Digital Transformation of Vaccine Manufacturing

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The Life Science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.
Agenda

1. Trends in Biopharma Manufacturing
2. Building Blocks and Enablers
3. Convergence of Technologies
4. Summary And Takeaways

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Our core businesses

Every day, our nearly 64,000 employees work in 66 countries to make a positive difference to millions of people’s lives by creating more joyful and sustainable ways to live.

Life Sciences

Impacting life and health with science
Cutting-edge technologies, products and novel services for diagnostics, research, development and the manufacturing of biological and novel therapies (mRNA). Focused on Pharma Biotech, Diagnostics, Academic and Government Research and Industrial

Healthcare

As one for Patients
Biologics and small molecule prescription medicines for cancer, multiple sclerosis, fertility and general medicine. Research focus: Oncology, Immunology & Immuno-Oncology

Electronics

Advancing Digital Living
Advanced solutions for the Semiconductor & Display industries focused on materials, equipment and services

Pigments and active ingredients for the Automotive, Cosmetic and Industrial industries
Bioprocessing

We anticipate and shape the future of biopharma manufacturing for the betterment of our planet and its people.

A vision for the future

• Lead the acceleration of sustainable and digital solutions to enable better health outcomes globally
• Blaze new development and manufacturing paths to deliver life-enhancing biologics
• Emphasize quality. Always.
TRENDS IN BIOPHARMA MANUFACTURING
Industry is driving towards ambitious targets for output and flexibility. 

Bioprocessing can drive transformation by focusing on key technology areas:

**Market Trends**
- Market Growth
- Uncertainty
- New Product Classes
- Cost and Pressure to deliver

**Business Drivers**
- **Speed**
  - Reduce facility build times
  - Compress production lead times
- **Agility & Scalability**
  - Reduce product change-over time
- **Quality**
  - Increase robustness
  - Reduce cost of poor quality
- **Value**
  - Reduce cost to manufacture and CAPEX
- **Sustainability**

We need to bridge with the right building blocks and enablers to realize the Facility of the Future.

Adaptive Plant
- “Plant of the future”
- Autonomous
- Self-optimizing
- Plug-and-play

Predictive Plant
- Process modeling & monitoring
- Advanced production technologies
- Predictive analytics

Connected Plant
- Automated production layers
- Industry standards
- Semi-automated analytics

Digital Siloes
- Islands of automation
- Recipes on systems
- Offline analytics

Pre-digital Plant
- Paper-based
- Manual processes
- Isolated unit operations

Industry is driving towards ambitious targets for output and flexibility.

Bioprocessing can drive transformation by focusing on key technology areas.
Achieving Manufacturing Success Requires a Paradigm Shift

**Evolution: Batch → Intensified → Integrated & Continuous**

**Convergence of Evolving Process, Analytics & Digital Technologies**

**END-STATE**
- Continuous
  - Real-time
  - Process Simulation
  - Predictive Analytics
  - Electronic Batch Record

**MID-TERM**
- Intensified
  - On-line
  - Orchestration Process
  - Process Analytics
  - Data Analytics

**TODAY**
- Batch
  - Off-line
  - Harmonized Unit Operation Control

**Digital Technologies**
Building Blocks and Enablers
How can we enable a Paradigm Shift?

Building blocks and enablers of Biopharma 4.0

Building blocks

- Digital Technologies & Data Management
- Process Analytical Technologies
- Process Technologies

Enablers for the Future

- Standard / Templated
- Connectivity & Interoperability
- Data Integration & Contextualization
- Flexibility
- Modularity
- Extendibility
- Model Driven Design
- Future Ready
- Ease of Use

Convergence of technologies and enablers create an ecosystem for BioPharma 4.0 Manufacturing Execution Success

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The Digital Transformation Journey

A Step-Wise Approach

**Process Data Layer:** What happened? Why did it happen?

**Plant Data & Integration Platform:** Where did it happen? Where else can it happen?

**Plant Execution System:** What can happen and when?

**Plant Decision System:** When it is predicted to happen, how can I adapt and continue?

**Approach: one layer at a time**

- **Layer 1:** Digital Silos to Connected Plant
- **Layer 2:** Connected Plant
- **Layer 3:** Predictive Plant
- **Layer 4:** Adaptive Plant

**Plant Decision System** – Optimize and Adapt

**Plant Execution System** – Model and Predict

**Plant Data & Integration Platform** – Data to Information

**Process Data Layer** – Collect Data
Converge, Intensify and Evolve. Together.

Convergence of technologies
BioContinuum™ Platform

Enterprise Portal

- Reporting
- Analytics
- Sharing
- ML/AI & Digital Twins

Process Data Layer (Historian +)

Digital

- Bio4C ProcessPad™ Software
  - Data integration, management and analytics and visualizations
- Bio4C Orchestrator™ Software
  - Equipment connectivity
  - User, recipe management
  - Reporting and approvals
- Bio4C ACE™
  - Equipment control

ProCellics™ Raman Analyzer & Bio4C® PAT Raman Software
- In-Line/on-line sensors
- Chemometric modeling software to analyze Raman spectra for real-time process analytics

MAST® Autosampling

Processing Technologies
- Hardware Systems
- Consumables
- Single-Use Technology

Process PAT

- Perfusion Bioreactor
- Continuous Capture
- In-Line Viral Inactivation
- Flow-Through Polishing
- Continuous UF/DF

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Bio4C® Software Suite

**Bio4C ACE™ Software**
- Remote control and automation software
- Built on Industry 4.0 principles
- Supports easy and fast integration – vertical and horizontal

**Bio4C Orchestrator™ Software**
- Centrally connects disparate Merck & 3rd party bioprocessing systems
- Gathers machine data into a Centralized Historian – A Process Data Layer
- Enables real-time monitoring and visualization

**Bio4C ProcessPad™ Software**
- Data management and analytics platform
- Offers bioprocess monitoring, lifecycle management, reporting, investigations, and continued process verification (CPV)
- Enables forecasting, prediction and process improvement

**Digital Islands**

**Connected Plant**

**Predictive Plant**
Process Analytical Technologies
Enables real time feedback, modeling and optimization

1. In-line Traditional Sensors
2. Procellics™ Raman analyzer with Bio4C® PAT Raman Software
3. MAST® Automated sampling
4. Liquid Handling & Sample Prep
5. Online/At-line Analytical Integrations
IT/OT Convergence: Towards Adaptive Plant

User 1

User 2

User 3

User 4

Manual Records

Process Data Layer

Bio4C ProcessPad™ software

LIMS

Quality Control
Sample data

QMS

Quality Assurance
Data

ERP

Raw Material or
Warehouse data

eBMR

Manufacturing
Data

Enterprise Data Lake

Bio4C Orchestrator™ software

Central Historian
PI/Wonderware

ProCellics™ Raman Analyzer
with Bio4C® PAT Raman Software

Bio4C ACE™ software

Bio4C ACE™ software

Bio4C ACE™ software

MAST® Autosampler

Manual Records

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SUMMARY & TAKEAWAYS
Summary and Takeaways

From This

- Lack of standardization
- Long development time
- Expensive investments
- Limited flexibility
- Complex and Manual Processes
- Disparate Data lacking contextualization
- Siloed Operations
- Process Variability

To This

- Data analytics
- Automation
- PAT

- Process Efficiency
- Data-Driven Decision Making
- Control from Anywhere
- Seamless Integration
- Facilitate Regulatory Compliance
Thank You!

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