



Perceived Risks to the Quality Conduct of Clinical Trials

Kate Haratonik, Genentech



Question posed to expert interviewees

- ▶ What are your concerns, if any, about the quality of how clinical trials are conducted?

Primary Concern: Data quality

- Are adequate processes are in place to ensure data quality and that data are not fabricated?
- What is the impact on data quality from having both paper source documents and electronic data collection?
- Is data collected at non-dedicated research sites reliable?
- Is early monitoring of protocol compliance sufficient, or even being conducted?
- Are staff following ALCOA principles in collecting, recording, and transferring data?
- What is the generalizability of study findings when only “perfect” participants are enrolled?

Primary Concern: Data quality

Investigator quote:

*...if you didn't do something as a procedure for a particular visit, so don't go making it up that you did it and just putting something down. That's very basic things as far as data entry. You have to collect the data, and what you collect has to be accurate. Also, you need to make sure the first place you document it is not the back of your hand or something like that. There's a lot of training done, but that's at our site level. The ethics of making sure that you are collecting data correctly, and some of the ALCOA principles. **So, you have to collect it in real time, put it down correctly, transfer it correctly, don't make up anything. If it's not done, it's not done, and then you take a deviation. Sometimes that's hard to deal with.***



Primary Concern: Data quality

Sponsor quote:

- *I think that we probably don't do enough to detect early that the protocol is being adhered to. But, it's very easy for a protocol deviation to happen before awareness is raised, if it's ever raised. And, therefore, we miss data, or we have inaccurate data or patients participate, subjects participate to no good or useful ends. Their data can't be used.*

Frequent Concern: Informed consent

- Are we ensuring truly voluntary consent, particularly among vulnerable populations without access to medical care?
- Are investigators able to work to ensure that their participants' consent is truly be informed given the long length and complexity of informed consent forms?
- Are investigators and their delegates able to help participants understand the commitment and responsibility required of trial participation?
- Are investigators sufficiently involved with the informed consent process?

Frequent Concern: Informed consent

▶ Sponsor quote:

- *I think investigators aren't as involved as they probably should be in the consent process, and this is one that they tend to delegate to study coordinators. And I think absent a clear understanding of both the clinical and the medical aspects of a clinical trial, an informed consent process can't be most effectively accomplished if the delegate doesn't understand those key details; again, clinically and medically, to explain them in a way that is fair and balanced that potential participants can understand. I think it's a little too easy to review the approved informed consent form, and then try to address questions as they come up.*



Frequent Concern: Informed consent

▶ Investigator quotes:

- *...frankly the informed consent document is so long, patients and family rarely read the whole thing, but are dependent on the verbal discussion that goes with the consent process*

Frequent Concern: Informed consent

▶ Investigator quotes:

- *The other thing that is part of our informed consent that's really difficult, and that's vulnerable subjects. I don't know if you get to talk about that very much, but there are a lot of people out there who have no medical care, they have no medical insurance, and we know they are coming in to do a clinical trial, because they don't have access to care, and they need care. So, it's a really fine line to try to determine if it's appropriate for this person to be in a clinical trial. Sometimes they absolutely need medical care and not be randomized to a placebo, and not getting medical care. But, if they are voluntary, if they want to proceed, that's a choice they can make. But, it's a fine line sometimes for me, knowing somebody is in a study that they might not want to participate in, if they didn't have to financially.*

Other Concerns: Processes and Procedures

- ▶ Clinical research has become very bureaucratic
 - Too many systems and processes
 - Time and resources are spent on using multiple systems, which duplicates efforts and is confusing
- ▶ High staff turnover rate impacts the quality conduct of clinical trials



Other Concerns: The inclusion/exclusion criteria, screening, and enrolling the appropriate study population.

- ▶ Pressure to enroll participants
- ▶ Concerns with enrolling vulnerable populations
- ▶ Trying to recruit participants who represent a broad demographic

Other Concerns: The impact of competing demands and time constraints

- Difficulties that investigators face with balancing clinical practice with clinical research
- Difficulties faced by both investigators and sites from being overextended from overseeing many studies, which makes it challenging to properly screen and comply with the study protocol
- Understaffed sites that have insufficient understanding of GCP and which are unable to perform well without extensive sponsor oversight

Other Concerns: Study oversight and medical care

- Concerns with ensuring that the entire team is well trained on the study protocol and GCP—and takes GCP seriously
- Concerns with the consequences that could occur from improperly delegating tasks to unqualified team members who do not fully understand the protocol
- Concerns with coordinators making decisions about causality and severity of AEs rather than Pis
- Concerns with study oversight—keeping timelines, documentation, and follow-up to avoid putting the clinical trial at risk



Discussion