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Digitalisation in the Pharmaceutical Industry

Digitalisation practice applied to tablet packing

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Acknowledgement : Andy Birch, MTC, (andy.birch@the-mtc.org)

The Manufacturing Technology Centre

- The Manfacturing Technology Centre (MTC), is part of the High Value Manufacturing Catapult
- Supported by Innovate UK and established to prove innovative manufacturing processes and technologies in an agile environment in partnership with industry, academia and other institutions.
- Through the Digital Manufacturing Accelerator project, designed and built the automatic tablet packing line as a demonstration of new technology
- The line uses digitalisation to ensure right first-time operation including continuous monitoring of all critical parameters

mtc where progress happens

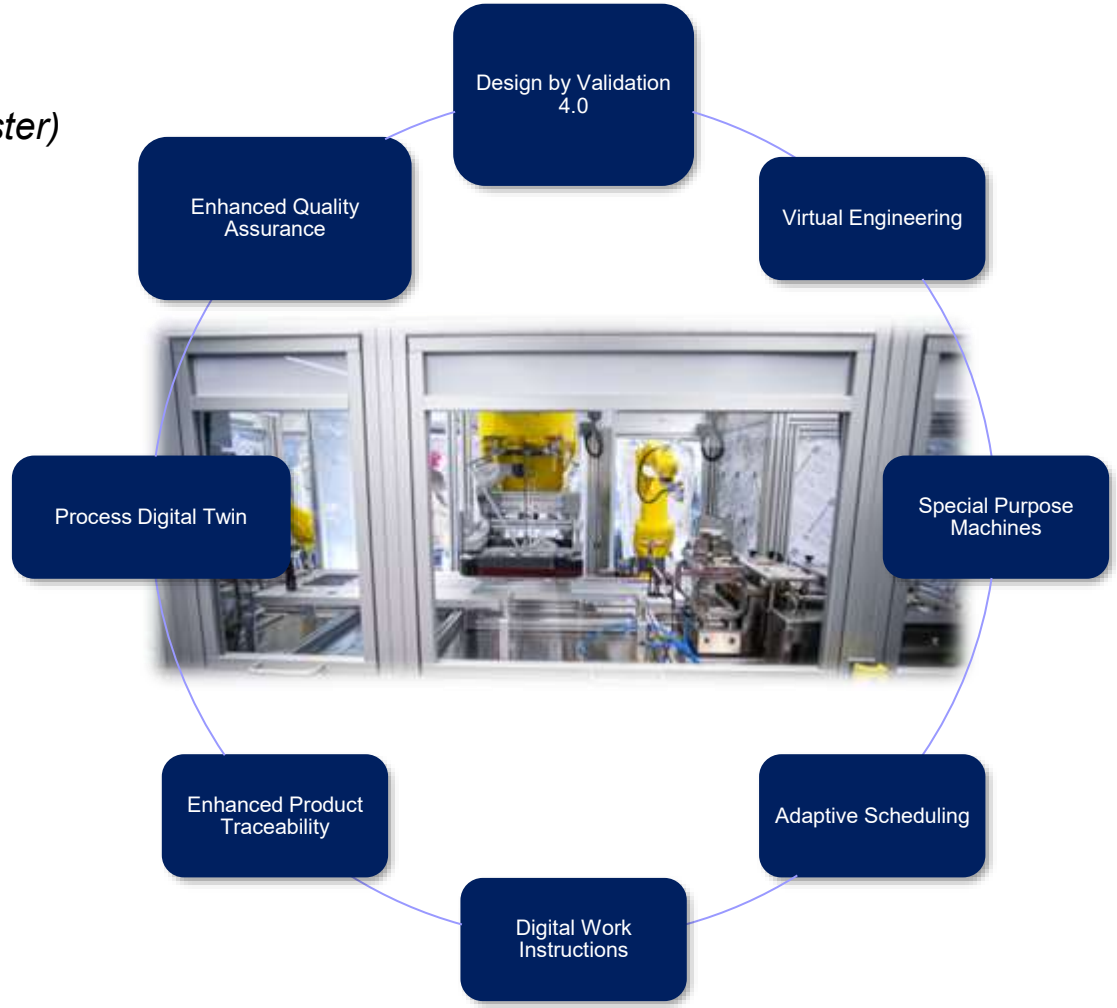
The Challange

“*Digitalisation enabling customised products*“

Production solution to meet the market need for customised (multi-drug blister) medication and productive small batch production.

Challenges:

- Existing packaging technologies **lack adaptability** with low OEE.
- Production changeover is **labour and time intensive** and prone to human error.
- **Lack of control** of product requires manual inspection.
- **Basic equipment monitoring**, lack of connectivity & industry 4.0 adoption.
- Paper-based traceability with **labour intense** manual batch sign off.
- New production introduction is expensive, time consuming with long downtime.



Project Objectives

- Able to pack patient specific pack formats (eg possible different tablets in the same blister)
- Complete automation of line operation and quality checks of all Critical Process Parameters especially the heat seal and the printing
- Complete recording and display of all data
- Systemised data management across recipe and master data and across the Manufacturing App (MES) Platform, the Process Control System, and the Electronic Batch Record (EBR), from manufacturing orders to finished packs
- High efficiency in- line setup and clearance that can handle the complexity of the possible packing formats to enable rapid and flexible changing of the pack make-up for a defined range of tablet types and dimensions
- Reduce any risks of cross contamination
- Innovation using Validation 4.0 principles in the equipment qualification and process validation

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Virtual Engineering

Starting from Virtual Engineering

- Multi-disciplinary use of integrated simulations as virtual prototypes to design, analyse, and optimise production systems, before physical prototypes are built
- Test, assess, debug, commission, demonstrate digital manufacturing solutions in a virtual environment

Benefits

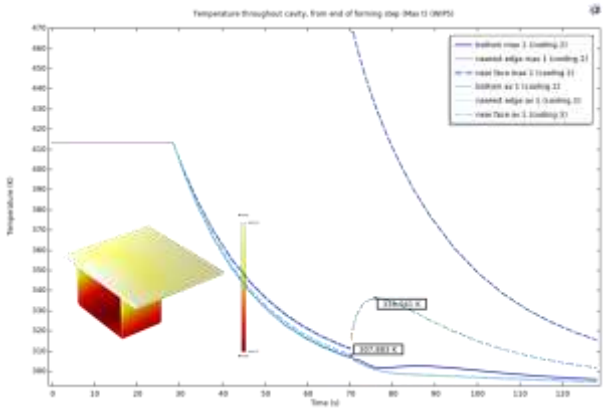
- Reduce prototyping
- Cost and lead-time benefits

Rapid adaptive packaging production

- Facility layout for reconfigurability
- Assess need for cooling around thermal processes
- Validate material handling processes quality
- Quantify impact of pick-and-place capacity on productivity

Production simulation

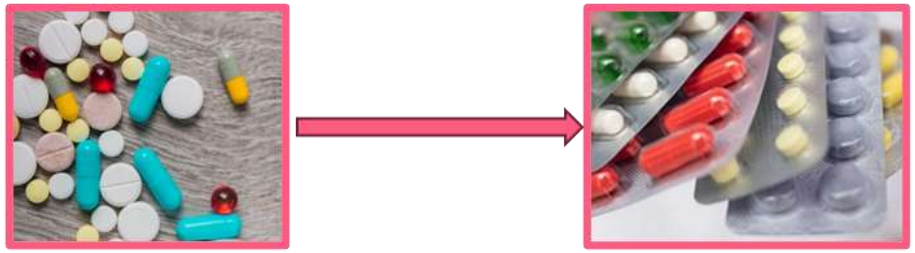
Tablet placing model

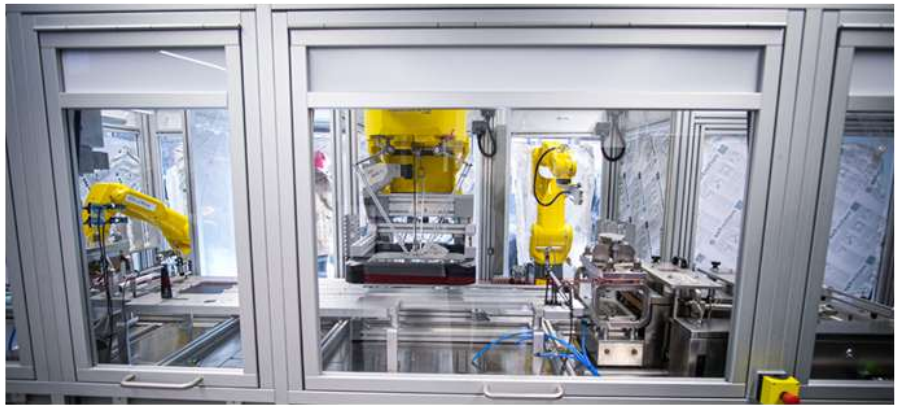


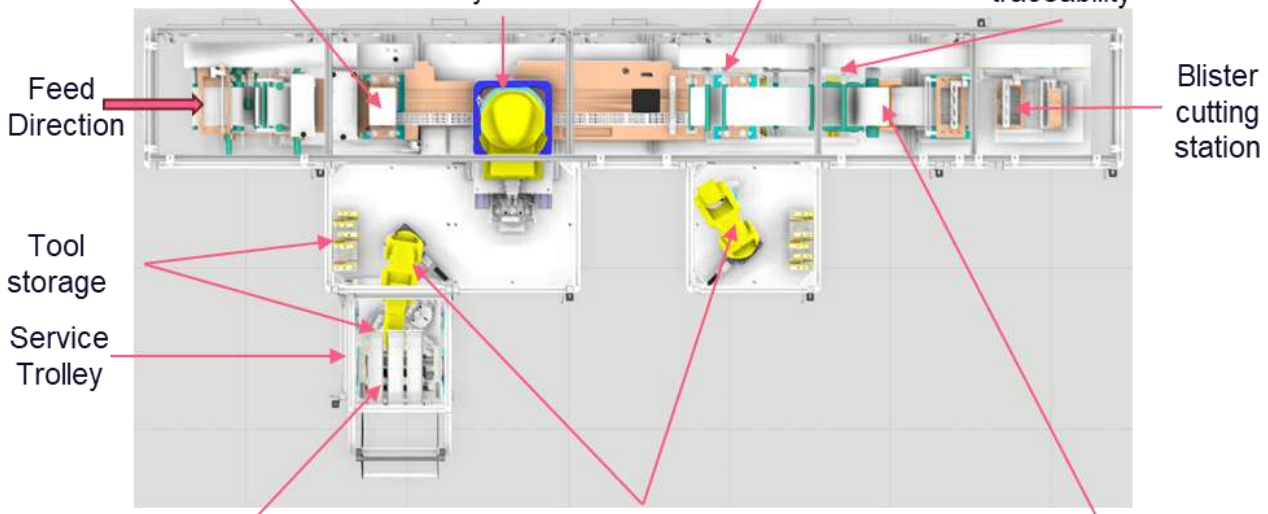
Thermal model

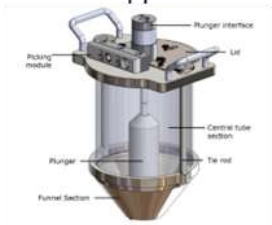
The Packing Line

An automated production solution for packaging customised (multi-drug blister) medication with enhanced productivity in small batch manufacture.









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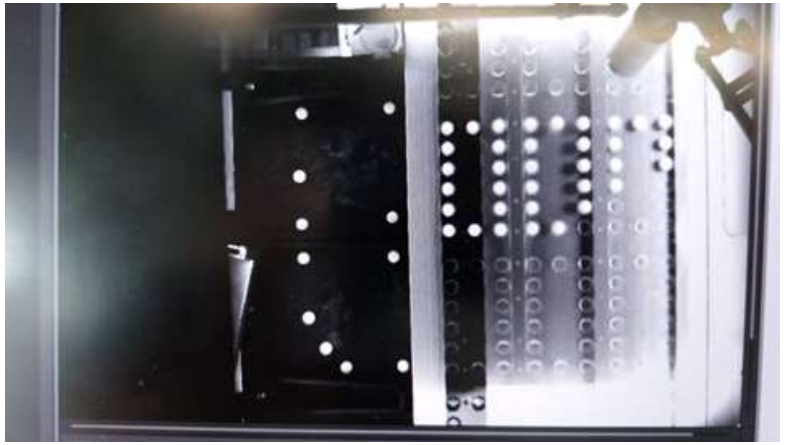
Line Operation

- The line is completely automated and embodies state of the art camera checks to ensure correct operation. The line is managed with a light no code management system (MES) with the process control system running below this. There is a lean batch record system to collect the packing batch record.
- A production order is created in the MES and started. Two robots select the changeover parts to match the order depending on the size of tablets. It places them in the forming and heat seal stations.
- The line forms pockets in PVC film and a robot fills each pocket with a tablet.
- a foil sheet is fed on to the top of the filled pockets and a heat sealer seals the packs
- A laser printer prints the variable data on each pocket including the seal temperature
- A cutter chops out the individual packs which are collected at the end of the line.

Line Monitoring

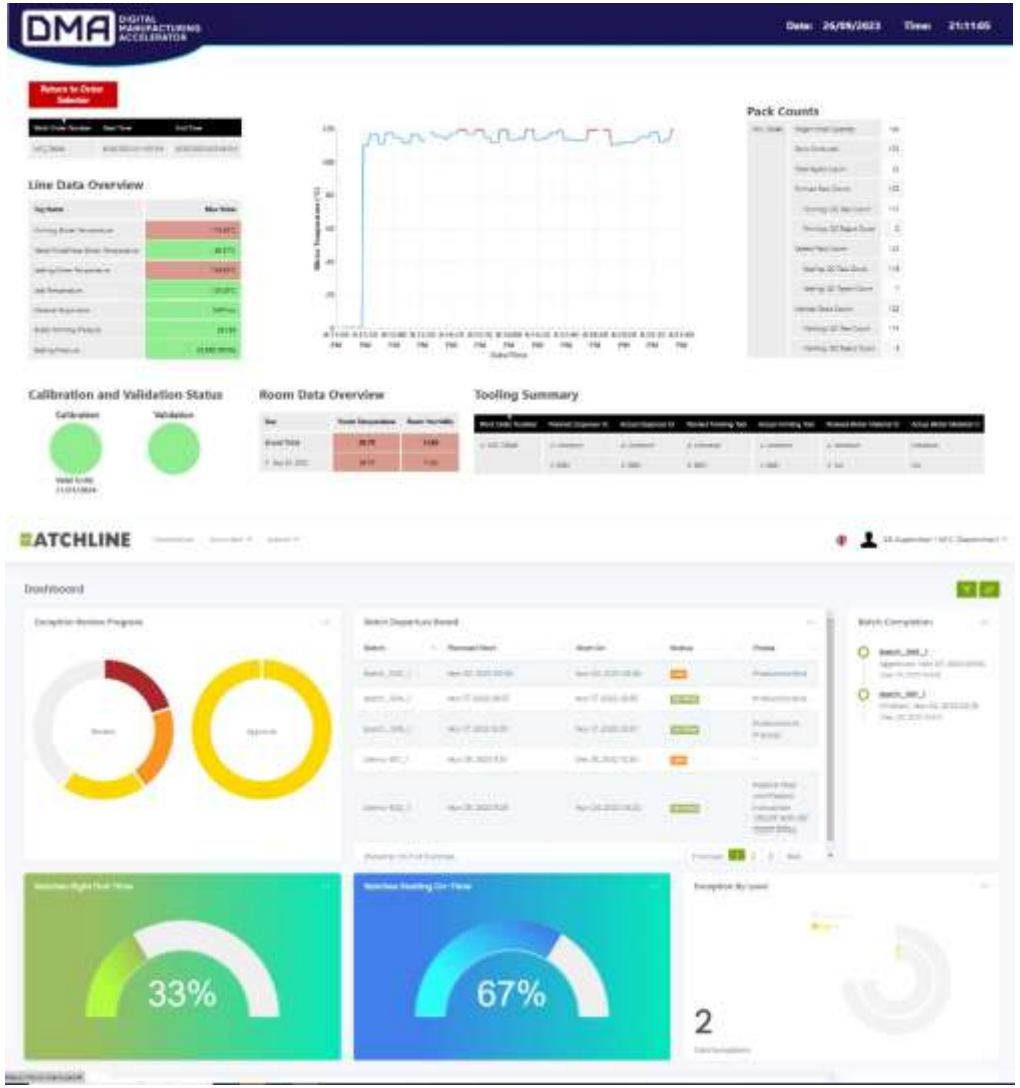
- Everything is continually monitored and any faults rejected. The monitor functions include detection of :
  - malformed PVC pockets
  - chipped or damaged tablets
  - pockets with no tablets
  - heat seal defects
  - print problem

- These potential problems are monitored with high definition cameras which are able to pick up any problems and correct them as they occur. Any faulty strips are rejected after cutting.



Details of Line Monitoring

- Malformed pockets are not filled
- Damaged tablets are not picked by the robot
- If a pocket has no tablet the robot will return to fill it
- The heat seal setting is determined by validation testing and the set temperature is printed on the strip and monitored . Any deviation of the heat seal temperature is monitored and alarmed
- The print definition is continually monitored and wrong or poor printing is rejected
- Key parameters are recorded and continuously displayed during the run
- The line makes an auto reconciliation at the end of the run.
- The MES provides guidance to the operator, collection of all data and simplified validation. For example
- the heat seal temperature which is a critical parameter is printed on each patient strip.



Digitalisation supports the continuous checking and right first time operation, in particular:-

- Packing of patient specific pack formats (eg possible different tablets in the same blister)
- Complete automation of line operation and quality checks of all Critical Process Parameters especially the heat seal and the printing
- Complete recording and display of all data
- Systemised data management across recipe and master data and across the Manufacturing App (MES) Platform, the Process Control System, and the Electronic Batch Record (EBR), from manufacturing orders to finished packs
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Electronic Systems

TULIP

Out of the box solution configured using composable apps to :-
Manage the whole operation from manufacturing order to finished packs
Provide operator guidance with human centric interfaces
Store all the data
Display critical parameters
Affordable

BATCHLINE

BatchLine is a compact and robust cloud-based digital Batch Record system built on modern web technology. Off the shelf configured solution with the advantages :-
Automatic Generation of Final Batch Report
Review By Exception, less time spent on the QA process
Automatic data completeness check
Data entry checked against specification on input
Cycle time reduction

Siemens PLC

Machine control

TULIP

What is Tulip?

- A platform for Developing No-Code Software Apps for Manufacturing
- Supports Composable Digtitalisation – Compose Apps to match operations
- Drag and drop, easy to use.
- Customers can develop their own Apps and/or use Factorytalk
- Many interfaces to the process
- Validateable – built for GxP use
- Cloud native, highly scalable.

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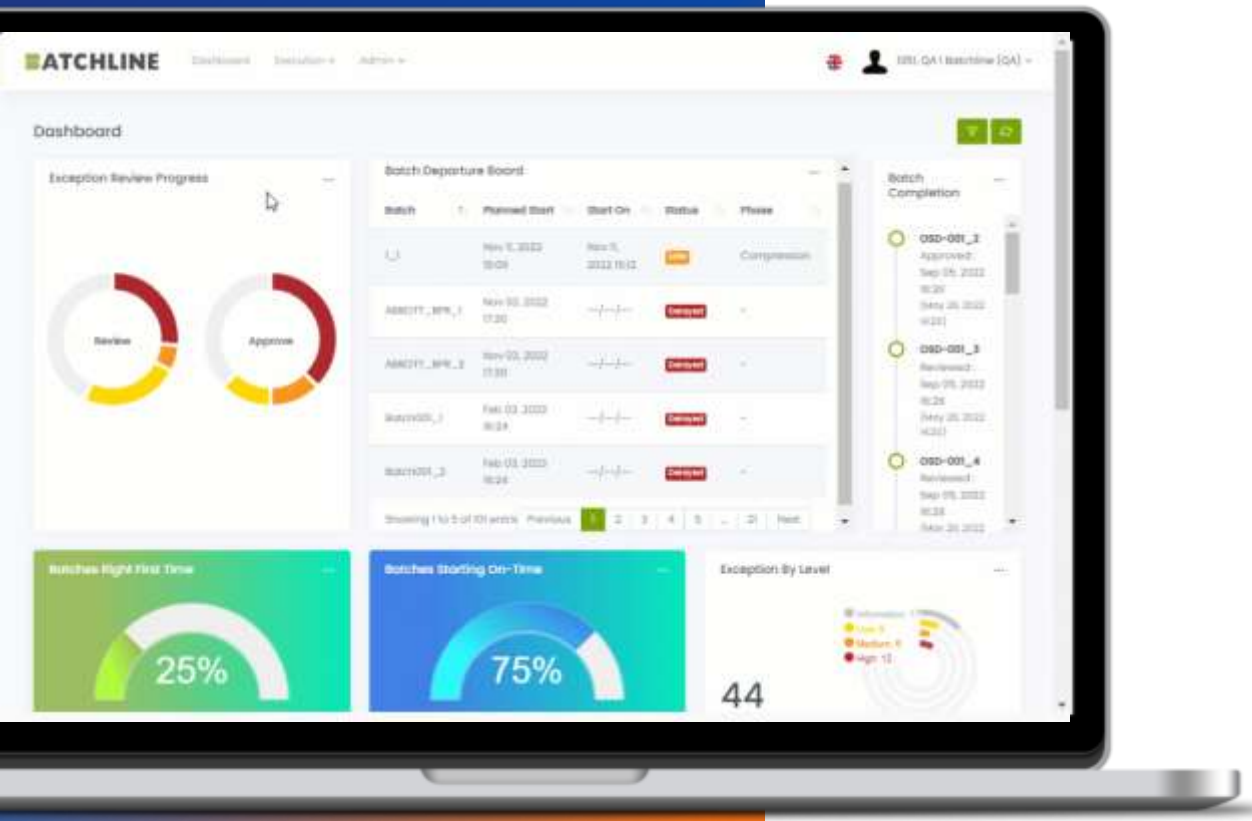
BATCHLINE

What is BatchLine Lite MES?



BatchLine offers a Lite MES with Electronic Batch Record (EBR), purpose built for Pharma and other GxP regulated companies to digitize production and quality for more efficient manufacturing operations.

With advanced technology and Pharma expertise we provide unparalleled benefits in an affordable product. Our experienced teams facilitate fast and simple onboarding, enabling EBR accessibility for all companies.

Smart, efficient, digital GxP manufacturing.
Made simple, compliant and affordable.

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MTC Machine Qualification
&
Validation Plan

Innovation using Validation 4.0 principles in the equipment qualification and process validation

The following validation documents were produced

- Validation Plan
- URS
- Risk Assessment
- Design Review
- Acceptance testing
- Validation Report

Risk Assessment

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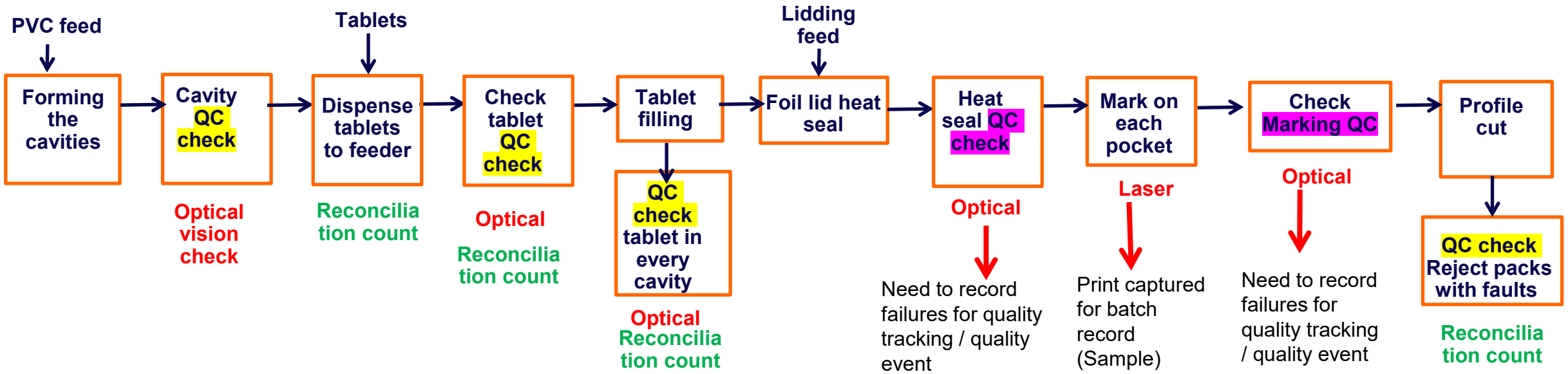
Tablet Packing Process & Critical Instruments



The qualification checks ensure that the QC checks are working and that any faults are rejected at the reject station . The batch record does not need to know about these faults

Efficiency / predictive maintenance does need to know about these faults

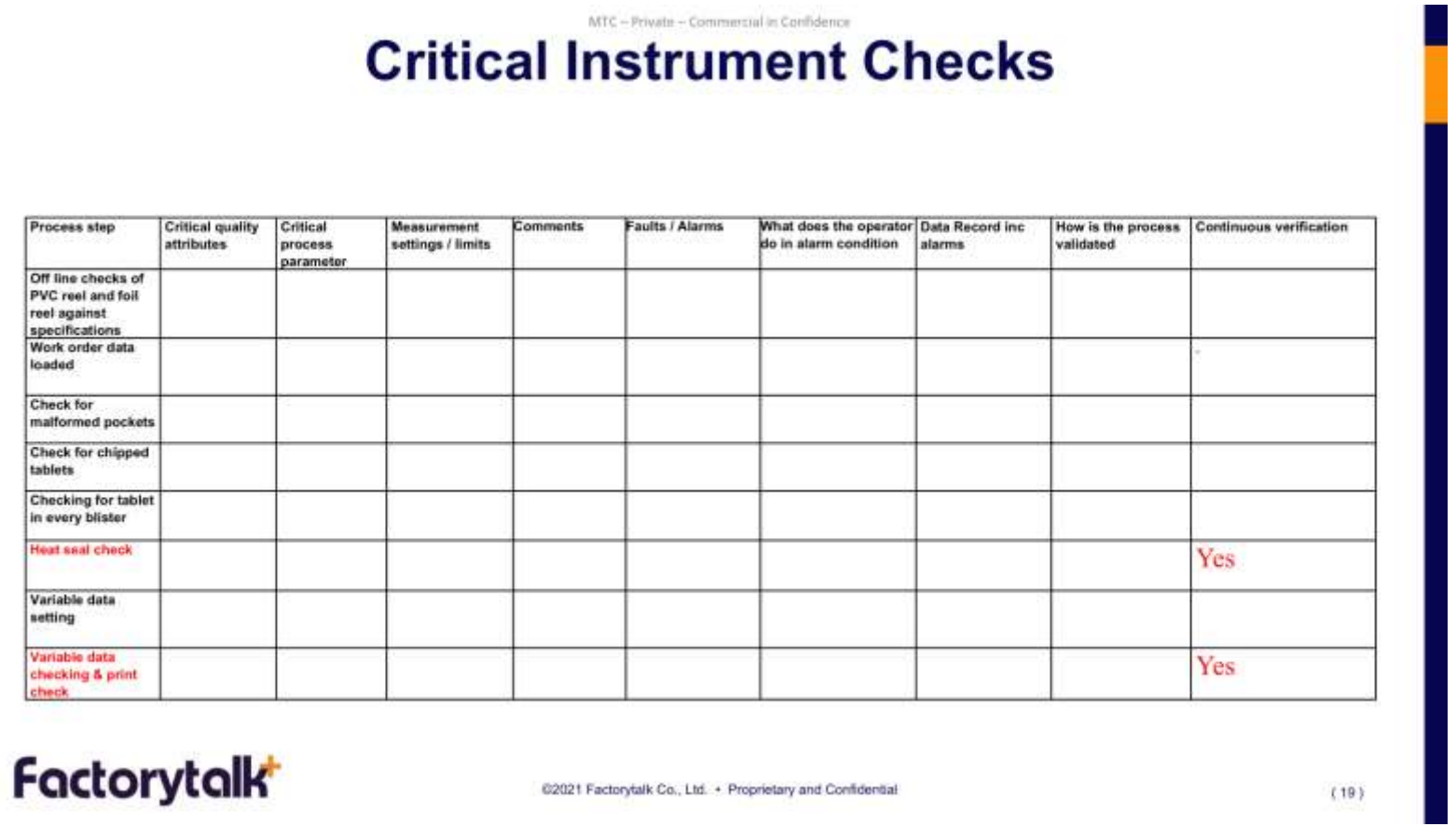
QC checks are quality events and do need to be recorded in the batch record

GMP record includes :-

- Issue of batch number & expiry date
- Raw material identification and status
- Change parts identification & status
- Line clearance
- Set up tests which check the QC checks and line speed
- Reconciliation, number started, rejects, number completed
- Printed information
- Any major failures eg heat seal or printing recorded as quality events
- Final approval by QA

Critical Instrument Review (Design Review)

- The critical instruments directly affect the product or product data
- Line speed as part of line set up
- Check on chipped tablets
- Check on tablet in every cavity
- Check for deformed cavity
- Heat seal temperature and dwell time
- Heat seal QC check (batch record)
- Marking QC check (batch record)



MTC – Private – Commercial in Confidence

Critical Instrument Checks

Process step	Critical quality attributes	Critical process parameter	Measurement settings / limits	Comments	Faults / Alarms	What does the operator do in alarm condition	Data Record inc alarms	How is the process validated	Continuous verification
Off line checks of PVC reel and foil reel against specifications									
Work order data loaded									
Check for malformed pockets									
Check for chipped tablets									
Checking for tablet in every blister									
Heat seal check									Yes
Variable data setting									
Variable data checking & print check									Yes

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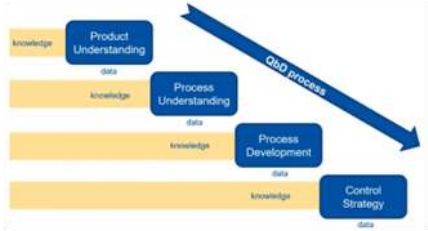
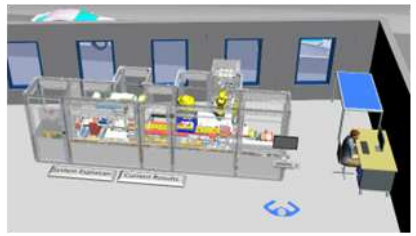
The Packing Line Summay





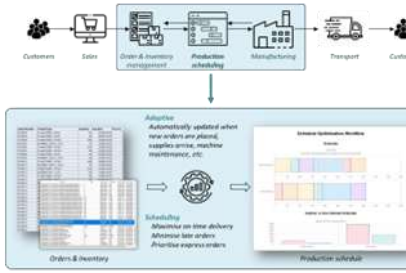
Machine Design

Design by Validation 4.0

Virtual Engineering

Enhanced Quality Assurance

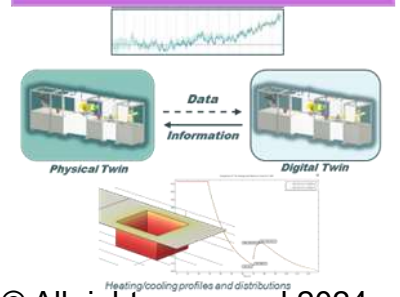
Adaptive Scheduling



Enhanced Product Traceability

Process Digital Twin

Digital Work Instructions



https://factory-talk.com

About Factorytalk ..

Specialist Consulting and Software Solutions for Life Sciences Manufacturers

Found in 2004 in Bangkok, Thailand

Teams in UK, Thailand, Indonesia, Brazil.

20+ years experience in MES, EBR, eDHR, eQMS, and CSV for GxP Regulated companies

Operate in Asia, Europe, and USA

75 staff + extensive freelance/ partner network

ISO 9001:2015 certified Volunteer for ISPE since 2004

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https://www.icheme.org/Visit-to-MTC

Visit to The Manufacturing Technology Centre

- Next week
- The Manufacturing Technology Centre, 131 Mount Pleasant, Liverpool L3 5TF
- Free
- 09.30 to 15.30
- Morning talks about the design
- Afternoon visit to the line
- The registration is available here :
- https://www.icheme.org/Visit-to-MTC

mtc where progress happens

Conclusions - Advantages of Digitalisation

- Automatic checking of :-
- Good heat seal (off line testing not required)
- Heat seal temperature continually monitored
- Print quality continually monitored
- Every blister has a tablet
- Tablet damage checks
- Auto reconciliation at the end of the run
- Continuous validation – correct operation is continually monitored
- Questions ?