SciTech Engineering

Commissioning & Qualification Team Brief

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ISPE launch GAMP 5

Good Automated Manufacturing Practice.

1.0 BACKGROUND

After over 4 years of re-work the GAMP Guide has been reissued at version 5. Gamp 5 is a major rewrite of the document and also has some significant changes in approach. These changes are to bring the procedure in line with the changing nature of the industry and to reduce cost of compliance.

Below is a summary from the ISPE:

The GAMP Guide has been significantly updated to align with the concepts and terminology of recent regulatory and industry developments.

These regulatory and industry developments focus attention on patient safety, product quality and data integrity. This is a key driver for GAMP 5.

Coupled to this there is the need to:

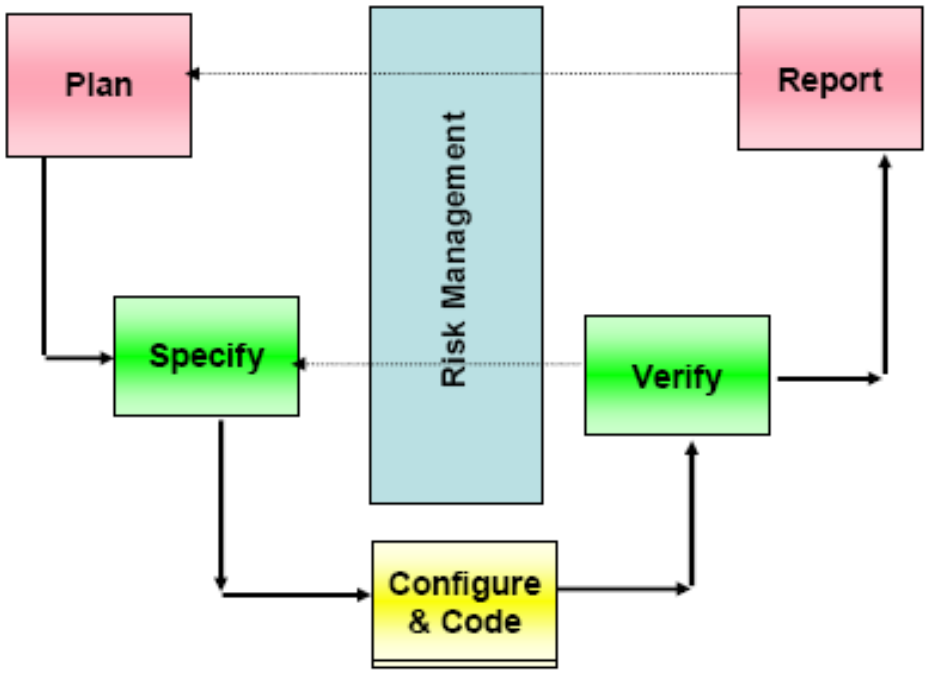
- *Avoid duplication of activities (e.g. by fully integrating engineering and computer system activities so that they are only performed once)*
- *Leverage supplier activities to the maximum possible extent, while still ensuring fitness for intended use.*
- *Scale all life cycle activities and associated documentation according to risk, complexity and novelty.*
- *Recognise that most computerised systems are now based on configurable packages, many of them networked.*
- *Acknowledge that traditional linear or waterfall development models are not the most appropriate in all cases.*

2.0 IMPORTANT POINTS

GAMP 5 is now formally launched and it contains a number of changes from GAMP 4. The biggest change being to provide more clearly defined scalability for effort / deliverables versus the size / complexity of projects, and to align with the various regulatory bodies' emphasis on risk / science-based GxPs.

Below are a few of the important point gained from the launch and pre launch meetings held by the ISPE and the GAMP Forum:

- GAMP 5 is not prescriptive. All lifecycle activities and associated documentation are to be scaled according to risk, complexity, novelty. (Some examples):
  - Risk: manufacturing process control = high risk, database containing training records = low risk.
  - Complexity: SAP = high complexity, Excel spreadsheet calculating lab results = low complexity.
  - Novelty: Excel = used by millions worldwide, lab instrument PC software = used by thousands worldwide, in-house developed application - used only by the company that developed it.
- GAMP 5 - all about risk. Increasing complexity and/or novelty = higher risk = more effort and deliverables.
- Moving away from traditional qualification terminology (e.g. IQ, OQ, PQ). Terminology confuses people outside of the validation and QA departments. Terminology is still available, but optional. See the updated V-Model below



- Most computerised systems now based on configurable packages, many of them networked.
- Validate only if there could be an impact on patient safety, product quality, data integrity. If none of these, no need to validate, good engineering practice is sufficient.
- Need to be clear on the differences between system owner and process owner.
- QA less involved than in the past. For example QA should review a URS against the applicable regulations. URS technical review is for technical subject matter experts (SMEs). QA does not need to sign a design spec, as they do not understand it (technical SMEs to sign). QA can verify that design specs are being produced for projects (i.e. verify that processes are being followed) but QA does not need to sign

every document in a project. In other words QA should sign quality documents (e.g. URS, validation plan), not engineering documents (e.g. design spec).

- Historically far too many signatures on documents, moving to limit to more reasonable numbers. Suggested maximum of three signatures per document (and QA not always needed, as mentioned above) Ask if signatures really add value.
- GAMP category 2 (firmware) has been removed; firmware has become so complex that it is no longer functionally distinguishable from software. Some minor changes to the descriptions of the GAMP category types.
- Important to know if suppliers are outsourcing / off-shoring. Will need careful control of where/how work will be done, whether people are suitably qualified. Also have a Quality Plan with supplier, verify suppliers have quality processes such as continuous improvement, change control, root cause analysis. Support post go-live needs to be considered, especially with small suppliers.
- Leveraging of supplier documents encouraged, but need to carefully evaluate suppliers to ensure that the provided documents will be of suitable standard.
    - Integrate the Life Cycle Phases:
        - Build,
        - Acceptance Testing (FAT/SAT/UAT),
        - Commissioning (“go live”),
        - Qualification.
    - Integrate the Computer System & Process:
        - Function based testing & qualification,
        - Tested with the equipment & process
    - Benefit from previously completed activities:
        - Check it once, but check it at the appropriate time
        - Develop the documents to fully support subsequent activities.
- Avoid duplication of activities, e.g. by fully integrating engineering and computer system activities to make sure they only happen once.
- Moving away from supplier audits. Has proved to be difficult to audit suppliers in many cases (how do you audit Microsoft if you use Excel?). Depending on system risk / complexity / novelty, supplier assessments are fine. (i.e. postal).
- When doing risk assessment, assess the probability of harm to the patient if a fault occurs, rather than the probability of the fault occurring. Also assess the severity of the potential harm. Increasing system complexity = increasing risk likelihood. The basis of all risk assessment is intended to be the understanding of the business process that is being assessed. Risk assessment aligned with ICH Q9.
- GAMP 5 approach is consistent with ASTM E2500-07 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment

3.0 SUMMARY

This new ISPE GAMP guidance is another step in the right direction and a general alignment with industry over the use of a risk based approach to qualification and validation. Again this is nothing really new, and is something that has been adopted by some of the industry for automated systems and new equipment over the past few years, but it has formalised this change.

The only new guidance is the emphasis on system upgrades and changes to existing systems rather than just considering major new builds. This reflects the changing shape of the industry and is a welcome change.

So is this really a big change? Apart from the welcomed clarification of current practice and the emphasis shift to upgrades and changes, I don't think that this makes a real big difference to the approach that we have been taking recently.

What the guidance really does, is fully support manufacturing and validation consultant organisations in defending their risk based pragmatic approach that may have been criticised by some of the more conservative organisations in the past.

I'm sure that the industry will talk about the new GAMP guide for quite some time yet and I will try and keep you all up to date with the current thinking and how this turns out.

Hope this helps,

Best regards,

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