From: OC GCP Questions
To: [redacted]
Subject: Question on Computer validation
Date: Tuesday, September 06, 2016 12:03:00 PM
Attachments: [redacted]

Good afternoon –

I cannot specifically answer your question but can offer the following information on electronic records and validation.

The agency has officially adopted the SAS program as a standard statistical program and recognizes it as validated software. To ensure that an analytical program coded using SAS accomplishes what the user intends, it would be important to perform functional testing on the coded program. Our Part 11 Scope and Application guidance notes that the agency plans to use enforcement discretion with regards to systems/software validation requirements. Since any coded program will be manipulating critical study data, again for this reason, functional testing of the coded program would be necessary.

I would expect an FDA investigator would like to review the records documenting the kind of testing that is to be performed on the coded program, as well as records documenting test results. Because SAS is a COTS program, we appreciate the fact that validation data of the SAS program itself may not be available from the vendor. I would not expect FDA investigators to ask to see validation information on the commercially available SAS program.

Also, the regulations governing electronic records/signatures/computerized systems can be found at 21 CFR 11 (see www.fda.gov/oc/gcp/regulations.html for this and other regulations governing the conduct of research in human subjects). Section 11.10(a) requires that systems used to create, modify, maintain, or transmit electronic records shall employ procedures and controls designed to ensure the authenticity, integrity, and, when appropriate, the confidentiality of electronic records, and to ensure that the signer cannot readily repudiate the signed records as not genuine. These procedures and controls must include "validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records".

This being said, you should also know that in 2003, FDA announced via its publication of the guidance entitled "Guidance to Industry Part 11, Electronic Records; Electronic Signatures- Scope and Application Guidance" that it would use enforcement discretion with regard to specific portions of the part 11 regulation. Enforcement discretion means that FDA will not normally take enforcement action to enforce compliance with specific sections (i.e., validation, audit trail, record retention, and record copying requirements of part 11) provided the records still comply with predicate rules. FDA notes that it can take regulatory action for noncompliance with those predicate rules. (In the case of clinical trials, predicate rules are customarily accepted as those found at 21 CFR 312, 812, 511, 50, 54, and 56.)

As you can see, validation is one of the part 11 controls for which FDA has elected to use enforcement discretion (see Section III.C of this guidance). The Part 11 Scope and Application guidance explains that when a company decides to validate computerized systems (and computer software), and decide on the extent of validation, that it take into account the impact the systems have on the company's ability to meet predicate rule requirements. A company should also consider the impact those systems might have on the accuracy, reliability, integrity, availability, and authenticity of required records and signatures. Even if these is no predicate rule requirement to validate a system (as is the case with regulations governing the conduct of clinical trials), in some instances it may still be important to validate the system.

FDA recommends that a company base its approach to validation on a justified and documented risk assessment and a determination of the potential of the system to affect product quality and safety, and record integrity. For example, validation would not be important for a word processor used only to generate SOPs. However the extent of validation efforts to evaluate the performance of database

and/or analytical software would be because data created, maintained, and archived in these software programs will be relied upon to meet the regulatory requirement that study records be accurate and complete [see 21 CFR 312.64(b) and 21 CFR 812.140(a)].

For data accuracy (and in the case of system/software validation), we rely on sections 812.140(a) for devices and 312.62(b) for drugs as the basis for requiring that all data (e.g., case histories and supporting data) be accurate, complete (and with devices, current). These regs lead us to the question: "How can data be considered reliable when entered/created/stored/ etc. in a computerized system?" We conclude that the system must be validated for this to happen. The level and frequency of validation efforts will be dependent on the conclusions a firm makes through its risk-based analysis.

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov should you have additional questions.

Kind regards,

Doreen M. Kezer, MSN
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Office of Good Clinical Practice
Office of the Commissioner, FDA

From: [redacted]
Sent: Friday, September 02, 2016 6:16 PM
To: OC GCP Questions
Cc: [redacted]
Subject: re: Question on Computer validation

Hello FDA staff,

We have 3 desk top computers with SAS on them (SAS stand-alone installations). On these 3 computers, we conducted the SAS Operational qualification and the SAS installation validation. Please advise if we only need to validate these 3 computers in which data manipulation is done on the desktops or do we also need to validate the central location where the files are stored. Additionally, please advise if we need a CSV also.

Thank you for your guidance and assistance. We look forward to hearing from you soon.
Kind regards,

[redacted]