Simplifying the Process of Managing Complex Country-by-Country Regulations in Clinical Trials

Clinical trials themselves have their own complications. Regulatory compliance and safety reporting are of the utmost importance in managing clinical trials. When you add to this how the regulations change in various countries across Europe – and the world – the complexities are exponentially greater.

The onus is on the clinical trial sponsor to ensure that all regulations have been met throughout the process of managing a clinical trial. They must also be able to trace and defend each step in the reporting process. Essentially laws, these regulations require interpretation by experienced and qualified individuals to gain a full understanding of what exactly the requirements are and how they can best be applied in the context of drug development. However, due to the complexity of the task, this effort is commonly supported by a network of professionals with different backgrounds: Clinical trial teams, Regulatory Affairs and Pharmacovigilance.

Automated technology has many befits for managing the process for safety and compliance information. This article will review how a central hub can simplify tracking country rules for compliance. This approach can feature dynamic templates, which can be modified to meet local requirements, help to set a standard for tracking each country's regulations and upon distribution to clinical trial investigators, can be blinded to avoid putting clinical trial information in jeopardy.

Managing Cross-Border Regulations and Languages

Regulations are generally high-level, which means that guidelines are provided but do not offer the specific details and processes that are necessary to attain compliance. This is where interpretations become exceedingly important. The country-level guidelines need to be translated into practical actions that can be applied across trial sites and institutions. In many countries, local competent authorities can apply their own interpretations of these guidelines, creating complexities for the clinical trial management team in safety reporting to authorities. Additionally, local and central ethics committees often add their own subtleties and don't always distribute notifications as to updates or changes. This causes even greater challenges to the sponsor in maintaining up-to-date information on regulatory compliance and to apply this information correctly during the course of a trial.

We also witness many countries that publish their regulations in local languages. This requires knowledgeable interpreters who can grasp nuances of the language and deliver accurate and transparent regulatory updates and alerts to clinical trial managers and sponsors.

Thus, for a sponsor that is evaluating a compound with clinical trials in various global geographies, management of regulatory compliance becomes even more complex. For example, if you are conducting a trial in Poland for a drug that will be marketed across Europe and North America, you need to not only consider regulations that apply to the country trial site but also to regulations in all of the countries where the drug will be available for distribution. Compliance with multiple countries' requirements obviously requires significant resource allocations and standardisation of data capture and reporting. This is where a centralised hub becomes a tremendous opportunity to take away some of these complexities and deliver data to customers who only have to focus on just a 'yes or no' acceptance of the standards.

Tracking Countries' Regulatory Alterations with Humans

Generally, in larger countries such as the U.S. and most European countries, there is ample notice when a regulation is changing. However, it's not the same in every country in which trials are being conducted.

To remain in compliance, clinical trial regulators need to be certain that a mistake hasn't been made in reporting. This also means devising methods to capture new requirements or delayed information regarding regulations to the sponsor. When there are automated processes in place, this can be documented and explained. But it's when issues in reporting are deliberate, i.e., specifically not reporting something critical like safety documents, it can become a significant problem that could seriously impact the progression of the trial. It's particularly challenging when someone is not advised of changes if there are a number of countries participating in the trial.

Subscribing to a regulatory database may be helpful but due to the issues occurring when countries do not issue notice of changes, there still needs to be human oversight, a quality check of sorts, plus of course the interpretation into a practical 'what needs to be reported, how and when.' Again, this takes time and experienced resources, particularly when trials are being conducted in multiple locations and in multiple languages. While databases may be helpful, complexities still exist that require human intervention.

Simplifying the Process

The clinical trial sponsor always has the ultimate responsibility of adhering to regulatory guidelines during the trial. However, the management of regulatory compliance documentation can vary from a sponsor's in-house team to a CRO or other vendor that supports safety regulatory affairs. For example, a vendor specialising in pharmacovigilance can support the trial sponsor with an automated system, i.e., a dynamic data hub that is designed to manage contact information for recipients at all clinical trial sites, distribution of safety documents uploaded or linked from existing data sources, provide audit trails as well as manage reporting requirements per country and per recipient type. For example, in

a typical safety document distribution scenario, ethics committee members would receive specific reports, i.e., periodic reports, line listings, SUSARS, defined for each role and document type.

Templates can be very helpful in supporting this distribution process – with designs based on role and document type. These are based on local values and will apply to the vast majority of all the rules but are able to be modified if necessary. Recipients are identified as to whether they would receive blinded or unblinded reports, critical when an unblinded report is inadvertently delivered to an unvetted recipient. This kind of mistake can seriously jeopardise a trial by creating bias. The data hub can be updated, when new contacts are onboarded, or new safety documents created – all of which are automatically entered into the system. The messages that are sent out are then tracked, with a detailed audit trail, allowing you to drill down from a document to see who it was sent to, and when it was acknowledged.

Most countries accept the standard report formats: MedWatch, CIOMS-I and CIOMS-II. The forms are generally distributed using English as a single language. However, specific processes or local forms are often translated into local languages, again which require translation and transparent interpretation. Another interpretation challenge may come from CROs operating in different countries where processes may be similar but not exactly the same. Therefore, there is still human intervention involved for a quality check on accuracy and 'clean-up' of any errors.

Regulatory bodies in both the U.S. and Europe are offering directives to streamline reporting processes. For example, in the EU the regulations for drugs and medical devices have become far more aligned than they had been in the past. But while regulations for safety document distribution often remain in place for several years, the reporting processes may change slightly, particularly with countries just learning to manage clinical trials where laws may change more often.

In Summary

Technology advances are supporting the automated reporting of clinical trial efforts. This will vastly simplify the tasks required to coordinate regulatory changes. This will positively affect the transparency in data reporting and greatly reduce labour, manual errors, and their associated costs. The key to this journey forward is a basis in which the information flows are interactive and dynamic via a central dashboard and where humans and machines work in tandem to assure prompt reporting with accurate results pre-determined to meet global guidelines.

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