Clinical Trial's Role in Compliance and Patient Safety

Although James Lind conducted the first controlled clinical trial back in 1747, it wasn't until The Nuremberg Code in 1947 and The Declaration of Helsinki in 1964 that patient safety in clinical trials became paramount. We now have a whole assortment of guidelines and regulations for clinical trials across the world. How can investigators and sponsors comply with all these rules to ensure that patient safety is protected?

Good Clinical Practice (GCP) was an initiative developed by The International Conference on Harmonization (ICH) back in 1990. Compliance with GCP provides assurance that the rights, safety and wellbeing of trial subjects are protected. It also ensures the clinical trial has credible data, hopefully resulting in a marketable drug at the end (having worked in pharmacovigilance for a few years I sometimes forget the end goal!). The new ICH GCP E6 (R2) Addendum released in November 2016 gives the investigator more responsibility for clinical trial oversight. The investigator can delegate tasks but they are ultimately responsible for supervision. The investigator or sub-investigator must also be a qualified physician. GCP R2 has a new quality risk management section requiring early identification of processes and data integral to patient safety.

Many countries have adopted GCP principles as laws and regulations. The ICH GCP principles are embedded in clinical trials legislation of the UK, European Union, Japan and the United States. So, not only do site staff and sponsors need to get to grips with GCP; they also have to comply with their local regulations too!

The sponsor is responsible for ongoing safety evaluation of the investigational drug. They must notify investigators, regulatory authorities and ethics committees of issues that could affect subject safety. Maintaining safety information and reporting adverse events are critical to ensure that the welfare and safety of human subjects is protected.

Each clinical trial will also have its own set of risks and considerations associated with patient safety. Clinical trial protocols need to be well designed and identify all potential risks to patient safety and include ways to minimise them. Compliance with the protocol is essential for keeping trial subjects protected.

Some of the challenges facing compliance include facilities, equipment, data storage, inexperienced personnel and training. Such challenges are often more common in resource limited countries being used more and more in clinical trials.

So, What Tools do we Have to Ensure there is Compliance to Protect Patient Safety?

Compliance can be measured by checking documents and systems. Inspections and audits of sponsors and sites conducted by individuals independent of the clinical trial also assess compliance. But probably the most important players are the clinical research associates (CRAs). Monitoring of study sites by CRAs involves overseeing the progress of the clinical trial to ensure it is

conducted in accordance with the protocol, GCP and all regulatory requirements. And if it isn't documented somewhere, it didn't happen!

If non-compliance is detected, prompt action is needed. If required by local regulations, the sponsor must notify regulatory authorities when the non-compliance is a serious breach of GCP or trial protocol – this can result in a trial being halted. New to GCP R2 is the need to implement appropriate corrective and preventative actions, and to incorporate these during trial design and protocol development. Planning is key to identifying processes and data critical to ensure compliance and protect patient safety… and of course to execute a successful clinical study!

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