

Avoca Quality Consortium Leading Change Collaborative Forum

Meeting Highlights

Topic: ICH E8 (R1): Building Quality into Clinical Trials

Meeting Date: November 16, 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. 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.

[ICH E8 \(R1\)](#), which goes into effect April 14, 2022, provides guidance on the clinical development lifecycle, including building quality into clinical studies. Brigid Flanagan, Senior Consultant, WCG Avoca, led a discussion focused on that topic, with considerable emphasis placed on one aspect of the guidance: stakeholder engagement. She observed that there’s been less discussion of ICH E8 (R1) than she would have expected. “I think everyone is focused on the clinical trial implementation system that’s going live in Europe on January 22nd, so this may be on their back burner at the moment.” But sponsors and service providers need to be paying attention.

Fortunately, she said, E8 (R1) builds on ICH E6 (R2). Having been through E6 (R2), people are already focused on identifying critical data and processes, the risks to those data and processes, and how they’ll manage those risks during a trial. “So, I think people, particularly after COVID, are very much in tune with what can go wrong and how we might address it.” But first, organizations need to have systems in place. That begins with providing some training on the requirements of E8 (R1). “We’re all avidly keeping an eye on the different regulatory agencies to see where else it might be adopted, but certainly being prepared is half the battle.”

Discussion Summary

Building a Culture of Quality

A pharma company participant discussed adopting the culture of quality as it applies to ICH E8 (R1). It starts at the top but must be communicated through the organization: It's not just a quality assurance activity. To accomplish this, her company developed a quality model that covers five areas: communication and collaboration; leadership commitment; employee ownership; technical excellence; and continuous improvement--all of which align with E8 (R1).

Stakeholder Engagement: Service Providers

What is "new and exciting" about E8 (R1) is the engagement of stakeholders in the design phase, Flanagan noted. A technology company participant heartily endorsed this. "Early engagement and open discussion across the clinical trial ecosystem may be key and critical to success. It certainly supports a risk-based dialogue. It's clearly outlined in the guidance" (section 3.2).

He added: "We've certainly seen use cases, where the mad procurement and outsourcing rush to identify key partners and experts prior to first patient first visit or SIV dates for screening has led to a lack of expert feedback in protocol design." And that keeps life-improving therapies from those who desperately need them.

Another technology provider participant concurred: To build in quality from the outset, engage all the stakeholders, including developers and programmers, medical affairs, the client, and quality assurance. It's important to take an agile approach, "because those critical quality factors may change during the course of development of that system."

Stakeholder Engagement: Sites

A participant representing a site network explained that although they receive draft protocols before the trial is activated, Investigators typically don't have much say in the final protocol design.

"We've found that some of the studies that get assigned to the investigators have very strict eligibility criteria where the indication does match the patient population, but these patient populations have other comorbidities and are taking several medications, which can make them ineligible to participate."

His recommendation: Let an investigator provide input on the eligibility criteria from the outset, so the criteria are more typical of an average patient from their patient population. "I think that's one of the important things for designing a protocol, which isn't too common right now, but hopefully with this new guidance being adopted, more investigators and sponsors will work together in designing the protocol."

Flanagan agreed. "In any other business, they speak to the end user," but not in pharmaceutical trials. "So, you've this beautifully designed protocol with all these complex procedures, multiple inclusion exclusion criteria (which nobody's going to meet all of them), and then that's passed over to ClinOps and they're expected to enroll that trial, and then people are surprised when enrollment falls behind schedule and all these patients are failing screening."

Stakeholder Involvement: Patients

“We need to involve the patients in designing the protocol, which this guidance document does address,” said the site participant. “And hopefully it will be adopted in the US as well.” When patients are involved early on in designing the study, it’s likely that patient recruitment will be higher and that participants will be more compliant with the protocol, he said.

Several participants pointed out that patients and patient advocacy groups are becoming more sophisticated and vocal about trials. If sponsors aren't paying attention to what potential participants are looking for, they could be putting their reputations at risk.

Critical-to-Quality Factors

One audience member wanted to know “how companies are distinguishing identifying critical-to-quality factors versus critical data and process to include in study-level risk management.” The answer? They are one and the same. It’s all about generating quality data that can be used to make decisions about the product or the medication, Flanagan said, adding that the appendix of E8 (R1) lists the critical-to-quality factors.

One participant further noted that section 3.5 of the guidance clearly overlays the two--critical-to-quality factors and operational practice. “There’s a very tangible discussion around the scientifically sound protocol, but also operational feasibility, and very clearly it doesn’t differentiate the two.”

Getting Up to Speed

Flanagan asked: “If you think about the change management around E6 (R2) and how long it took for that to be adopted, do you think we’re likely to run into the same challenges with E8 (R1)?”

None of the participants made a prediction, but they agreed that training was essential to adoption. “It’s very much forefront in our minds, certainly to know that, because it does take a long time, we need to start getting that process created and rolling out,” said one participant.

There’s a lot to learn: E8 (R1) covers many more topics than those raised in this discussion. As several participants noted, the clinical development team needs to make sure that they’ve read it and are planning to address it.

As one participant put it, “You don’t want inspection findings to be your catalyst for change.”

*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.*