# Expert Examines Key Requirements for Computerized Clinical Study Systems

Despite the fact that federal regulations governing electronic records and signatures have been in place since 1997 and the FDA issued guidance in May 1999 designed to further clarify these requirements, many clinical research entities remain confused about the agency's expectations for computerized clinical systems, according to Len Grunbaum, president of META Solutions Inc., a McLean, Va.-based clinical consulting group.

Speaking at the Association of Clinical Research Professionals annual meeting on May 16 in New Orleans, Grunbaum elaborated on the main features of electronic clinical trial systems, discussed why industry is struggling with the regulation and offered advice on how to proceed in the future (see 21 CFR Part 11, App. II).

## Necessary Controls

When a computerized clinical system is used, researchers must ensure that the quality of the system and the results it produces are equivalent to paper-based systems used for the same purposes. To achieve this goal, controls for every process used to operate the system must be maintained, Grunbaum said. Specifically, researchers must validate and test the computer system to prove that it works in the way it was intended.

According to Grunbaum, researchers should write detailed testing plans and have them approved by management before conducting the tests. Formally written test plans that are subject to company approval help to focus in on the expected functions of the computer system, he said. After initial testing has been performed, researchers should conduct continuous operational checks of the systems to ensure that the system "does what it's supposed to do, that it only updates the files it's supposed to update, that it doesn't erase or override anything else, and that it continues to operate properly," Grunbaum said.

## System Features

Under the requirements, all computerized clinical systems must allow for the copying of records so that FDA inspectors can review the system in detail. Inspectors need to view data and tables contained in individual files, check source codes and determine how the system was built. Similarly, computer-generated audit trails also are required as a way to show why changes were made, by whom and when.

Staff access to computerized systems should be limited to ensure data integrity for the records contained there. One way to do this, Grunbaum said, is to build a system that allows for "authority checks" — electronic firewalls that prevent unauthorized individuals from entering or changing data or adding passwords to gain access to files. Verification controls are particularly important for companies that intend to use electronic signatures, because they prevent potential forgeries in clinical records, he said.

Because computerized systems are only as good as those individuals responsible for their use, research staff should be adequately trained in the operation of systems and provided with current standard operating procedures (SOPs) that explain how the equipment works. According to Grunbaum, the FDA will inspect these SOPs and verify that adequate policy and documentation controls are in place and determine whether procedures include security and data recoverability measures.

## Industry Difficulties

Although using computerized systems in clinical research offers many potential benefits, a recent META survey of contract research organizations, pharmaceutical sponsors and software companies revealed that the clinical research industry is merely at the planning stages for utilizing computerized systems. The primary reason for this hesitancy appears to be concern over how to comply with 21 CFR Part 11. For example, a number of companies that participated in the survey had concerns about how to bring older, legacy computer systems up to speed

*(See Computerized Systems, p. 5)*

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## Tracking, Training

To prevent drug accountability problems, investigators should create a schedule for dispensing and returning study medications, and provide clear instructions for nursing home staff regarding drug study orders and dosing instructions, Segal advised. Patient documentation problems can be avoided by providing nursing home staff with easily understood descriptions of the study's inclusion and exclusion criteria and by conducting thorough and regular chart reviews.

Although tracking down patient LARs for consent purposes can be difficult, researchers should look to the nursing home's billing department or the social services administration to track down that individual, Segal said.

To accommodate nursing home staff turnover, sponsors should provide regular ongoing study training for the staff. By doing this, sponsors protect themselves against a complete study disruption in the event a key staff member leaves, Segal noted, and may spur greater interest in the study among new staff members. Facilities should also be educated about the FDA and NIH requirements for reporting serious adverse events.

## Planning Ahead

To address concerns about the location of medical records in nursing homes, sponsors should obtain facility storage policies upfront and incorporate the policy into the standard operating procedures for the trial.

Although there is little that can be done to forecast whether a particular nursing home will stay in business or merge with another facility, sponsors should choose sites with positive survey reports.

## A Rewarding Experience

Although nursing home studies may sound a bit daunting, they offer a very large and growing patient population and can be highly rewarding, according to Segal.

"Nursing homes offer increased opportunities for sponsors to diversify their research efforts and can be a very gratifying experience for everyone involved," Segal said. ◆

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with the regulation and how to determine whether to scrap an old system and build or purchase a new compliant system.

Some respondents also were confused about certain technical issues, such as how to transfer data from legacy systems to new applications, how to build local date and time stamps into computerized records and how to tie electronic signatures with electronic records.

Another industry concern was that many currently available computerized systems — particularly vendor systems — do not have the ability to provide computer-generated audit trails as required by the FDA, Grunbaum noted.

"Industry thinks that the FDA is expecting too much," Grunbaum said. "Many believe that the available technology has not matured to the point of being able to meet agency expectations and that clinical investigators and hospitals are not prepared to meet the stringent requirements of the regulation."

## Recommendations

Even though the FDA has agreed with this argument to some extent, it is clear that the agency intends to push forward with electronic records enforcement. Therefore, companies that choose to use computerized systems should heed the following advice, according to Grunbaum:

- document everything in the system, including its hardware, operating system and communications network, and all actions taken in the computerized system;
- maintain a detailed Part 11 compliance plan that describes the system, its purpose and its potential risk factors;
- stay abreast of regulatory developments to ensure ongoing compliance;
- maintain adequate technical resources and provide practical training to staff; and
- use existing regulations and FDA guidance documents relating to good clinical practices (GCPs) as a foundation for establishing and maintaining electronic records.

"M[any] of the quality assurance and process controls that are discussed in the GCP requirements can be applied directly to computerized systems," Grunbaum said. "Investigators, auditors and monitors need to have a good understanding of those principles." ◆