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Some Quality Food for Thought

By John R. Wilson, Jr.

I'm more than a little perplexed by the perpetual quality conversation in clinical research. On one hand, I work in an industry that employs people who care, who understand the significance of their work, and who want to make a difference. On the other hand, anyone with tenure in the industry knows that clinical research quality is far from optimal and improves glacially, if at all. We're still talking about the same problems — protocol deviations, informed consent violations, ineligible subject enrollments, etc. — that we were talking about when I first started in quality 23 years ago. And, our colleagues at FDA routinely document the same findings on 483s that were appearing decades ago. Are we working in an industry that time forgot?

It's not like we aren't aware of the issues. There is no shortage of training programs. I recently received flyers for conferences on "Quality Improvement in Clinical Trials," "How to Ensure High Quality Clinical Data," "Auditing for Higher Quality," etc. And, I'm not saying there has been zero progress. For example, the FDA and some sponsors have started looking for systemic problems rather than focusing on isolated errors. But the overall picture is barely changing. We still hear the same messages: Improve quality. Do more audits. Be proactive. Be lean. Adopt Six Sigma.

The implications are more chronic than acute, and revolve around topics like waste, delay, and inferior data. Our quality is not disastrous, just mediocre. Nevertheless, sub-acute, chronic ailments are still a burden— ask someone with diabetes, high blood pressure, or kidney disease. Bit by bit, mediocre quality accumulates to create costly delays in new product approvals, preventing effective therapies from reaching clinical use, to say nothing of their detrimental impact on the drug and device industries, as well as the clinical research industry itself.

You might say, "OK, genius, what do you want us to do?" I could provide a long list of specifics, but let's start by committing to systematic, practical and measurable applications of basic principles. Otherwise, we will just bounce from one quality flavor of the month to another, without consolidating progress. Playing quality Whac-A-Mole without addressing root causes in a systematic manner is a recipe for mediocrity. Instead, I suggest that there are four places to start — four places that are overlooked in the current dialogue on clinical trial quality.

The Quality-Time-Cost (Q-T-C) Triangle

First, I suggest we start with a radical reinterpretation of the Q-T-C triangle as it applies to clinical trials. The Q-T-C triangle has been the holy grail of project management for as long as I can remember. The idea is that we have to sacrifice one of three objectives to achieve the other two. For example, we can achieve high quality quickly, but only at a high cost. Or, we can compromise on all three objectives to deliver mediocre quality on a mediocre schedule at a mediocre cost.

I challenge this theory. Yes, it's a zero-sum game (or worse) if, rather than building quality in, we try to inspect errors out by adding more monitors and auditors. If these are the only tools in our toolbox, yes, we have to spend time and money to increase quality. But it's the wrong model.

In 1979 — 33 years ago — Philip Crosby published the book, "Quality is Free," popularizing the idea that improving quality does not cost money or even not cost money, but actually saves money through lower inspection costs, lower rework rates, faster work-in-process turnover, and other reasons. Sound familiar? A typical clinical trial spends as much on site monitoring and data cleaning as it does on site payments. That's like a production line with an inspector standing behind every production worker. How many clinical trials are delayed because of the same old problems with the protocol, poor site selection, delayed data lock, etc.? It's time for us to start saving time and money by *improving* quality.

Role Clarification

Second, let's re-examine the role of the principal investigator (PI). Clinical research is conducted at study sites, where the PI is the accountable person. But, the PI is first and foremost a physician. Our approach to clinical research is premised on the assumption that physician PIs view study subjects first as study subjects and secondarily as patients. Surprise — physicians almost always view study subjects as patients first and study subjects second. A Form 1572 really can't compete with the Hippocratic Oath.

This is not to say that physicians shouldn't be PIs, but expecting them to easily step out of that role into the research role is asking a lot. The roles are different, and, all too often, we expect them to move fluidly between the two. This is just unrealistic.

What other industries primarily rely on vendors who see their business as a minor sideline? Asking a busy physician to focus on arcane, time-consuming, and often unprofitable clinical trials is like asking car companies to focus on manufacturing airplanes. Sure, they can do it, but it's hardly their strong suit. If we want serious investigators, we need to treat them as serious business partners, not as waiting rooms with warm bodies.

Engineering Controls

Third, and on a very nuts-and-bolts level, I suggest we look to the equivalent of engineering controls to help tackle problems like incorrect dosing, failure to draw samples, missed assessments, etc. In the pharmaceutical manufacturing arena, controls like specially fitted hoses make it almost impossible to accidentally introduce inappropriate materials into the product manufacturing process. The clinical trial version of engineering controls could be bar-coded wrist bands or wallet cards that clearly define what is to happen to the subject on a given day and in what order. My health club employs a bar card system that is more technologically advanced than the typical clinical trial system as it applies to subject procedures.

Rehearsals

Fourth, we are all familiar with investigator meetings in which sponsor personnel lecture PIs and study coordinators about the protocol, case report forms, introductory GCP, etc. A site monitor then presents a condensed version at a site initiation visit. Unfortunately, these educational experiences are usually more boring and theoretical than engaging and practical.

There must be a better way and, in fact, there is: rehearsals. I suggest that our colleagues in the Sales Department might be able to help out here. Yes, the Sales Department — those same colleagues who push us to use key opinion leaders as (lousy) PIs. Sales departments routinely use rehearsals to train their sales representatives. Someone plays the role of physician and new sales reps are coached in simulated sales calls. Why not apply this

technique to clinical trials? I know the first study subject through each site would be grateful.

Conclusion

None of these steps will eliminate every defect, but in the realm of clinical trials, zero defects isn't the goal anyway. Clinical trials are designed by humans, conducted by humans, and use humans as research subjects. Human errors are bound to occur. We need to try new, high-impact solutions rather than just the same old techniques that we have proven, beyond a doubt, to be inadequate. There must be a better way. Instead of just pretending that our goal is high quality, let's actually take steps to achieve it.

The drug and device industries must cope with reduced R&D productivity, higher regulatory burdens, widespread patent expiry, and a host of other challenges. Could re-examining our approach to clinical research quality be part of the solution? As an industry, we owe it to clinical trial subjects, future patients, investigators and ourselves to find out.

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