ENGINEERING PHARMACEUTICAL INNOVATION

Parenteral Filling Facility Automation Case Study

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System Overview

- Greenfield Parenteral Filling facility with two filling lines (Commercial Line and Clinical Line), Microbiology Lab, Inspection, Packaging, Waste Treatment, and Warehouse Storage

- 8 Programmable Automation Controllers (PAC) provide direct control of non OEM equipment and batch/sequential control.

- 15 Thin client Human Machine Interface (HMI) provide visualization to the facility via redundant terminal servers

- 8 Mobile devices (ruggedized tablets and handheld computers) provide wireless access for visualization and data entry

- Data historian provides historical data collection

System Overview (cont.)

- Monitor and control of all HVAC (Direct and Indirect Impact)
  - 7 AHUs
- Monitor and control of clean utilities storage and distribution
  - WFI, Clean Steam, etc
- Monitor and interact with 28 pieces of skid equipment
  - Various PLC/HMI vendors
- Provides overall batch execution and control for major operations
- Serves as the traffic cop for all data transfer
- Aggregates data for production reports

System Goals

- Develop a layered but unified system for the entire facility
  - Displays, actions, etc are consistent for all parts of the system
  - Access to key functions, displays, data, reports for all operation and equipment from one system
  - One stop shop for the facility
- Provide overall coordination for all batch activities on the line
- Provide a central repository for recipe data and data management
- Provide a central repository for batch and process data
- System needs to produce electronic batch reports
- Act as interface to ERP system in order to provide MES type functions

Consistency Throughout

- A system must appear consistent to users at all layers in order to serve as unified system
- The Easy Things
  - Graphic color schemes, borders, symbols
  - Navigation of system, printing activities
  - Starting equipment, entering set points, changing modes
- The Not So Easy Things
  - Common login for all equipment, most importantly OEM skids
  - Consistent method for initiating batch and unit operations whether it is an autoclave, isolator, or CIP process.
  - Batch reports for all process and equipment appear similar in the type of data provided and the method of presentation
  - Interface to a partswasher looks the same as the interface filler, just different data.
  - Data transfer methods are transparent to user, it just works!

ERP Integration

1. Process Orders, Bill of Materials, and Inventory are transmitted from SAP

2. Decoupled interaction via XML file drops over FTP on 15 minute cycle.
   - Current schedule is less than 5 unique orders per week so real time data exchange is of little value.

3. Orders are available for selection by operators upon receipt.

ERP Integration

1. Order status is communicated as phases (compounding, filling, packaging) advance through different states (started, held, aborted, completed)

2. At the completion of each phase consumption data is transmitted with direct linkage to received inventory, supported by Asset Tracking system.

3. Production Data is transmitted at order completion

Real Time Asset Tracking

- If a material is received from Inventory (SAP) or Cleanliness/ Sterility is tracked the item receives a unique barcode for tracking.
  - Operators “Receive” consumable materials from SAP Inventory, generating a new barcode.
  - All materials passing through a partswasher or autoclave receive a barcode.
  - Barcodes are marked clean, sterile, and dirty based on equipment activity.
  - Operators scan barcodes as they move the materials in the suite.
  - Barcodes are associated with cycles and reported in electronic batch reports.

Batch Control

- How do you provide batch control of a process when:
  - The equipment involved is standalone and not necessarily designed with a higher level system in mind.
  - You do not have direct control over the equipment involved.
  - The equipment needs data that it does not own.

ANSWER:

GET INVOLVED EARLY WITH THE VENDOR AND GET IN THE MIDDLE OF EVERYTHING

Batch Control (cont.)

- Every production operation is governed by a predefined procedure in the facility system regardless of what equipment provides final control.
  - CIP, VHP, vial washing, filling, compounding, manual cleaning, autoclaves, etc

- Acts as the gatekeeper and enforcer for all production operations
  - All production procedures must be initiated from the facility system

  - All prerequisites must be met before proceeding in a procedure
    - Room conditions, utility status, equipment status (clean/dirty), environmental monitoring. These are things that the gatekeeper knows but the equipment does not.

  - The system must have the ability to enforce and issue both hard and soft stops to the equipment should something go wrong.

Batch Control (cont.)

- System must act as the data traffic cop
  - Any data needed by another piece of equipment comes through the system, including interlocks and permissives
  - Data quality, value, status is always known and can be conveyed to the user
- Procedure structuring is important
  - Everything is considered an operation or cycle to allow flexibility

Batch Control (cont.)

- Step 1 – Track your Cycles

  1. Complete control and visibility of GMP cycles
     - Autoclaves, Partswashers, Filter Integrity
     - CIP, SIP, Decon
     - Compounding Operation
     - High level Filling and Packaging Procedures

  2. Filling Line, Packaging Equipment
     - Equipment requests “release” for specific cycles
     - Operator driven from equipment HMI
     - Each release is assigned a unique Cycle ID

  Associations are made at the cycle generation stage whenever feasible. (Compounding and Packaging)

Batch Control (cont.)

- Step 2 – Associate Cycles
  1. Direct association at cycle generation

  2. Equipment Cleanliness and Sterility (CIP, SIP, and Decon)
     - Time and Event Based
     - CIP → SIP → Equipment Use Cycle → Decon

  3. Consumable and Durable Good Cleanliness and Sterility
     - Barcode and Event Based
     - Partswash → Autoclave → Equipment Use Cycle

  4. Sequence of Events

  5. Associate with SAP Process Order by operator selection at the start of the cycle.

Batch Control (cont.)

- Pulling It All Together
  - SAP Process Order
    - Component Preparation
      - Autoclaves
      - Partswashers
    - Compounding
      - Compounding Vessel CIP and SIP
      - Hard Good Association to Component Prep Cycles
    - Filling
      - Equipment CIP and SIP
      - Hard Good Association to Component Prep Cycles
      - VHP (Sterility) Cycles for Isolator
      - Cool Zone Sterilization for Depyrogenation tunnel
      - …
    - Packaging

Batch Control (cont.)

- Why use a batch procedure to control everything, even manual activities and operations carried out solely by underlying equipment?
  - The obvious reason – procedures enforce workflow of both manual and automatic activities
  - The not so obvious reason – event and data context for the batch report

Recipe Management

- Recipe and cycle parameter managed in a single location - “recipe database”
  - Provides ease of management and tighter control of validated parameters
- Non-production recipes (maintenance, setup, cycle development) not stored in the recipe database to provide flexibility.
- Recipe data is either downloaded to the equipment or verified prior to allowing a batch to start.
- Some vendor equipment was set up to receive recipe parameters from the facility system.
  - Required early coordination with the skid vendor (need a place to send the data)
  - For these systems, recipe data is downloaded from the recipe database directly to parameters on the equipment PLC.
  - Data is verified after download completes to check integrity of the transfer.

Recipe Data Management (cont.)

- Some vendor equipment was NOT set up to receive recipe parameters from the facility system recipe database.
  - Either the vendor refused to set their system up to receive recipe data or we were to late to get the requirement into the specification.
  - For these systems, recipe parameters residing in the equipment PLC are compared/verified against the recipe parameters in the recipe database.
  - Recipe parameters must match prior to issuing the permissive to start a cycle.
- Able to utilize off the shelf capability of system for recipe management and recipe transfer
  - Allowed for viewing and editing of recipe parameters by authorized users in a familiar format.

Recipe Data Management (cont.)

- Benefits of controlling and consolidating ALL recipe data
  - Central location for management
  - Consistent structure of data, regardless of destination
  - Guarantee the right recipe data gets used every time
  - Dynamic access to data for batch reporting: comparing data against limits, comparing run times against targets, recipe version, author etc.

Data and Access Management

- Followed the idea that a single system should hold all important "data"
  - Data Historian – monitored and logged continuous data. HVAC fan speed, Room DP, Autoclave temperature, stability chamber temperature, etc.
    - Data historian logged data from ALL equipment, including OEM skids
  - Alarms and Events– monitored and logged alarm and event data. Process alarms, interlocks, overrides/bypasses, starts/stops, setpoint changes, etc
    - Alarms and events logged from ALL equipment, including OEM skids
  - Material Tracking – material tracking data stored in system database
    - Location, quantity, expiry, lot information,
  - Equipment and Room status – status tracked and stored in system database
    - Last CIP, current state, time left, room status, etc

Data and Access Management

- Followed the idea of a single login for all operations, including OEM equipment
  - Utilized Active Directory for all logins
  - Users centrally managed
  - OEM systems utilized our login system, takes vendor buy-in up front of course
  - Users assigned access to areas and equipment based on training qualifications
  - Record of all users at all equipment at all time

Batch Reporting

- Major Goals
  - Electronic batch reports for all automated equipment (no more strip charts)
  - Production of cycle level reports that could be combined to create the final batch report.

- Common layout for all reports
  - Common headers and footers for all batch reports
  - Common sections for similar types of reports:
    - Recipe parameters/targets
    - Charts with dynamic limits (based on recipe) and data specific to time of batch
    - Pertinent cycle data
    - Exception reporting – alarms, events, excursions

Batch Reporting (cont.)

- Data from various sources
  - Process Data – Temperature, pressure, humidity
  - Alarm and Event Data – Bypass, override, manual control
  - Recipe Data
  - Cycle data
  - User data

- Reports are available for all operations
  - Autoclaves, parts washers, compounding, CIP/SIP, filling line, packaging line
  - Reports identified by cycle ID and batch ID as appropriate

Batch Reporting (cont.)

- Report presentation
  - Online, on-demand access as the product moves through the production cycle
  - Retrieve online reports by batch ID
  - Reports can be printed and attached to the manual batch record
- Report Storage and Distribution
  - Available via web page
  - Data stored electronically for reports
  - Reports are saved to PDFs
  - Reports can be printed
  - Reports can emailed to a distribution list