Paper 232-27

Is It Harder for a Pharmaceutical Company to Move from SAS® V6.12 to V8.2 Than It Is to Qualify for the World Cup?

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ABSTRACT

This paper will discuss the experiences of a pharmaceutical company during the validation of their SAS® environment.

The validation takes place as part of the migration from SAS V6.12 to V8.2. However, the discussion on the validation process could apply to any upgrade between SAS versions.

The current regulatory requirements will be discussed and the degree of validation necessary for SAS and the hardware it resides on. The members of the project team and their role in the validation process will be covered and a general overview of the documents required. The areas that should be considered for testing are summarized. And finally, the importance of training the users and the format of this training will be debated.

As a break from the world of validation, during my presentation I will also present some quotes which will highlight the difficulties in qualifying for the football world cup. These quotes are not included in this paper.

INTRODUCTION

Migrating from one SAS version to another should be a simple process for the single user. For a a large scale company with over 400 SAS users this process requires extensive planning.

In the pharmaceutical industry regulations since 1997 have addressed the validation of software and harware as a regulatory requirement. The forward thinking companies are acting on these changes by validating all software and harware used to produce data for regulatory submissions. The Boehringer Ingelheim company wide move from SAS V6.12 to SAS V8.2 was seen as an ideal opportunity to start this validation process, as it is the first major version change under the new regulatory requirements for validation.

This paper will discuss how a company tackled one slice of this validation headache by setting up a project team to validate their SAS environment. This was not a simple project and the validation required almost a year to complete.

On the positive side, now that this process has been performed once, it will make the move to future SAS releases a more straightforward task. This is especially true since the majority of the documentation required relates to the hardware and not the SAS software. This documentation will need to be reviewed for future SAS releases (every 2 years) but the majority will remain unchanged

REGULATORY REQUIREMENTS

I can only discuss the regulatory requirements for validation from the perspective of the pharmaceutical industry.

The regulation which has the greatest effect on the pharmaceutical industry is the FDA 21 CFR Part 11 for electronic signatures and records. It states that “under the controls for a closed system certain procedures and controls need to be followed. These should include validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records”.

I will not go into this definition in any further detail but the message is that in order to use electronic submissions, validation is a regulatory requirement. The definition of what level of validation will be discussed in the next section.

In addition to the regulatory requirements, Boehringer Ingelheim have adopted the standard that all software/hardware is validated if it is used to import, manipulate or report data used for a regulatory submission.

VALIDATION VERSUS QUALIFICATION

As a company we had already validated other software products, some specific to Boehringer Ingelheim and some tailored to our own environment. SAS is a product we have used for many years and have had vast experience working with. In the majority of pharmaceutical companies SAS is the standard software used for analysis and reporting. Regulatory authorities are familiar with SAS and comfortable receiving SAS data sets or programs.

Regulatory requirements only state validation as a requirement via the FDA 21 CFR Part 11 regulation. There is no regulatory guideline which discusses validation outside of the area of electronic signatures.

So the question we asked ourselves, was do we need to perform a full validation on SAS? With the current regulations the answer is no but seeing the speed of change in this regulatory area it would be unwise to do nothing. The main point that came out of all discussion was that it would be good business practice to perform a validation but from a resource point of view extremely intensive. As an alternative it was suggested to qualify SAS instead of validating it.

Qualification of computer systems is done because, while no regulatory requirement clearly indicates the need for validation, the activities the system is used for is critical in nature and/or closely supports a regulated activity. The driving force for the activities that take place in computer validation is regulatory compliance. In qualification of computer systems the driving force is elimination of business risk.

A document was then produced which listed all the main steps in the validation process, beside each of these was placed an importance flag relating to the qualification of SAS - “Not Required”, “Desirable” and “Highly Desirable”. Therefore, while some tasks were highlighted as desirable or highly desirable – none were mandatory, as is the qualification process itself. It was done merely as good business practice.

PROJECT TEAM

One of the first tasks in the project was for me as project leader to pull together all the experience that would be needed to perform the qualification. The final project team contained the following members:

Project Leader
Validation Manager
Validation Consultant
Quality Assurance Consultant
Information Services (IT) Member
Oracle Clinical Team Member
CARE Team Member
SAS Expert

As project leader my main responsibility was to co-ordinate the group towards achieving our main objective of migrating to SAS V8.2 by the end of March 2002. This involved producing a detailed project plan, highlighting pivotal tasks and the timelines associated with them. This plan continued to evolve throughout the qualification process.

Two project team members were specific to our environment at Boehringer Ingelheim. Firstly, the Oracle Clinical (OC) team member, who was required to assess the impact moving to SAS V8.2 would have on our database. Test cases were created to ensure all interaction between the two sets of software would remain the same after the migration, or if differences existed then we were aware of the them. Secondly, a CARE (Clinical data Analysis and Reporting Environment) team member was included. The CARE environment was created by Boehringer Ingelheim and is our main link between SAS and the reports that we send to the regulatory authorities. Extremely detailed test cases already existed for testing new versions of our CARE environment. These were used to test the effect moving to SAS V8.2 would have.

The validation manager is responsible for producing some of the main documents and also for collating all the documents produced by other project members. They will also conclude the qualification by writing a close out report.

The validation consultant, quality assurance consultant and SAS expert assisted by advising the group and reviewing the documents produced.

The IT member co-ordinates all IT aspects of the qualification regarding hardware and the SAS software. They should form a sub-team of IT representatives with all countries involved in the qualification process.

DOCUMENTS REQUIRED FOR VALIDATION

The main documents required for the qualification process are as follows:

- Project Plan
- Project Request
- Functional Requirements
- Functional Specifications
- Risk Assessment
- Qualification Plan
- Qualification Protocol
- Installation Qualification (IQ)
- Operational Qualification (OQ)
- SOP's
- Test Strategy
- Functional Test Plan
- Functional Test Cases
- Training Plan
- Training Documentation
- Document Archive
- Qualification close out report

The following sections will now give a brief overview of each of these documents.

PROJECT PLAN AND PROJECT REQUEST

The project plan has already been discussed. The project request document is written by the company SAS sponsor and explains why the project was created and its main purpose.

FUNCTIONAL REQUIREMENTS AND SPECIFICATIONS

The functional requirements and specifications describe what tasks we as a company require SAS to do. This is useful when assessing if SAS meets our current needs and can be a basis for looking at other packages as an alternative to SAS. For example, as a company we now require output to be produced in HTML. Does V8.2 of SAS meet this requirement?

RISK ASSESSMENT

This document highlights any risk in performing the qualification. It should not just focus on areas of greatest risk but also areas with little or no risk. For example, the reason behind performing a qualification and not a validation should be discussed here.

QUALIFICATION PLAN AND PROTOCOL

The qualification plan gives an overview of the qualification process:

- the scope of the qualification,
- roles and responsibilities
- project organization
- description of our usage of SAS
- sites involved
- documents required
- process for re-qualification

The purpose of the Qualification Protocol is to describe in detail the qualification activities outlined in the Qualification Plan. It is here that much more detail on the IQ and OQ documents should be given. The appendices contain many of the forms required for verification of validation activities.

The qualification plan and qualification protocol are written by the validation manager with input from the project team.

INSTALLATION AND OPERATIONAL QUALIFICATION

This is a massive part of the qualification process and concerns not just how we install our software and how we are going to be using it. It also involves qualifying the hardware we put the software on. The benefit of a qualification is severely reduced if we have qualified software located on unqualified hardware.

The Information Services member of our team was responsible for all the activities in this area and the completion of many required documents.

I do not want to go into the details of either the IQ or OQ as this could be a paper in itself. Much of our discussions at the project level revolved around some of these questions:

- How will the test cases be run without giving all SAS users access to V8.2?
- How will we qualify a server which is currently in use when we need to re-install the operating system?
- The test server should be separate from the production server, is this possible with the servers we have available?
- SAS output is stored on a separate server at some sites to the server the SAS software is on. Do we need to qualify these additional servers as well?

Most of the issues involved the hardware and not the software and was a direct result of not having a qualified server to run SAS. One message for the future is that new servers should be qualified as soon as they are purchased and before any software is loaded.

STANDARD OPERATIONG PROCEDURES (SOP)

Any SOP's related to the qualification should be documented in the qualification plan. The SOP's should be updated as part of the qualification if they are now out of date.

TEST STRATEGY AND CASES

The project team produce a test strategy based on what they feel is necessary to qualify the environment. Testing should discover any changes or potential changes, which might occur when the new SAS release is rolled out. Some of the findings should be included as part of the training material. Testing, including the test cases, will be discussed in more detail later in the paper.

TRAINIING PLAN AND DOCUMENTATION

The training plan highlights the who, what and where of the proposed training. The training documentation is the material that will be disseminated or presented to the SAS users

DOCUMENT ARCHIVE

How will all the documents relating to the qualification be stored? What filing structure? Electronic and/or paper copy? At more than one site?

CLOSE OUT REPORT

The final assessment of the qualification, checking that all necessary documents have been completed and signed off. A discussion of any omissions and the reasons behind them is included. This task is performed by the validation manager.

TESTING SAS IN OUR ENVIRONMENT

The testing performed for our qualification did not include any formal testing of SAS itself. Any changes or bugs are documented by SAS and it was not the task of the qualification to detect any that were missed.

The standard test streams provided by SAS were used to check SAS functionality at each site after the new version was released.

Although no formal testing of SAS was done, informal testing was used. We wanted to know how the new version of SAS was going to affect our environment. Sixteen users were asked to use the new version of SAS for two months and record anything they felt would be useful to new users of the SAS version. The following questions were asked:

- What new functionality is most useful to Boehringer Ingelheim?
- What functionality is difficult to understand or implement?
- What tips can we give new users?
- What SAS bugs (if any) were found?

The results of the testing were very positive for the new version of SAS. We collated all the comments from each of the users and created a "Boehringer Ingelheim Guide to SAS V8.2". At the training the document was discussed and it's benefit for new users highlighted.

The other test cases that were run included a complete comparison of a single clinical trial, compatibility with O*C and compatibility with CARE. Performance testing at each of the sites using SAS was not within the remit of this project but was assessed by another group.

TRAINING THE USERS

At Boehringer Ingelheim we have more than 400 SAS users worldwide. We also have many different levels of experience in SAS, data managers, programmers and statisticians. The level of interest in SAS also had to be considered. For example, some statisticians program just to get the required output, others want to know how SAS calculates the output and how the program can be made more efficient and re-usable. Another major factor when presenting the training worldwide was language differences.

The main subjects for the training were agreed as:

- How the SAS environment has changed
- The ODS system
- Changes that need to be made to old programs so they produce identical output in V8.2
- Features we can use in V8.2 to make our programming more efficient

Two methods of giving the training were discussed.

Demonstration with a projected computer screen, with each user having access to a computer terminal. The difficulty with this method was mainly the large number of users to be trained. Would we have adequate computer facilities at each site to be able to train in this way? Additional supervisors would be needed to try and gage the level of understanding of the material and help balance out the different levels of experience in SAS.

The alternative was for the users to follow a presentation with screenshots and interactive sessions, but no hands-on experience. This is easier to mange but less effective, although was our only option due to the difficulties with the first option. To help with the difficulty in keeping attentive for long periods of time the presentation was broken up by several interactive tasks that could be performed without a computer.

IS IT ALL REALLY NECESSARY?

With previous releases of SAS we moved to the new version within a

few weeks. This project started in May 2001 and will finish with the roll out of SAS by the end of March 2002. So was this drastic change necessary?

The qualification of Boehringer software and hardware is a compnay requirement. It is also a regulatory requirement for electronic signatures. Most importantly, it's good business practice!

One important aspect is that for future upgrades to new SAS versions the majority of the work has now been completed. The major tasks in qualifying any new versions will be the running of the test cases.

CONCLUSION

Validation is now a regulatory requirement for electronic signatures in the pharmaceutical industry. It is likely that this will expand to include other regulatory areas.

Informal testing of SAS is a useful tool as it benefits by testing without constraints and in your own SAS environment.

Careful thought should be given on how we train users in a new version of SAS. The right training in a new version will gain the support of the users and help them understand how it can benefit them most. The alternative may be a resistance to change.

Moving versions of SAS is no longer a simple task if validation is going to be considered

The majority of the documentation has been completed and hardware qualified. Hence, future migrations to new SAS versions will be much easier than this one.

REFERENCES

FDA 21 CFR Part 11 Regulation for Electronic Signatures (this can be ordered via the www.fda.com web site)

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