

Take Back the Research

If you do not read the Editor's Corner by Mikkael Sekeres in *ASH Clinical News*, you should. It is a good read. Mikkael's piece in the June 2017 issue, "Contract Research Agonizations," had me chuckling mightily. He mocks (correctly in my view) contract research organizations and their monitors, who routinely torture those of us who try to make the cancer world a better place.

We never know if our rants will gain traction, but I think that Mikkael may have started something. Not long after publication, a Letter to the Editor appeared that was authored by Steven Le Gouill and Simon Rule and signed by more than 80 prominent European clinical investigators. Whereas Mikkael had made his point with humor, Steven and Simon took their gloves off and struck bare-knuckled at the CROs. Here is an excerpt:

We, the doctors and researchers who treat patients, are the true clinical research specialists. It is therefore our duty to stop the administrative inflation introduced in the name of "good practice" that is beginning to kill clinical research, demotivate clinical research teams, scare away young clinicians, and unnecessarily disperse the limited financial resources that should go toward improving care and science. How could we not denounce a business model that does nothing for patients, unreasonably increases the cost of clinical trials, and ultimately benefits only the industry that invented it?

It's no secret that the CROs generate revenue for themselves by creating work. They generate this work in the name of data quality and patient safety, but anyone who truly understands this world can see right through the charade. How did this happen?

I believe it all goes back to the "Feds." The FDA, the Office for Human Research Protections, and other governing bodies put out vague rules, leaving drug companies and institutions to interpret them. Most organizations will automatically gravitate toward the most cautious interpretation of these rules in an effort to mitigate risk. If you're a pharmaceutical company that just put \$200 million into a drug development package, the last thing you need is the FDA bouncing it back to your feet and saying the data are unreliable. So you hire a CRO, with its impressive and endless stack of SOPs (standard operating procedures). The CRO will clean and scrub the data until everyone knows exactly at what second of which day a particular grade 3 pneumonia "resolved."

Although much of the CRO behavior can be directly traced to perverse financial incentives, other factors come into play. Watching anyone with regulatory jurisdiction over anything is a fascinating study in human behavior. The

narrower the scope of authority, the more rigid the enforcement. I learned this the hard way in college when I attempted to mail a package to a friend overseas. I walked into the post office, package in hand, and waited patiently. When my turn arrived, I handed my package to a postal worker for weight and costs. The look of horror on his face was something I will not forget. Apparently my choice of tape and taping strategy were not up to US Postal Service standards. The worker went "postal," equating my attempt to tape this package with "building a house on quicksand!" I did a walk of shame out of the post office, humiliated by a Cliff Clavin wannabe.

I recall a clinical research audit done a few years ago. The study required baseline PET and CT imaging of the neck, chest, abdomen, and pelvis. In one case, the PET was done and the CT of the chest, abdomen, and pelvis was done. A dedicated CT of the neck was not. I admitted that we had missed the dedicated neck CT but pointed out that the PET included CT of the neck. "Not good enough," declared the auditor. The protocol states that the scans must have IV contrast! This was true, but the patient had no disease in the neck on the PET scan—our error had no impact on data quality or patient safety. "Doesn't matter," declared the auditor. "You enrolled an *ineligible* patient because you failed to get all required baseline tests. This is a *major* deviation. Report this to your IRB immediately!"

This auditor was an MD who does clinical research! My point is, there needs to be more room for judgment. Although a protocol violation had occurred, it was one that had no impact whatsoever. Cite us for a protocol violation if you must (a minor violation, in my view), but do not declare the patient ineligible!

As I get a bit older and potentially wiser, I acquire increasing admiration for folks who fight for what is right. I sincerely hope that Mikkael has started something significant, although I admit I am not sure we have the power to roll back the craziness. I hope I am wrong, and that we (clinical investigators) can lead the charge back toward sanity. There appears to be a precedent; the physician rebellion against the ABIM recertification shakedown seems to be having a meaningful impact. That gives me hope.

Until next month ...



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