Avoca Quality Consortium Leading Change Collaborative Forum

Meeting Highlights

Topic: Reducing Site Burden in Safety Reporting

Meeting Date: June 15, 2021

Background Information

The emergence of the COVID-19 pandemic has caused the pharmaceutical industry to rapidly adapt its processes and technologies, including clinical trials. In Avoca's Leading Change Series, AQC Members have discussed the QMS Ecosystem Divide, FDA Voluntary Remote Inspections, Diversity in Clinical Research, Protocol Design, Patient Engagement Trends and Solutions, and more.

Safety reporting--more specifically, the unnecessary reporting of safety events to investigators--creates a tremendous site burden and puts patients at risk. At present, it shows no sign of abating. As a result, sites, already overburdened and currently severely under-resourced, may overlook critical patient safety information while focusing on activities that are not value added to the clinical trial process. The fear of misinterpretation of regulations by the Sponsors in conjunction with the lack of global regulatory harmonization compounds the overreporting crisis.

The problem: Sponsors and CROs are sending large numbers of reports to sites for acknowledgement by study investigators instead of analyzing events and sending only those reports which are required by the FDA.

"From the FDA's perspective, getting it right is a fundamental responsibility of Sponsors", said WCG Avoca Founder Patty Leuchten. Sponsors and CROs must do a better job analyzing suspected adverse events before sending out safety reports, both to reduce site burden and to protect patient safety. "Obviously, if we can't identify a signal through the noise of overreporting, patient safety is hanging in the balance, as well as quality. So, it couldn't be more important to us."

VP of Client Delivery, Crissy MacDonald, PhD, expanded on the threat to patient safety. "We're burying them in information, at the risk of ultimately then missing the one alert that matters. And not only the one that matters from a patient safety perspective, but the one that matters for us as Sponsors, because that's the one that's going to be the inspection finding. They missed the one that really did count, that really did matter."

The issue seems to be flying under the radar of Sponsors and CROs while at the same time sites are forced to do more with fewer resources, due in large part to the COVID-19 pandemic.

Discussion Summary

Complexity and Ambiguity Demand Interpretation

Sponsors need to analyze safety reports if they are to send only the appropriate ones to sites. It requires work. “The regulations are typically quite gray. They're not black or white, they are open to interpretation. We don't have a consensus as an industry” But deciding how to interpret the regulations is part of the job.

Overreporting to Avoid Noncompliance

Some sites don’t want to do any interpretation, any “triage,” as one panelist put it. One reason: There is a clearly understood penalty for underreporting, but not for overreporting. Overreporting has become a “cautious step,” said one panelist. The attitude appears to be that overreporting isn’t ideal, but it’s better than being cited for noncompliance.

Sponsors and CROs need to understand the downstream consequences. “If we overburden sites, we really are not doing ourselves any favors as CROs and as Sponsors, to the investigator or to the ethics, because overreporting could potentially bury something important, and that most important valuable piece of information then gets lost,” said one panelist.

It’s not only patient safety at stake. Sites may not have the capacity to take on new trials, for example. “Cost is a factor, too. It's not the driving factor, but I think we're all completely breaking the banks and overspending on these reports as well,” said one of the Sponsor participants.

Sites are Pushing Back

Some sites are starting to push back by increasing the cost to Sponsors, essentially saying, “If you're going to burden us with this, we're at least going to get paid for it,” reported a panelist representing the site perspective. Some sites refuse to acknowledge Suspected Unexpected Serious Adverse Reactions (SUSARs) that don’t meet the reporting criteria.

They have good reason, she said. “If the event already is listed in the drug brochure, and it's a known risk factor, why is it being distributed to the clinical trial investigators, who already trained on that brochure? The sheer volume is staggering, and don't forget for each event which happened, we have initial reports, follow-up reports, second follow-up reports, third follow-up reports, and final reports, which if determined that there is no relation then we'll have to process a retraction of that initial report.”

Lack of Global Harmonization a Significant Factor

"One of the most difficult things for Sponsors is that the philosophy in Europe and the US is different. So, in Europe they really do say, 'Send everything to the EMA','" explained Steven Beales, Senior Vice President, Scientific and Regulatory at WCG. (Beales will be working with a new AQC Leadership Advisory Board described below.) "But the policy for the FDA is the opposite." The variation in local country rules provides even more incentive for Sponsors to overreport.

One Sponsor representative reported integrating more than 60 local country regulations with an automated system. By reducing overdistribution, it improved site acknowledgement compliance by 20%. It also enhanced audit readiness. "I know it's not all about the tool, but there are benefits to having an automated system."

Make the Case to Sponsors

Sponsors "want to do the right thing, and I think it's really about being able to help people understand what's going to be the most meaningful and the most effective," said a Sponsor representative. "I think it just takes time, and maybe you start small, and you start with one small study, and then maybe you can see the successes, and build on that."

Next Steps

To address this challenge, Avoca will form a Leadership Advisory Board, to do a deep dive into the global requirements; the objective is to create very practical tools to support the industry. The board will, among other tasks, develop a Safety Reference Model, a framework for defining safety reporting rules. It will launch in September. Interested AQC Members can contact Caryn.Laermer@theavocagroup.com.

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