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Qualification of Windows Servers (Part 1)

IT Quality in the Life-Science Industry

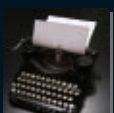
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Compliance Corner

A Pragmatic Approach to the Validation of Excel Spreadsheets – Overview

Many GxP critical spreadsheets need to undergo validation to ensure that the data they generate is accurate and secure. This paper describes a pragmatic approach to the validation of Excel spreadsheets using the principals of GAMP 4. The validation lifecycle requirements are met using a generic documentation set which allows spreadsheet validation and implementation with two documented deliverables. Compliance with the user's applicable regulations is achievable using this flexible and cost effective process.

By David A Howard & David Harrison

Key Words: Validation, Compliance, Spreadsheets, MS Excel, 21 CFR Part 11, Pharmaceutical, GAMP, GxP, GLP, GMP, GCP, End User Computing.



Introduction

This is the first of a series of short articles describing a generic process, as developed by ABB Engineering Services, for validating Excel Spreadsheets; future articles in this series will include the following topics:

- A Pragmatic Approach to the Development and Specification of Excel Spreadsheets
- A Pragmatic Approach to the Testing of Excel Spreadsheets

It is recognised that Excel Spreadsheets have been widely used in all industries for many years. A major attraction of spreadsheets is their ease of use and flexibility – anybody with a minimum amount of training/experience can create and modify spreadsheets. The downside of this versatility is the potential for developer and operator error, and the difficulty in verification of the spreadsheet and the data it produces. Additionally there are inherent security and audit

trail deficiencies in the standard MS-Excel product, leading many experts to consider spreadsheets as 'unvalidatable'. These factors have led auditors to consider spreadsheets as a common system in which data can be incorrectly calculated and reported, both due to accidental, and intentional operator actions.

Many companies within the pharmaceutical industry initially took the approach of removing, or at least planning to remove, spreadsheets from all critical areas of the business. This approach has had some success; however it has been an extremely costly and time-consuming process and is by no means complete except in a handful of companies. Often the replacement of Excel simply moved the compliance concerns to other systems, and the process of migration greatly inconvenienced a large user base of experienced Excel users and in-use spreadsheets. In addition change always brings about a level of risk, and often migrating the process to a new system actually increases the risks to the data, especially in the short term. Many companies are confident in their data produced from the Excel processes, but have found it difficult to demonstrate that confidence to inspectors and auditors. The argument for maintaining the use of Excel, but in a controlled and validated process is therefore well founded.

ABB have developed and optimised the validation approach outlined in this series of articles over a number of years, enabling implementation of compliance improvements and improved business processes whilst continuing to use Excel. A major benefit is that the process can be implemented rapidly in all regulated environments; it has been successfully applied to many hundreds of spreadsheets in major pharmaceutical companies worldwide.

Does the spreadsheet need to be validated?

One of the first things that need to be determined is whether or not the spreadsheet needs validating. There are two related questions here

- a) Does the data flow involve GxP critical data that needs to be validated? and
- b) Which spreadsheets within that data flow should I validate?

The answer to both of these questions can be determined by producing an inventory of all spreadsheets and then performing a risk based assessment of the data used, the functionality of the spreadsheet, and the data reported.

These principal questions should address whether the spreadsheet is used to support an activity governed by any applicable regulation, typically GMP's^{1,2}, GLP's^{3,4}, ERES⁵, Medical Devices⁶ etc.; if the answer is Yes, then the simple answer is that it should be validated.

Field audits have demonstrated that 94% of real-world spreadsheets contain errors⁷. It therefore makes good business sense at this stage to analyse the 'business impact' of each spreadsheet to ensure that all critical spreadsheets are documented and checked to ensure they are accurate. Financial spreadsheets are increasingly becoming subject to scrutiny to ensure compliance with regulations such as the 2002 Sarbanes-Oxley Act. Although the "validation" process described in this series of articles has most commonly been used for compliance with pharmaceutical regulations, it is simple and flexible and can be applied to all spreadsheets to provide assurance that the system performs as intended.

The resulting spreadsheet inventory should assign a priority for each spreadsheet and thus a framework for the validation project. The maximum gain will be achieved by concentrating effort on the spreadsheets with highest regulatory and business risk; these should all be completed prior to commencement of work on the lower risk spreadsheets. There is usually no correlation between regulatory risk and spreadsheet complexity, but if possible, dealing with high risk yet simple complexity spreadsheets allows a ramped introduction to the topic, and allows compliance teams to become familiar with the spreadsheet validation process.

Project/Validation Preparation

Project planning is essential for the successful execution of any validation exercise; this is particularly true when embarking on spreadsheet validation. It is likely that a large number of spreadsheets will be involved and therefore efficiency and repeatability are critical factors in the validation process; the key to the efficiency and minimising the validation costs is to keep the process simple. This is achieved by introducing streamlined processes throughout the validation lifecycle, and the use of a generic yet adaptable set of documentation.

It is essential that the validation process is documented and commonly this may require a formal Validation Plan to satisfy local procedures. Alternatively it may be possible to document your process in other project documents such as Standard Operating Procedures (SOP) or the Spreadsheet Specification. However, one of the biggest strengths of a Validation Plan (and subsequent Validation Report) is that it presents an excellent "condensed" document set to present for an inspection. It demonstrates you have a well thought through and controlled validation process, and the Report summarises the outcome and validated status of your spreadsheets. For any project with more than a few spreadsheets a Validation Plan is highly recommended.

A formal validation plan should where possible cover all spreadsheets in the company/department. This can be achieved by cross-referencing the spreadsheet inventory as a separate 'living' document. The production of separate validation plan for each spreadsheet should be avoided – this is simply duplicated work and additional documentation.

Resources

Many spreadsheet projects fail due to a lack of communication between the spreadsheet users and the people responsible for validation of the spreadsheets. It cannot be over emphasised how important it is to get full and complete buy in from the spreadsheet users. The key reasons for this are detailed below.

- Often the spreadsheet users were the developers of the spreadsheet, and they have both intimate knowledge, and a sense of ownership of their creation.
- The users know where and how the spreadsheets can be improved, and exactly where the deficiencies lie between the spreadsheet and the business process being undertaken.
- The users are the people who defined the User Requirements, and an error when defining the requirements cascades throughout the lifecycle to result in a spreadsheet that may not be fit for purpose.

The user/owners invariably have the highest burden to bear during a spreadsheet validation project, their buy-in is critical to remaining on time and on budget. The project should be planned such that they are fully aware of the benefits of validation, and wherever possible additional benefits, such as improved working practices, should be incorporated.

Action should be taken at an early stage to resolve any resourcing issues; and it is recommended that suitable temporary/contract staff are recruited if there is any doubt as to the availability of internal resources to complete the project on time. In a project where repeatability and efficiency are key factors, the project team need to maintain a momentum to get maximum benefit from the streamlined process.

Inventory Review

Following on from the inventory generation described in section 2.0 the inventory should be reviewed with the goal of minimising the workload and simplifying the inventory.

Often the spreadsheet inventory will include 'populated' spreadsheets (i.e. ".XLS" files) containing data and it is strongly recommended that these are NOT subjected to validation in their native format. In order to facilitate validation, it is preferable to install controlled and 'empty' spreadsheet templates (i.e. ".XLT" files); hence some reformatting / data cleaning will be necessary prior to validation. This reformatting step (see Section 3.4) is an opportunity to review and rationalise the spreadsheets that are going to be subject to validation. An inventory review should be performed with the following questions in mind:

- Are there any new requirements for existing spreadsheets?
- Can any spreadsheets be combined to produce a single template?
- Can spreadsheets be 'genericised' to allow future flexibility?

The combination/genericisation steps are crucial to reducing the validation workload; the following are examples of how this can be achieved:

- Use multiple worksheets in a single template.
- Make column headings data input areas.
- Add extra input areas to a worksheet to allow it to be used for multiple purposes.
- Add configuration sheets/tables and lookup cells to allow future modifications with minimal/no revalidation effort.

ABB managing compliance enabling performance

ABB is an international technical consultancy providing a range of services including licence to operate, asset management, manufacturing improvement and capital investment to customers in the Life Sciences business sector.



ERP Systems

ABB is a world leader in helping clients manage and implement ERP systems to achieve early success and payback from IT investments. Our proven SAP validation approach centres on a holistic analysis of how the system is integrated with the business operation, directly aligning business and project aims. Combining experienced leadership and our ERP project accelerators we can deliver high quality ERP validation projects at up to 30% less cost.



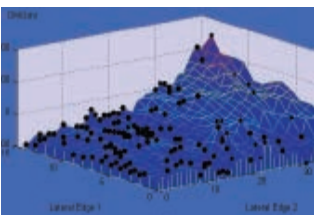
End User Computing

End User Computing provides the optimal environment for users, however the inherent flexibility can bring compliance concerns and lead to extended validation effort. ABB are the world leaders in spreadsheet and database compliance, providing cost-effective and pragmatic solutions through the use of technical controls and efficient validation processes. Our proven turnkey solutions ensure your systems meet both regulatory and user requirements.



Computer Systems

ABB has a proven track record in providing world class consultancy and validation on Computer Systems (DCS, PLC, WMS, LABS, LIMS etc) throughout the pharma industry. Whether on new implementations or upgrades, the combination of our widespread experience and risk based approach to validation ensures a cost effective, pragmatic solution that fits your business, resource and budget needs.



PAT

Quality by design (QbD) concepts based on Process Analytical Technology (PAT) is fast becoming a corporate development imperative for many of our pharmaceutical clients. ABB are at the leading edge of this drive, combining our excellent technology, regulatory consultancy and change program management skills to offer the perfect technology partnership for our clients.

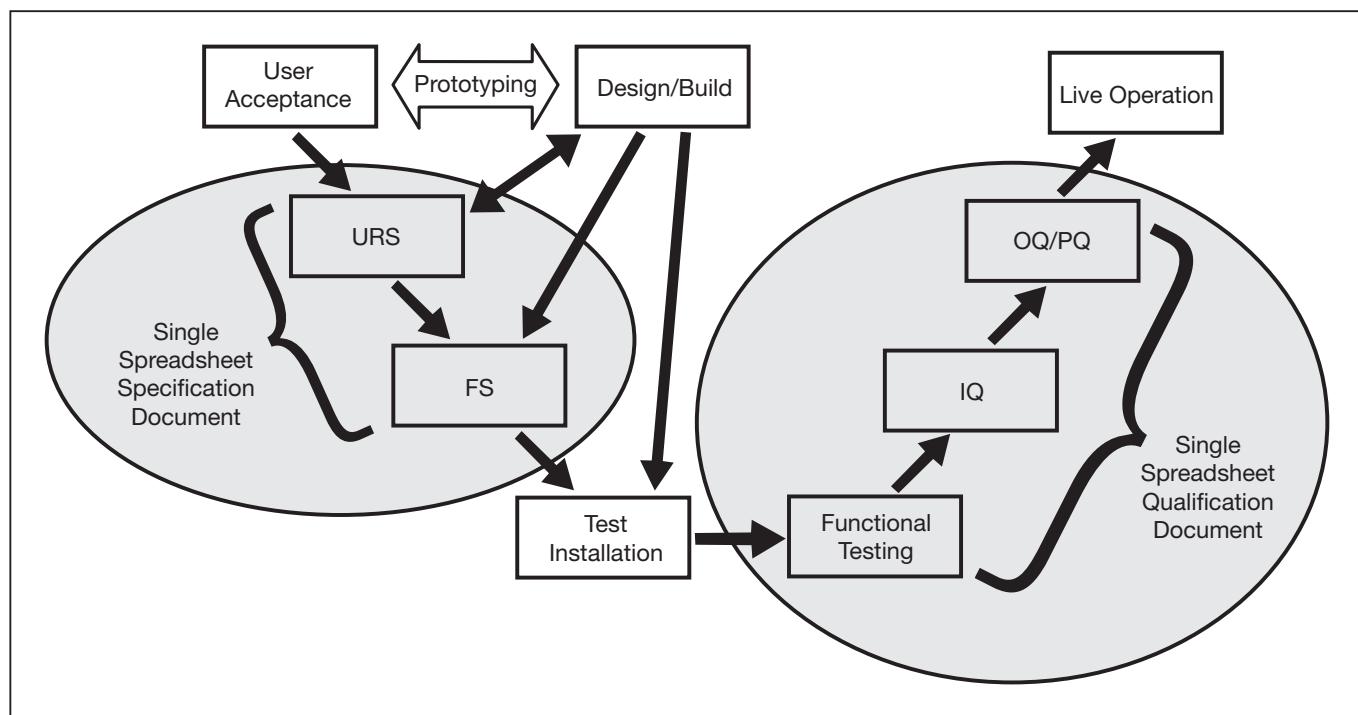


Figure 1: Amended V model for Excel Spreadsheet validation

Spreadsheet Validation Lifecycle

The simplified software development lifecycle (SDLC) for validating spreadsheets is depicted in Figure 1.

The principal features of this simplified SDLC, and key considerations for a cost-effective validation, are summarised below:

User Acceptance

The 'final' spreadsheet design is developed in conjunction with the end-user(s) via a 'prototyping' methodology. Excel is an ideal tool for rapid application development and prototyping. In many instances the user will already have developed a "working" version and may even be in a position to submit the final design without modification. This prototyping process allows flexibility, is amenable to change/improvement and ensures communication between the developer and the end user.

When a final design has been agreed by the user, the spreadsheet must be locked down and further development stopped. Strong project management is required at this step to avoid the danger of 'scope-creep', the tendency of users to modify and extend their requirements throughout the project. The recommended approach is to baseline the agreed version, and any subsequent requests for change are forced into a separate project. Failure to manage this stage results in a never-ending "improvement" cycle resulting in no finalisation of the validation.

Spreadsheet Specification

A User Requirement Specification (URS) and Functional Specification (FS) are only produced once the spreadsheet design has been locked down. The URS and FS are combined into a single document generated from a generic specification template. The main body of the document is very generic, requiring only minor modifications for most spreadsheets, with a number of appendices containing the specific spreadsheet information.

Spreadsheet Specifications will be covered in more detail in a future article.

Spreadsheet Qualification

A qualification document is also produced once the spreadsheet design has been locked down. This is developed from a generic document template with separate appendices covering functional testing, installation qualification, and operational and performance qualification. The appendices provide flexibility to add additional specific test scripts for any 'non-standard' spreadsheet functionality; typically this would include functionality such as macros or data import/export.

The qualification document optionally includes a summary report sign-off page that acts as an authorising report for final approval of the spreadsheet template.

Spreadsheet Testing/Qualification will be covered in more detail in a future article.

Live use

Prior to live operation, a number of procedures need to be in place, checks are incorporated in the spreadsheet qualification for the presence of a specification, backup/restore procedure and a spreadsheet operation SOP. Additionally the following procedures (which may be generic departmental SOPs) may need to be in place to ensure compliant operation:

- System administration including system access/authorisation
- Error logging / resolution
- Routine testing / Periodic Reviews / Re-qualification.
- Change Control / Configuration Management.
- Disaster Recovery / Business Continuity
- Records Retention
- Decommissioning / Data Migration procedures

Spreadsheet reformatting

Design, development and reformatting of the spreadsheets should be performed with a view to facilitating validation. If spreadsheet reformatting is to be performed repeatedly in-house, it is preferable to have predefined design guidelines

and standards. When the work is contracted out then the design standards should be agreed in advance, typical guidelines to be followed include:

- Workbooks should have an ‘intuitive’ lay-out with discrete/manageable sections, for example separate areas for data input and results
- Where possible lookups should be used to “pull” data from other locations and worksheets rather than having repeated data input areas.
- Macro use should be kept to a minimum, especially if they are not critical to the accurate or efficient use of the spreadsheets. Macros can save time when in use, but will bring an additional burden for validation.
- Incorporate any add-in modules such as electronic signatures and audit trail modules (see Section 3.5), so that they can be validated as generic systems/modules, and then do not require full validation on every spreadsheet.
- There should be a consistent ‘look and feel’ to all spreadsheets, e.g. colours for input cells, consistent use of comments and cell validation etc. This will assist in user training and acceptance, and aid the implementation of a single spreadsheet operation SOP.

Technical Controls

In order to meet specific regulations, for example audit trails within 21 CFR Part 11 [5], it may be necessary to add additional technical controls to Excel. These controls can normally be added in one of two ways.

- Custom developed macros and functionality provided either on a spreadsheet by spreadsheet basis, or as a

generic module which is added in the same format to multiple spreadsheets. These customised developments will generally be classed as GAMP category 5 software [8], and as such merit a rigorous validation effort due to the risks associated with customised application and coding.

- Third party software packages that add additional technical controls to the Excel environment. These off the shelf software packages will generally be classed as GAMP category 3 / 4 software⁸, and as such require specific validation.

When either of these “add-on” options are implemented, the project should be planned such that the validation effort be performed only once for the add-on. Each subsequent spreadsheet validation should then reference the add-on validation. The investment in additional, extended validation of these types of add-on components is usually repaid as it reduces the effort required to show security and traceability on each individual spreadsheet. The larger the spreadsheet inventory, the more beneficial these options become.

These options are most commonly used to comply with the necessary technical controls of 21 CFR Part 11. A typical spreadsheet validation project would include the installation of these additional controls, combined with the implementation of multiple spreadsheet templates. An example process for a project incorporating the DaCS add-on⁹ is depicted in Figure 2. The validation of the technical controls (lower half of Figure 2) is only performed once; the validation of these add-on features can then be referenced on the streamlined validation of each spreadsheet (upper half of Figure 2).

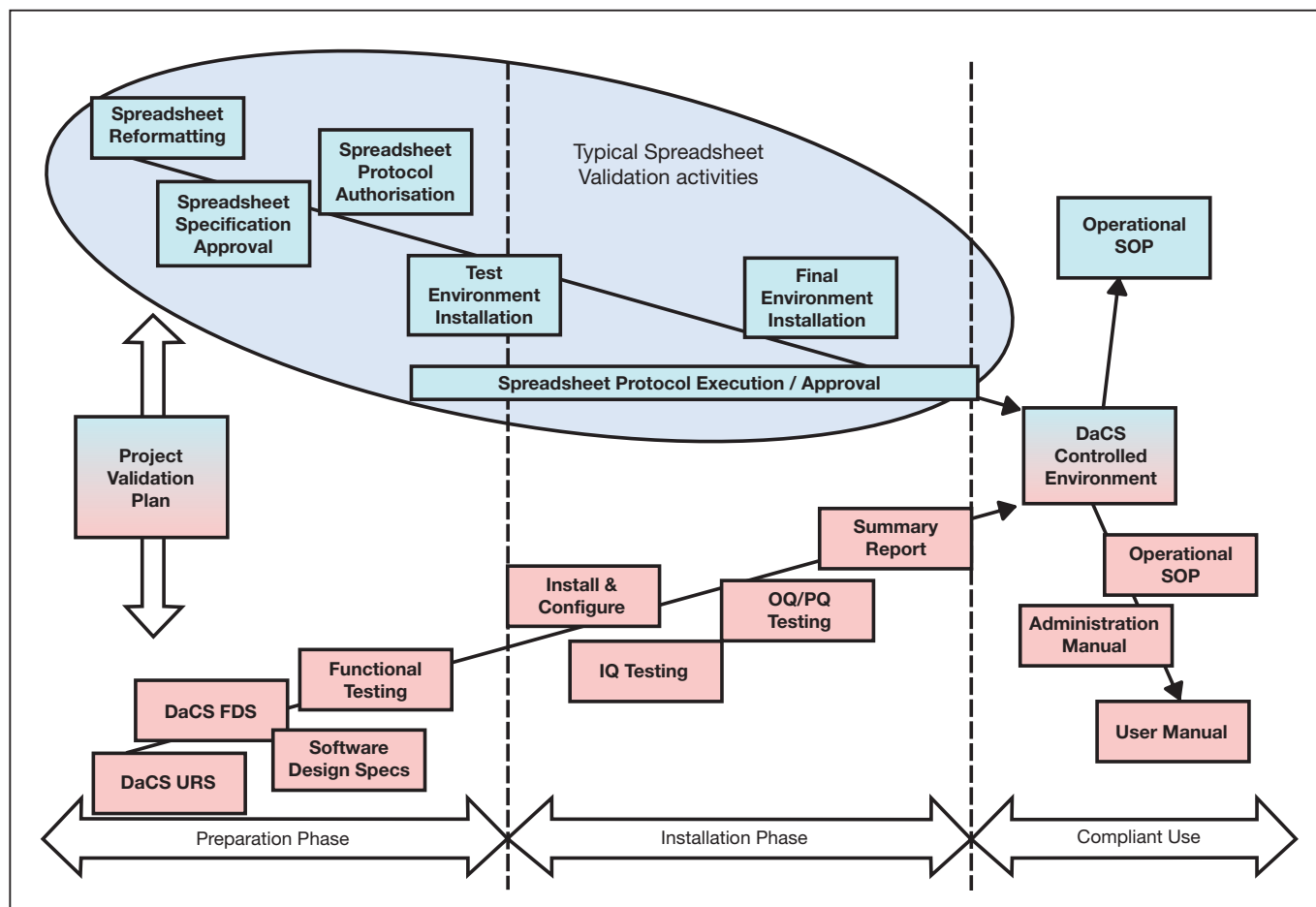


Figure 2: Process Overview including add-on validation

Conclusion

An introduction to a simple, streamlined approach to the validation of Excel spreadsheets has been outlined in this article. This approach condenses best industry practices and guidelines into two generic documents, further details of which will be presented in future articles. Using these principles, the full validation and implementation of a typical spreadsheet can be achieved with less than four days effort.

The approach provides a pragmatic solution to a common compliance concern, reducing risk with a cost effective and repeatable process. The approach can be adapted to any sized inventory of spreadsheets and remains flexible enough to fit into individual company's computer systems validation policies.

More information on spreadsheet validation can be found at www.spreadsheetvalidation.com ■

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