JOURNAL OF CLINICAL RESEARCH BEST PRACTICES
Vol. 16, No. 8, August 2020 "Happy Trials to You"

Tales from the Field: Site Monitors Tell Their Stories

By Eric Ceh

The COVID-19 pandemic has accelerated the transition from on-site to remote monitoring. But will remote monitoring ever completely replace on-site monitoring? The true-life, first-person stories below suggest not. Certainly, remote monitoring will never generate these stories of misadventure.

1. The study patients were supposed to be the ones getting the headaches.

I was monitoring a migraine study and visited our top enroller. I discovered why he always had great, clean data: he was changing study data and tossing the old records. At this visit, I found duplicate records and notes where he instructed the coordinators (each of whom I later found out were patients of his—a real conflict of interest) to change "XXX" to "YYY" so the patient would show a good response and to delete the adverse events that were reported. He had been very thorough until then about getting rid of the duplicate records.

I also found notes erroneously filed in a couple of the patients' charts. These notes were for other patients, although that was not initially clear because the initials were the same as those of the study patients. Digging into the data, which was slightly off, I realized that the investigator was giving these non-study patients an anti-epileptic drug (AED) and collecting data for migraine relief. That would not be a big deal if properly set up in an investigator-initiated study, but that's not what he did. Instead, he took our study's case report forms (CRFs), on paper at the time, copied them and used those data points in his own, separate "study." The CRFs were misfiled in our study's records because they were the same forms with the same patient initials. As if that were not bad enough, he was collecting data on these other patients without signed consent forms.

To make matters even worse, I found email correspondence in which he was offering to sell this data to a very well-known AED pharmaceutical company. I notified my project manager, who reported the investigator to the FDA and removed him from our study. When I returned a month later to close the site out, the FDA showed up completely unannounced. Needless to say, the inspection did not go well.

As an aside, my monitoring station for this site was the bathroom (AKA "sample room"). I laid my notes, CRFs, etc. out on the passthrough shelf that opened to the exam room.

2. Who doesn't love a good train wreck? Well, the FDA for one.

I took over a site in Atlanta in an ongoing pulmonary hypertension study. The investigator was the high enroller. We had been informed that, as the high enroller, he would be inspected by the FDA as part of an upcoming routine study audit, so everything needed to be really clean.

The previous monitor had been the site's monitor for about a year before she left the study. When I showed up for my first visit, the coordinator made it clear that she expected me to buy her lunch every day, just as the previous monitor had. Immediately, red flags were flying.

I was told in advance that there were concerns about the data from this site, so I did a retrospective review of all patients and found a ton of problems, including multiple patients on study without signing consent forms, no signatures from most patients on consent forms

© 2020 MAGI and the Author(s)

related to protocol amendments more than six months earlier, multiple other protocol violations, no notes by the investigator in the past six months on any patients, and tons of unreported adverse events.

When I met with the investigator at the end of the visit, he had no idea how many patients he had in the study. He told me he saw every patient at every visit, which was highly unlikely. It was abundantly clear that he had started the study because he was a very well-known opinion leader and was pegged as the lead author of some of the planned study articles. He had turned all study activity over to his sub-investigator and assumed everything was going as planned. He was unaware of all the patients newly enrolled without consent. He was aware of the multiple protocol amendments but was not aware that they had not been implemented or that the revised consent forms had not been signed.

Because an FDA investigation was coming soon, I made a list of all the issues and we discussed the necessary corrections. To his credit, he immediately assembled his team and had them sit with me to discuss the issues and corrective measures necessary over the next few weeks.

At subsequent visits, the coordinator refused to make corrections or complete tasks from the previous monitoring visit. The issues were so overwhelming to her that she just didn't care.

The site was inspected and received a long 483 with Mandatory Action Required. One-third of the investigator's patients were tossed from the study, costing the sponsor a LOT of time and money.

After the initial FDA inspection, the sponsor contacted me to ask for a copy of all my monitor notes, as per FDA request (a good reminder to all clinical research associates (CRAs) that the FDA will demand to see these notes in some cases). I was happy to provide them and VERY glad that my documentation was extremely thorough, including discussions with the investigator and his staff as well as the state of things when I started monitoring.

The previous monitor (no longer working with the sponsor) emailed me and also asked me for copies of my notes, which I did not provide to her. Clearly, she was within the scope of FDA's inspection as well, another good reminder for CRAs.

3. Sometimes, all you can do is take deep breaths.

I was consulting with a contract research organization (CRO) on a Parkinson's disease-with-psychosis study, assisting them with their high-risk (difficult) sites and trying to mend the CRO's and sponsor's relationships with these sites. The CRO was running the study very poorly, utilizing inexperienced CRAs and project managers. They were giving sites misinformation, not following up, and providing sites with little-to-no post-visit detail or instructions.

One of these sites was a key opinion leader in Denver. The CRO's project manager told me that the previous CRAs thought he was making up patients because there were never any patients in his office. However, during my first visit, I discovered that the investigator had retired from his neurology practice and only saw patients through his research site.

The other complicating factor was that he had had very little research experience over the previous 20 years. Clearly, the previous four CRAs (yep, four different CRAs in about a year) had not taken the time to speak with the investigator and fully understand his situation and capabilities.

I also discovered that, perhaps because of his lack of research experience, he thought that vital signs were not important and didn't need to be accurate, so he often recorded the

same heart and respiration rates for all patients seen in a day. He would also change borderline scores on tests like the Mini-Mental State Examination (MMSE), so the patients would qualify for the study because, as a clinician, he wanted to help them and give them some semblance of hope. He was using good, old medical judgment and not following Good Clinical Practice (GCP) with its black-and-white regulations for conducting clinical research.

After working with him for a few months, we got the relationship repaired with the sponsor but not with the CRO. There was just too much damage that could have been avoided by simply using properly trained and experienced CRAs.

4. Did they expect me to be the life of the party?

I was monitoring a couple of studies at a large academic institution. For a period of time, I was usually placed in a cubicle in the general vicinity of the clinical research office. However, they moved me to the entrance to their large office (40+ people) with a work space of two by three feet. People were constantly coming in and out of the office with the door making a distinctive thud each time. To make matters worse, people sometimes put food out on a ledge next to where I was working, so now I had people standing around me eating and talking. No one seemed to care that I was trying to concentrate on my work. It was so frustrating. This went on for a number of visits before arrangements were made for monitoring space in an office area down the hall.

5. Clean data has to start somewhere.

During a SWAT team clean-up, a strange and uncomfortable situation occurred. I should mention that the investigator was a key opinion leader and had the reputation of a high enroller.

We had arrived at the site on schedule and were working in an area near the bathroom. We observed the study coordinator leaving the bathroom with wet hair, as if she had just taken a shower. Close behind her followed the investigator, also with wet hair. Nobody said anything. At future monitoring visits, we preceded our arrival with a call or text to avoid what, to us at least, would be embarrassing situations.

6. Did I mention he’s not a key opinion leader on tax preparation?

While disembarking from my flight en route to a monitoring visit, I received a call from the investigator requesting a check for the completed data entry modules. I explained that I do not deliver checks; they are sent directly from the sponsor to the sites. I also explained that he would receive a check once I had verified the data. The investigator said he needed the money now since the Internal Revenue Service was about to shut him down. He could not guarantee that the site's doors would be open the next day.

I immediately called our budgets person and tried to expedite payment, but it was a holiday in the country where the sponsor was located. I arrived at the site that afternoon to hear the investigator screaming over the phone to the IRS agent.

I completed my two-day visit and a check was sent to the site.

7. You can bring an investigator to a study but you can’t make him do much of anything.

I was assigned to a women’s health study, which started off with a large investigator’s meeting that featured a key opinion leader on the disease. Her talk was informative but I didn’t hear much about her research experience. I was told that this doctor would be one of

my sites, so I introduced myself to her and asked a few questions. I had a sinking feeling that I already knew what the future held.

Sure enough, at the initiation visit, the site had no idea how such a visit is conducted. The investigator was nowhere to be found. The study coordinator hadn't even opened any supplies or read the protocol. I tried to go over the protocol and explain how to order drugs from the call-in service but was met with resistance.

A couple of weeks later, I heard that the site had enrolled a subject so I had to conduct a monitoring visit ASAP. The study coordinator presented me with a patient record consisting of two very vague paragraphs describing how the subject presented and that the study drug had been handed out. The informed consent form wasn't fully completed and there was no record about most of the eligibility criteria.

I asked the investigator and study coordinator about using the call-in randomization process and discovered that they had just handed the subject one of the study meds. I told the sponsor about the situation and we scheduled a training session. We spent two days at the site but it appeared that they still did not know what they were doing. It was like the Keystone Cops.

Luckily for me, I was reassigned to a different site. About six months later, I got a call from a sponsor quality assurance auditor. He had followed up on the informed consent issues and, during the visit, had extra time to go over recently enrolled subjects. He found the same issues with those subjects. He was going to recommend that the site be barred from further enrollment.

8. FedEx must be really expanding their service lines.

At a site I was monitoring there was a change in study coordinators. From the start, I noticed a distinct decrease in the quality of the documentation of study visits and also observed that lab samples were not being processed correctly.

The study coordinator did this little stunt around noon when she would excuse herself and then not be available for hours. So, on one of my visits, I followed her out of the room. A FedEx man was by her office. He proceeded to go into the room with her. Later, I came out and went by her office. The lights were out and door was locked. I knocked but no one answered. The next day, I noticed the same FedEx guy standing around and the coordinator again leaving. I tried to discuss the situation and other issues with her but she was evasive. I then spoke with the investigator and suggested that the coordinator be changed. After much discussion, he agreed to the change, although he thought the rendezvous with the FedEx man were farfetched.

I completed the study with another coordinator. At the closeout visit, the site manager said, "I met the FedEx man and he no longer comes here."

9. It's always winter somewhere, in fact, it's always winter here.

At one site I monitored, I was taken to what appeared to be a lab area next to a very large freezer. It was very noisy, and a vent was blowing the coldest air. I had to wear my heavy-duty winter coat to work in that room. I told the study coordinator that I wouldn't recommend putting an auditor in there as they would most likely not react kindly.

10. I guess I didn't know what it meant to be treated like a lady.

Early in my career, I was assigned to monitor some sites for a huge infectious disease study. The investigator meeting was held at one of the nicest hotels in California. One of my

assigned sites had a rather flamboyant study coordinator, who indicated she expected to be treated like a lady when I conducted my monitor visits. Unclear of her meaning, I made sure I fully understood the sponsor's entertainment policy.

I went to the site for the initiation visit. Luckily, my manager accompanied me on the visit, so I could follow her lead. The coordinator was very touchy-feely with the investigators, consoling them about difficult study details and how she would be there to help them along the way.

I later got a call from the site manager that they would be bowing out of the study. It turned out that the study coordinator was having an affair with *two* of the docs. The site manager was so embarrassed that we never heard from them again. I still remember my manager's comment: "She (the study coordinator) didn't have nice teeth."

11. At least they didn't give me a mop.

One site had me monitor in a cleaning supply closet, complete with a chain-link fence around it. In addition to having to breathe the chemicals around me, it was so cold I had to keep my coat on. They didn't even give me a real desk; I had to manage with a makeshift counter made of two-by-fours. I discussed the situation with the sponsor, but they did nothing about it. After that study, I refused to go back there again.

12. They were way scarier than any investigator.

At one site, I sometimes did work in the medical records office, which was way down in the basement of the hospital. On several occasions, I could not believe what my ears were hearing. The women in that office weren't discussing knitting and baking. I thought I had a knack for colorful language but those ladies made me feel my guy talk was totally lame and nondescript.

13. Sometimes, you can just let the data speak for itself.

Early in my career, I was monitoring an infectious disease study at a hospital. There was a change in study coordinators and the new coordinator was not particularly friendly. On my first monitoring visit with her, she took me to a room at the hospital that was as close to the attic of a house as possible: hot, smelly and crammed full of one-arm schoolboy desks. I would be working in this room.

The study averaged four to five thick medical records binders per patient, there being no electronic medical records at the time. I changed to a short-sleeve shirt, rearranged the desks to lay out the patient binders as best I could, and gutted out a couple of visits. At a subsequent visit, the sponsor came along as part of a good-will tour and met the investigator in the "attic." When the investigator said how okay everything was, I interrupted to state otherwise. An active conversation ensued.

Luckily for me, the study coordinator was very lazy and, so far, she had never completed the concomitant med and adverse event (AE) case report forms for any study visit; she just waited for me to make queries and enter that data. I had not been able to discuss this issue with the investigator, so I blurted out, "Just go ahead and grab any of these patient CRF binders and you'll see the blank con-med and adverse event pages." The investigator angrily quickly grabbed four subject binders, slammed them on the desk, and began to go through them. They all had blank con-med and AE CRFs. His facial expression abruptly changed. He offered an apology and said the study coordinator had other issues and the blank pages confirmed his suspicions. He indicated he intended to fire the study coordinator.

Sure enough, I had a new study coordinator at my next monitoring visit and a much better room to conduct my work in.

Conclusion

Thank you to the monitors who contributed to this article.

I hope you have enjoyed these stories and now have a better appreciation of what monitors can go through in the course of their work. Are site monitors the least-appreciated people in clinical research? I think so.

Author

Eric Ceh, SEC Clinical Consulting, can be reached at sec_consulting@sbcglobal.net.

© 2020 MAGI and the Author(s)