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ICH GCP Guidelines Amendments (R2) 2016

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The International Conference on Harmonization of Good Clinical Practice Guidelines, also known as ICH GCP, must be adhered to in US, EU and Japan. However, if an organisation intends to market its drug or device in these territories they need to include these countries/regions in their clinical development plans and consequently observe the guidelines. The addendum to ICH GCP (R2) is due out shortly (expected in November 2016) and organisations need to be aware of the addendum, how it will impact the way they work today and the changes they will need to consider in a relatively short timeframe.

Although a draft guideline was issued, the exact details will not be clear until the final amendment is published, nor it is it clear if there will be a period when organisations will be able to adjust their processes, systems and most importantly the behaviours of clinical staff, to meet the changes required. In order to optimise the efficiency of approaches in line with this opportunity presented by ICH GCP, a fairly rigorous review of processes particularly around quality is needed.

Why is ICH GCP changing?
The last significant change in the ICH GCP Guidelines was around 10 years ago, so why the need for change now? According to the regulators these changes are being introduced because of the evolution in technology and risk management processes and the opportunities these offer to increase efficiency, by focusing on relevant activities.

This is a positive move, recognizing that the clinical trial of a decade ago is not the same as today. Previously the staffing structure on trials both at pharma and investigator sites was simpler, protocols were more straight-forward and generally the execution of assessments was more easily monitored with the consistency of staff and devices. Clinical trials today are much more sophisticated. Protocols are more complex and there are a long list of protocol events, multiple investigators involved and potentially a different nurse for each shift. This can result in protocol assessments being executed differently from day to day. Since the data needs to reflect the evolution of the patients health, not variability because of different approaches in measurement, this can cause issues in the reliability of the data generated.

Due to the change of size and structure of study teams, which may include multiple functions and various vendors, the sources of emergent study data to be analysed and assessed has increased. Clinical monitoring today is more complex. CRAs need to go to multiple hospital departments in order to verify procedural compliance. SDV only verifies errors in transcription between the source and EDC and not the possible variations in the execution of the protocol assessments. In recent years, we have seen some very exciting technological developments which support advanced data analytics and the introduction of medical device and wearables which all bring advances in execution but challenges to regulatory requirements.

And yet, the objective of clinical trials remains the same. We still have to put the patient at the centre of all decisions, enhancing patient safety and being able to confidently rely on the study results, with a protocol, an investigator brochure, essential documents, investigational products and a CRF. The upcoming changes recognize the need for a new approach to enable consistent detection of errors in site procedures, and the detection of trends in possible non-compliance in protocol assessments at site.

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What is changing?

In summary, the addendum focuses on three key areas: technology and systems, risk based quality management and monitoring, and oversight.

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Ã?Â **Technology and systemsÃ?Â**

To encourage sponsors to adopt innovative technologies, the ICH GCP 2016 is introducing a new framework that resolves previous ambiguities in compliance requirements. This is a positive development since previous guidance stifled innovation, at times. There will be an increased requirement to safeguard validity and integrity of data in systems, in particular, over time and as technologies evolve. Organisations will need to manage access and training through technology, specifically to avoid improper use of systems and they will also need to be able to issue certified copies of documents and data.

The guidelines specifies requirements for the validity, longevity and fidelity of trial data as sponsors transition from paper systems to digital records, update their digital systems, or change from one technology to another. It also encourages standard processes to avoid situations where real-time data aggregation and visualisation may inadvertently reveal trial outcomes inappropriately early in the trial process. Finally, to resolve concerns that digital trial databases can obscure unauthorised changes to primary data, the framework expands on the need for control by investigator and institutions of their generated data and documents.

Risk based quality management and monitoring
The changes will impact the focus on relevant risks to human subject protection and study data reliability, with a need to focus

on critical data and processes. It will be necessary to plan, evaluate and control risk more diligently and in a way that reporting of errors can lead to the right corrective actions and show any deviations to the plan. This will require a more adaptive approach than currently exists in traditional monitoring. In particular the guidelines mandate deployment of;
Ã?Â¯Ã?â??Ã?Å? Risk based approach to monitoring
Ã?Â¯Ã?â??Ã?Å? Site and central monitoring based on risk assessment
There will be a need for a process to be in place to systematically address significant non-compliance with root cause analysis and respond with corrective, as well as preventive, action.

Increased oversight
The new guidelines will see the need for sponsors to have enhanced oversight and for investigators to maintain oversight on tasks they delegate, including services deployed to third parties. The investigator and institution will need to maintain control of data at all times and essential documents will need to be provided to sponsor. Sponsors and CROs alike will need to consider how to enable effective and efficient support to sites in order to meet this increased oversight.
There will also be a requirement for sponsors to maintain oversight of tasks delegated to CROs. This will put the onus on CROs to provide effective systems for transparency of data and tasks to enable effective oversight of both their operations and any third parties that may be engaged during the trial. Subcontractors appointed by the CRO will also need to firstly seek the sponsor's approval on delegation.

Increased quality and efficiency
In conclusion, the guidelines are what we need to adjust our processes to the changing paradigm of more complex clinical trials. They herald a more positive approach to integrating technology and a risk management approach that should see an increase in quality and efficiency in clinical trials.

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