

## PHARMA IT

Excerpted from  
*Pharmaceutical Formulation  
& Quality* magazine,  
October 2004



### PART 11 COMMON SENSE

# Now that the Smoke has Cleared

“Common sense” practices and creative alternatives to address 21 CFR Part 11

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**T**HREE SIGNIFICANT PRINCIPLES ARE AT THE HEART of the 21 CFR Part 11 Legislation and the new guidance associated with this law. First, companies must perform a risk assessment to determine the status of computer systems and their “risk of importance” to the manufacturing and delivery to consumers and public safety according to the Guidance surrounding FDA’s cGMPs for the 21st Century initiative.

Second, PC-based systems should not be capable of inadvertently overwriting files without user alerts, intervention, maintaining the original file, documenting date and time, documenting the reason for changes and authorization.

Third, FDA is actively trying to encourage the industry to use technology to improve the efficiency of operations and is committed to making the Part 11 rules sensible and helpful rather than presenting an obstruction to progress.

### History

The genesis of the 21 CFR Part 11 regulations was in 1991, when members of the pharmaceutical industry met with FDA to determine how they could accommodate paperless record systems within the then current GMP regulations. In response to this meeting, FDA created a taskforce which, through much iteration with the industry, came up with the final Part 11 regulations in 1997.

Even though the regulations were fairly succinct and just 10 pages long, they were quite comprehensive and it was clear that FDA intended to apply them across the board. For example, there was no exclusion for so called legacy instruments—instruments put into service prior to 1997. This was not a guideline document; it was effective immediately and it was a regulation, meaning that it had the full force of law behind it.

Through subsequent guidelines and interpretations, FDA also made it clear that even if these electronic records were printed and signed and submitted as paper records, the electronic records were also subject to regulations.

Since the industry also needed FDA support to migrate from paper-based systems, the goal of both parties was to save time, money and resources, and improve compliance by using validated electronic systems.

### Initial Hard Line Interpretation

The regulations received relatively little attention in its first few years of existence as they were overshadowed by concerns around Y2K. Recently, the pharmaceutical industry has renewed its focus on the requirements of these new Part 11 regulations and has begun to realize its full implications.

FDA was starting to pay close attention to compliance with these regulations and every company covered by the regulations had to have in place a GAP analysis. This analysis had to list each and every instrument in the labs and state the extent to which they met or did not meet the regulations and establish an action plan for remediation. During this period, there were frequent new guidelines from FDA and each one seemed to interpret the rules more stringently than before.

Response of the industry was mixed. Some companies made a serious effort to comply and spent hundreds of thousands of dollars in upgrading instruments and establishing tighter administrative controls. Others were more deliberate in their actions as costs were a major deterrent.

Industry representatives were also making their thoughts known to FDA that this regulation, as it was then being interpreted, was way too costly for the industry and represented a major deterrent to their adopting electronic systems at the pace they had planned earlier.

These messages found a receptive ear within the agency and in February 2003, FDA issued a sweeping new interpretation of the Part 11 regulations. All existing guidelines were withdrawn and the agency issued a new guideline that dramatically softened all previous interpretations.

### The Risk-based Approach

The new guidelines were specifically designed to meet the industry’s concerns with regard to cost and provided incentives for using electronic systems more effectively. Even though the new guidelines did not directly state that the interpretations would be risk based, the corresponding guidelines on *Pharmaceutical cGMPs for the 21st Century: A Risk Based Approach*, makes it abundantly clear that FDA will adopt these principals when interpreting Part 11.

The new guidelines emphasized that the industry could now focus on the most important applications, the ones that most directly affect the health of its consumers, and ensure that they are 100 percent compliant, and it does not have to ensure a similar level of compliance where the risks to the consumers are minimal.

The agency explicitly excluded legacy instruments in the new guidelines and also hybrid systems, where the paper record is considered the valid retention document.

## Back to Common Sense

Hundreds and thousands of applications and instruments built on operating systems allow files to be created, saved, edited and re-saved with ease. And, we have been using these for many years. So in a high quality, compliant environment, the age old question remains, who cares about complying with 21 CFR Part 11?

We all do. We want to maintain the integrity and history of electronic records supporting the discovery, development and manufacture of pharmaceutical products. These records represent knowledge and history for us to improve our processes to reduce cost and enhance quality.

An approach to address numerous applications, computer systems and instruments that are in everyday use in today's laboratories without spending tens of thousands of dollars in upgrades, is to deploy generic technology that provides a "shell" around each independent application or computer system. This allows complete technical remediation on an application basis and provides a standard generic set-up for any PC-based operation. These technologies ensure that:

a) Only properly authorized persons may access the systems and the records

b) The record shall be maintained in a secure repository

c) No record shall be changed without recording

i. a before and after copy of the record,

ii. the electronic signature of the person changing the record,

iii. the date and time of the change and

iv. a reason for change (predicate rule).

By utilizing simple generic approaches to the multitude of PC-based instruments, desktops and stand-alone applications, the original vision of Part 11 can be achieved with a cost-effective, high quality approach.

Many alternatives today address the 21 CFR Part 11 challenge for the industry. The law and its latest interpretations continue to be for "the right reasons." Innovative, simple technologies are available to remediate non-compliant applications in a very straightforward and cost-effective deployment model.

In the end, Part 11 represents an enabler to move our industry towards paperless operations, dramatically reducing cost, accelerating cycle times for new medicines and assuring high quality operations.

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