



To meet today's competitive challenges, pharmaceutical manufacturers must bring new products to market quickly, deliver products configured to the specific needs of their customers, and do it in collapsed time frames.

- Production capacity must be optimized and inventory "right-sized" to reduce costs and maintain profitability.
- The right products must be made at the right time for order fulfillment.
- Full regulatory compliance must occur without draining resources.

Many pharmaceutical companies have implemented new enterprise resource planning (ERP) systems in order to manage and control the supply chain and order fulfillment processes. These systems support financial management, order management, and planning and scheduling; they make the supply chain process visible to management to enable informed decision making. When coupled with an advanced planning system (APS), an ERP system can greatly strengthen a company's ability to compete. These systems do not,

however, impact the basic manufacturing process: production of quality pharmaceuticals.

***ERP systems do not address the manufacturing process itself.***

Manufacturing execution is a complex web of activities and information flow. Without a system to orchestrate these activities, plant capacity is underutilized. Materials may not be where they are needed, when they are needed. There are unnecessary delays in the production process and the manufacturing process as a whole cannot be optimized. Without a system that coordinates manufacturing information, ERP systems may actually increase costs; headcount may have to rise just to meet the need to manually feed batch data from the plant floor into the ERP system.

In a pharmaceutical company, the flow of information includes extensive requirements for FDA-verifiable cGMP (current Good Manufacturing Practices) compliance. Without a computer-based compliance system, a company must rely on paper-based manual data collection to verify batch data at every step. Collecting hundreds of measurements for multi-

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ple batches on a daily basis creates delays, errors and overhead costs, and impedes productivity. The real cost of paper records is even greater; the cost of not locating needed batch documentation in a situation requiring a product trace—potentially months after its manufacture—may be very high indeed.

#### **MES: THE MISSING LINK**

A manufacturing execution system (MES) can fill the execution gap for pharmaceutical companies. An MES "deliver[s] information that enables the optimization of production activities from order launch to finished goods."<sup>1</sup> An MES is the formulation of plant floor production methods, procedures, knowledge and experience, captured in a computer system. This information controls the execution of the manufacturing process—orchestrating and synchronizing resource allocation, material movement and production activities from ERP production order release through product shipment. An MES functions as the backbone for all plant floor automation and information management activities.

As MES instructions are executed, the system captures, stores and synthesizes information for data analysis and reporting. A subset of the real-time data captured and

reported in the MES can be sent to the APS and ERP systems to accurately depict production status.

An MES can help pharmaceutical companies optimize their manufacturing process and fully support FDA reporting. By linking ERP systems with control systems, an MES can be used to improve the manufacturing process where it is most needed and most cost-effective. An integrated ERP/MES system can:

- Significantly reduce manufacturing cycle time.
- Increase production capacity through elimination of production errors and minimization of resource delays.
- Improve overall product quality and consistency and decrease product defects.
- Minimize inventory and work in progress (WIP).
- Ensure that plant records are fully compliant to cGMP standards, and provide audit trails that withstand regulatory examination.
- Create a database of detailed, timely and accurate operational information that provides a foundation for continuous quality improvement, performance measurement, and best practice searches.

- Reduce time to market by simplifying scale-up from clinical to commercial production.

These benefits translate to improved manufacturing prowess and agility.

While the benefits of an MES are significant, there are challenges in implementing these systems. An MES implementation provides a major opportunity for a company to significantly raise its overall level of operational performance. This requires optimum implementation of software, concurrent with reengineering the processes to which the software will be applied. Defining manufacturing "best practices" can be challenging, given the number of people, processes and locations

involved for a particular manufacturing process. Organizational units, line functions and processes which have historically operated autonomously must now work together to ensure that an MES implementation supports the company's business objectives. There is more variation from one plant to another than from one corporate office to another. This diversity of manufacturing plants means that software must be configured to match the plant model and business rules.<sup>2</sup>

Significant effort must go into choosing the right MES product from a multitude of vendors, then integrating the selected MES with existing systems. Affected processes must be assessed and, if necessary, optimized. Finally, paper-based or electronic

### Case Example: Impact of MES Implementation at a Major Pharmaceutical Company

- Reduced manufacturing cycle time by 30%
- Reduced work-in-progress (WIP) cycle time by 30%
- Reduced manual data entry time by over 40%
- Reduced lead time for batch and continuous-process-flow manufacturing operation by over 20%
- Reduced risk of noncompliance due to product deviations or faulty/missing records by replacing paper-based reporting with a real-time, on-line system

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manufacturing process instructions must be transformed into dynamic instructions for both people and machines in a flexible and maintainable manner.

Given all of these factors, selection and implementation of an MES must be tightly managed, both to ensure that the system provides the required functionality and benefits and to prevent the project from taking two or three times as long as it should. Results of poor selection or implementation can include extensive and excessive system customization, failure to address the core needs first, a lack of appropriate integration with other company systems, or attempts to use the MES for purposes for which it was not designed.

#### MAXIMIZING BENEFITS FROM A MANUFACTURING EXECUTION SYSTEM

CSC experience indicates that there are five keys to achieving optimal benefits from an MES:

1. Implement where opportunity is greatest.
2. Use an MES as a vehicle for process improvement.
3. Link MES and APS/ERP systems strategically.
4. Coordinate clinical and commercial production.
5. Select the right implementation partner.

#### **I. Implement Where Opportunity is Greatest**

Implementation of an MES should be directed first to the company's greatest operational business challenge. The case for action may place priority on inventory improvement, FDA compliance and risk reduction, or rapid turnover of production lines from one product to another. The priority could be increasing production yields per asset. It could be increasing throughput or reducing time to market. The company needs a clear understanding of what the value of an MES

#### **Five Keys to MES Success**

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would be in each aspect of the manufacturing process.

For most pharmaceutical companies, compliance and risk reduction are key issues. This means that the first stage in automation may be capturing the manufacturing process in the electronic batch record, utilizing electronic signatures and data validation for key data input fields, thereby forcing compliance. As more manufacturing processes are encompassed by the MES, screen displays can be put in place which reduce risk by controlling the data presented to the operator or machine by the MES. As a company seeks to increase coordination of people and machines on the production floor, MES implementation may include the incorporation of intelligent devices. Where the biggest business challenge is inventory management, an MES can be used to coordinate materials handling, reduce inventory and minimize movements through devices such as radio frequency terminals.

Whatever the company's business situation, MES implementation should be aimed at addressing the operational problems the company most needs to solve.

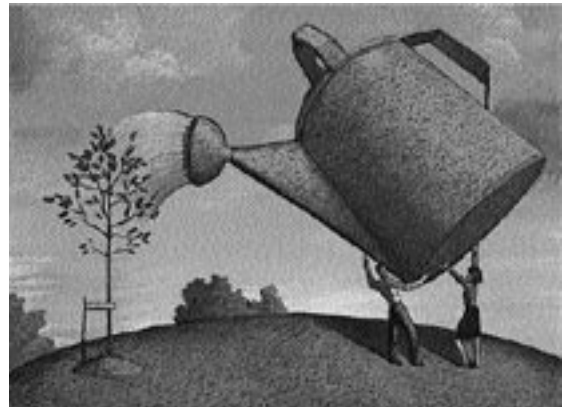
## **II. Use MES Implementation to Drive Process Improvement**

Operational management should take maximum advantage of the MES as a vehicle for achieving process consistency and standardization.

Without this consistency, process improvement through business process reengineering and best practice identification is impossible.

Within a single plant—even within a single production line—it can be difficult to obtain consistent operation across operators on all shifts without an MES. By assuring consistency from operator to operator and from shift to shift in the way a product is produced, an MES eliminates unintentional variation, and enables examination of the results of intentional production changes. The MES controls the way the product is made, captures production data and records the results consistently.

The data produced can be fed into a data warehouse that facilitates analysis to support continuous process improvement. For example, since FDA revalidation requirements mean that even one simple change to a



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production line setup can cost \$3,000 – \$5,000, changes should be made only where there is objective support for the value of a change. An MES can provide the data to determine this value with confidence.

At later phases of implementation, the challenge may be to use an MES to standardize processes across multiple plants with diverse operations and procedural dissimilarities. The benefits of this form of standardization are significant:

- Reduce costs of system development work and of overall future system maintenance.
- Simplify development and reporting requirements through standardization of the system platform across multiple production sites.
- Allow rapid dissemination of system fixes, enhancements and best practices through knowledge-sharing across plants.

Process simplification and standardization across sites can result in staff utilization advantages such as reducing the number of job skill-set categories and increasing opportunities for cross-training and cross-staffing. There may also be opportunities to reduce staffing require-

ments. These advantages, in turn, result in cost reductions and quality improvements.

### **III. Strategically Link MES and Other Systems for Greatest Benefits**

The MES is at the center of the enterprise's entire fulfillment cycle, where ideas and raw materials connect to produce value for the customer. As such, the MES can provide the greatest benefit for the enterprise through its potential to link with the critical pieces in the enterprise. Maximum value is achieved where there is some degree of integration between the systems that control finance, the supply chain and the manufacturing processes, in order to support cross-functional business processes and information flows.

The MES can consolidate and right-size data for other systems, such as the ERP system and the APS. For example, linkages between the MES and APS provide translation of demand forecasts into production requirements that make the APS plans truly effective, using accurate, real-time data on plant capacity and its sub-elements. Systems integration can also allow automatic scaling and sequencing of recipes and specification of raw material requirements,

consistent with demand forecasts. Quality data feedback from the MES to the APS can enhance demand forecasting.

Linkage of financial and production reporting can greatly improve strategic understanding of business operations. Realistic information on costs and effort enables more accurate product planning, while accurate plant performance information improves sourcing decisions and maximizes profit.

#### **IV. Coordinate Clinical and Commercial Production**

An MES can knit together the commercial and clinical environments to produce faster technology transfer, easier FDA validation, and proof of batch equivalency. Coordination of clinical and commercial production can accelerate the process of scaling up production recipes and greatly reduce time to market, with significant impact on a company's bottom line.

Without automation, scaling up is often difficult and costly, due to the complexity of formulations and methods of delivery and dosage. During drug development formulation, dosage and method of delivery are constantly changed to produce the most efficacious product. Clinical

production is highly labor intensive and if not synchronized with the FDA filing process, can cause FDA submissions to be delayed.

By providing a way to move smoothly between the divergent technologies found in the clinical versus commercial manufacturing environments, an MES can provide a major opportunity to shorten new product time to market.

Appropriate integration of the MES with other systems such as document management allows clinical production procedures to be captured so that modifications or scale-up of the processes can be performed easily.

#### **V. Select the Right Implementation Partner**

For the great majority of pharmaceutical companies, an MES implementation partner will provide the most effective implementation with the most immediate payback, for several reasons.

- Most MES vendors are small organizations that will not have the resources or business vision to assist with the complex organizational, process and systems integra-



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tion tasks required to achieve significant benefit from an MES.

- Few pharmaceutical companies have enough in-house staff with the skill sets most needed for MES implementation—experience in large systems integration, MES configuration and developing global architectures.
- Selection of the appropriate product from the hundreds of MES vendors available is a formidable task for in-house staff.
- An MES implementation partner has experience dividing projects to provide a series of small successes and can therefore deliver payback more quickly.
- An outside partner can be impartial with regard to modifying existing processes, which can reduce internal conflict during implementation.

To maximize the benefits of an MES to the business as a whole, management should seek a partner with an in-depth understanding of the strategic and business process framework within which the MES should operate. A partner should have extensive experience in IT-enabling manufacturing process redesign and should possess the skills to integrate MES with ERP, APS and process control systems.

AMR Research, a leading research organization on manufacturing applications, has identified three types of companies doing system integration work. The first type focuses on business strategy and configuration of business processes; the second on control systems integration; and the third on integrating control systems and IT applications in the plant.

### **A Systems Integrator for Manufacturing Projects Should Have:**

- A successful track record of applying a repeatable methodology on similar projects.
- Technical capability.
- An organizational model to pull together components from all system levels.
- A value proposition.
- Relationships with specific software package vendors.

Adapted from: Roddy Martin, "Who Can Integrate My Manufacturing Plant Systems?" AMR Research Report on Manufacturing for December 1998.

## Impact of Well-Managed Implementation of Manufacturing Execution Systems at Several Pharmaceutical Companies

Category	Impact
Manufacturing Cost Savings	<ul style="list-style-type: none"> <li>• Reduced batch waste by \$500,000/year</li> <li>• 5% overall manufacturing cost reduction</li> <li>• 25% reduction in paperwork</li> <li>• Batch errors reduced to zero</li> <li>• Elimination of 1 million points of data entry</li> </ul>
Labor Savings	<ul style="list-style-type: none"> <li>• Batch review time reduced by 52 person-days/year</li> <li>• Batch deviation reviews reduced from 2 person-days to 2 hours</li> <li>• Elimination of 8 person-years annually from electronic batch record and release</li> <li>• Reduction in labor force of 20 people/plant</li> </ul>
Increased Production Capacity	<ul style="list-style-type: none"> <li>• Production of an added batch/week (batch value \$1 million)</li> <li>• Batch changeover reduced from 30 minutes to 5 minutes</li> </ul>

AMR notes that plant integrators, particularly those with an orientation towards business processes, can best offer the broad scope of capabilities needed to integrate the manufacturing plant. Plant system integrators can best build appropriate links between the advanced planning and manufacturing execution systems in order to leverage manufacturing competitiveness. The ideal partner will have alliances with the leading relevant software application vendors

and will be able to show that they have partnered successfully with those application providers and with other leading systems integrators.

### CONCLUSION

Defining MES as a necessary system to remain competitive in the marketplace is only the beginning. In order to maximize the success of the system, pharmaceutical organization leaders need to keep in mind the drivers to a successful MES imple-

mentation. The MES should be directed to the company's greatest business challenge, while using the implementation as a vehicle to drive process consistency and standardization. For greatest success, the MES must link to other critical systems in the enterprise. Coordinating the clinical and commercial production will reduce time to market while significantly impacting the company's bottom line. Finally, to maximize the benefits of an MES, it is important to seek a partner with an in-depth understanding of the strategic and business process framework within which the MES should operate.

A manufacturing execution system can increase the strategic agility of a pharmaceutical company and provide significant cost savings and regulatory advantages, but implementation can be formidable. By employing the five keys to successful implementation, organizations can keep an MES on schedule and quickly obtain maximum business value from the system.

- 1 MESA International, *MES Explained: A High Level Vision*, White Paper Number 6, September 1997
- 2 Roddy Martin, "Who Can Integrate My Manufacturing Plant Systems?" AMR Research Report on Manufacturing for December 1998

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