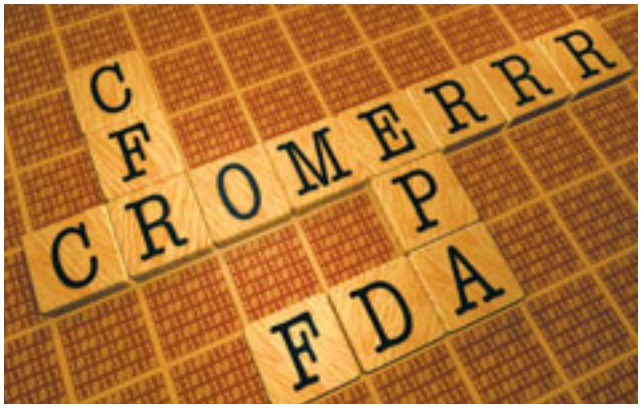
EPA and FDA Spell Out the Rules

Victoria Lander

Responsible record keeping and efficient data management are critical in this digital age.

It's panic time. Your company is being sued over an environmental issue, and the company attorney wants all the site files from 1996 by the end of the week. The stack of GC-MS printouts is as tall as you are. Your geologist is on vacation this week, and you can't decipher his handwritten field notes. The lab tech mistakenly discarded the chain-of-custody sheets when the lab analyses were completed. You compiled a report for the district manager in 1998, but it got lost in the 1999 computer system upgrade. You go through a similar paper chase every time you have an environmental audit, your division manager is on your case to improve your productivity statistics, and you only have 24 hours in a day.



Chemists working in industries regulated by the Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) are only too familiar with this hypothetical scenario. The pressure to reduce costs and improve profit margins competes with the need to comply with significant new government regulatory policies, creating an atmosphere of anxiety that can inhibit decision-making and the implementation of solutions.

The last decade has seen astounding growth in the generation of production, quality control, and laboratory data. Converting this data into meaningful information becomes difficult, however, when data are held in disparate, unconnected systems. Capturing data and transforming them into viable information not only ensures compliance with FDA and EPA regulations, but can enable companies to use this information with greater agility.

21 *CFR* Part 11

Industries that deal with food, drugs, cosmetics, nutraceuticals, or medical devices are subject to regulation under 21 *CFR* Part 11, the FDA's Rule on Electronic Records and Electronic Signatures (*www.fda.gov/ora/compliance_ref/part11*). This rule is based on GxP, the "good practices" applications. (GLP is good laboratory practices, GMP is good manufacturing practices, GCP is good clinical practices, etc.)

Part 11 has been "final and effective" since August 1997. Firms are expected to have their procedural and administrative controls in place by now. They must also have plans for upgrading their legacy systems (existing computer infrastructure) with the technical controls for Part 11, which address electronic record security, integrity, traceability, and the proper use of electronic signatures. These plans must be detailed and contain a reasonable timeline, and firms must show progress toward implementing them. Records covered by Part 11 include inventories, calibrations, preventive maintenance, validations, training, customer complaints, and adverse events. There is no determined date when all firms must be in total compliance with *CFR* Part 11, but the FDA has recently increased active enforcement of this rule. The basic intent of Part 11 is to ensure that scientists working in labs governed by predicate (previously published) rules keep certain records in electronic form, and that these records are trustworthy, reliable, and legally equivalent to paper records and handwritten signatures.

CROMERRR

Most of the EPA's data collection protocols were implemented years ago, before there was a clear appreciation of data quality principles and in the absence of standards that protected the trustworthiness of data. Most of the data currently collected by the EPA is acquired by regulated organizations and local agencies using vastly dissimilar collection and analysis methods. Lack of consistent standards not only increases the time and resources needed to review results, it can also lead to erroneous conclusions when incompatible data are compared incorrectly.

For example, in the mid-1980s, one environmental testing lab in New Jersey analyzed soil and water samples for priority pollutants using GC-MS. The instruments were not networked, and there was no protocol for the handling and long-term storage of the data. The paper printout of the analytical report was the protected data entity. It never occurred to management that electronic records would need to be protected for accurate and ready retrieval in a compliant environment. Today, anyone needing to re-examine and reprocess those unprotected, unsearchable tape backups would face quite a challenge.

Developed with 21 *CFR* Part 11 in mind, the EPA's proposed Cross-Media Electronic Reporting and Recordkeeping Rule (CROMERRR) will provide the legal framework for electronic reporting and record keeping under the EPA's environmental regulations (*www.epa.gov/cdx/cromerr/propose/index.html*). The rule was proposed on August 31, 2001, and the public commentary period closed on February 27, 2002.

CROMERRR will apply to most, if not all, reporting and record keeping currently required of EPA-regulated organizations (currently regulated under GLP). These

records include master schedules, protocols, standard operating procedures, and quality assurance inspection reports; the electronic documents will have the same legal and evidentiary force as their paper counterparts.

CROMERRR technical controls specify

- the ability to generate copies of records in human-readable and electronic forms,
- logical and physical protection against record compromises,
- secure computer-generated date/time stamps and audit trails,
- a means of retrieving records readily in the normal course of business, and
- a means of searching and retrieving archived records that preserve the context, metadata, and audit trails.

Comparing Regulations

Although there are commonalities between the intent and technical and procedural controls for 21 *CFR* Part 11 and CROMERRR, they are two separate regulations, conceived and maintained by two different governing bodies. However, it is likely that some firms will be regulated by both CROMERRR and Part 11, since they currently comply with EPA and FDA regulations.

Both regulations establish the requirements for trustworthy electronically maintained records, substantiate electronic reporting requirements, and set up the functional capabilities of electronic record retention and document receiving systems. Unlike Part 11, CROMERRR establishes a Central Data Exchange (CDX) system for receiving e-records. EPA-regulated entities that use electronic systems to create, modify, maintain, or transmit electronic records must use procedures and controls designed to meet the minimum criteria to ensure that e-records are admissible in court to the same extent as previously kept paper records.

Neither CROMERRR nor Part 11 dictate the specific software and hardware needed to meet electronic record keeping requirements. Thus, industries can take full advantage of emerging technologies as long as e-record trustworthiness and reliability are preserved. The systems' users are responsible for understanding the requirements and adopting appropriate compliance controls into their overall business practices.

Data Management Solutions

In future response to CROMERRR, many EPA-regulated laboratories may compile comprehensive reports for electronic submissions to the EPA. Like their pharmaceutical counterparts, these laboratories are challenged by their need to coordinate disparate data from a wide variety of sources. These data are ideally assembled from multiple sites and collected, archived, and used at one convenient location. Scientists might also be called on to locate and readdress the data even after they have submitted their final reports.

Developing a regulatory compliance strategy is not an easy task. Many software suppliers have enhanced their product's features and devised internal technologies to address the technical controls required by these regulations. Such fixes tend to be proprietary and thus become only partial solutions. Any regulation intended to protect the reliability of records generated by computer-controlled systems not only relies on the regulatory technical controls, but also on the implementation of procedural and administrative controls. These are

the policies and procedures that govern conformance to the technical requirements of a regulation—for example, a written procedure prohibiting users from sharing their passwords for system access.

In practical terms, a thorough approach to data and knowledge management requires a flexible, Web-based platform that integrates with multiple analytical and software systems to provide an enterprise-wide record keeping solution. Such a platform must also incorporate the technical controls for e-record maintenance and e-signature regulation. This information must be stored in a database that is compliant, easily retrievable, and reusable.

Pulling It All Together

One large pharmaceutical company learned firsthand how such a data management system could help them make the most of their data. This organization was interested primarily in increasing its ability to meet the Part 11 requirements for laboratory data. In the existing system, report data was stored on paper, and raw data files were deleted from analytical instrument computers when free disk space was required. It was difficult to find data when it was needed, and the company was not protecting its raw data throughout the file-retention period required by Part 11. The company implemented the NuGenesis Scientific Data Management System (NuGenesis Technologies Corp., Westborough, MA), a program that unifies data from various sources into a common Web-based electronic format.

By installing, validating, and using this software along with the appropriate Part 11 procedural and administrative controls, researchers were able to capture the raw analytical data from their HPLC, LC-MS, and other instruments and store human-readable report data in a secure relational database. Metadata was extracted automatically and cataloged, enabling successful data searches. Access to the data was controlled by system logins, automatic computer-generated time-stamped audit trails, and other security features. At this point, the researchers in this laboratory felt that they were in 90–95% compliance with Part 11, a significant improvement over the previous system.

CROMERRR has not yet been finalized, but its record-keeping requirements are based on those in place for 21 *CFR* Part 11, the software requirements will be similar for both sets of regulations, avoiding the need for two separate systems.

The general feeling in the industry is that although implementing these rules on trustworthy record keeping is costly and time-consuming, when the dust settles, these regulations will pave the way to more reliable data management and utility. In our current corporate environment, trustworthy records will undoubtedly add an element of confidence to the regulated arenas.

Suggested Reading

Information on 21 *CFR* Part 11 and CROMERRR; http://pw1.netcom.com/~jlboet/esiglinks.html.
NuGenesis Technologies' 21 *CFR* Part 11 page; www.21cfrpart11.com.

Victoria Lander *is the market manager for compliance for NuGenesis Technologies Corp. Send your comments or questions about this article to tcaw@acs.org or to the Editorial Office address on page 6.* ◆