Maintaining GxP with a 21 CFR Part 11–Compliant Tracking System

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For global pharmaceutical companies, maintaining a GxP (the collective term for good laboratory practice, good clinical practice, and good manufacturing practice) environment while upgrading quality systems and moving from paper-based systems to an electronic records and signatures (ER/ES) structure requires a comprehensive and fail-safe method of tracking all quality-related issues and exceptions in real time throughout the organization. Some companies have been preparing for this challenge for the past few years and already have begun implementing tracking systems to record deviations, nonconformance, defects, out-of-specifications, and consequent corrective and preventive actions. Other companies will find themselves scrambling to come up with a solution in a timely manner. All of them must ensure that their tracking systems comply with 21 CFR Part 11.

A brief history
In the beginning there was paper. Paper forms and templates were developed to document problems, events, deviations, corrective actions, and so forth. This approach created its own problems, however: Records were easily misplaced or lost when forms and files circulated among staff members in various offices or distant locations. The inconvenience of paper media prolonged the process of follow-up and approval and made it difficult to bring projects to a conclusion in a timely manner. In addition, management had no way to effectively assess the status of projects in the organization or to detect trends on the basis of recurring events.

Realizing that paper-based systems gave managers and staff no immediate access to information and no effective control in tracking issues, individual departments started to develop their own electronic systems to address these problems. They used tools such as e-mail systems, spreadsheets, and databases to publish and keep track of deviations. Band-Aiding one problem led to others, however. Portions of records still were being kept on paper, whereas others were saved electronically, thus inviting errors. Each department or location typically had a different system in place, resulting in inconsistency in the way the company was operating. Systems with little or no security enabled unauthorized users to access and modify records. Even worse, no audit trail for records existed, so records could be duplicated, altered, or eliminated. Finally, because no validation was performed on these systems, it was impossible to demonstrate that the data being kept were complete and accurate.
Recognizing the need for a systematic way to address these problems, FDA and the healthcare industry began meeting to determine how they could adapt ER/ES systems to the current good manufacturing practice regulations. 21 CFR Part 11 was released 20 March 1997 with an effective date of 20 August 1997. Parry because of this five-month implementation period and partly because the broad scope of the regulation created widespread difficulty and confusion, the implications and potential effects of the final rule were not immediately recognized. In the past few years, however, through the combined efforts of FDA and the Industry Coalition on 21 CFR Part 11, companies have gained realistic assessments of the time and expense required and the risks associated with modifying or replacing current systems and their related business processes.

The need for a tracking tool
Many companies have adopted an approach to Part 11 compliance along these lines:
- Read and completely understand Part 11.
- Identify all systems that must be compliant.
- Develop a checklist or other method to create a gap analysis.
- Determine the functional requirements for each system.
- Determine the appropriate workflow to perform system remediation or replacement.
- Implement a Part 11 compliance schedule and execute it accordingly.

Somewhere between the fourth and fifth steps, the need for a tracking tool became apparent. A centralized tracking solution would enable all affected departments in the organization to participate in their relevant portion of the workflow in a collaborative environment. Some companies attempted to develop their own in-house tracking system. Information technology (IT) departments were assigned to the development and deployment of yet another system, a task that put a strain on ongoing efforts such as Y2K remediation and e-business initiatives. Faced with this added burden, many IT departments chose to create compromise and stopgap solutions until the other mission-critical initiatives were completed.

Once the smoke cleared and full attention was given to the compliance-tracking application, many IT organizations realized they were lacking the necessary resources to develop a strategic tracking tool (see sidebar “Desirable features of an electronic quality-management tool”). It quickly became apparent that developing a tool that complied with all Part 11 requirements and met the users’ business requirements could take years and would cost millions of dollars just to develop, let alone to implement and validate. Furthermore, an application being developed in house would have required a software programmer to make changes to the source code every time a business process was created or modified. Clearly, some companies needed an off-the-shelf solution that was easy to configure and was Part 11 compliant.

A quality-management software tool
TrackWise (Sparta Systems, Inc [SSI], Hazlet, NJ) is a configurable Web- and Microsoft Windows–based quality-management software tool used for tracking nonconformance, deviations, customer complaints, corrective and preventive actions, audit observations, and other regulatory issues such as commitments and validations (see Figure 1a). Because the Part 11 regulation is subject to interpretation, it is difficult to determine whether software is truly compliant. SSI’s approach was to use the Good Automated Manufacturing Practice (GAMP) Special Interest Group document Complying with 21 CFR Part 11 Electronic Records and Recognizing the need for a systematic way to address these problems, FDA and the healthcare industry began meeting to determine how they could adapt ER/ES systems to the current good manufacturing practice regulations. 21 CFR Part 11 was released 20 March 1997 with an effective date of 20 August 1997. Partly because of this five-month implementation period and partly because the broad scope of the regulation created widespread difficulty and confusion, the implications and potential effects of the final rule were not immediately recognized. In the past few years, however, through the combined efforts of FDA and the Industry Coalition on 21 CFR Part 11, companies have gained realistic assessments of the time and expense required and the risks associated with modifying or replacing current systems and their related business processes.

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Electronic Signatures as its basis for implementing all of the features necessary for a company to be compliant (1).

The GAMP Special Interest Group document offers a practical Part 11 interpretation that is an assembly of views taken from FDA, published articles, GAMP Forum meetings, and International Society of Pharmacoeconomics and Parenteral Drug Association (PDA) members. Part of the document outlines the technical and the procedural controls that are required for any Part 11–compliant system and describes who is responsible — software vendor or pharmaceutical company — for each control.

As an example, consider 21 CFR Part 11, Subpart B, 11.300(b):

"Controls for Identification Codes—Passwords: "Ensuring that identification code and password issuances are periodically checked, recalled, or revised (e.g. to cover such events as password aging)." The software itself must be able to force passwords to be periodically changed and also enable user ID–password combinations to be rendered inactive without losing the record of their historical use (see Figure 1b). However, it is up to the pharmaceutical company to establish policy for how long a password can be used until it expires. The time period could be 90 days, 120 days, and so forth.

Another example can be found in Subpart B, 11.300(d): "Use of transaction safeguards to prevent unauthorized use of passwords and/or identification codes, and to detect and report in an immediate and urgent manner any attempts at their unauthorized use to the system security unit, and, as appropriate, to organizational management." The software system must be able to detect any failed attempts to use a password and after a certain number of failed attempts alert system administrators to the attempted breach, take swift preventive action (e.g., lock the user's account), and also alert management that the breach occurred and what action was taken.

The TrackWise system is fully configurable to allow the system administrator to set the allowable number of failed attempts as well as determine who is alerted and how, such as by means of an e-mail, a page, or both (see Figure 1c). In addition, SSI works closely with FDA-regulated clients and trade associations to follow and implement all of the critical features necessary to assist with a 21 CFR Part 11–compliance effort. Compliance audits, which follow PDA or other process models, help companies weigh various alternatives and solutions on their route to compliance. In April, TrackWise was successfully audited by a third party following the PDA process model (2).

21 CFR Part 11 and beyond

Although addressing and implementing Part 11 requirements is a must, several other key considerations exist for effectively selecting and deploying a compliance-tracking tool. One significant aspect of any tracking tool is its adaptability to one's business rules — that is, is it configurable? Configuration should not be confused with customization. A customizable product requires changing the source code and/or specific "stored procedures" in the database to implement functional requirements, thus necessitating a call to the product vendor. These developments could introduce delays in the process and could require substantial additional validation. In contrast, a configurable product is one that allows the customer to take the software out of the box and configure it to match any business requirement. For example, the TrackWise system can be used to set fields to reflect divisions, departments, products, and batch codes. It also can be used to set fields to specify workflows, security rules, and more. The system is user-configurable, meaning that it has built-in point-and-click tools that enable users to configure it without requiring them to be technology experts.

Choosing an off-the-shelf, fully configurable tool can substantially shorten implementation time and reduce validation costs. Customers then can validate that their configuration matches their business and functional requirements.

Other very important attributes of any tracking solution are robustness, scalability, and maturity of the product. The TrackWise system, for example, is designed to work with enterprise database-management systems such as Oracle and Microsoft SQL Server, which can support a large number of users. Date and time stamps are stored by means of the Universal Time Code, so the time displayed is in local time no matter what time zone a user is in. Web-based systems require no client-side installation and thus simplify use. Most important, when choosing a tracking tool it is essential that one chooses a mature product with a proven track record. It also is important to consider the reputation and stability of the software vendor. One not only is purchasing the product, but also is committing to a long-term relationship with the supplier. SSI supports the TrackWise tool with professional services to install and configure the product, train users, and support deployment. SSI also offers its customers extensive documentation and test cases that can be used throughout the validation process.

Conclusion

Investing in a quality-management system is one of the most important decisions an organization will face. Considering 21 CFR Part 11 compliance as well as all other aspects will be key to a company’s success, so make sure your company chooses wisely.

References