Cover Story

Improving Operations Through Electronic Batch Records

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Electronic record keeping can save effort and money.

Pharmaceutical companies are often on the cutting edge in terms of research, but when it comes to manufacturing they are, in many ways "tied up with paper". Regulatory reporting burdens have historically driven complex procedures and paperwork in order to ensure compliance. Once established, companies tend to stay with these systems – even though there are significant efficiencies to be gained by exploring other methods.

Establishing these benefits are especially important in world areas, such as Asia, where the impact of global regulatory considerations is relatively new, and instituting a more efficient compliance culture in pharmaceutical manufacturing can be a decided advantage. This article will explain some of the problems caused by the historic paperwork approach, and point the way to newer methods and tools that improve efficiencies, reduce delays and improve revenues.

The Problem

A significant problem with historic paper-based systems is that managing the paperwork takes a great deal of time and effort, and has substantial financial implications on pharmaceutical manufacturing operations. For example, while corrective actions and associated problem resolution are being completed, significant inventory

(Source: Emerson Process Management)

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of Active Product Ingredients (API) can remain in a warehouse while all analyses and documentation reviews are completed and approved. That product sitting in the warehouse represents working capital tied up, fewer inventory stock turns, and lost profits.

What is needed is a way to eliminate the paperwork and optimize the paperwork process: converting to Electronic Batch Records (EBR). They will electronically capture and improve workflow activity, replace paper logbooks, keep track of everything that has affected a batch, manage the approval process, and more. Utilizing EBR would have a dramatic impact on the process of releasing active pharmaceutical ingredients if it did no more than provide better paper handling and record keeping. Improving workflow management and information flow can dramatically improve quality, throughput and reduce manufacturing costs while satisfying regulatory requirements.

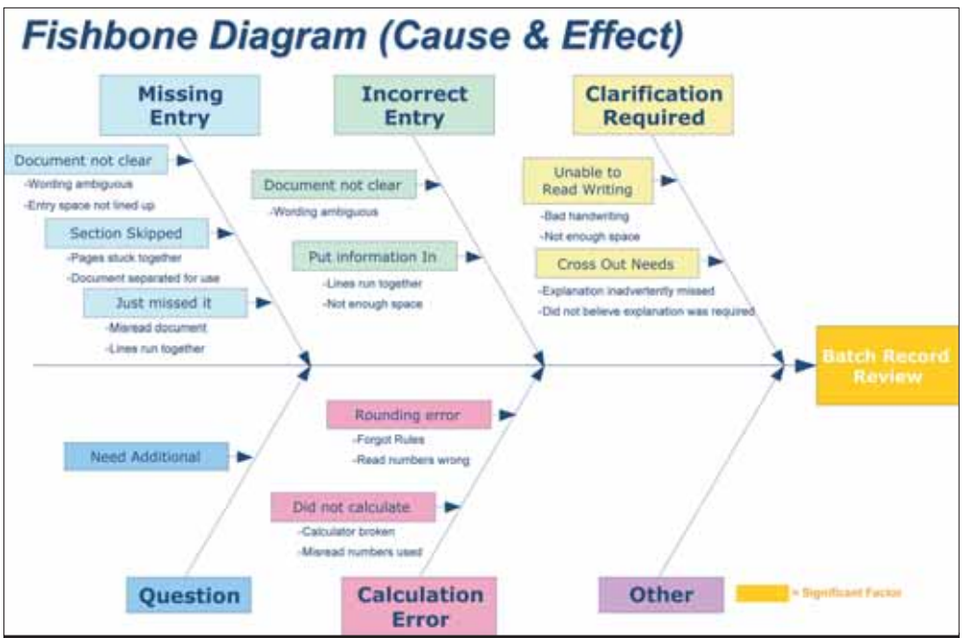

Figure 1: A fishbone diagram is an excellent tool to evaluate None-Value-Add (NVA) activity. (Source: Emerson Process Management)

Harmonization of Regulations

While there are differences among countries in specific regulations, a fair amount of global harmonization has already taken place. The International Conference on Harmonization, which today includes 33 countries, has aligned many key elements of Good Manufacturing Practices (GMP). These harmonized GMPs require ensuring the approved production process is followed, the right materials are added correctly, the equipment is properly calibrated, the operating environment is properly controlled, and the operator is qualified to perform the required tasks.

The historic answer to these regulations was to utilize a paper-based management process. However, most countries have changed their reporting requirements such that electronic signatures (and therefore electronic records) are legally binding. China's acceptance of electronic signatures as legally binding for e-commerce is one of the latest examples of this trend.

How Far We have to Go

A benchmarking study published in the July/August 2004 issue of Pharmaceutical Engineering showed that the UK pharmaceutical industry compared poorly to an award-winning company in that country and even worse when compared to world-class benchmarks. For example, a typical pharmaceutical company managed three

(Source: Emerson Process Management)

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to five stock turns per year, compared to 14 for the award-winning company, and 50 for world-class benchmarks. Right First Time (RFT) percentages were 85 to 95 for the typical pharmaceutical company, 96 for the award-winner, and 99.4 for the world-class benchmark. Perhaps the most telling number was cycle time in hours: 720 hours for the typical pharmaceutical company and 48 hours for the award winner. The world-class benchmark was eight hours. Switching to EBR can deliver significant improvements in this performance.

A good idea of the shape of the ideal arrangement can be found in the Instrumentation, Systems and Automation Society or ISA's S88 and S95 standards, which cover batch production, and the architecture of information flow among the plant floor automation systems and enterprise resource planning applications. All of this should be found in a good EBR.

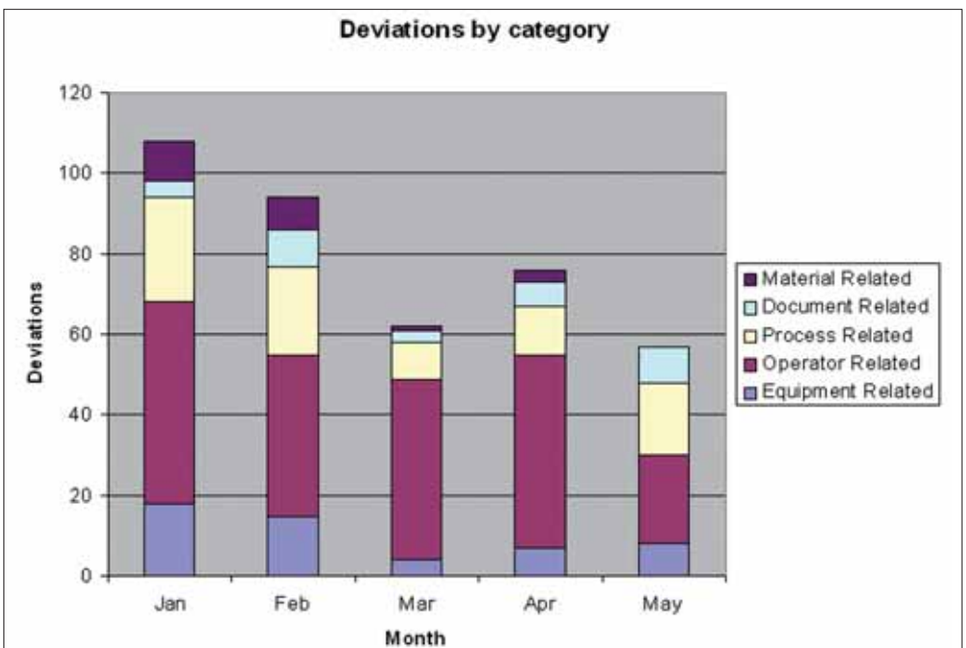

Figure 3: Root cause analysis of cycle time deviations.
(Source: Emerson Process Management)

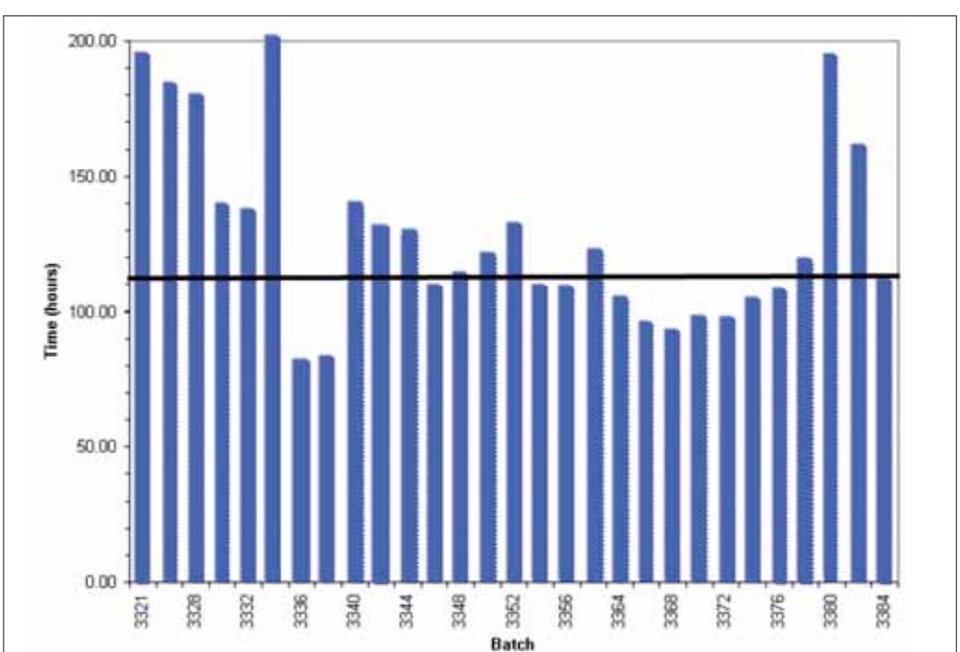

Figure 2: Cycle time deviation during batch production.
(Source: Emerson Process Management)

Components of the Ideal System

Today's integrated EBR systems can be applied from one end of the plant floor to the other, including the facility design and day-to-day maintenance. A representative EBR system includes components for the following:

- A security and audit component that addresses 21 CFR Part 11 concerns for electronic records and signatures, and provides audit trail services of all production and operations activities for all modules in the system.
- A content repository that provides controlled access to manufacturing documentation, and gives the company full control of all documents and version information.
- A training and development function that manages training courses and comprehensive training records, including the tracking of GMP training courses, scheduling of personnel, and real-time status confirmation of operator qualifications.
- An equipment tracking function that maintains the facility equipment hierarchy model, documents equipment states and properties, and tracks definable equipment events like usage, cleaning, and maintenance in any manufacturing environment. It should provide paperless calibration records and equipment logbooks with real-time updating.
- A materials management module that provides both work in progress and centralized material management capabilities with container level tracking, material genealogy, and quality controls.
- A weigh and dispense function that ensures the proper material has been measured, containerized, and then added at the correct time during the order.
- A modular recipe authoring function that simplifies and speeds the process of generating documents and workflow such as batch records, test methods, validation protocols, and other manufacturing documents.
- Configurable electronic workflow that man-

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Table 1: Examples of typical measurement.

CATEGORIES	CURRENT STATE	POTENTIAL IMPROVEMENT/ FUTURE STATE
Quality		
Deviations	Deviations/lot	Percent reduction
Investigations	Investigation efficiency	Percent improvement in efficiency
On Spec Results	Percent right first time	Percent improvement
Correct/Complete Batch Records	Percent right first time	Percent improvement
Training to Comply	Number of deviations due to deficient training	Percent improvement
Throughput		
Yield on process/unit ops	Percent yield/unit operation	Percent improvement
Repeatability (reduced variability)	Variability in critical quality attributes and batch yield	Variability reduction
Reduced cycle times	Unit cycle time	Percent improvement
	Batch cycle time	Percent improvement
Availability		
Reducing unplanned shutdowns	Percent downtime – equipment and line	Percent improvement and increased production revenue
Improving equipment status management (clean, calibrated)	Manpower to get information	FTE reduction
Reduced cleaning time and setup time	Percent planned cleaning and setup time	Increased production revenues
Reduced changeover	Percent planned changeover	Increased production revenues
Improved planning	Manpower to get information	FTE reduction
Operation and Maintenance		
Eliminating NVA activity (in operations, compliance and maintenance)		Hours reduction/improvement
Reduced overtime (in operations, compliance and maintenance)		Overtime hours reduction/ improvement
Manpower efficiency improvement		Hours reduction/improvement
Capital		
Reduced WIP (normal production)	Current WIP	Cost reduction
Fast time-to-market (new capital projects)	Current calendar from design to conformance lot	Time reduction
Reduced cost of new capital projects	Current cost from design to conformance lot	Cost reduction

(Source: Emerson Process Management)

ages and sequences batch records, collects and consolidates all batch data and generates facility performance metrics, graphs and charts.

- An electronic batch records module that provides routing, review and approval of paperless manufacturing records for current good manufacturing practices (cGMP) facilities with complete product and activity genealogy.
- A scheduling module that provides real-time production scheduling and updates so that plant floor events and equipment changes can be immediately accommodated
- Easy integration to all existing plant floor systems and connectivity to high level applications such as Enterprise Resource Planning.

Where to Begin

A good way to begin to develop an EBR system is to benchmark current or planned workflow through Six Sigma and Lean Manufacturing techniques. This evaluation will provide many opportunities to gain efficiencies. Excellent tools, including Fishbone Diagrams and Value Stream Maps, can be effectively used to evaluate Non-Value-Added (NVA) activities (see Figure 1).

Examine the roles of equipment, people, materials, documents and existing information. Using these benchmarks it becomes a straight-forward task to see where improvements can be made and, just as importantly, to quantify the results.

Examples of typical measurement are in Table1.

Example

Recent experience with a major pharmaceutical site confirms these benefits. This site has shown significant deviations in overall cycle time, as shown in Figure 2. Root cause analysis of the deviations shows various causes, with the largest cause being operator error, as shown in Figure 3. Resolving the deviations during the release approval process is the largest component of the cycle time variability.

Implementing an EBR system has reduced the deviations by more than 20%. Cycle time variability reduction has also seen significant improvement.

Conclusion

The opportunities are real and significant. Taking advantage of changes in regulations and leveraging new technology such as EBR systems are making pharmaceutical manufacturing more competitive. **PA**

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