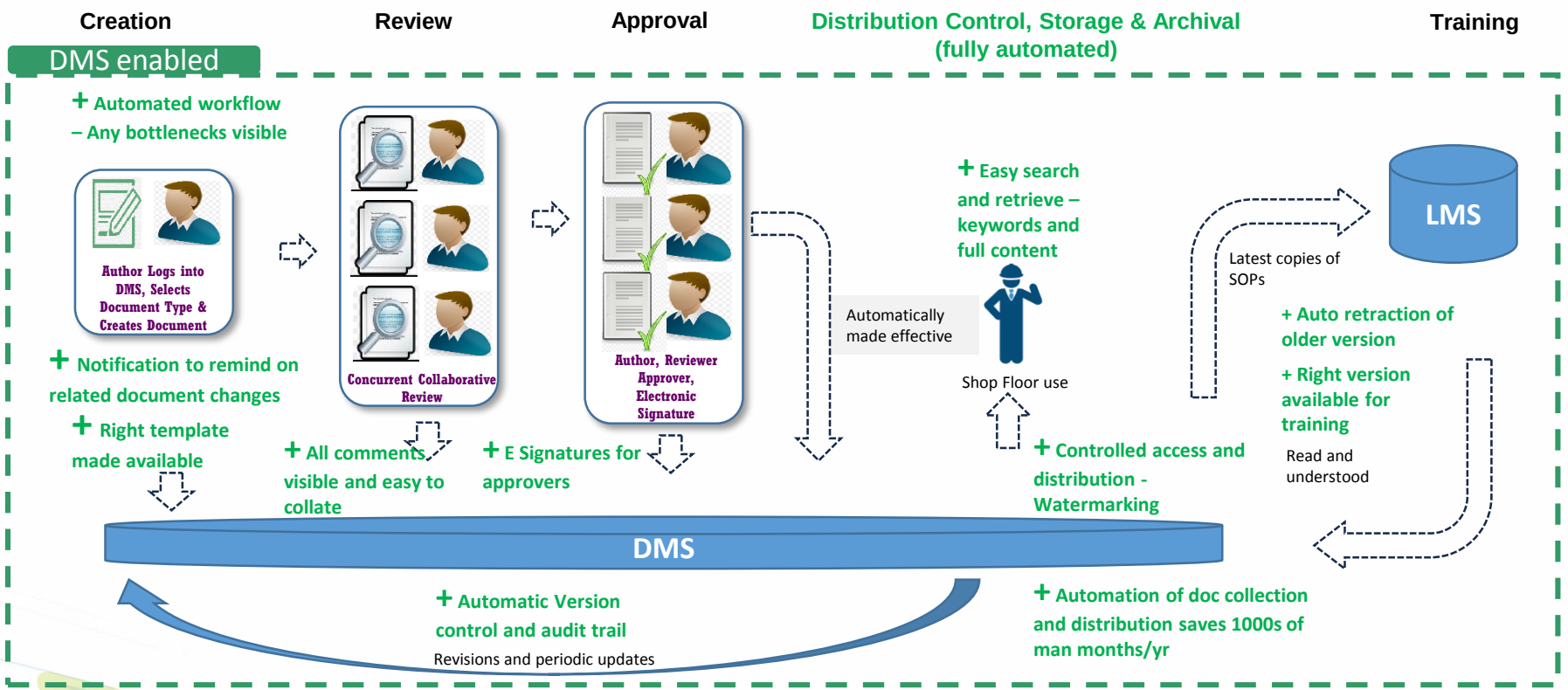
Document Management System



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DMS Key Benefits

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Audit Readiness & Data Integrity

> 25 process interlocks for compliance

Audit preparation time reduced by >60% to 1-2 days

No more document movement or misplacement

- Change control mandatory for all doc changes
- Templates, numbering, work flows, signatures auto enforced
- Traceability of prints; recall; reconciliation
- Easy search and retrieval of documents
- Easy identification of all related documents
- Availability of soft copies ensures Audit prep does not deprive information for other activities

Productivity/ Cost Improvement

QA - 400 man months (40% of DCQA resources)
RA -250 man months;
End users – 1150 man months

1800 man months (150 FTE) saved/year

~INR 9 Cr/year in manpower savings

60 lakh sheets of paper /year reduced => ~ INR 2 Cr

- No more printing, stamping, filing of documents
- Eliminate manual movement of a paper doc for review and approval
- Reduce constraints on prints and reprints; manage w/ better governance
- Recall and reconciliation made easy
- Easily find docs with full content search

User Experience

Over 2.5 lakh Emails eliminated

Single dashboard for all pending document tasks

Compliance built in. Fewer decisions to make

Harmonised processes across all units.
Easy to follow and assure

Visibility for decision support

Bottlenecks in workflows visible and actionable

Interconnectedness of documents – simplification made possible

Insights into cycle time and quality of work

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Analytics for simplification and continuous improvement

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How to put the data to use

- KPI Dashboards
  - Turn Around Time Analysis
  - Pending Samples Analysis
  - OOS Analysis
  - Incident Analysis
  - Change Control Analysis
  - Product scorecard & CQA analytics
  - Stability alerts
- Support in investigation (Root cause predictor)
- PAT
- Process improvements
- Continuous Process Verification
- APQRs

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Analytics Dashboards

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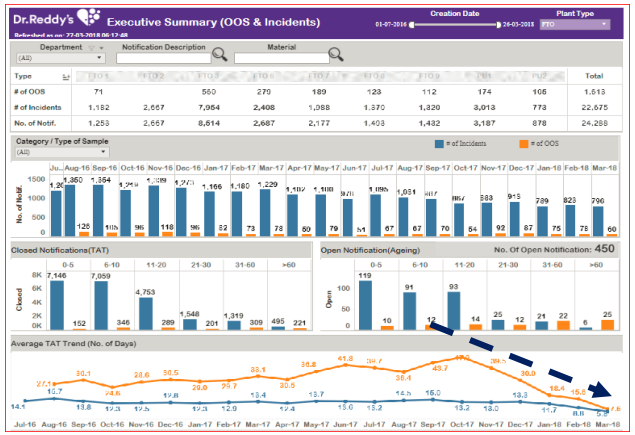
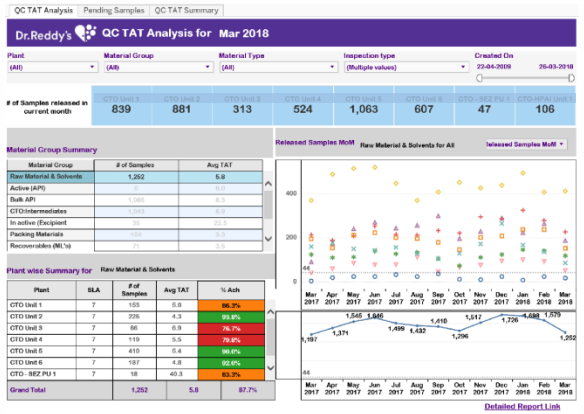
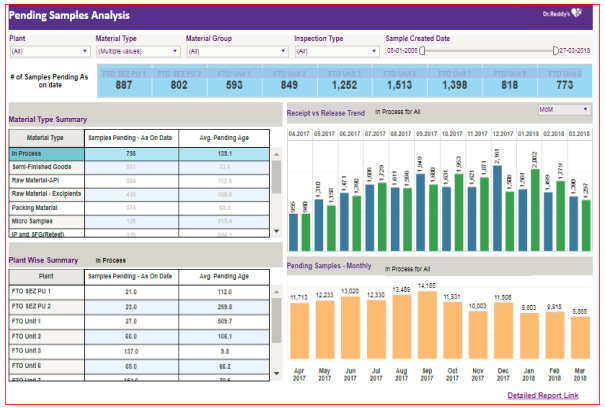
OOS & Incidents



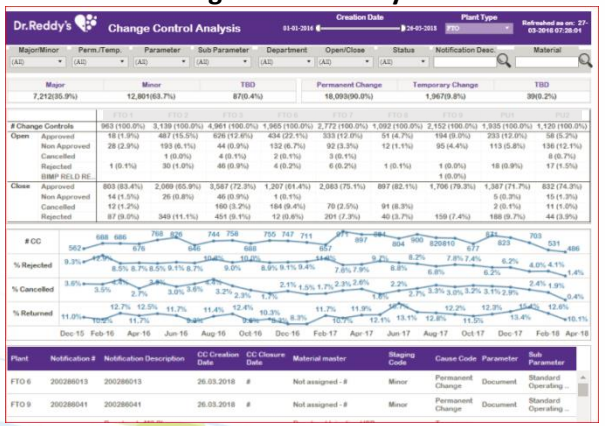
QC TAT



Pending sample analysis

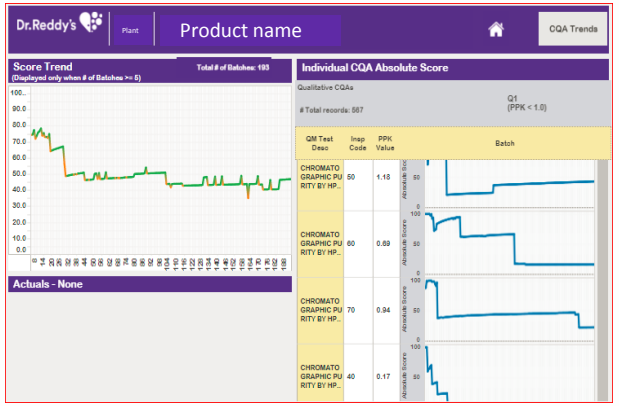


Change control analysis



Stability Alerts

Product score card



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Support in investigations

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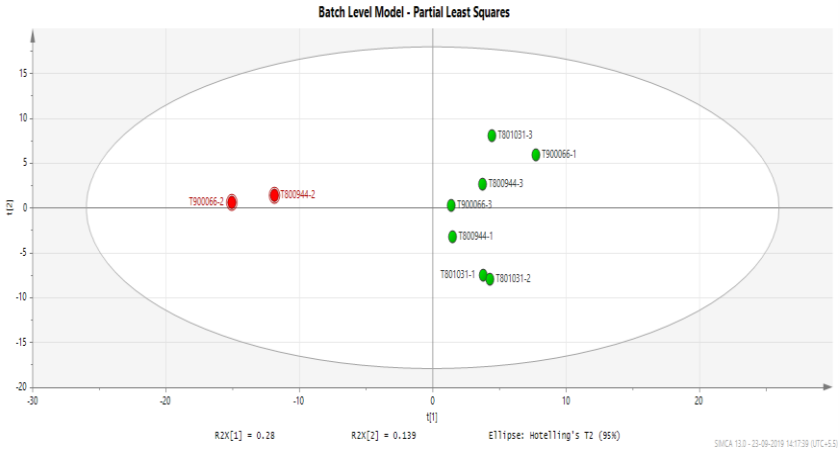
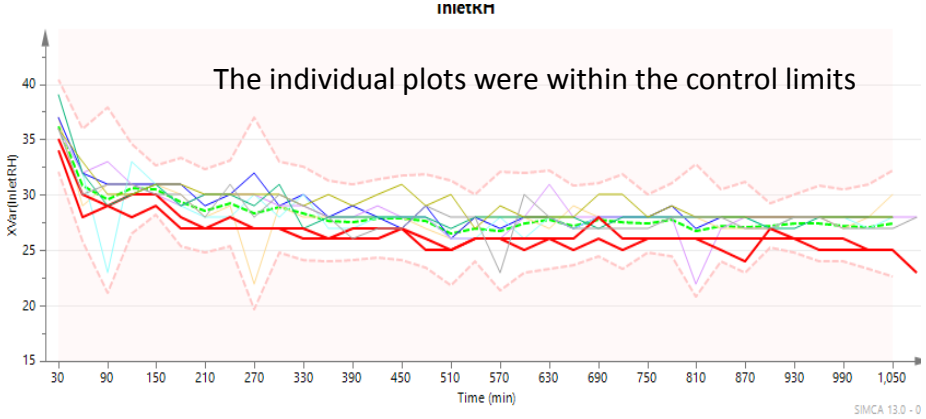
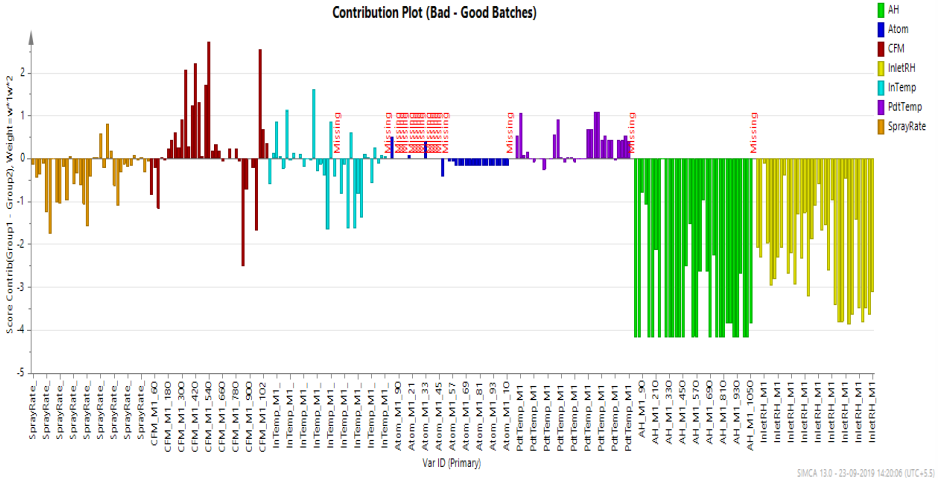
Problem statement

Low dissolution in one batch of ER product.



Multivariate analysis (using partial least square regression) showed two lots were different compared to good lots





The contribution plot of the difference between bad and good lots in terms of standard deviation indicated bad lots were run at low AH and RH in comparison to good lots

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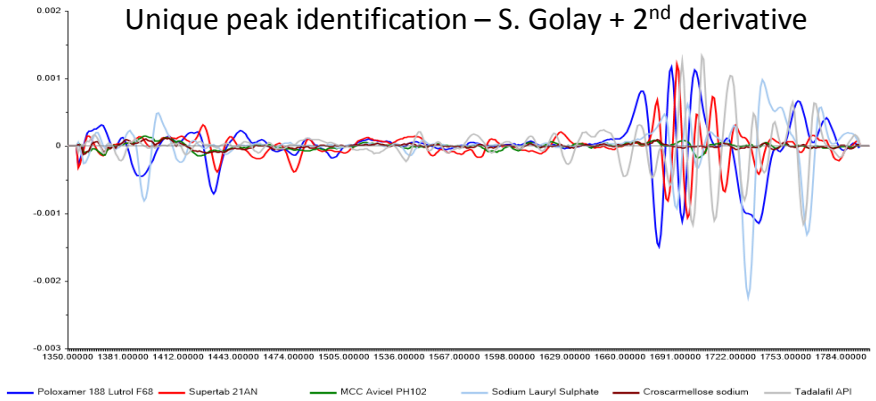
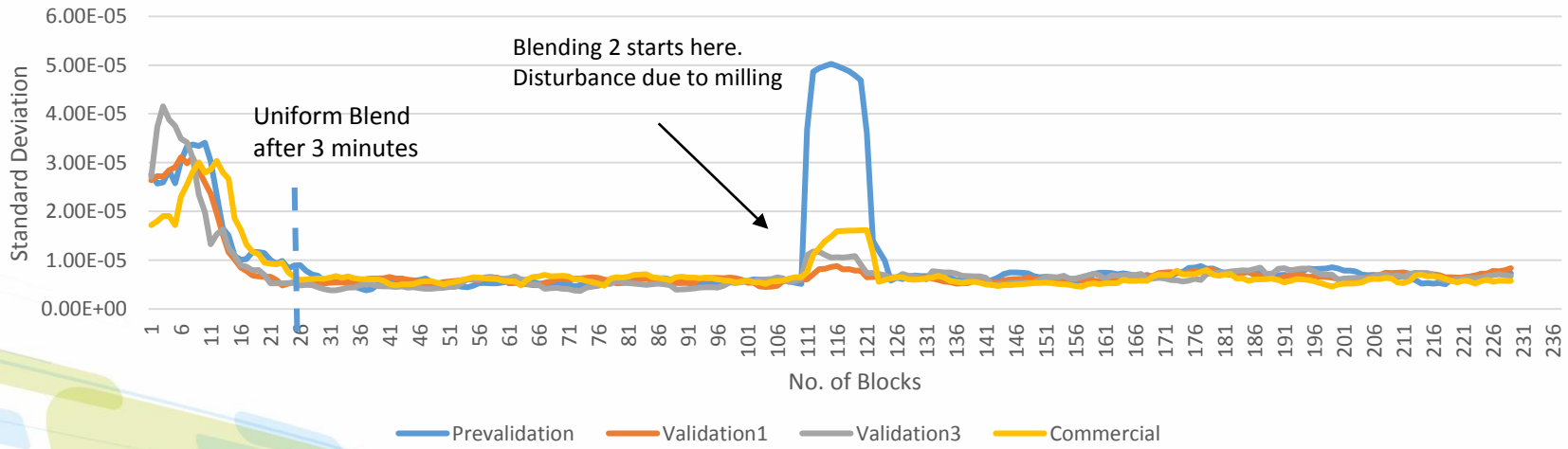
PAT for process improvement & parametric release





Outcome : Reduction of process time & Deletion of blend analysis

Golden Tunnel based process monitoring

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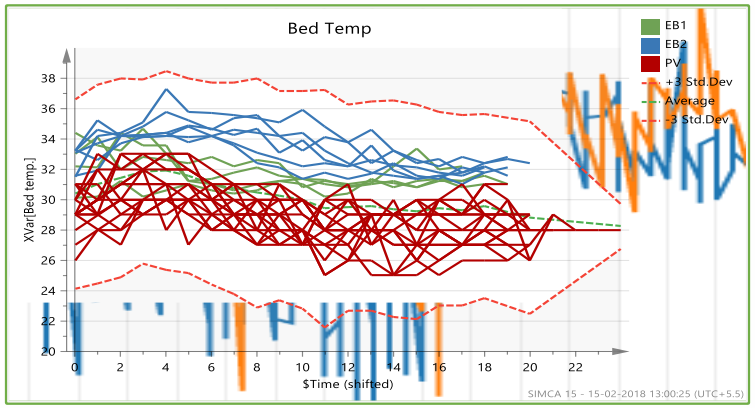

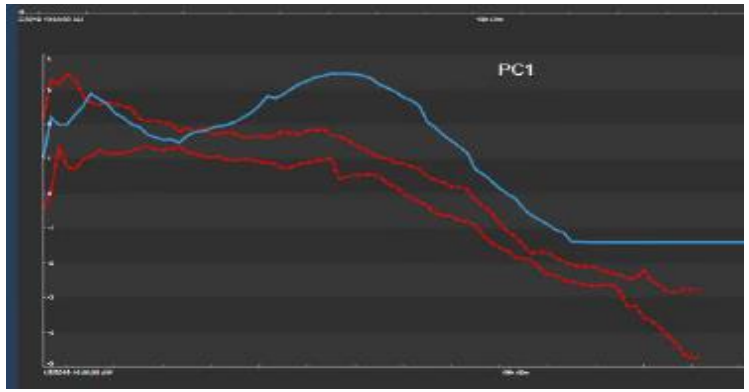

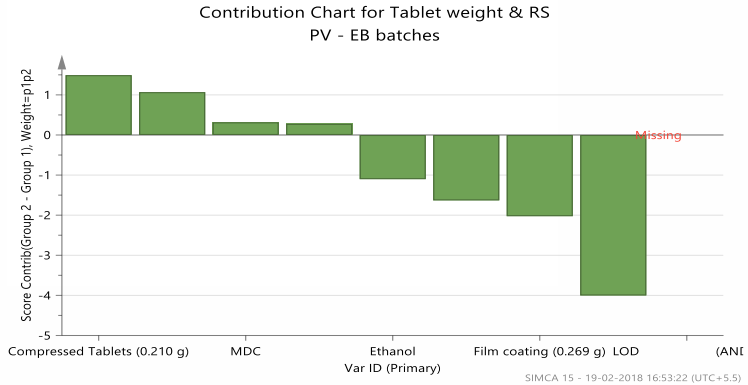

Building PLS Model

- *Identify Batches with desired CQA*
- *Build "Golden tunnel" of process parameters based on these "good" batches data.*
- *Build Machine learning models to arrive at principal components that explain the behavior of process*

Online Monitoring

- *Create Score Plot - 1 Principal component that combines effects & interactions on all Process Parameters.*
- *Alerts when current production parameters deviate from "golden batch" conditions.*

Contribution Plots

- *Highlight contribution of individual process parameters*
- *Identify corrective actions in real time.*

Classification | RESTRICTED

Yield Optimization

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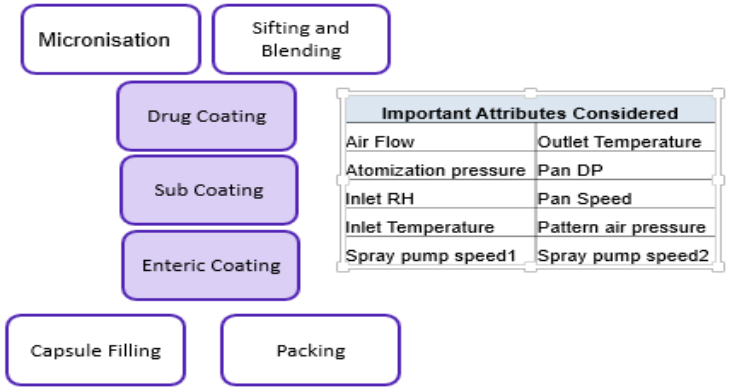
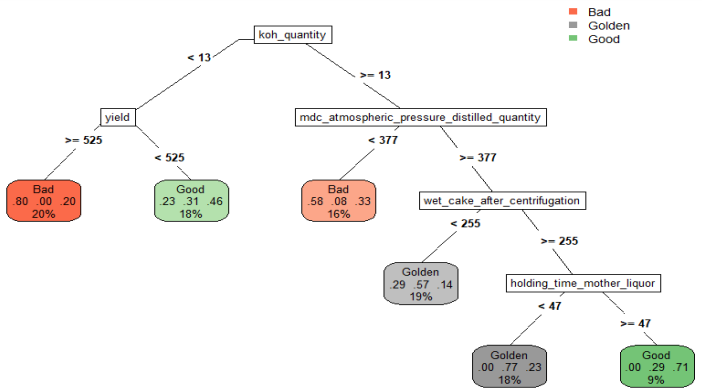
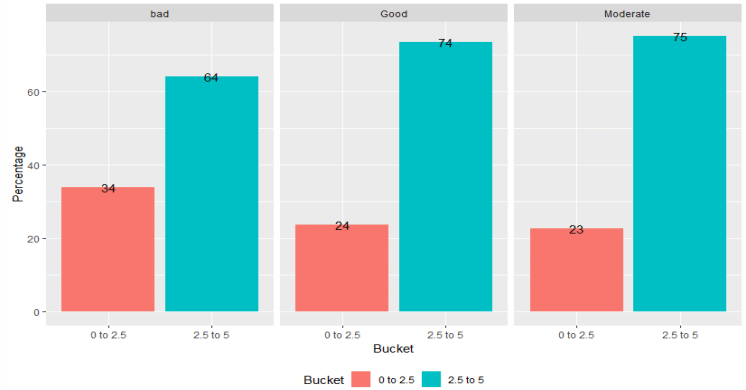
Use of Machine Learning based approach



Important Attributes Considered	
Air Flow	Outlet Temperature
Atomization pressure	Pan DP
Inlet RH	Pan Speed
Inlet Temperature	Pattern air pressure
Spray pump speed1	Spray pump speed2





Understand Process Flow

- *Understand Process Flow and identify Process parameters to be analysed*
- *Random Forest and Lasso Regression etc. models are used to identify the important parameters.*

Decision Trees

- *Create Decision Trees to identify the set of "golden batch" parameters needed for target yield.*

Deploy Model

- *Deploy model in commercial manufacturing and categorize effects based on obtained actual yield.*

Prescriptive model to Optimize machine setup

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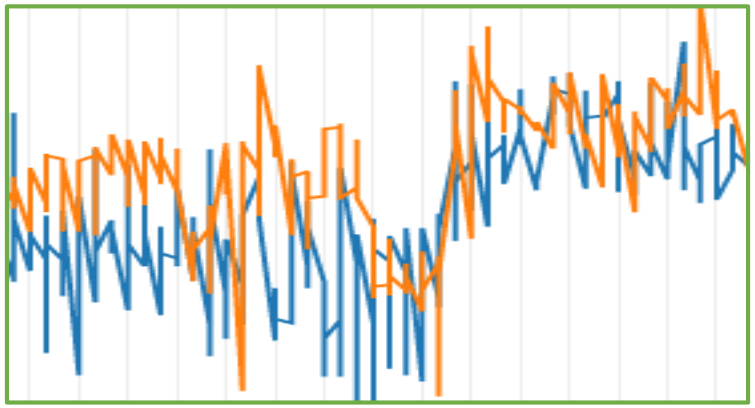
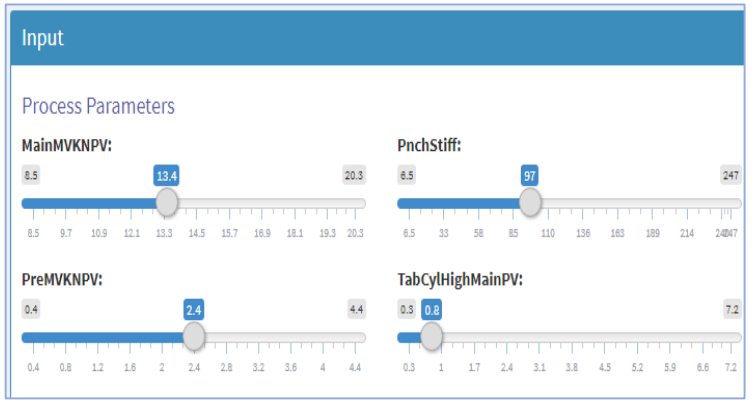
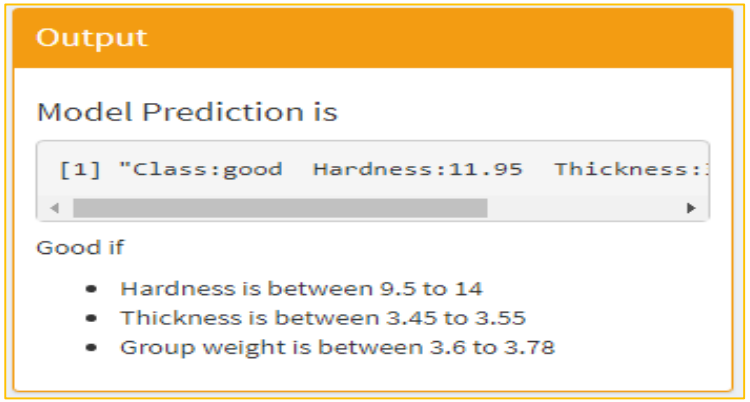
Faster Setup & Reduced Scrap to improve Op. Efficiency







Identify Correlations

- *Through data models, study the data and detect Inputs that have a strong correlation with outputs.*

Run Simulations

- *Operator to run simulations by keying in Batch to be compressed.*
- *System retrieves necessary specifications, compares with operator selected Inputs.*

Throw Predictions

- *Help the operator with prediction of CQA values that the machine will produce if the selected batch is run with simulated CPPs.*

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Integrated Planner & Scheduler

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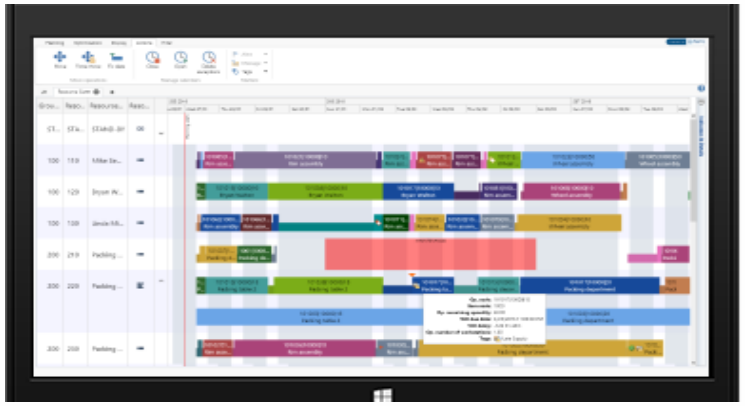
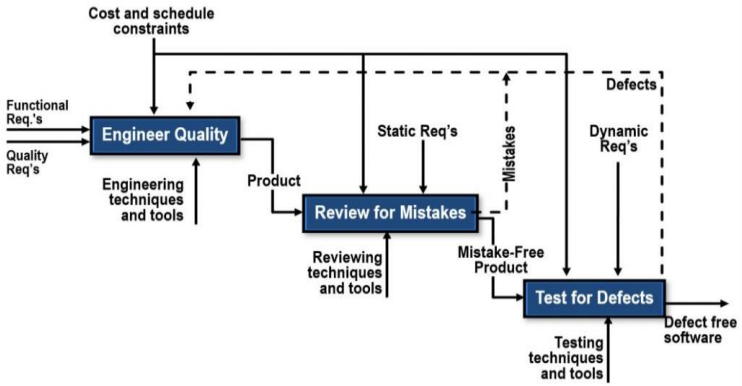
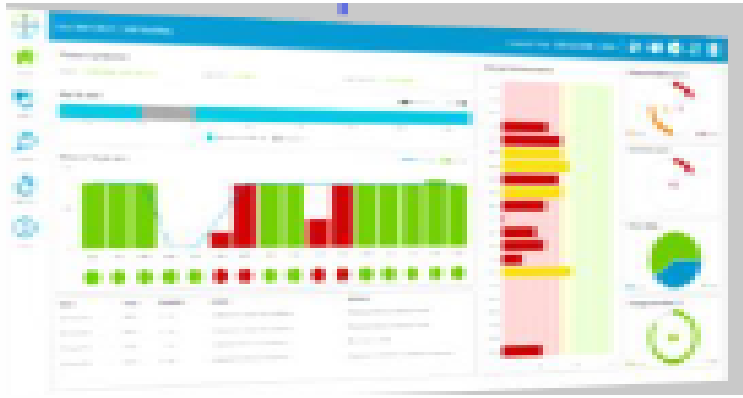
Focus on Core Operating Process







Integrated Planning

- *Digital Value Stream Map*
- *Flow Optimization(Ageing)*
- *Capacity Planning Optimizer, Planner for Equipment & Manpower including QC Lab Scheduling.*

Proactive Decision Making

- *Scheduling model automatically generates optimized schedule*
- *Web app for manual adjustments and building scenarios*

Digital Performance Management

- *Leverage big data to create real time transparency of performance.*
- *Live tracking of test completion on performance board*

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Challenges of Automation

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- Cost
  - License cost, Hardware, Implementation, Computer system validation, AMC,
  - Escalations
  - Upgrades
- Data migration
- Increased Regulatory scrutiny
  - Design (security, integrity, access controls, privileges)
  - Computer system validation
  - Data storage (backups, retrieval, control, audit trails)
- Change management
- Training of people
  - Operators & Supervisors

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Thank you