SyberWorks and Veracord GAMP5 Webinar

Attendee Questions

1. In automated medical equipment, is a PLC recommended over, say, a PC with a Windows XP operating system?

To answer your question adequately, we would need more context. Typically, it is not required that PLC must be used if the functionality can be accomplished by other software. Whatever satisfies the user requirement specification (URS) and meets the functional aspects can be used, provided the intended software is kept under control per GAMP and CFR GxP Guidelines. We cannot answer your question in regards to Windows XP about replacing the PLC type software because more information is required on this question to better explain if needed.

2. Do you have any examples of scalability in the validation approach to system changes?

Small change example: A software patch is required for an MES application. Make an assessment within a change management or change order system, write an IOQ test script to meet the CR or CO test objectives, gain preapprovals to execute, and then execute the test script after deploying the code to validation environment. If it passes, then deploy to production and close out the CR or CO. Typically, companies use Trackwise or ARS Remedy for CR or CO management. Other programs are also available and can be used.

Large change example: A version upgrade is required that changes software from non-part 11 compliant to 21 CFR Part 11 compliant as supplied by the vendor. Treat this as a project and perform complete set of validation life cycle documentation and activities. Combine other changes at this time. This would require a revision to URS, FS. DS and development of VP, IQ/OQ protocol with test objectives and test scripts for each or combinations of test objectives.

3. How is commissioning applied by the industry to reduce validation costs?

GAMP V and ICH Q9 are being used in the industry to roll out a risk based validation approach by using a company's quality risk management processes and supporting tools. Commissioning is a terminology to differentiate from validation. Lower risk functionality or components can be "commission tested" and may not need QA approvals, since QA has already approved the risk assessment and risk control strategy supposedly up front. Higher risk ranking items will require full validation testing and QA will have to review and approve the validation package. Also, see other answers below to gain more understanding on cost reductions. Also, ensure a commonly agreed upon template is in place so that time can be reduced on template issues. Make it simple yet compliant by working with quality organization or unit.

4. Are you just concerned about quality requirements here? What about other regulations: SOX, etc?
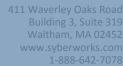
In the context of webinar, we were addressing the compliance related to FDA CFR and other international agencies. SOX is a very important and required regulation on its own. In the case of an ERP such as SAP, GxP, GAMP and SOX would be applicable if the financial module is implemented.

5. Does GAMP5 cover quality systems software validation (for example, training software or document control systems) or just manufacturing systems?

It covers all software systems used including learning management systems (LMSs). Since training records are maintained of the staff performing manufacturing tasks, the LMS becomes part of the whole equation of GAMP V. You should use a risk based validation approach to decouple the non-GxP aspects of a training system. It is a bit tricky to validate such hybrid systems. You don't want to over-validate or under-validate.

6. The problem with using vendor documents is normally the way they document execution. If using vendor documents to leverage qualification, will they be required to follow GDP?

Yes, GDP and GEP both are required of vendors selling into biopharma or medical device industries. However, some vendors cut corners and sacrifice quality and compliance and do not have much documentation to share. A vendor audit can reveal many of these obvious gaps, and you should then take steps to make your validation study more robust to compensate and ensure that critical aspects of software are fully validated and documented. This helps out in production because it helps to avoid many calls to the helpdesk and leaves a better impression on user community of IT teams including validation. Also, look at the track record of the vendor on how many patches they issue per year. This would be one indication that they do not have a good quality system in place throughout the SDLC process.

7. Does the requirements document need to be signed by the quality unit?

Yes. This ensures QA involvement is up front and they would better understand the validation testing package.

8. The history slide references wqCFRPt11 D1, D2 and Final (2007). Was Part 11 reissued? What is the difference between these various Part 11's?

Part 11 came about as a result of the natural increase in dependency on computerized systems in the life science industry. Computerized systems have been governed by the FDA since the mid 1980's, but the technology has evolved significantly. The original regulations presented hindrances, so in 1991 industry representatives and FDA members came together to figure out how to accommodate paperless record systems. That led to 21 CFR Part 11 becoming effective in 1997.

Unfortunately, the life science industry was unprepared both technically and procedurally for the 1997 release of 21 CFR Part 11. Lots of confusion resulted about the scope and enforcement aspects of Part 11, so the FDA released the "*Guidance for Industry Part 11, Electronic Records: Electronic Signatures – Scope and Application*" in August 2003. The objective of that document was to present a more limited scope and to clarify the FDA's current thinking on how Part 11 compliance should be implemented and enforced. In particular, "systems that were operational before August 20, 1997" were grandfathered in, meaning they are not subject to compliance rules. Additionally, the 2003 guidance encourages the risk-based approach. However, the 2003 guidance had some areas that contradict requirements in the 1997 Final Rule.

In May 2007, the FDA issued the final version of their guidance on computerized systems in clinical investigations. This guidance supplements Part 11. The last news is that a new Part 11 will be released on a date that is "flexible."

9. What do you consider the validation cost and non-validation cost of projects?

Validation costs include:

Conducting system impact assessment, risk assessment and risk control strategy, validation plan, all IQ/OQ/PQ, RTM, data migration plan, software test scripts development, test dry runs in IT environment, actual validation testing in VAL or QA environment, documenting and resolving deviation, ensuring SOP and training is complete, and validation summary report. All related activities such as review cycles of URS, DS, FS and editing documents, back/forth discussions, deployment verification and change management tasks.

Non validation costs include:

Requirements development (URS), functional and design specifications (FS/DS), software development and configuration, and actual deployments or installation.

10. Does the 2-5% validation cost reflect that the system was evaluated to be low risk?

The 2-5% validation cost reflects the common relative cost of validation as it relates to all other costs combined, including system cost, overhead of FTE & consulting cost, impact on all involved parties, planning, execution, etc.

11. You say that review time can be reduced using these guidelines. Which roles in a company are required to approve validation documents?

Using risk based validation (provided your company has a guidance document in place for such a standard or quality requirement); the total validation can be divided into two tracks. One track would follow full validation for critical risks identified and mitigation listed in a risk control strategy document. Reviewers/approvers should be at minimum: QA, business process owner (BPO), also known as system owners, and IT validation manager. For the second track, low to medium risk items, only BPO and the IT validation can review and approve the documents, therefore, saving review time needed from QA. The second track documentation can be considered as "commissioning test or CT" as opposed to typical OQ and PQ. CT only scripts can also be streamlined with simple template that has yes/no answers with initials and date as opposed to fully writing out each step with actual results. Only critical steps can be written out to ensure adequate documentation. Of course, any screen shots can and should still be captured.

12. How important is the supplier (vendor audit) qualification, and leveraging the vendors FDS and qualifications for your system intended use? Which audit should be done Postal on-site?

As discussed during the webinar, the vendor audit is a critical component to address any compliance gaps. Especially in COTS configurable packages, make sure a vendor site audit is performed by qualified staffs or a contracted vendor. This is to establish if the vendor has a quality system in place that can be substantiated with documents and testing results. The vendor is responsible for following good engineering practice (GEP), SDLC and any additional guidelines such as GAMP V and 21 CFR Part 11. More often, vendors don't want to release internal sensitive information, so a site visit may become unavoidable. If a postal audit is thorough and can be substantiated with the required documentation, then it may suffice as well. It really depends on the situation. An audit report must be written for internal use only; you don't have to share this info with FDA in my experience. Rather, use this report to gain confidence in the vendor's capabilities to comply with guidelines and an insight into the future software releases.
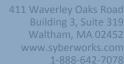
13. How do the system classifications break down in GAMP 5? Are there any changes from GAMP 4?

The GAMP categories have been revised in GAMP 5 and category 2 firmware has been removed. The table below shows the difference.

Category	GAMP 4	GAMP 5
1	Operating System	Infrastructure Software (such as OS, middleware etc.)
2	Firmware	No longer used
3	Standard Software	Non-configurable software
4	Configurable Software Packages	Configured Sofware
5	Custom Software	Custom Software

14. What compliance risks do you foresee at organizations where development teams are isolated in terms of separate business units within the company and pre-agreed-to SLAs that allow the non-sharing of imperative documentation such as hardware and software installation, server maintenance, etc. How can such risks be incorporated in the risk mitigation strategy?

On the surface it seems like a bad idea and indeed a compliance risk to isolate development documentation. There must be an organizational need for such a separation. As such, teams can report to different managers to map the

organizational need, but the information flow within the required validation documentation must exist. There is a way to decouple the infrastructure related tasks and documentation by documenting in the risk assessment and risk control strategy (RA/RCS) of hardware server IQ and database IQ. After you establish this strategy, and have some documented way of managing it, it may be possible to keep these documents in a separate work stream and follow a different process than the application software validation process. We can help design such quality risk management (QRM) approach and document RA/RCS if there is a need from your side.

15. How do you differentiate major and minor changes and change management in terms of implementation?

From what I have seen practiced, minor changes are those that require less than 100 man hours of total work. 100 to 200 man hours are considered medium level changes and should be treated as small projects. 200 man hours or more of work constitute major changes. Minor changes can be bundled in quarterly releases by working and setting expectations with the business user community. We can provide a guidance document to this effect if needed. You should also keep quality gates in mind when processing these changes so the quality by design (QbD) is integrated in your change management process.

16. Compare GAMP5 to IEEE. Is one more acceptable for software development/validation in the Pharma industry?

GAMP V is more prevalent and acceptable in computer software validation and related software development activities.

17. Since GAMP5 actually cuts down on validation activities based on the system risk, does this imply that if we are compliant with GAMP4 that we are actually doing more then would be required by GAMP5, and therefore can draw the conclusion that our CSV process meets the regulation requirements?

The short answer is yes. It is to your company's benefit to take advantage of GAMP V: you declare what guidelines are followed in your validation document so that keeps you compliant.