Werum: The Leading Manufacturing IT (MIT) Partner for Life Sciences

<table>
<thead>
<tr>
<th>Year</th>
<th>Employees</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>380</td>
</tr>
<tr>
<td>2010</td>
<td>400</td>
</tr>
<tr>
<td>2011</td>
<td>450</td>
</tr>
<tr>
<td>2012</td>
<td>470</td>
</tr>
<tr>
<td>2013(e.)</td>
<td>490</td>
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</tbody>
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490 Employees

21-Sep-15  MES in Single-use Biomanufacturing Facilities
PAS-X market approach: more than software

Comprehensive offer for fast & efficient MES projects
The growth of Single-use Systems has been slow but steady in GMP Plants:

**Upstream Equipment Market**

- More growth in GMP vs. R&D (23 to 64% of SUS market)
- Increased cannibalization of stainless market (from 10 to 20% of spending)
- $\frac{2}{3}$ of new small / mid size facilities are Single-use
Dramatic growth also expect for Downstream as new technologies become available:

- > 100% growth in the downstream market
- Still a fraction of the traditional stainless market
What is driving Single Use trend…and what is the impact?

- Small Sites
- Lower Staffing Levels / Skills
- Contract Staff
- IT “Cloud”
This drives certain operational behaviors... and risks:

- **Increased Manual Activities**
  - Risk: Human Error

- **Increased Complexity of Consumables**
  - Risks:
    - Genealogy
    - Material Tracking

- **Designed for Increased Flexibility**
  - Risk:
    - Human Error
    - IT Efficiency

- **More Material “in space”**
  - Risk: Material Tracking
Can automation mitigate these risks?

Systems supporting BioPharmaceutical Manufacturing have made progress

<table>
<thead>
<tr>
<th>Purpose built software with content designed to support BioPharmaceuticals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mature philosophies on organization of IT systems in the architecture</td>
</tr>
<tr>
<td>New technologies will improve access to IT at smaller sites</td>
</tr>
<tr>
<td>Integration standards (i.e. OPC) and APIs simplify integration across systems</td>
</tr>
<tr>
<td>Regulators acceptance of and, in some cases, encouragement of shop-floor technology</td>
</tr>
</tbody>
</table>

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ISA S95 IT Concept

**Level 4**

**ERP (SAP)**
- Source, Plan,
- Manage Inventory,
- Delivery, etc

**What?**
Managing the end-to-end supply chain
Establishing plans - production, material use, delivery, and shipping. Maintaining costs of operations.

**Time Frame:** Months, weeks, days

**Level 3**

**MES**
- Dispatch Production,
- Detailed Scheduling, Make product,
- Manage events/exceptions

**What?**
Work flow / recipe control, stepping the process through states to produce the desired end products. Maintaining batch records and optimizing the production process.

**Time Frame:** Shifts, hours, minutes, seconds

**Level 2**

**DCS**
- Batch Control

**Continuous Control**

**Discrete Control**

**What?**
Monitoring, supervisory control and automated control of the production process.

**Time Frame:** Milliseconds

**Level 1**

**What?**
Sensing the production process, manipulating the production process.

**Time Frame:** Milliseconds

**MES in Single-use Biomanufacturing Facilities**

21-Sep-15

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Growth of MES has been steady in life sciences

More than 70% of top companies have established global MES programs

Growth driven by:
- Compliance
- Visibility
- Efficiency
- Control
- Complexity
Where we were

Level 4 - ERP

Challenge:
• Many point-to-point connections
• Expensive and time-consuming to validate and maintain
• Importing lots of raw data into MES

Level 3 - MES

Challenge:
• Chance for transcription error or “missed value” by operator
• Inefficient, with lots of human interaction

Down:
• Process Parameters
• Recipe start/end

Up:
• Tag Structures
• Process Data
• Alarms/Events

Historian
A Better Approach

Level 3- MES

Benefits:
• Leverages existing historian connections
• Reduced validation / maintenance efforts
• Easier management of statistical data

Level 2/1 SCADA / DCS

Down:
• Process Parameters
• Recipe start/end

Up:
• Tag Structures
• Process Data
• Alarms/Events

Historian

EBR

PAS X

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MES in Single-use Biomanufacturing Facilities

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The Electronic Batch Record is often seen as the single source of production information for a produced product.
This drives certain operational behaviors...and risks:

- Increased Manual Activities
  - Risk: Human Error

- Increased Complexity of Consumables
  - Risks: • Genealogy • Material Tracking

- Designed for Increased Flexibility
  - Risk: • Human Error • IT Efficiency

- More Material “in space”
  - Risk: Material Tracking

21-Sep-15
Increased Manual Activities

- Paperless Production drives “Right First Time”
- Electronic Work Instructions
  Strong User Guidance
- Launch visual guides for operators (video, photographs)
- Optimized User Interface for Shop Floor Environment
Increased Complexity of Consumables

- Material verification by barcode scan checking material number, batch number, expiry date
- Can be performed with stock material and with WIP materials
- Automatic population of batch record triggered by scan
- Full genealogy assembled real-time
- Materials can be managed as equipment
Libraries: Pre-defined, process specific building blocks to rapidly build recipes (by Unit Operation)

Generic Recipes: Eliminates needs to re-build recipe for each new SKU

Plug / Play with Equipment Integration: Pre-defined tags in MES for specific process equipment
More Material “in space”

- Real-time tracking of material / container movements and location
- Storage condition monitoring to prevent expiration of critical materials
- “Intelligent” containers and equipment that can move process relevant information between orders and areas
What more is on the horizon?
Case Study 1: Traditional Large Molecule

**Background**
- Top Biopharma Company
- New, single-use facility
- New technology and approach for company
- Multi-product
- Low cost basis
- New manufacturing model moving forward

**Scope**
- COTS Software Model
- Architecture:
  - ERP (Global)
  - MES (EBR, Mat., W/D)
  - DCS
  - Historian
  - Multi-variate monitoring
  - Plug and Play Equipment
  - Clinical and Commercial
- 5 to 10x reduction in construction cost

**Key Learnings**
- Parallel development of recipes on Level 2/3
- Generic recipes apply to some areas, but not all, for BioPharma
- Need proper modularity of recipe structures to achieve “plug-n-play” goal
- Lots of change in early plant -> recipe changes...
- Simulation systems for each level of architecture critical for testing and minimizing timeline risk
Case Study 2: Autologous Therapy

**Background**
- Autologous Therapy
- Table-top manufacturing with fully SU technology
- Expecting huge growth, with specific challenges:
  - Batch sizes of one
  - Material tracking failures can have fatal consequences
  - High tracking requirements for raw materials
  - Global alignment of processes across multiple sites

**Scope**
- Focus on Scale-Out vs. Scale-Up
- Chain of Identity (CoI) from outside -> inside four walls
- Architecture:
  - ERP (Global)
  - Scheduling / Clinics
  - MES (EBR, Mat.)

**Key Learnings**
- MES requirements not unique to the industry
- Guidance and electronic control for operators key to maintaining quality at volume
- Future of automated Level 2 is murky
- MES provides a platform for harmonizing recipe across sites via central deployment
Thank you for your attention.

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References