IT Focus: The Great Mediator

How MES can optimize the pharma supply chain

By **Rolf Blumenthal**
Werum Software & Systems AG

In any production-based business, a successfully implemented Manufacturing Execution System (MES) program can be the glue that binds a company together. Indeed, this role is intrinsic in the very definition of MES: an electronic interface between personnel, equipment automation, orders, logistics, equipment and processing instructions. MES is a go-between, a facilitator, a translator. It mediates between business administration — core functions such as sales and production planning — and the automation of the production process.

When properly incorporated, MES enables a business to reduce production costs and, in the pharmaceutical industry, significantly increase compliance with regulatory requirements. This is, of course, an exceedingly exacting, thoroughly inspected, and critically scrutinized business. For today's pharma company to perform on as high a level as possible, its MES must operate as seamlessly and efficiently as possible.

Pharma and MES: Roles and Goals

MES plays a big role for big pharma: controlling, optimizing and documenting business processes executed on facility floors in full compliance with pharmaceutical requirements, regulations and restrictions. For pharmaceutical companies, MES not only makes manufacturing smoother but also safer, by increasing security and reliability in the manufacturing process and improving overall product quality.

A lengthy list of additional goals can be achieved through successful MES implementation:

- Recognition of deviations at an early stage
- Immediate documentation of process steps
- Improved data quality for assessing processes and products
- Visibility and transparency throughout the entire production process; because only deviations are analyzed, a detailed examination of the normal flow of operations is no longer required
- Reduction of storage costs for work in progress (WIP) material due to reduced lead time
- Reduction of administrative work for maintaining manufacturing documents
- Creating and approving master batch records
- Reducing the number of lost batches
- Reduction of operating costs due to a high level of integration, and thus prevention of isolated solutions
- Rapid access to current data; management decisions are based on up-to-the-minute information for all critical business cases
- Full 21 CFR Part 11 compliance for lower-level systems

The Architectural Design of Pharmaceutical Production

There are a variety of industry-specific production structures for manufacturing active pharmaceutical ingredients (APIs) or dosage forms such as tablets, ointments or liquids. These structures can be classified according to specific criteria and used to define differing, tangible benefits of an MES. This practice is a kind of production architecture that weighs methods against goals and investments against opportunities.

Production of API is characterized by natural fermentation

Rolf Blumenthal is Senior Director of Consulting & Product Management with Werum Software & Systems AG, an MES supplier for the pharma and biopharma industries. As a member of the International Society for Pharmaceutical Engineering (ISPE) he contributes to the Good Automated Manufacturing Practice (GAMP) forum. He can be reached at rolf.blumenthal@werum.de.

processes of germs (Figure 1). Characteristic features of biopharmaceutical production include:

- Highly automated production
- Sub-recipe control by means of a DCS
- The process running "on rails" with just a few buffering possibilities
- The need for reliable verification of the cleaning status of various equipment.

Dosage Form Production

One of the concerns in the production of pharmaceutical dosage forms (Figure 2) is correct and consistent material flow. A master batch record indicates fixed batch size limits based on the corresponding container size. Material input quantities and other operations also stem from these limits. Often, the process is conducted across a large number of work centers with multiple in-container manual transports — all of which is conducive to various independent and minimally-supervised systems.

Here, the solution for quality control lies with integration. In the production supply chain, MES can substantially contribute to vertical integration. All of these individual systems — from enterprise resource planning (ERP) to plant operations to equipment — merge into one overall mega-system. Regarding integration, the level of technology achieved to date provides good technical safety if adhering to standards like ISO S95, ISO S88, or Namur NA 94.

Let's examine one of these certifications/standards more closely. ISA S95 consists of three individual parts:

- Part 1 defines models for describing the distribution of tasks between ERP and MES systems (ISA-95.00.01)
- Part 2 describes the associated data models (ISA-95.00.02)
- Part 3 defines a catalog of functions (ISA-95.00.03)

According to the specifications of ISA S95, pharmaceutically relevant data are to be handled by the MES system when the MES and ERP systems are integrated. Therefore, Part 3 has the following parameters in terms of what is applicable to this catalog:

- Data required to maintain "regulatory compliance"
- Data adding to the reliability of plant operations
- Data relating to the required equipment

Figure 1

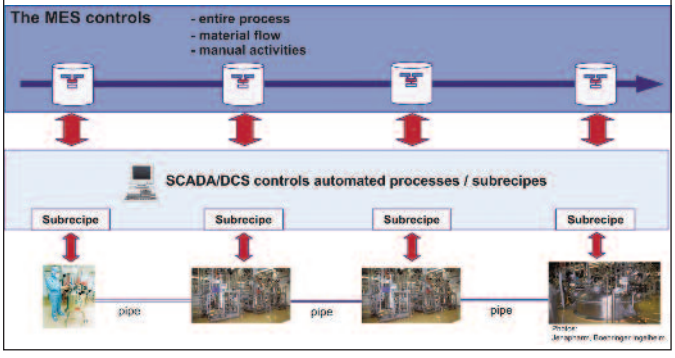
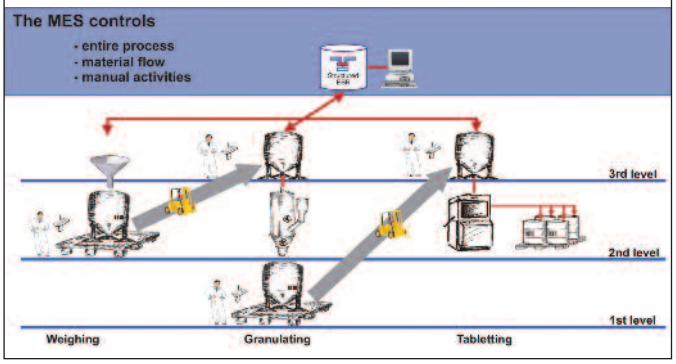


Figure 2



- Data required to enable supervisor to control plant operations

Equipment Integration

Equipment interfacing by means of programmable logic controllers (PLC) enables the MES system to use automatically acquired data. Such data are more reliable than manually collected data, since errors during manual data entry can be eliminated.

Of course, equipment interfacing involves effort for integration and qualification. But once such a system is running and validated, MES users can add originally acquired operating data or highly sophisticated conversions to their batch records — and do so quite seamlessly.

The list of production functions includes definition management, resource management, detailed scheduling, dispatching, data collection, and tracking. And scores of sub-functions could be listed under these categories.

Regulatory Requirements

Regulations are a necessary challenge, and the integration of a robust MES solution can greatly enhance compliance. On top of the myriad "standard" manufacturing data issues, an MES in the pharma industry helps achieve compliance withregulatory authorities in various destinations worldwide, including GMP requirements and FDA mandates for electronic records and e-signatures.

High on this list is required validation of computerized systems. The fundamental prerequisite that qualifies any system for validation is that clearly defined quality assurance (QA) policies have been observed throughout all project phases. In essence, all process phases must be concluded with a verification to prove that all regulatory requirements for that step have been fulfilled.

Real-World Implementation: MES in Phases

The last issue is practicality. Manufacturing Execution Systems are an investment of time, training and money. But like most widely-held best business practices, MES is not an all-or-nothing concept. It is, rather, a 21st century solution that can, classically, be incorporated into existing manufacturing capabilities incrementally. MES is not an elevator; it is a flight of stairs to be taken one step at a time. But at the end of the climb, the long-range view can be well worth the effort. ■