Computer validation rules challenge bio industry

By Kip Wolf

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It's no secret that advances in the field of biotechnology are tightly bound to advances in data processing and information technology. Less well known is the dramatic impact of the criteria set forth by the Food and Drug Administration (FDA) in the Code of Federal Regulations (CFR) on computer validation practices in the biotechnology, biopharmaceutical, medical device and other regulated industries. Simply stated, *computer validation* is the documented process that ensures a computer system is installed as designed, operates to specification, and performs as required. But complying with validation requirements can be far from simple.

Who needs to be concerned with compliance?

Companies that manufacture, process, pack or hold pharmaceutical products must comply with Good Manufacturing Practices (GMP),[1] including computer validation. Companies that use "records in electronic form that are created, modified, maintained, archived retrieved, or transmitted, under any records requirements set forth in [FDA] regulations"[2] must be concerned with computer validation compliance. Companies in pharmacology and toxicology testing also need to be concerned[3]. Companies involved in medical device research and manufacture, biologic license and human subject testing must be concerned due to regulations regarding Good Clinical Practices (GCP).[4] And last, if your company sells products or services to regulated industries, you need to be concerned with compliance.

Owner Awareness and Interpretation of the Rules

Along with GCP, GLP, and GMP, the final rule for the regulation of electronic records and electronic signatures (21 CFR Part 11) makes the task of computer validation compliance more complicated. Compliance with 21 CFR Part 11 is not the responsibility of the QA or Validation department, but the responsibility of the "persons who use closed systems"[5].

Computer Validation Policy

Consistency in the computer validation process is as important as the validation documentation itself. One of the best ways to ensure consistency is for your company to develop and implement a computer validation policy. The policy should describe the company's interpretation of the regulations, rules and other company procedures, and their impact on the validation effort. The validation master plan should reference rather than detail and duplicate the policy, so that policy modifications necessitate changes to fewer documents. Finally, the policy must dictate the full system life cycle approach to the validation effort, beginning with specifications, through validation and commissioning, and ultimately ending with a retirement plan.

Life Cycle Methodology

Using a system life cycle (SLC) model for project management paves the way for a readily validated system. The SLC model is a systematic, phased approach to system

[1] 21 CFR Part 210 & 211; Good Manufacturing Practices (GMP)
[2] 21 CFR Part 11 § 11.1(b)
[3] refer to 21 CFR Part 58; Good Laboratory Practices (GLP)
[4] These include 21 CFR Parts 11, 50, 54, 56, 312, 314, 601, 812 & 814; Good Clinical Practices (GCP)
[5] 21 CFR Part 11 § 11.10

design, development, installation, integration, testing, maintenance and retirement. It imposes discipline on the management of the project that ensures efficiency and quality for the entire life cycle of the system.

The SLC approach starts with preparation of the often overlooked but crucial User Requirements Specification (URS), which enumerates system requirements. The URS and a Quality Plan, including validation plans and risk analyses, are prepared as part of the Request For Proposal (RFP).

Requirements and Validation Documentation

During the development phase, system documentation progresses with a Functional Requirements Specification and Detailed Design Specification, which refine the URS requirements. Vendor audits, along with factory and site acceptance testing, ensure vendor accountability. Meanwhile, a traceability matrix, created directly from the URS requirements, provides a tool to ensure that no requirements are missed in system development, test planning, or qualification protocols.

On-site testing leads naturally and efficiently into validation. Installation Qualification (IQ) and Operational Qualification (OQ) may overlap installation and on-site testing. In Performance Qualification (PQ), system owners put the system through its paces to ensure acceptable accuracy, reliability, and consistent intended performance.

The Final Product

The result of following the SLC model is a comprehensive documentation set that is "readily available for, and subject to, FDA inspection."[6] This documentation, along with ongoing change control and maintenance documentation, provides defensible proof of validation to inspecting authorities.

This article describes best practice approaches to computer system validation, and the approaches familiar to and employed by GxP Data Services. GxP Data Services is a premiere information technology consulting firm specializing in the integration and validation of technology solutions for regulated industries. We provide solutions for compliance with 21 CFR Part 11 and GxP regulations, and have experience working with a wide variety of systems used in GCP, GLP and GMP applications. With experience ranging from bench top laboratory systems to distributed manufacturing and process control systems, we are prepared to design, integrate and validate systems to meet your business and regulatory needs. For more information, please visit our web site at www.gxpdata.com.

Mr. Wolf is president and Chief Executive Officer of Manheim, Pennsylvania-based GxP Data Services. His professional experience includes over thirteen years in Information Technology and over ten years in regulated industries and the Department of Defense.

[6] 21 CFR Part 11 § 11.1(e)