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Is there such a thing as simple validation?

Recent guidance from the EMA emphasises that the sponsor of a clinical trial remains responsible for the conduct of that trial irrespective of how much of it is outsourced. As a result, CROs can expect continued or greater scrutiny from their customers of their computer systems validation processes and the evidence that they follow them. PHARMASEAL can help CROs efficiently validate our system and provide information and evidence of their compliance to their customers and inspectors.

How can the responsibility for Computer Systems Validation be outsourced?

The EMA Notice to Sponsors on Validation and qualification of computerised system used in clinical trials, on 7th April 2020 states:

> "
> Both Directive 2005/28/EC and Regulation (EU) No 536/2014 contain the provision that regardless whether a sponsor delegates all or part of the clinical trial related activities to an individual or an organization, the ultimate responsibility with regards to the clinical trial conduct — in particular related to the safety of subjects and the integrity, reliability and robustness of the data generated in the clinical trial — remains with the sponsor.

The EMA have recently followed this up by issuing a draft of their comprehensive "Guideline on computerised systems and electronic data in clinical trials" (released for comment on 10th June 2021) which states "Irrespective of whether a computerised systems is installed at the premises of the sponsor, investigator, another party involved in the the trial or whether it is made available by a contracted party as a cloud solution, the requirements in this guideline are applicable".

This responsibility to ensure that the system is being operated, and is working correctly, starts when you implement the system, and continues with each update and change that the supplier makes while you are using the system. With a reputable supplier, this should be a lot easier than doing everything yourself, but still requires you to be able to demonstrate why you are confident that the system is, and will continue to, meet your, and the regulators, requirements and expectations.

The responsibility ultimately lies with the sponsor ,but the operation can be subcontracted to CROs, who can in turn subcontract IT operations to software service providers.

No software vendor can take away the operator's ultimate responsibility to ensure that they are managing their computer systems in a compliant manner but they should have the expertise and capacity to help in ways that should minimise the regulatory compliance burden on their customers.

Change can be seen as a documentation burden in a validated system, but change is a good thing.

You want the systems that you are using to continually develop and improve - that is a key benefit of buying a commercial system.

PHARMASEAL can help you reap the benefit of updates without the burden of excessive documentation.

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What does this mean to CROs?

When a Sponsor outsources all or part of a clinical trial, they are outsourcing compliance with the applicable laws and expectations at the same time. They will also expect that the CRO will ensure that any subcontractors that it uses are compliant as well. The extent to which the customer will verify the CRO's compliance will vary from a quick review to a comprehensive audit.

A CRO can proactively provide a good level of assurance through pre-prepared documentation. This will protect customers that might have done a lower level of verification from unexpected inspection findings, and might preempt customers that might have done a higher level of verification, from digging as deep - hopefully saving both parties time and effort.

PHARMASEAL's Regulatory Compliance Offering:

Computerised Systems Validation is basically just good business practice and PHARMASEAL has a goal of minimising the effort of achieving compliance by eliminating waste through duplicative testing and other activities that do not address the true risks in using our system.

To do this we offer:

1. A ground-breaking continuous validation software development lifecycle (SDLC) that ensures that every change to the source code meets all the validation requirements for release at the time the change is made.
2. A comprehensive Validation Package with every release that you can reference in your validation documentation.
3. A set of Disaster Recovery provisions that protects your data and the system from damage and downtime.
4. Extensive security controls that are compliant with industry standards and ensure our systems are well engineered to resist attacks.
5. An implementation package that includes dedicated validation support, featuring:
   a. 20+ years experience in implementing validated systems
   b. Validation approaches that take advantage of the FDA's Case for Quality initiative and EMA risk-based validation guidance
   c. Customer validation plan, test plan, and validation report templates

When you buy Software as a Service (SaaS), you are buying a working, tested computer system and you should only have to test the way that you set it up and use it.

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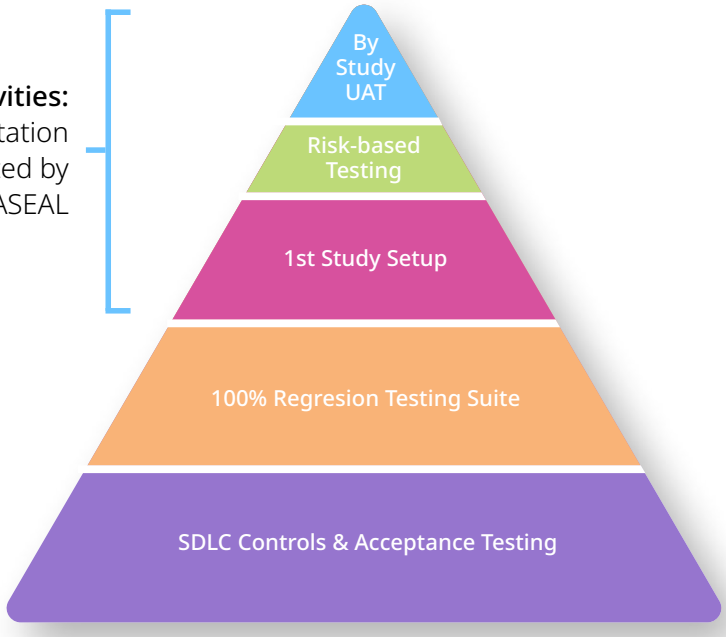
The Testing Pyramid:

Customer Activities:
During implementation and supported by PHARMASEAL



Documented in our Validation Package Accompanying each release

Your validation approach should reflect the testing pyramid:

1. Understand and establish trust in the vendor's SDLC process, including how changes to the source code are specified, tested and accepted into the system.
2. Ensure that you have access to the vendor's testing documentation and how each release is tested before it gets into the production system.
3. When you implement the software, you will spend a fair amount of time learning how to use the software and setting it up to run your first study. During this period you are effectively testing the software and gaining confidence in how it works. If you both plan and collect evidence of your activities during this process, you can use this phase as part of your validation process.
4. Before initial production use, do some risk-based testing. There are some aspects of the system configuration that are higher risk, for example the configuration of role-based user access levels, and you want to have some formal testing of these aspects, such as verifying the access each role has in the system.
5. Each study is different and you want to have a process for the testing or verification of each additional study as it is set up to ensure it is working according to the protocol. This could be a standard process with document templates.

This approach should be topped and tailed with a Validation Plan and Report that explains what you planned to do and how it went.

This should not add a large amount of time to your project and will pay back in terms of your own confidence in the system and your ability to defend your use of the system to inspectors when required (or, for CROs, their customers).

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Summary:

The Sponsor is required by law to ensure that each system that is used to support their clinical trial(s) is validated, and any CRO that provides clinical trial services will inherit this delegated responsibility.

However, the process should not be a burden or complicated. Your software supplier should do most of the work as part of their service and can provide supporting documentation and support so that you only need to add the parts that you need to do.

Below are a few guidelines:

- Plan the validation approach up front so that you can build in documentation creation during the implementation.
- Don't repeat testing that has already been done by the vendor! For example, PHARMASEAL runs thousands of automated test cases on every release so you can have confidence that the system works as specified. You should focus on verifying how you have set up your use of the system, your processes and study designs.
- Use the time and effort you spend setting up your first study to collect evidence that the system does what you need - this can form a significant chunk of your verification testing.
- Use our fact sheets on Disaster Recovery, Security and Regulatory compliance, plus our validation document templates to build a comprehensive but also easy to understand validation package that you can present to inspectors or customers with confidence.

For further information about PHARMASEAL's validation services and the Engility® Trial Management Platform contact **info@pharmaseal.co** today!