Avoca Quality Consortium Leading Change Collaborative Forum

Meeting Highlights

Topic: EU CTR 536/2014 Readiness

Meeting Date: January 18, 2022

Background Information

The emergence of the COVID-19 pandemic has caused the pharmaceutical industry to rapidly adapt its processes and technologies, including clinical trials. The AQC Leading Change Collaborative Forum features compelling topics designed to encourage provocative discussion. The priority is providing practical and actionable support and having immediate "peer-to-peer" benchmarking about how other organizations are managing the topic at hand, all while ensuring prioritization of patient safety, data integrity, and regulatory compliance.

In this session, the moderator began with an overview of the new clinical trial regulation [(EU) No 536/2014](#) (EU CTR), which went into effect January 31, 2022. A decade in the making, EU CTR introduces a centralized authorization procedure based on a single submission via a single EU portal, an assessment procedure leading to a single decision, rules on the protection of subjects and informed consent, and transparency requirements. The purpose of the EU CTR is:

- to harmonize the approval processes with maximum timelines through a single electronic submission, the EU portal. The portal will be the single point of entry for submission, storage, and authorization of clinical trial applications.

- to support close coordination among the EU member states to ensure that European countries work more uniformly.

- to make it easier to conduct clinical trials in different EU member states.

The change took effect January 31, 2022, and it includes a one-year transition period for new trials. That means each new clinical trial will need to be registered, submitted, and authorized under the EU CTR by January 31, 2023. For ongoing trials, the transition ends January 31, 2025.

"I must be frank and honest with everyone: This is about diving into unknown territory."
--participant

Discussion Summary

Implementation of CTR into Company Processes

Organizations will need to rethink clinical and regulatory operations. Most have already started; the changes were first announced in 2014.

One participant described how his organization began with a gap analysis that revealed many gaps. "Some minor, some major, some in between, but all needed to be taken care of." It covered a vast number of documents. "Thus, there can be a lot of stakeholders embedded into just one gap and thus a huge alignment needs to be performed. That is something I've been working a lot with. It's been a huge journey of filtering down the vast amount of documents until … we knew, okay, this is the batch of documents that we need to work with."

With implementation, timing matters, several participants noted "It's a balance. If we push the 'go' button too early, we might strip some departments of resources," said one. This could hurt important ongoing projects--especially in a major pharma company.

Implementation comes down to basic change management principles, explained another. "We're identifying the impact on the business, on our procedures, on our people." That involves assessing the impact of the regulation on processes, documents, guidelines, working instructions, etc.

Communication--and the timing of communication-- is therefore critical. Stakeholders need to understand the impact of the regulation on their procedures, training, and timelines, but, as one panelist noted, communication is challenging because of the magnitude of the changes that will take place.

All of this is a huge undertaking for the largest companies, so how do smaller biotech prepare? They can leverage CRO expertise, noted one panelist.

"Parallel Universe" of SOPs

Organizations will have to manage different sets of standard operating procedures. They'll have trials already underway following the old procedures while starting trials that must follow the new regulation. "You have a parallel universe of your SOPs, and that is also something I think will be a bit challenging," noted a participant.

That point also came up in the discussion of implementing the 25-year record retention into SOPs--part of the discussion of transparency and data protection.

Transparency and Data Protection

Several conversations arose around this area. Among them:

- **Archiving requirements:** As one participant explained, it comes down to this: "Do you make one new big global SOP and force all the other countries where this is not applicable to forcefully be implemented under this umbrella as well? Or do we create two different archiving SOPs? That's the big question." A panelist's answer: "For right now, I believe the most pragmatic way we've solved it is that we've just simply added a small parenthesis in our SOP stating that it's only subject for studies submitted under EU CTR."

- **Consistency in data protection rules:** "Harmonization is a big thing, and it's also important in relation to when you're talking transparency. Because if you have individual requirements on what you are allowed to redact and take out of your document, and that is different for different regions or different countries, then you might eventually be able to piece the whole thing together," said one participant.

  "From an operational perspective, it's very, very challenging," she continued. What happens if you can share the data for a trial if patients come from the UK and Germany, but not from the U.S. or from Japan? The whole idea behind having one trial, according to the ICH E17, will break apart if we don't have the same rules and apply the same rule on data protection."

- **Reporting serious breaches:** A key aspect of the regulation--a requirement to report serious breaches--generated questions. For example, when does the seven-day window begin? Companies need time to make those determinations, explained one. "As you can imagine, the definition is extremely subjective, and it does take time to come to a conclusion of what qualifies as a serious breach."

  One participant offered the following solution: "What we're working on, and what I recommend our peers and industry do, is have very, very clear processes. In terms of, within your business rules, what truly qualifies as a serious breach." "The definition of breach is subjective", he added. "We look to develop that clarity within our own business rules. That should cut down the number of instances where you're having to evaluate for breach reporting."

Managing the Centralized CTA

"The changes in the clinical trial application (CTA) process will lead to some role changes within the organization," said one panelist. "But I'd say the biggest challenge we have is onboarding our staff with these new ways of working."

Another challenge: "Cross-functionally nailing down the clinical trial application, the study design, the protocol, in an early stage. We've already had many, many challenges in that space. So, really tightening that process, I think, is going to be a very steep learning curve for us."

One participant shared that, at least for now, they've "decided to be a bit sparse on the initial steps," limiting CTA access to a tight centralized group. "We are not absolutely sure on how the system will work and we feel it's better to have that knowledge in as few hands as possible."

The change in the submission process brings both risk and reward. As one panelist summarized, "I think the opportunity of this is that we get one approval. We have fixed timelines, so we know when we are going to get it, but that is also the risk. Because if we are not meeting the timelines, then we risk starting all over again. The opportunity comes with a risk."

If you are interested in learning more about the [WCG Avoca Quality Consortium (AQC)](#) or its Leading Change series, please contact [Dawn.Auerbach@theavocagroup.com](#).