GIG CYMRU NHS WALES
Partneriaeth Cydwasanaethau
Shared Services Partnership

Semi-Automated Medicines Manufacture

NWSSP Pharmacy Division

Discussion Points

- Background
- Adopting semi-automation
- Batch vs Campaign
- Method development
- Validation & Bracketing
- Staff Training
- Learning in Practice

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Background

- From perspective of CIVAS@IP5
- MHRA Special Manufacturing licence since Jan 2021
- Over 18 months testing and validating several devices
- Manufacture of:
  - Critical care syringes
  - Monoclonal antibody infusions
- Current work on
  - OPAT
  - Insulin syringes

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Adopting Semi-Automation

- Understand the processes to be automated
  - Current state
  - Desired state
- Understand target/desired product portfolio
- Look for efficiency gains outside of automation
- Key to understand end-to-end process
- Key URS features should include:
  - User profiles & permissions specific
  - Barcode scanning
  - Batch specific report downloading
  - Gassable!!!!

Batch v Campaign

Batch

- Long shelf-life products
- >28 days
- Standard batch sizes
- Standard batch on cost
- Predictable prescribing patterns
- Balance batch sizes vs time in critical zone vs financial risk of failure

Campaign

- Short to intermediate shelf life
- High usage
- <14 days
- Variable on-costs
- Items with unpredictable supply
- Validate maximum campaign sizes with novel segregation processes

Methods Development

Process

- **Starting materials**
  - Reconstitution?
  - Full, part or multi vial dose
  - Barcoded?
- **Process**
  - Transfer……gassing
  - Batch or campaign?
  - Syringe, infusion bag or OPAT?
  - Is further dilution required?
  - In-line filter
- **Process Completion & Inspection**
  - Labelling and process completion
  - Release criteria?
  - Product Inspection?
- **Quality Control**
  - Batch records
  - Device printouts

Method Considerations

- One device vs two devices
- Manual aseptic manipulations
  - Spiking
  - Luer lock
- Transfer
  - Gassing allows larger batch sizes
- Clean room segregation and process completion

Validation & Bracketing

Validation of Equipment

- DQ & IQ essential
- PQ in a bracketing approach
  - All similar equipment pass DQ/IQ
  - Rotation of equipment for ongoing processes
- Annual calibration
- Equipment can also have manual calibration by staff
  - Each batch
  - Periodic time frames

Validation of Processes

- Identify maximum and minimum batch sizes
- Max and min volume additions to final containers
- Each process validated every 6 months
- Validate equipment changeover mid-batch
  - In case of equipment issues
- Frequently change equipment serial number to ensure statistical significance of process data

Staff Training and Validation

- Staff validated on all equipment before using any.
- “Aseptic technique” – spiking and “luer-locking”
  - Focus on adherence to WPI
  - Comportment
  - Critical zone set up
- Equipment is designed to prevent intentional deviation
- Supervisors more focussed on control of finished goods and clean room behaviours

Learning in Practice

- Improved repeatability and reproducibility
- High batch yield
- Improves capacity
- Low ingredient waste
- Data integrity
- Reduces single use plastics
- Cost-effective
- Remote control of manufacturing schedule
- Branded-generics without barcodes
- Need a backup – expensive
- Local technical/engineering knowledge advisable

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50 INFUSION BAG ADDITIONS IN 90 MIMUTES

70-80% REDUCTION IN SINGLE US PLASTICS

200 5mL SYRINGES IN 90 MINUTES

>350 BATCHES – ZERO BROTH SIMULATION FAILURES

£75 STANDARD CONSUMABLE COST PER BATCH

YIELD OUTPUT
97.5 – 99.6%

ANY QUESTIONS?