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EU CTR Pushes Sponsors and CROs to Clean Up Their Act

The European Medicines Agency's plan to harmonise all clinical trial information requires a significant change in how companies collect and store trial data and records.

On 31 January 2022, European Union pharmaceutical legislation known as the Clinical Trials Regulation[1] entered into application – hoping to harmonise the processes for assessment and supervision of clinical trials throughout the EU.

The regulation aims to make it more efficient to carry out multinational trials by enabling sponsors to submit one application via a single online platform – known as the Clinical Trials Information System (CTIS) – that would grant approval to run a clinical trial across several European countries. The regulation also intends to make it more efficient for EU Member States to evaluate and authorise such applications together, via the Clinical Trials Information System. Prior to the new set of regulations, clinical trial sponsors had to submit clinical trial applications separately to national competent authorities and ethics committees in each country to gain regulatory approval to run a clinical trial.

The Clinical Trials Regulation1 represents a milestone on the journey to a more competitive European R&D environment, particularly for multinational studies. Improved trial transparency – and EMA has recently opened a public consultation in this area – will make it easier for patients to participate in research. A harmonised approach to clinical trial applications across Europe should lead to faster approvals.

However, despite being given a year transition period to adapt to the incoming regulations, companies have been facing challenges in several areas since EU CTR became mandatory for all new starting trials in January earlier this year. Sponsors and contract research organisations (CROs) find it difficult to coordinate submissions cross-functionally and meet tight deadlines, partly due to fragmented and time-consuming data collection. Redactions are another sticking point. Disclosures must be fully integrated within the standard clinical trial process yet occur more frequently across the trial lifecycle than before.

Some issues are outside companies' control and will only ease once the Clinical Trials Information System (CTIS) reaches a steady state. Still, companies don't need to wait for the next phase of CTIS to improve their oversight of the complete submission file. Changing the resourcing of their regulatory and clinical teams and adapting their data collection, request for information (RFI), and redaction processes will provide much-needed visibility sooner. The benefits are not limited to EU CTR. Clarifying ownership and creating a single source of trial information would also make rest-of-world studies more efficient.

One Crew at the Helm

Many small, single-country studies are well-suited to being pilot submissions to CTIS, and have been used to identify the limitations of existing processes and systems. Insights from these first submissions have helped sponsors decide on an effective resourcing model for subsequent studies, including whether or not to outsource to CROs.

Sponsors that insource have improved alignment by creating a single EU CTR cross-functional process and team structure, spanning from regulatory and clinical to quality, safety, and trial disclosure. In the past, these teams had independent responsibilities. Regulatory managed the submission of health authority approvals while clinical teams handled ethics committee approvals at the site or country level. Condensing regulatory and ethics committee approvals into a single process requires adjustments to team structure and responsibilities.

Companies have set up their centralised submission teams for success by clarifying ownership of the end-to-end process and confirming new responsibilities. Among Veeva customers, there isn't a consensus on which team should be in the driver's seat: roughly half point to regulatory while the remainder opts for clinical operations. Irrespective of which team leads, its submission responsibilities are broader than before, extending to regulatory, ethics, and disclosures.

As the nominated team is pivotal in collecting trial-related information, its remit should be clearly communicated to the broader organisation. Understanding who is accountable for gathering information from different stakeholders (e.g., quality, regulatory affairs, clinical) is critical, particularly during RFIs from EMA, which require a response within 14 days. A tracker specifying ownership for each task can make it easier to collect RFI answers across the organisation.

Customers are also exploring new ways of working to counter the challenges of fragmented data collection and dynamic redactions. Some sponsors have delegated data entry into CTIS to CROs for outsourced studies, eliminating a few extraneous steps. Similarly, centralising responsibility (whether internally or outsourced) for redactions helps to manage this process more effectively because training, guidelines, and SOPs can be implemented in just one dedicated team.

Reaping the Benefits of a Streamlined Approach

Already, some customers have become familiar enough with the regulation to submit Parts I and II together. Leading companies go further during the initial submission by including many countries under Part II. Submitting multi-country studies in parallel decreases the number of evaluation cycles, reduces the risk to patient recruitment, and shortens the overall approval timeline. But it's a heavier upfront lift, for which easy access to trial-related information is essential.

While it may be tempting to navigate a submission with pre-existing data collection processes, this could prove shortsighted. Currently, CTIS lacks an API capable of receiving data and documents from either

sponsor systems or technology partners (including Veeva). However, the next phase of CTIS will probably involve API capabilities, which could make company integrations more straightforward. Doing the hard work now to create a robust data foundation will pay dividends if (and when) the API is introduced by EMA.

Sponsors and CROs that have centralised data entry into one team (resourced with up to 10 people in enterprise biopharma) are already seeing the benefits of the new model. Having one part of the organisation accountable for data entry and upload to CTIS streamlines user access management and reduces the training effort required. However, data entry teams often need external support to create a repository of all the data points for each CTIS submission and then scale this structured approach across the company. This CTIS data collection tracker[2] should be a single source of truth of all reportable data from different systems.

It can also be helpful to reflect on the spirit of the regulation when setting up a process to manage redactions. Companies need to balance disclosure risk with the benefits to patients of greater trial transparency. Usually, the two main types of data anonymisation activities (commercially confidential information and protected personal data) take place using a hybrid approach. Redactions of company information are often centralised because they require legal knowledge (*e.g.*, information relating to patents), and personal data redactions are decentralised so local teams can apply their national legal understanding.

Modifying redactions can quickly become messy in a hybrid model. Information that is confidential today might not be in a few months when the trial ends. Nor do all redactions involve obscuring text. Some content may need to change or be rephrased. The complexity of managing redactions could hinder patients and sites from enjoying easy access to study-related information envisioned in the regulation. To address these areas, sponsors should work in a system that maintains a close relationship between source and redacted documents so that teams can easily manage changes to content before public disclosure.

Centralisation is the New Benchmark

The main aim of the Clinical Trial Regulation was to ensure the EU offers an attractive and favourable environment for carrying out clinical research on a large scale, with high standards of public transparency, robustness of data generated and safety for clinical trial participants.

A single point of access to European clinical trial information will benefit patients, as participation in ongoing trials becomes more straightforward.

Mandatory use of the same system should enhance stakeholder access to trial information without compromising robust data privacy standards.

However, EU CTR also challenges sponsors and CROs to reconsider how they collect and store trial data and documents for EU and non-EU studies. The European Medicines Agency has thrown down the gauntlet – and for some companies, this provides a welcome opportunity to get their houses in order.

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