

# Production Information Management

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**Production data must be collected and checked to ensure that validated process operations**

**are being executed consistently to produce a product within the established limits. Additional information to explain alarm excursions and other possible variances must be added to the batch database and electronically signed by authorized manufacturing personnel. Produced lots will be released for sale only after the batch data, relevant to each production lot, are evaluated (manually or automatically) and approved. Production data must be securely collected and stored as well as safeguarded from any kind of alteration.**

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**P**roduction information is part of a company's intellectual property and is as important as the materials the company produces. Production information must be accurate and available in real time for management to make informed decisions about the product or business, a process that must be completed with the least amount of time and cost.

Production data collection is the process used to gather information to confirm that manufacturing business requirements are achieved. A common problem in data collection is that this information generally is embedded in various management and process control systems. These data are often difficult to extract and align with other production data to develop informative reports. An important aspect of this process, throughout the enterprise, is to record data once, at the source. Once recorded, the data must be available to all enterprise users so they can acquire necessary information to make decisions.

Production information can be categorized in several main areas such as

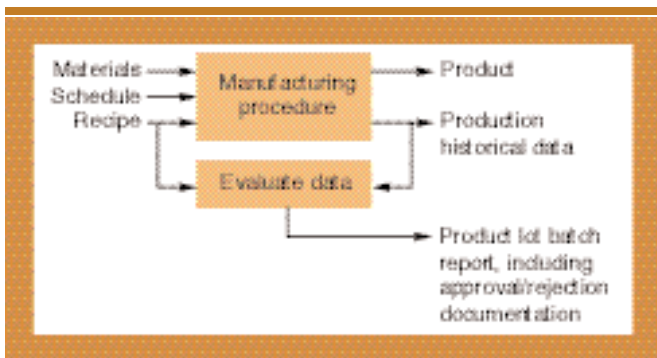
- recipe-management information — instructions that tell how to make a product and are retained in tickets, recipes, and in standard operating procedures (SOPs)
- production planning and scheduling information — descriptions of the schedule of the manufacturing facility activities and material availability
- production information — information that is used to approve or reject a product. These data are obtained during the production process and used to make decisions about the quality of the process execution and product. Generally, large quantities of these data are collected for each manufactured product lot.

Production data are collected so that decisions can be made for a variety of topics, including but not restricted to the following:

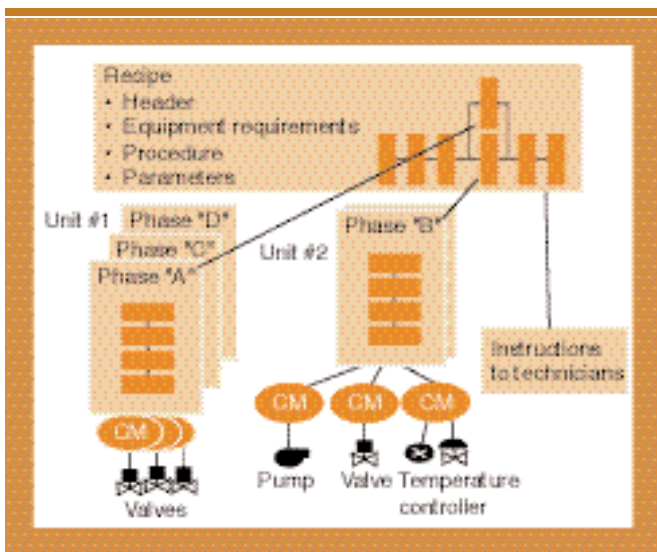
- product yield calculation
- production variance resolution
- product approval and release
- material genealogy tracking
- batch reports
- product development improvement
- equipment-use logs and maintenance scheduling.

Production information collection must be managed in a way that minimizes the time and effort required to inspect and review the detailed data. The objective is that, at the comple-





**Figure 1:** Product manufacturing approval process.



**Figure 2:** Recipe system for sending instructions to equipment and technicians.

tion of the product cycle, all critical alarms and actions are resolved, making it unnecessary to review the collected batch data (see Figure 1).

To maintain control of the product throughout the manufacturing process, the collected data are continually compared with expected values to determine the approval or rejection of the product. Production data are collected from equipment measurements and phase activities, manual technician activities, and laboratory analysis. It is crucial that critical parameter approval limits are well known throughout the life cycle of the production batch and that corrective actions are established if the limits are violated. To reduce cycle time, information about these limits must be readily available so that appropriate decisions can be made about the production lot.

### Evolution of batch control systems

**Paper tickets.** Paper tickets have been used in manufacturing facilities for more than 30 years to maintain control of production procedures and the quality of the manufactured product. The ticket serves a two-fold purpose: it tells the technician how to make the product and directs the technician to collect and record the necessary production information. The ticket becomes the production record and is reinforced by one or more SOPs.

The information collected on a completed ticket is reviewed for possible variances and must be approved (by a signature on paper) by manufacturing quality assurance (MQA) before the lot is released. This still is the most common way to maintain control of CGMP processing in the pharmaceutical industry. Because paper is lightweight and easy to handle and read, it is still a very good material to use to convey information. However, it requires manual activity that can consume valuable resources and time, especially if many variances or incidents are observed that must be resolved before a product can be released.

**Manufacturing execution systems (MES).** MES is a manual instruction system that gives operating instructions to technicians and collects the corresponding information automatically from validated equipment and manually from the technician with a confirming electronic signature. This system mimics the ticket by means of a computerized procedure. It fosters consistency throughout the production process or the manufacturing facility by allowing instructions and corresponding data to be retrieved from a common master recipe database, thereby ensuring less chance of introducing errors. The possibility of using an out-of-date ticket is reduced drastically, and the collected and entered production data are entered in a database for common production reporting, tracking, and approval of the product. MES can be integrated with automated equipment and sent start and stop instructions and, at the same time, can collect process information automatically. Automating the product approval process by collecting data in a relational database reduces cycle time and is cost effective.

**Automated equipment control systems.** Traditionally, distributed control systems (DCS) and other process control systems are developed to control equipment operations automatically. Through the years, equipment data have been collected in various forms to satisfy operating, process engineering, maintenance, and technicians to verify the proper function of equipment and process operations. These forms generally are continuous-trend data or activity logs that are linked to equipment control and not directly related to the product lot being manufactured. The data are difficult to retrieve and too incomplete to be used for management reports.

**Automated production control systems.** With the development of modern batch control systems, which are based on S88.01 control model and database technologies, automated production control systems are becoming more integrated with MES functionality, which includes electronic signatures, and are used more frequently in the automation of the production process. Information about a change in a product's status executed by technicians or automated equipment helps determine conformance of product operations and must be recorded. These systems tell a technician what to do when an alarm occurs and allow a technician to record what action was taken. This information shows product-state changes and is required for verification of production and product progression (see Figure 2).

An S88.01 control recipe contains instructions that include parameters and process limits for automated equipment phases or is given to an operating technician for manually operated activities. Appropriate data, as instructed by the recipe, must be collected to verify the correctness of the actions taken, re-





This photo depicts an intelligent data and information management terminal on the manufacturing floor.

regardless of whether they are executed by automated equipment or manually by technicians. Equipment-phase action results are reported automatically to the historian after phase completion. Technician actions must be entered with the appropriate comments, including an electronic signature indicating that the action was performed as instructed. The collected data must be bound to the production lot number. Recipes that change the status of equipment rather than product, such as with clean-in-place and steam-in-place procedures, are processed in the same manner. The equipment status and the corresponding data and information must be referenced to the recipe lot number that produced the equipment status. Product made in the equipment can be traced to the cleaning procedure of that equipment. These new batch control systems, in addition to maintaining consistent product quality, are designed to record the production data from all phases of the production process and provide up-to-date production quality confirmation.

### Attributes of batch data

Collecting more-specific data can help ensure product quality, but at the same time, this data should be used to make the decision process simpler and to reduce work. Data collected during the manufacturing process are used for several purposes; however, in FDA-regulated industries, the most important use for data is to confirm, approve, or reject the product by verifying that the production process has achieved the expected or validated processing steps and the actual product parameters are within the processing limits.

Throughout its life cycle, a product should be approved after each operation in the manufacturing process to reduce work, manage risk, and to prevent an unapprovable product from continuing to completion. In the production process of biologicals, the production time for one lot of product may require from four to six weeks. Therefore, approving or rejecting a lot

as soon as possible to save production time and material cost is advantageous.

Other unplanned or unscheduled data that are collected during the operation of a batch must be related to the batch lot and must be explained before the batch is released. To accomplish this procedure, all necessary data must be available (such as recipe parameters) to make a comparison of validation conformance.

**Batch data.** Batch data are the collected data related to the manufacture of a unique lot as it is planned and instructed by the recipe. These data are generated by the sequence of operations such as phase start and stop times, equipment use and time used, actual parameter values, and operator confirmations, comments, and electronic signatures. These data elements confirm that recipe instructions have been correctly executed within the established limits.

**Measurements and attributes.** Parametric data are used in real time to verify the product stage or equipment measurement at a given time during the production process. In a batch process, the material goes from one stage or phase to another, and measurement trends follow a predetermined path. Alarm limits may be turned

off or on or may change depending on the processing phase of the product. In most production processes, alarms can be classified as equipment- or product-related.

Equipment and safety alarms indicate equipment boundary crossings and should be responded to in such a manner that the equipment and process are safe when a critical alarm point is reached. Product measurements can be classified as critical or noncritical. Noncritical product measurements are technician alerts and do not require identified alarm actions. Critical product measurements, which affect the quality of the product, should be identified in the recipe with their alarm limits and actions (see Figure 3).

A product must be manufactured within established limits. Critical product parameters must define a setpoint and target range. A measurement must remain within the target range to stay within specification. If measurements deviate outside the established target range, an alarm notice will occur. This alarm may be informational if the measurement is still within an acceptable range for product quality, and corrective action may prevent the measurement from deviating further. If the mea-

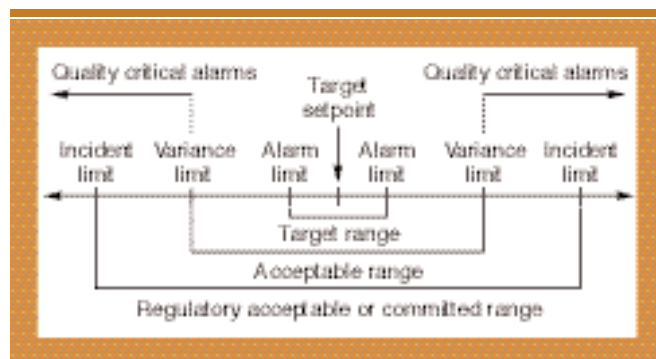


Figure 3: Critical parameter alarms.



surement does deviate outside the acceptable range, it becomes a more serious product-quality deviation, and quality critical alarms such as a variance or incident may occur. Either way, the occurrence of these alarms must be recorded and should include an explanation of the corrective actions. Discarding the product is not unusual if the parameter measurement crosses the incident limit, which is the regulatory acceptable limit.

**Operator-technician action log.** In an automated control system, any action performed by the operator that interferes with the automatic control of the system is recorded into an action log and batch historian. The record must refer to the equipment and lot number of the affected batch. For example, if a technician switches an automatic control loop to manual control, he/she must log the action's purpose and the time that it occurred.

The reason for this action must be noted in the batch history because any deviation from a normal production operation must be explained. If the equipment failed, which might affect product quality, the action log must contain an explanation of how the technician responded and must be authenticated with the technician's electronic signature. The comment must be attached to the lot number and retained as part of the lot history.

**Trend data.** Continuous-trend data collected during the processing of material in equipment must be logged to the historian with reference to the batch number. Generally, the trend data refer only to an instrument tag, which is insufficient for batch processing. Trend data must be tagged to the lot produced so that the data can be retrieved by a lot-related database call and will be available for insertion in batch reports. This generally is implemented to explain why parameters crossed product alarm or variance limits.

**Late entries.** Late entries are elements of data that are entered in the batch historian after the recipe has been completed and is no longer active on the control system. Although the recipe has been completed and no changes to the produced lot of material are planned, the lot still could be on hold in a processing vessel in the facility. For example, an intermediate material could be waiting to be acquired by another recipe for further processing. Meanwhile, vital information about the status of the lot — such as temperature, pressure, and other information — must be reported to the batch historian with reference to the lot number. This can consist of automatic measurement of the environmental conditions the lot of material is in or comments that are manually entered by the technician. Lot information must be monitored and entered in the batch historian until the lot is completed, stable, and ready for shipment. Late entries can be general environmental conditions, laboratory measurements, and MQA comments to approve the quality of the batch.

Material is not released until all variances are resolved and the batch record is approved. MQA comments pertaining to the resolution of critical alarms and variances must be entered. Any manually entered late entries must include an electronic sig-

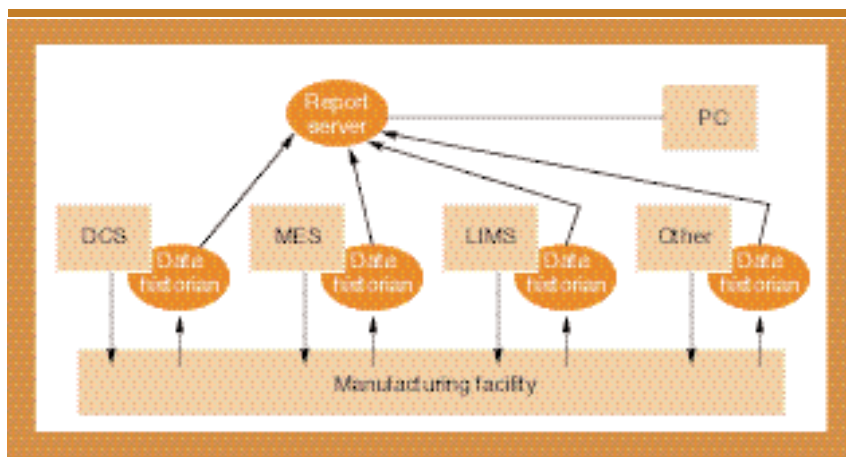


Figure 4: A manufacturing information strategy.

nature identifying and confirming the actions of the person entering the information. Also, all entries in the historian database must relate to the material's production-lot number.

### Automating data and reducing cycle time

**Data collection and information development.** Data about process operations can be collected in large quantities very effectively. Next, data must be managed to create information effectively. DCS or programmable logic automated control systems, provided that they are implemented with S88.01 recipe control concepts, are compatible with MES. Both systems must share their information when they are used in the same processing facility. This requirement also applies to data and batch information stored in additional systems such as laboratory information management systems and materials requirements planning systems. The objective is that key process information is collected and made available on-line by all systems for real-time production information reports.

Data that are required for the approval of a production lot, which may be part of different control and execution systems, must be made accessible for database queries. Specifically in a multi-manufacturing environment in which a product moves from one manufacturing area or facility to another, information must be readily available throughout the corporate network in relational databases on-line and must be accessible by means of personal computers.

Developing a business strategy for how information is collected and made available throughout the enterprise is of utmost importance. Technology should be perceived as a tool to help accomplish the strategic business plan. Technology will change very quickly, but the strategic business plan should not (see Figure 4).

A report server can be used to transmit preformatted information reports to standard corporate networked PCs, with data obtained from several databases located on the network. Approval of a manufactured lot means that all product variances are corrected and explained satisfactorily. If this is not the case, the product cannot be sold and must be discarded. The batch life cycle can be shortened by approving or rejecting material as early as possible in the manufacturing process.





For each production variance, a documented justification must be completed and properly signed off. Obviously, solving a variance issue and making a decision shortly after the occurrence is advantageous. To complete the production run and later destroy the product because of an earlier unresolved variance in the process would not be beneficial. To solve a variance issue in a timely fashion, MQA must have all the appropriate batch data available on-line to review and to make informed approval decisions for each critical processing operation and phase execution.

When all batch data are available on-line in relational database formats, MQA exception programs can search automatically for anomalies and then report them. When all issues are resolved satisfactorily in the database, the need for comprehensive batch reports is eliminated, work is drastically reduced, and money is saved.

**Automate the data.** Single or multiple batch-report servers with preformatted report applications can be used on the corporate network to extract data and information from multiple sources about a variety of subjects and objectives. The advantage of report servers and databases in a distributed architecture is that it will accommodate change. Additional control system databases can be added or new advanced report server technology can be implemented without affecting the present system and strategy. A current example of advanced report server technology is the formatting of personal Web pages with re-

quested corporate or production information. With this technology, considerable batch-review time can be saved by executing automated exception reports for production lot data confirmation. Data should not be duplicated or transferred to other systems because it is unnecessary work and may create additional errors.

### **Conclusion**

To maintain a cost-effective manufacturing environment, data and information must be automated and produced as efficiently as the product. Data should be automated to evaluate a product's approval or rejection throughout the manufacturing life cycle. A strategy must be developed in which various equipment and production control systems can work together and use the production process information. A sufficient amount of data from a particular process must be collected to make informed decisions, and report servers should be developed to transmit management reports with real-time information derived from interdisciplinary control and information systems. **PT**