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Implementing the ERES rule will do more than make your organization compliant with federal regulations. It will strengthen its intellectual property position for the information age.

21 CFR Part 11: (Un)Expected Added Value

Many great ideas start out as simple, innovative solutions to small problems. Rarely does an inventor anticipate the magnitude of solutions his or her invention will provide . . . but the solution to electronic record keeping for intellectual property development already lies waiting for us.

The convergence of science and technology is rapidly altering the operational landscape of research and development (R&D). Companies that control a promising technology must protect that technology, and they are forming partnerships, relationships, and alliances to expand their markets, raise capital, and increase their capabilities. The Internet is significantly altering R&D organizations, and leading-edge companies are exploring and using new strategies that enable them to compete in the modern marketplace. Increasingly, new tools are being made available for researchers that allow for more prolific, more productive, and more efficient work flow. Today, researchers generate mountains of data — both scientific and commercial. Business processes supporting their efforts are changing too. As competitive pressures force organizations to focus on core competencies, each company must align its efforts to achieve maximum returns on its investments.

All R&D organizations generate one common product, data, and these data are almost without exception electronically recorded. Although anyone in an organization can pursue an invention successfully, a preponderance of pharmaceutical patents relate to the New Chemical Entities (NCEs) identified and generated by chemists and biochemists. Their reliance on instruments and technology increases daily. The long-awaited information age is upon us, and now we must learn to manage this new landscape.

Why go paperless? Organizations use electronic records for straightforward, simple, and compelling reasons. Electronic systems facilitate and accelerate information (data)

exchange and the sharing of information among researchers. Such systems reduce internal costs and, in regulated industries, minimize legal as well as regulatory risks. Records are created partly in anticipation of future disputes: to record activities and/or transactions at or near the time of their occurrence and thereby establish a people-independent memory of events. The records of every business constitute its corporate memory. And even though the basic tenet of the American judicial system is “innocent until proven guilty,” that is not the case with regulatory compliance. Through its records, a company must be able to demonstrate through documented information that a pattern of behavior was so consistent as to preclude the possibility of any validity to an allegation of procedural wrongdoing.

The Electronic Records, Electronic Signatures Rule (ERES), 21 CFR Part 11, is both gatekeeper and enabler of the data-capture process in FDA-regulated industries (1). The rule defines stringent controls for the use of electronic records and signatures — but more significantly, it defines the requirements for capture, storage, retrieval, maintenance, and security of data to ensure integrity and acceptability for FDA. What is more important, ERES is a present “reality” promulgated by a world-recognized government agency to ensure governmental acceptance of electronic records and signatures as equivalent to their paper precursors.

Implementation woes. In industry, ERES is forcing all regulated organizations to reevaluate their information processes and controls. Organizations must review their documentation in support of all processes and controls because employees must be able to demonstrate confidence to the agency (FDA) that their electronic data are no less reliable than data contained in the paper format. To date, industry concern has focused on the many challenges to implementation, and that focus has been confined within the regulatory silo. Although compliance professionals are well aware of the new regulation, IT groups

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Laboratory Notebook Standards

1. Use bound notebooks or journals to record ideas and experiments. Loose papers get lost and are subject to challenge because temporal connectivity cannot be presumed.
2. Use permanent ink.
3. Record experiments contemporaneously with the actual work.
4. Date each experiment on the first and each subsequent day. It is common to see dates separated by two or three weeks. If the important work occurred between those dates, only the later date is usable in a patent proceeding.
5. Define the objective of each experiment, including the designation or name of the NCE to which it applies.
6. Record all relevant facts (such as the type of equipment used, conditions, times, materials), including sources and data. If standard procedures are used and not discussed in detail, note where full descriptions of such standard procedures can be found. Use only well-known or defined abbreviations and codes.
7. Attach or copy into the notebook equipment-generated data, or note where such data can be found. Cross-reference the notebook and data that are not actually in the notebook.
8. Have a noninventor who understands the work being recorded sign and date each relevant record. The corroborating witness must not be a coinventor, must have observed the work described in the notebook as it was being done, and must have understood what was done.

have offered widespread resistance to the changes that the regulation requires even though compliance will provide many ancillary benefits to their organizations when they become compliant.

The Rule Itself

21 CFR Part 11 defines the criteria under which FDA will consider electronic records equivalent to paper records and electronic signatures equivalent to traditional handwritten signatures (1). The rule is divided into three sections: Subpart A, "General Provisions"; Subpart B, "Electronic Records"; and Subpart C,

"Electronic Signatures." Records are defined as "Any combination of text, graphics, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system."

Under the regulation, signatures can appear in three forms (handwritten, digital, and electronic), which are defined in 21 CFR 11.3 as follows: A handwritten signature is "the scripted name or legal mark of an individual handwritten by that individual and executed or adopted with the present intention to authenticate a writing in a permanent form." The scripted name or legal mark may be applied to devices other than paper. An electronic signature is "a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual's signature." A digital signature is "an electronic signature based upon cryptographic methods of originator authentication, computed by using a set of rules and a set of parameters such that the identity of the signer and the integrity of the data can be verified."

Compliance with ERES focuses on three fundamental elements. First, a computer-generated audit trail with local date/time stamps of user entries and/or actions (creation, modification, or deletion) records and assures data integrity. Second, security practices limit access to authorized users, hold them accountable to written policies, and differentiate between open and closed systems to preclude tampering. Third, modalities must be put in place to ensure retention, retrievability, and reproducibility so that electronic records are archived in electronic form (on tape or disk) with accurate transcriptions or complete copies of data and "metadata" (data about data).

Organizations using electronic records in FDA-regulated environments, however, face certain challenges. They are, of course, required to validate any new computer-related systems and may well need to visit or revisit legacy systems in the same light. Validation will be an ever-increasing challenge as it spreads its influence through newly defined organizational functions and activities. Design of systems and their supporting architecture will become critical. What is most important, the security environment (documentation, change control, and adequate testing of security controls) will be paramount.

Intellectual Property Records

Extensive documentation is critical for determining proof of patentability. When competing applications or patents cover the same invention, the U.S. Patent and Trademark Office (PTO) may declare an "interference" between the contesting parties to determine who was actually (legally) the first to invent. The party establishing conclusive evidence that it invented first will be the ultimate winner.

Written evidence of who did what and when is almost always the critical determination factor. Because researchers increasingly use computers to conduct and document their work, issues have arisen concerning whether computer or electronic records meet the rigorous evidentiary standards imposed in interference proceedings. Electronic records are admissible as evidence in interferences to the same extent that such records are admissible under the Federal Rules of Evidence (2). Company practices that comply with FDA requirements should meet the federal test and thereby comply with the PTO requirements.

Links in the chain. In pharmaceutical R&D, especially in development laboratories, the most common forms of written evidence are laboratory notebooks and the instrument-generated documents that are included as part of them. Most scientists learn to keep notebooks in graduate school, and personal styles vary dramatically. The proliferation of new and nonstandardized electronic media further complicates the matter, along with differing institutional standards regarding notebook practices.

The operative point, from a corporate legal perspective, is that all scientists should view themselves as potential inventors. Large organizations recognize that and ask or require all new employees to acknowledge that anything they invent while employed is ultimately the property of the employer. More progressive organizations provide payment of "consideration" (a nominal financial transaction) for transferring rights to legitimize the relationship.

Because every scientist's ideas have the potential to be important, they should be accurately recorded. Journals and laboratory notebooks that could be important in patent litigation clearly should be of such quality and completeness that they can establish inventorship in court or before the PTO. The scientific development or "reduction to

practice” of an invention, along with the dates of all of associated inventive activity (including proof of the date of conception), must be supported with full documentation. Therefore, electronic records should be little different from their paper precursors. The “Laboratory Notebook” box lists generally accepted standards for paper records.

That was the way of the past. For centuries, paper was the medium for recording information, both in private and in

public environments. Today, the electronic medium is becoming the primary interface. Unlike paper documents, the visual record displayed electronically is only part of the true record. Users see the graphics and text of electronic forms, but the information that is entered into electronic forms and composes the underlying “record” is an amalgamation of binary codes and algorithmic reductions. Users do not generally see that part of the record. Point #7

in the “Laboratory Notebook” box (to copy electronically generated data into a journal) therefore violates a fundamental principle of electronic records and of the ERES rule.

Admissible. Preferable? The U.S. PTO affirms that electronic records are admissible as evidence before the Board of Patent Appeals and Interferences to the same extent that electronic records are admissible under the Federal Rules of Evidence (3). Therefore, if steps are taken to ensure the reliability of electronic research records, then those records can satisfy even the heightened evidentiary requirements that govern efforts to prove invention dates. In fact, use of computers for the creation and maintenance of research records can provide evidentiary and operational advantages over and above traditional paper records when proper logical, technical, and managerial controls are in place. The weight given to any particular record necessarily must be determined case by case. The “Coincidence?” box illustrates similarities between Part 11 and guidelines published by an intellectual property law association.

Questions concerning the evidentiary sufficiency of electronic records arise from the attributes that distinguish them from traditional paper records. The process of creating an electronic record begins with data capture through an input device, either human operated or automated. Once in the computer, information is generally held in some type of temporary memory until it is saved to a more permanent memory device. The process is completed by the output of the stored information.

In the United States, the general admissibility of electronic records as evidence in legal proceedings has been well established. Federal courts have over two decades of experience considering the application of their rules to electronic records and ruling on objections to their admissibility. The rationale underlying admissibility of any evidence requires that a series of obstacles be overcome. The evidence must be relevant and/or dispositive, and it must be authenticable.

Federal and state statutes, as well as case law, establish a sound basis for admissibility of “data compilations, in any form” that are “kept in the course of regularly conducted business.” To date, the law has focused on the process by which records are created. In the future, attention will look to accuracy,

Electronic Records Guidelines: Coincidence?

The American Intellectual Property Law Association also has published guidelines for electronic records and signatures.

21 CFR Part 11

Subpart A: General Provisions

Section 11.1: Scope

Section 11.2: Implementation

Section 11.3: Definitions

Subpart B: Electronic Records

Section 11.10: Controls for Closed Systems

Section 11.30: Controls for Open Systems

Section 11.50: Signature Manifestations

Section 11.70: Signature/Record Binding

Subpart C: Electronic Signatures

Section 11.10: General Requirements

Section 11.20: Electronic Signature Components and Controls

Section 11.30: Controls for Identification Codes/Passwords

AIPLA Guidelines

Subpart A: General Provisions

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Section 11.20: Identification Mechanisms and Controls

Section 11.30: Controls for Identification Codes/Passwords

authenticity, and completeness of information retention, the processes by which records are controlled for review, reproducibility, and retrievability. Records of electronic transactions will play an increasingly important role as evidence in legal disputes as well as regulatory audits and inspections.

To be admissible under the law, records must be “recorded, copied and reproduced by any . . . process that accurately reproduces or forms a durable medium for reproducing the original.” Establishing the authenticity of an electronic record (that it is what it purports to be) is a key foundational requirement for admissibility in evidence. Under the Uniform Rules of Evidence, accuracy also plays a role as one of the fundamental tests of authenticity: Evidence describing a process or system used to produce a result and showing that it produces an accurate result must substantiate any related claims. Therefore, it is important for the transaction information (including metadata resulting from electronic forms) to show that an accurate result was produced.

Audit trails. Establishing the authenticity of an electronic forms transaction record for business and legal purposes requires creating and maintaining data that can be used to establish an audit trail. Information necessary to both the audit (business) and

chain-of-custody (legal) processes includes, at a minimum, these elements: who used the system, when they used it or instigated a transaction, what they did while using the system, and the results of the transaction.

Properly implemented and maintained, audit trails as mandated by the ERES can establish that all pertinent information was captured at or near the time of an event, and ERES controls verify that procedures (SOPs) were followed to achieve an accurate and reliable result. That can add significant weight to establishing the authenticity of an electronic record for admissibility in evidence. Not only content but also the context (circumstances of creation) and structure (logical and physical attributes) should be preserved as part of an electronic forms transaction record.

Paving the Way

Change — rather than stability — engulfs us in a world of endless demands for reinvention and reinvigoration of processes. Something discomfiting is happening: Changes made have strategic implications beyond the sphere of a single decision maker or team. Management has long based its calculations on the traditional sectors and dimensions of power: finance, marketing, and manufacturing intertwined within and supported by a complex legal framework.

But a new field is emerging, “information strategy,” and although still inchoate, it promises to redefine the traditional dimensions of power. Moreover, it will seed the creation of an “information dimension” broadly understood to include technological conduits and conceptual contents. The keys to success will likely lie in managing informational capabilities and resources skillfully (that is, strategically).

Today, organizations increasingly rely on data, and data as a whole are increasingly the commodity and asset upon which business relies. Proactive organizations must establish a knowledge architecture that acknowledges these changing needs, meeting the compliance requirements and paving the road to the future paradigm. Data by themselves are not readily usable. They must be searchable, secure, and retrievable irrespective of their origin and organized into a usable format that can be applied to the crisis of the moment. Roughly 90 percent of all that we know in biology, chemistry, and physics has been discovered over the past 30 years. Our ability to process and store data doubles every 18 months, and that pace is increasing.

With a rapid transition to electronic systems (particularly Web-based applications on the Internet), business systems, practices, and procedures must be established to guide public and private entities through the potential minefield of electronic records management. What the courts require and what auditors expect — and therefore what commercial and public entities should be striving for — are systems and processes that are both accurate and reliable. As such, they will be viewed as trustworthy in the management of their electronic transaction records. The ERES, when properly implemented, provides just such assurance.

References

- (1) *Code of Federal Regulations, Title 21, Food and Drugs*, Part 11 (U.S. Government Printing Office, Washington, DC), July 1999.
- (2) “Admissibility of Electronic Records in Interferences,” *Official Gazette*, Patent Office, 10 March 1998.
- (3) *Code of Federal Regulations, Title 37, Patents, Trademarks and Copyrights* (U.S. Government Printing Office, Washington, DC).

For Further Reading

Code of Federal Regulations, Title 28, Judiciary and Judicial Procedure (U.S. Government Printing Office, Washington, DC). **BP**