

This article reports on a unified MCS architecture using commercially available MES and PCS. It explains the steps in moving beyond paperless functionality to a unified system helping manage information, processes, and people.

# Unified Manufacturing Control System (MCS) Architecture for Pharmaceutical and Biotech Manufacturing

by Ronald E. Menéndez and Darrell Tanner

## Introduction

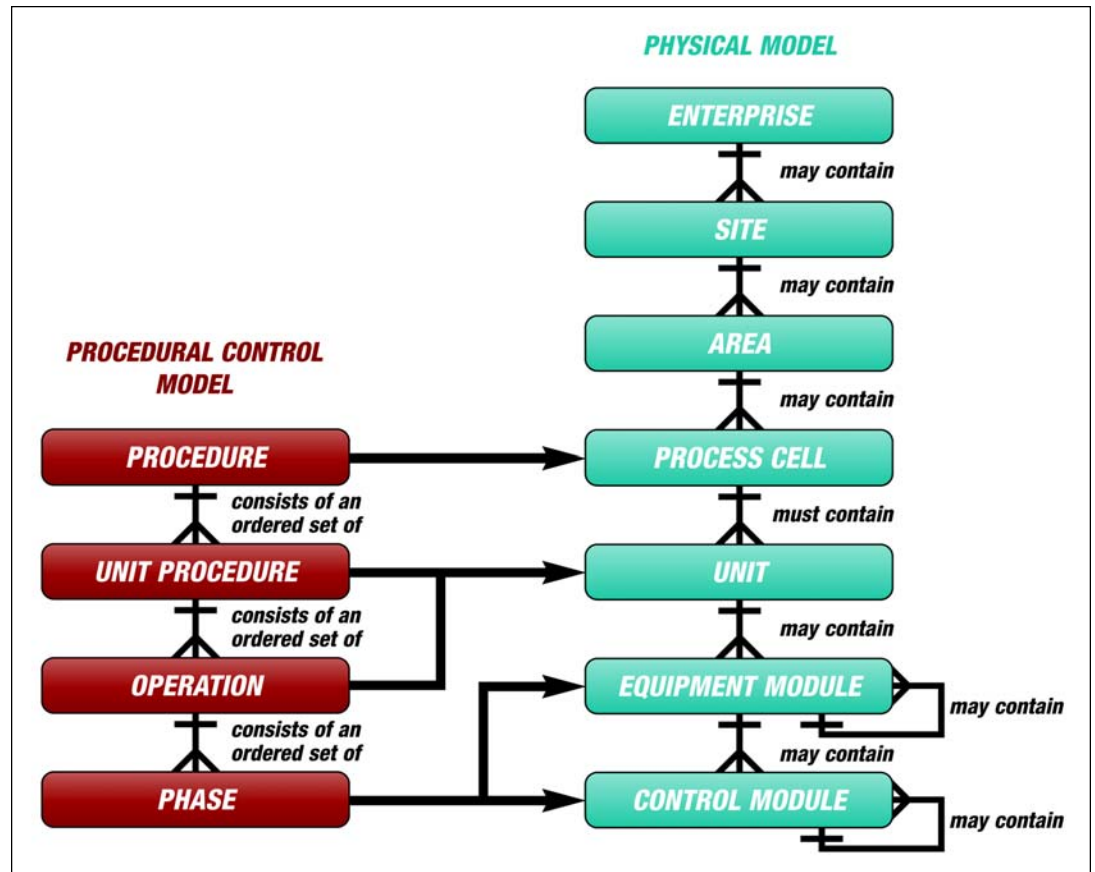
In recent years, Manufacturing Execution Systems (MES) and Process Control Systems (PCS) have gained wide acceptance in the pharmaceutical and biotech industries, due to the adoption of industry standards and technology advancements. PCS for bulk therapeutic and biotherapeutic manufacturing achieved uniformity in the past decade thanks to the establishment of the ANSI/ISA-88 models for batch control. During the same period, a broader range of industries used MES and

ANSI/ISA-95 standards to improve their manufacturing operations.

While MES and PCS found their place in the industry, they were typically viewed as separate solutions within a manufacturing facility. This approach often led to a disparity of systems and organizations responsible for development and maintenance. The resulting systems were usually hindered by a lack of interoperability and dependence on custom interfaces for connectivity.

As companies pursue MES and process au-

Figure 1. S88 models and methodology overview.



## Evolution of Batch Control

A key requirement for effective batch control is collecting useful data and information—and knowing what to do with it. To standardize the use of batch control technology in the process industries, the Instrumentation, Systems, and Automation Society (ISA) established the S88 standard. The ISA guidelines identified a common set of procedures that can be used to describe and define batch manufacturing systems in accordance with U.S. Food and Drug Administration (FDA) current Good Manufacturing Practices (cGMP).

### S88 Defines Manufacturing Methodology

The S88 methodology breaks down each manufacturing module into a pyramid of smaller and smaller process steps, known (in descending order) as “procedures,” “unit procedures,” “operations,” and “phases.”

The models and terminology incorporated in the S88 standard emphasize good practices for the design and operation of batch manufacturing plants. They can be used to improve control of continuous or discrete processes, and applied regardless of the degree of automation. The standard includes both physical and procedural models that are written once and then employed as templates.

Physical models define the equipment used in the process, such as units, equipment, and control modules, whereas procedural models, which include procedure, operation, and phase modules, define the control enabling the physical models to perform given tasks - *Figure 1*.

Proper implementation of S88 batch automation reduces the time required to reach full production levels for new products. It also helps vendors supply appropriate tools for implementing batch control, and allows users to better identify their needs.

### Standard Improves Process Design Philosophy

S88 isn't just a standard for software, equipment, or procedures; it's a way of thinking, a design philosophy. Understanding S88 will help you better design your processes and manufacture your products. Leveraging the knowledge and experience contained in the standard will enable you and your customers to better identify your needs, make recipe development easier, and help reduce the time to reach full production levels with a new system or for each new product. Following the concepts explained in S88, you can improve the reliability of your operations and reduce the automation lifecycle cost of your batch processes, including lowering the initial cost of automating your operations.<sup>2</sup>

tomation initiatives, they are often challenged by varying budgets, schedules, and project methods. That is because automation is traditionally viewed as an engineering discipline, whereas MES is regarded as an IT function. However, in a recent project at a brownfield biotherapeutic manufacturing facility, a new aggregate approach referred to as the Manufacturing Control System (MCS) was put forth as a solution to provide a single environment for manufacturing operations and process automation meeting all requirements of a paperless facility.

This article reports on this system integration effort and presents a unified MCS architecture using commercially available MES and PCS. It further explains the steps in moving beyond paperless functionality to a unified system that helps manage information, processes, and people.

## Advancements in Automation Technology

In the 1990s, the advent of open systems in process automation changed the way manufacturers operated their plants. Proprietary computer networks and control applications from automation vendors gave way to PC-based hardware using commercially available operating systems. Ethernet communications employing standard wiring, switches, and routers superseded proprietary communication protocols.

Modern control systems utilizing Web-based Human-Machine Interfaces (HMIs) provide a single, facility-wide view of operations. These systems, designed to integrate business processes with a common HMI across the plant, also provide seamless, third party integration through open Web standards. This trend toward third party integration enabled the advancement of batch control technology benefiting automation end-users throughout the process industries.

### Batch Management Increases Flexibility

Batch management software integrated in most PCS available on the market today provides a robust solution for designing, modeling, and automating batch processes. It enables flexible recipe building and management using object-oriented recipe structures aligned with the S88 models. On-line tools allow users to manage multiple batches from the same window, and navigate between displays based on batch execution activities.

S88 batch management applications for automated recipe management and unit procedural control reduce latencies and improve repeatability. This, in turn, improves production efficiency. S88 batch automation ensures procedures are executed in accordance with approved specifications and standard work processes. Using these applications, manufacturers have achieved faster response to production orders and schedule changes, flexible processing to support new product introduction, and increased throughput to meet expanding production demands.<sup>1</sup>

## Development of Manufacturing Operations Technology

In a variety of industries, MES has proven to be effective in managing all steps of the production lifecycle; from materials

receipt to product shipment. The technology and S95 standards assist production personnel in managing execution decisions and information during the processes of planning/scheduling down to production execution.

Typical MES provide specification management tools allowing users to define the materials, equipment, and procedures required for production. In many cases, the systems can be expanded to handle multiple production sites - enabling product development departments to quickly deploy new products or update existing product formulations.

Characteristically, MES benefits manufacturers by providing a scalable, Web-based architecture that is easy to deploy and maintain. MES can form the central system for synchronization of business systems with manufacturing and process control - *Figure 2*. Integration with other manufacturing systems can be achieved using Web services and industry standard technologies such as XML and OPC.

### Paperless Records Reduce Errors

Key to the adoption of MES technology was its promise of eliminating paper-based batch recordkeeping. With the FDA's re-examination of 21 CFR Part 11 and their issuance of *Guidance for Industry Part 11, Electronic Records; Electronic Signatures - Scope and Application*,<sup>5</sup> there is a greater understanding of the compliance requirements for paperless systems in the regulated industries.

MES makes it easier for pharmaceutical and biologics producers to meet regulatory compliance by managing and recording activities associated with personnel, manufacturing resources, and the process itself. In addition, the MES solution is a direct means to reduced human error during data entry. Users can reduce paperwork, improve overall resource management, and produce fully compliant, paperless production records.

MES provides a "paper-on-glass" replacement for traditional paper formulations, typically referred to as "tickets," by offering prompted data collection, electronic work instructions, and e-signature-based review processes.

### Challenges Facing MES Solution

Despite the merits of MES, the technology alone cannot advance the state of biologics and pharmaceutical manufacturing. This is because traditional "paper-on-glass" systems do not collect, organize, and manage all production information - particularly manufacturing and process data generated by the PCS.

Although MES applications have matured around integrated material management and paperless plant-floor operations, which provide significant production efficiencies and cost savings, often personnel find themselves manually managing vast amounts of information. Users are required to refine production data so operations and quality decisions can be made in a timely manner.

Combining today's MES with batch control provides a beneficial architecture for tackling activities such as material tracking/genealogy, barcode scanning, bills of material and work instructions, asset management, lab systems inte-

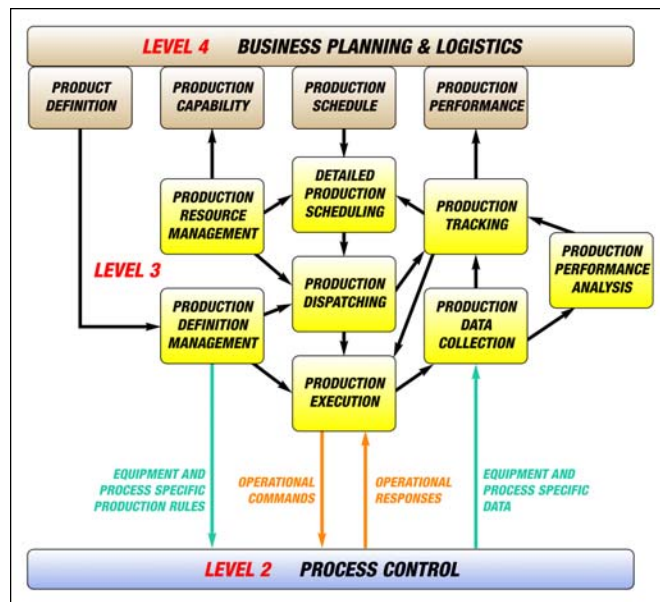


Figure 2. S95 production operations management model.

gration, and production dispatching and execution in single, unified environment.

### Benefits of a Unified MCS

The Manufacturing Control System (MCS) is the integration of MES and PCS technology to provide a single solution for production management, process automation, and reporting. This unified MCS design utilizes the strengths of MES for material management and plant floor applications, and at the same time, incorporates the latest advancements in PCS technology - particularly in the areas of automated recipe management and unit procedure control. Together, the two solutions are employed in a way that is most beneficial to operational objectives.

Tight integration of MES and process automation allows pharmaceutical and biotech manufacturers to move beyond "paper-on-glass" functionality and leverage all of the robust capabilities the two systems have to offer. These include: electronic work instruction execution and workflows, material reporting, asset management, laboratory data logging, production dispatching, and Electronic Batch Record (EBR) management.

### Open Communications Interface to ERP

Implementation of MCS requires an open, standards-based programming interface allowing communication between MES and ERP solutions and business logic. Such integration enables users to access production-related information from the MES and business applications in real time. This connectivity, made possible by S95 Parts 1 and 2 defining ERP/MES communications standards, is a precursor to MES/PCS unification - and a new level of plantwide integration.

Within the integrated manufacturing architecture, MES serves as an interface to corporate-level 3 and 4 systems, electronic document management systems, laboratory information systems, Material Resource Planning (MRP) sys-

## Evolution of MES

In the 1990s, with adoption of the ANSI/S95-95 (S95) standard, manufacturing companies began implementing MES technology to ensure their production operations were capable of delivering on their enterprise's supply chain commitments.

MES holds the potential to significantly improve manufacturing excellence and compliance to regulations. However, realizing this promise requires tight integration of information and work activity across all the real-time levels of the S95 model. Integrated recipe authoring and execution delivers the MES promise across both bulk production and finishing, while reducing the time and risk required to deploy electronic recipes.

### Understanding the S95 Control Hierarchy

S95 Part 1 defines the interfaces between business logistics systems and manufacturing operations systems. Part 2 doesn't add any new concepts to the integration model, but it contains additional details and examples to help explain and illustrate the Part 1 objects. Part 3 defines models for the disparate collection of activities that must occur in manufacturing operations for effective and efficient manufacturing. The goal is to provide manufacturing companies with a common language to describe requirements to vendors and let companies compare alternate architectures and solutions.<sup>3</sup>

Upcoming S95 Parts 4 and 5 will address object models and attributes for Manufacturing Operations Management, as well as business to manufacturing transactions enabling information collection, retrieval, transfer, and storage in support of enterprise/control system integration.

### "Shop Floor to Top Floor" Integration

S95-compliant MES systems fill the complicated gaps between the "top floor and the shop floor," linking business systems and the core automation, controls, and HMI/SCADA, and pure manual data collection systems existing in the manufacturing environment - Figure 3.

Although the S95 standard includes a model similar to S88 that defines terms and transactions, the scope of S95 goes on to define activities and models at all levels of the production process. Users who purchase systems from different suppliers for different levels of the organization can have confidence that they will understand how they communicate along with finding greater ease with the integration process if both are compliant with the S95 standard.<sup>4</sup>

tems, and other Enterprise Resource Planning (ERP) applications.

The MCS provides a platform for handling both inbound transactions (i.e., process orders and lab results) and outbound transactions (i.e., inventory updated and lab requests) - Figure 4.

### Typical MES/PCS Transactions

The benefits of the unified MCS approach are demonstrated through MES/PCS transactions, such as production execution, resource management, material tracking, and electronic work instruction management. Unit procedural control and phase execution with an MCS is more efficient than in a traditional environment with separate system domains. Transactions between different systems and personnel are seamless; operators see a unified interface with a common HMI environment, instructions, and displays.

### Production Definition, Dispatching, and Execution

With the unified MCS architecture, orders from MRP come down to the plant floor through the MES - Figure 5. The MES automatically dispatches recipes based on required equipment statuses and availability, and executes them in the process control system. This innovative approach eliminates the traditional requirement for operators to manually check equipment status, assign equipment, load recipes, and initiate batch execution. Rather, the MES handles these activities as the operator fulfills the order at the PCS layer.

Consider a typical MCS batch processing application: after dispatching a unit procedure, the MES binds to the process unit for execution and starts the sequences. The PCS then executes phases within operations at the equipment level, performs automated tasks, and requests information from the MES.

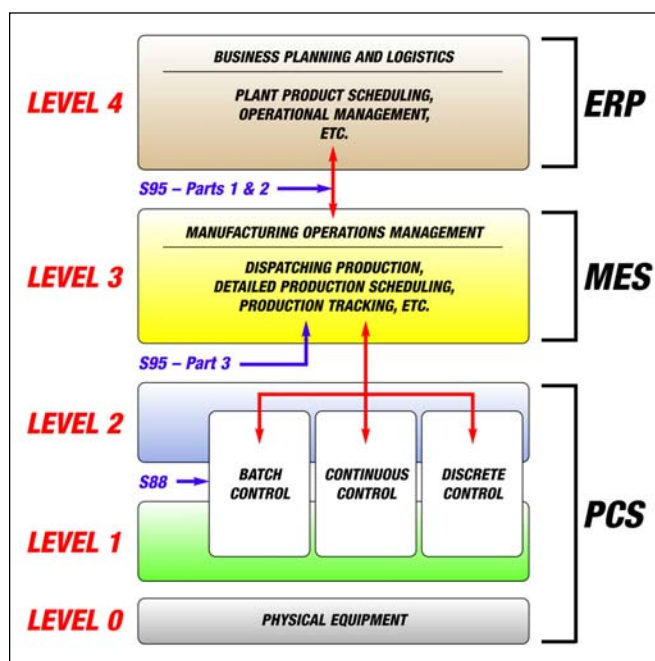


Figure 3. S95 control hierarchy levels.

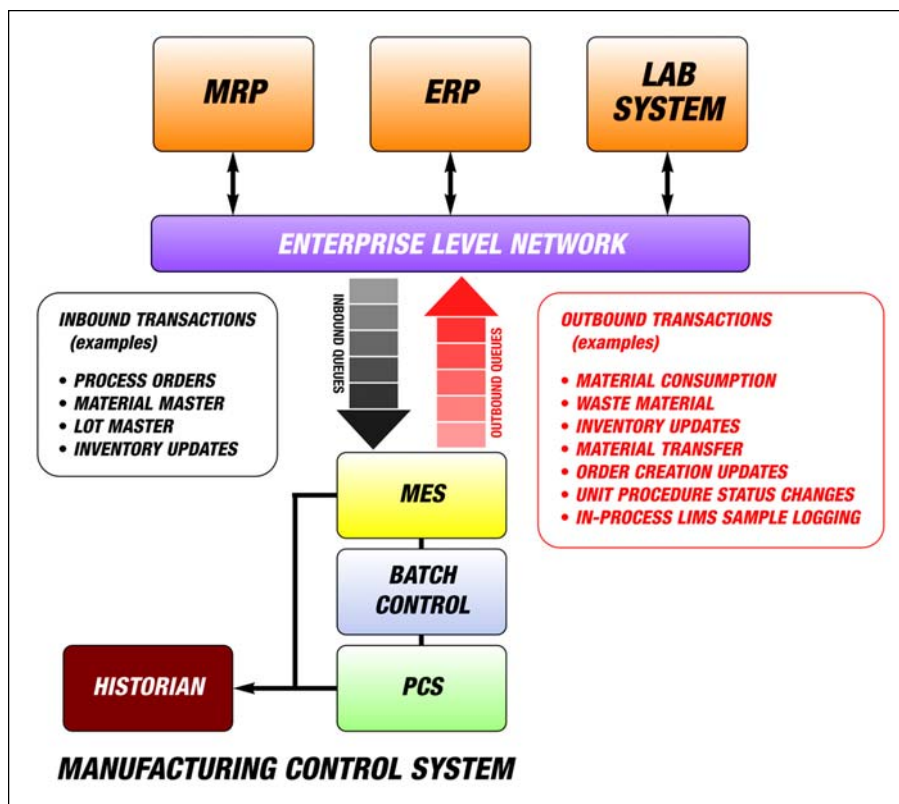


Figure 4. Typical system transactions.

### Management of Resources and their Statuses

At a typical pharmaceutical or biotech plant, operators are tasked with managing production resources and reporting on their statuses. The operator must verify the status of specified equipment in a paper log or database before a batch can be started or progressed.

The MCS solution automates this procedure since the programmed phase in the PCS controls specific equipment. The phase is designed to automatically request equipment and assets from the MES based upon their required status. PCS requests for information are handled by a transaction executed to the MES via an OPC service. The MES automatically allocates resources and performs arbitration should conflicts arise. This allows the automation process to continue without interruption.

For example, The PCS might issue requests such as, “This tank is needed - is it sterile?” The MES will respond, “Yes, you can acquire this resource because its status is correct for your requirements.” Once the operation is completed, the PCS phase will release the tank back to the MES with a message saying, “This equipment is being returned with a status of ‘dirty.’” Such transactions are carried out automatically, without operator intervention.

### Material Management and Tracking

When it comes to material tracking and reporting, the PCS phase again interfaces directly with the MES, which in turn, interfaces with Manufacturing Resource Planning (MRP) as required for inventory updates. During execution of a particular phase, the system might say, “Material ‘A’ for the

batch is needed.” The MES then reports, “The material’s quality is acceptable and the expiration date has not been exceeded. Here is the quantity that should be added.” It then provides results regarding bar code scanning and performs system data verification at the point of use (i.e., when the material is introduced into the batch).

When tracking material consumption, the PCS can send a transaction notifying the MES that it is time to automatically or manually consume a particular additive or ingredient. As the automated steps execute, a procedure pops up on the operator’s screen with prompts for completing the task.

Under normal circumstances using disparate MES and PCS systems, the operator has to pull up a ticket or paper-on-glass in the MES environment to check the status of materials, and verify information indicating that he is adding the prescribed material. Then, he must acknowledge the material addition is complete and instruct the PCS to continue execution.

In the case of manually consumed materials, standard material add pages prompt the operator to scan the required material and then automatically execute the quality checks prior to prompting the operator to deliver the material. For automatically added materials, the quality checks and consumption reporting are done without operator intervention unless required.

### Management of Electronic Work Instructions

The MCS strategy also revolutionizes the handling of electronic instructions and workflows and eliminates paper procedures. Unlike a standalone MES, the integrated system automatically presents instructions or workflows (i.e., SOPs) on the HMI screen whenever and wherever they are needed. Operators are no longer burdened with coordinating MES activities, while staying abreast of PCS execution. This enables a new level of plant production efficiency.

During a phase execution, for instance, the system calls up standard faceplates on the process control graphic that prompts the operator whenever his attention is required. The operator is presented with an “action list” displaying phases with their instruction, a button to display the detailed instruction, and upon acknowledgement of the action, the type of signature required. Operator instructions can be signed off directly from the HMI page - *Figure 6*.

Likewise, in the middle of a phase, required manual actions can appear on the MES page as a workflow that includes a variety of MES activities the operator must follow. Once the tasks are completed, the technician acknowledges the work with an electronic signature and the PCS resumes automated control.

## Discussion

For pharmaceutical and biotech operations, the unified MCS not only delivers new automation capabilities, but also presents new ways to manage manufacturing complexity and improve operational efficiency. Industry analysts estimate that as much as 20% of a firm's costs of operations are associated with manufacturing, which means even modest operational improvements can have a significant financial impact.<sup>6</sup>

### Greater People Collaboration

For a plant's technology personnel, the MCS merges disparate MES and automation departments into an integrated production team that works hand-in-hand to optimize manufacturing operations. Under the new architecture, components such as work instructions, bill of materials, and asset definitions are supported in the MES, but requested from

phases executed in the PCS. As a result, the two departments interact to ensure components are correctly configured and managed. This closer collaboration enabled a reduction of support staff between the two departments of over one-third and the restructured groups operate as a single organization as opposed to separate teams of engineers and IT specialists.

In addition, manufacturing personnel, quality departments, and engineering staff now utilize a single, unified system with a common environment for accessing production data, viewing process displays, and making critical operational decisions.

### Faster Review and Product Release Processes

The MCS solution eliminates the need to manage paper batch records. The system provides electronic records of each batch of products produced, as well as the means to collect, store,

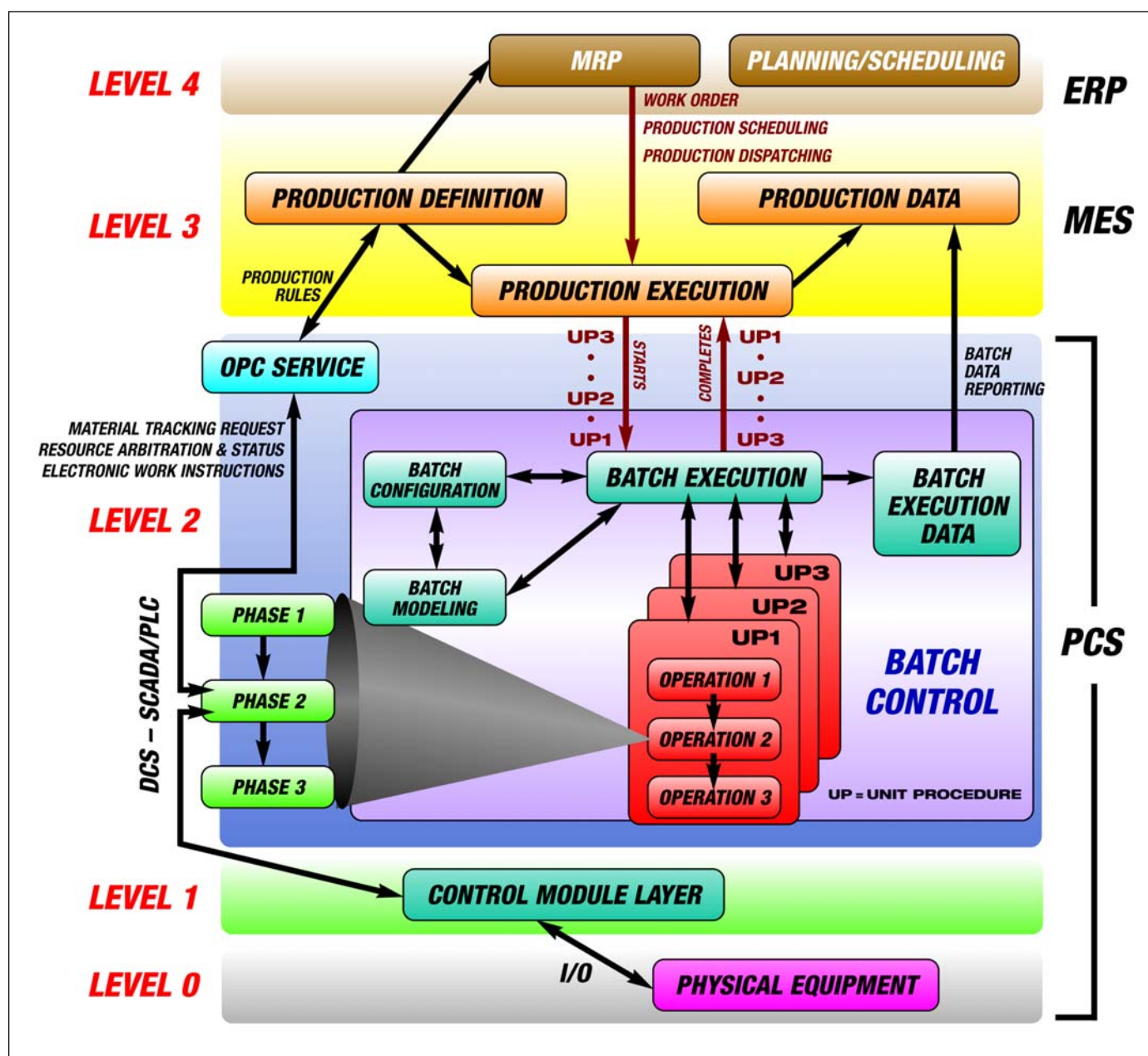


Figure 5. Unified MCS architecture.

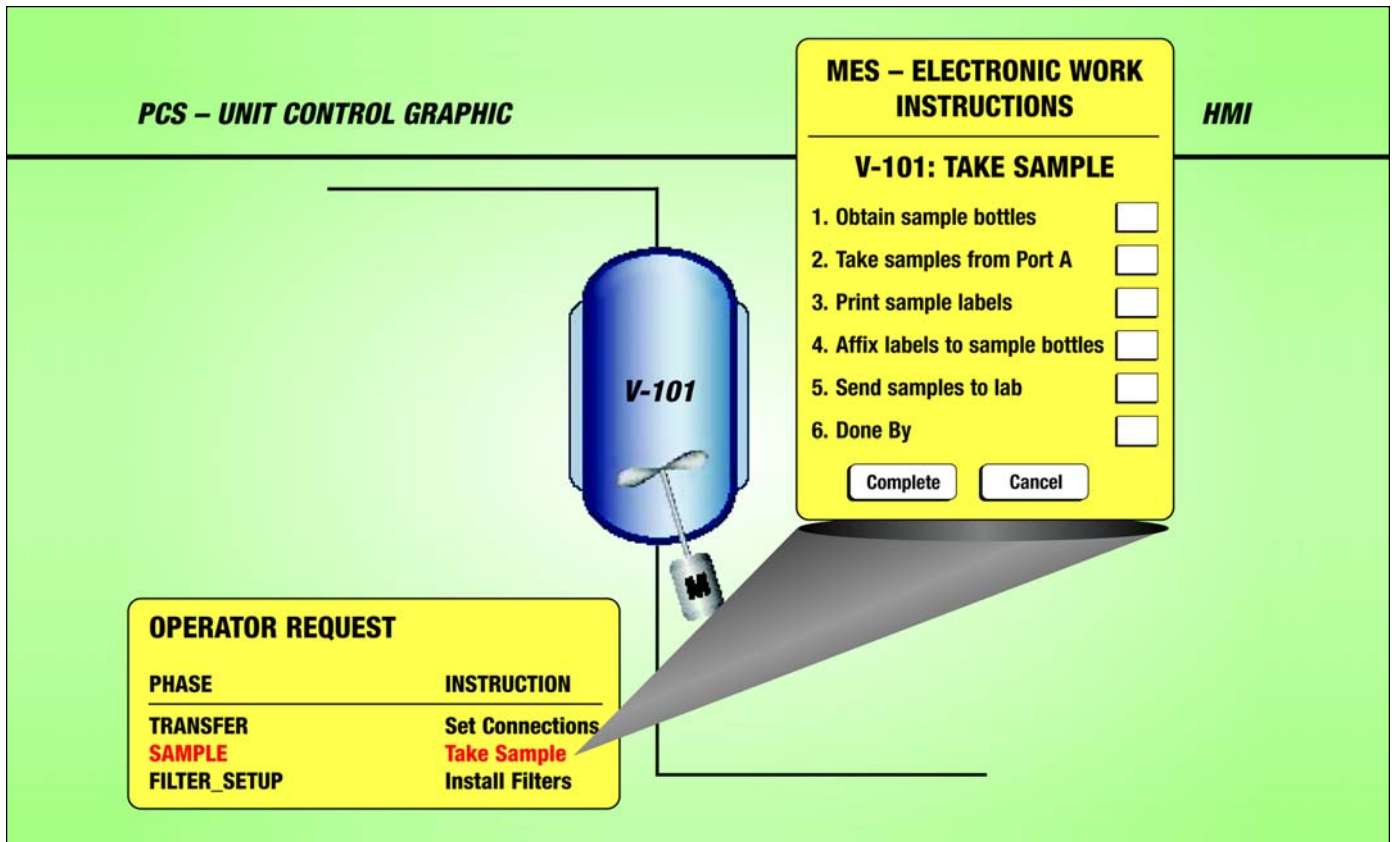


Figure 6. Unit control graphic.

and analyze data more efficiently. Documents within regulated environments can be created, reviewed, approved, and issued electronically in a collaborative manner with full change control by the respective departments. This approach simplifies the GMP-related document management process.

Manufacturers implementing MCS can streamline the effort required for regulatory compliance and expedite the release of manufactured product. The integrated system, with EBR and process automation information (i.e., alarms, unit control data, batch events, process history, etc.), enables easier compliance and verification. The plant's quality group can access robust, consolidated data assisting the review process prior to product release.

Previous paper-based systems required numerous weeks to collect paper records, review, reconcile discrepancies, and approve for release. Subsequent designs of disconnected MES and PCS architectures reduced the product release process to a couple of weeks, but the new MCS design is estimated to reduce this process to a few hours.

### **Better Information Equals Improved Performance**

The integrated MCS system approach brings together information from key areas such as process control, MES, and laboratory systems. This facilitates the discovery of new opportunities to improve operational performance and drive down costs.

Pharmaceutical and biotech facilities gain a world-class solution providing a single source of centralized manufacturing data. No longer must PCS data be duplicated for the MES

environment, and then migrated into the ERP system. Instead of distributing asset and process information between three different systems, users attain a "Single-Source of Truth."

Equally important, an interoperable MCS design with Web/HTML-based applications and open, industry standard communications protocols provides a secure and predictable path for future technology investments. Potential directions can include RFID, biometric security, and wireless hand-held mobile devices, to name a few.

### **Conclusion**

In the life sciences industry, the constant challenges for manufacturing are efficient, streamlined operations with fewer errors, greater consistency, and unfailing compliance with FDA regulations. Manufacturers seek shorter product cycle times, faster product changeover, and better maintenance scheduling - all adding up to improved operational performance.

To meet these challenges, a seamless MCS architecture providing common electronic batch records and production reporting for automation and production management with reliable traceability (i.e., materials, equipment, and personnel) can be employed as presented in this article.

Traditionally, many manufacturing facilities have had a disconnected view of their automation and IT solutions. As the lines between systems blur, a paradigm shift is likely to move the industry toward the next-generation MCS, merging current MES and PCS with integrated batch control technology. As this natural evolution progresses, companies will

actualize the benefits of managing plant-level and corporate-level systems as part of a single system. And, unified enterprise architectures, as discussed in this article, will likely emerge as the standard manufacturing solutions for new facilities by the end of this decade.

## Acronyms

EBR	Electronic Batch Records
ERP	Enterprise Resource Planning
IT	Information Technology
HMI	Human Machine Interface
MES	Manufacturing Execution System
MRP	Material Resource Planning
PCS	Process Control System
PC	Personal Computer
OLE	Object Linking and Embedding
OPC	OLE for Process Controls
RFID	Radio Frequency Identification
SCADA	Software Control and Data Acquisition
UP	Unit Procedure
XML	Extensible Markup Language

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