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DMC Regulations May Change, but Principles Won't

By William Myers

The FDA's guidance on Data Management Committees will expire by the end of the year, but even if it's not extended, the principles behind them will endure.

Cardiologist Jonathan Seltzer, president of ACI Clinical and a noted expert in DMCs, said the concerns that have guided regulations for nearly two decades — "Is this a vulnerable population? Is there a specific toxicity that should worry clinicians? Is this a lengthy, complicated trial?" — aren't going away.

Those concerns can help sponsors clarify their thinking about DMCs, Seltzer said.

It's important for committee members to be independent, but also responsible, Seltzer said. That's simple in description, but can be tricky in execution.

"The good thing is they're not working for the company; they don't have a stake in the success. The bad thing is if they make a mistake, or they don't do their jobs correctly, the consequences are enormous," Seltzer said.

An early warning sign of trouble can be that the committee begins ratcheting up its request for external analyses, Seltzer said. ACI typically budgets about 10 percent of its DMC consulting budgets for external analyses. An early run-up can be an indication that there is discord on the committee, or that early data may be revealing an unintended consequence.

DMCs aren't for every trial, Seltzer acknowledged. The sponsors who can benefit from using committees the most typically have one or more of three characteristics:

- A lack of staff, time or money. "Especially in smaller companies when maybe you have a chief medical officer who's running the trials, supposed to be looking over trials, who's meeting with investors, who has all these responsibilities — they may not have time to look over safety," Seltzer said.
- Low-resourced CROs. "They don't have the expertise," Seltzer said.
- Worries about unintended consequences. "If you're concerned about unexpected safety issues or things that might ultimately impact your development program. There's real value of a DMC detecting a safety signal early that allows you to modify your program, so you don't kill the drug," he said.

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—Jonathan Seltzer, president, ACI Clinical

A few years ago, Seltzer analyzed the impact of DMCs on trials. He expected to have to argue for DMCs' value proposition, but the data showed that there was a direct, positive cost/benefit proposition. The biggest positive impact seems to be that the committees help rescue trials from cancellation by spotting early problems and modifying the protocols, he said.

"I was stunned," he said. "And I felt bad writing it. I'm in the business, and there I was tooting my own horn."

Seltzer said that he worries that some sponsors seem intent on hiring the committees merely for what he calls "the optics."

"Really, it just reassures the public that someone else is looking at the data," he said. "You should not have a DMC unless you believe it brings value to your trial, period."

It is really important to bear in mind the principles behind DMC regulation and to build clear goals around them, Seltzer said. Some companies put together a committee as if they were hiring for portfolios — this person is for regulatory, another for efficacy, etc.

This can create the illusion of wide-ranging expertise and it may be that "you've set up a situation where your committee's going to go rogue," Seltzer said.

Sponsors typically make three other common errors, Seltzer said:

- Over-focusing on star power. "Trying to get the most famous person in the field — it's a reflexive thing to do," Seltzer said.
- Hiring friends. "I've gotten calls from people who know me and I have to say, 'I don't really know this,'" he said.
- Hiring someone just to keep them on a company's payroll. "Sometimes they're great, sometimes there's an issue," Seltzer said.

"The construction of the committee should be driven by the needs of the committee," Seltzer said. "What are the skill sets that are necessary for this DMC given what you want this DMC to do?"

Sites have a role to play, too, Seltzer said. Any trial that's particularly complicated, or that involves vulnerable populations or potentially risky new compounds probably should have a DMC working. "The sites should probably insist on it," he said.