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Clinical Research Fraud: The Case of the Errant Investigator

By Barbara Burkott

Managing pain during and after orthopedic surgery can be a major challenge. Multimodal analgesia addresses the challenge by employing two or more analgesic agents that affect different pain mechanisms. In addition to reducing pain, multimodal analgesia also reduces side effects by allowing the use of lower dosages of each agent.

Dr. Scott Reuben was Professor of Anesthesiology and Pain Medicine at Tufts University in Boston, Massachusetts, and Chief of Acute Pain at Baystate Medical Center (BMC) in Springfield, Massachusetts. As the leader in research on multimodal analgesia for post-operative pain management, especially in orthopedic surgery, Dr. Ruben published 21 journal articles on the topic, starting in 1996.[1] These articles were based on several investigator-initiated clinical studies conducted at BMC.

Dr. Reuben's work came under suspicion in 2008, when a routine review at BMC noticed that studies described in two articles did not appear to have received IRB approval. Further investigation revealed forged signatures by presumed co-authors and imaginary studies that enrolled imaginary subjects. As a result, BMC retracted Dr. Reuben's articles, his employer terminated his employment, the FDA conducted an inspection and debarred him, he lost his medical license, and a federal court sentenced him in 2010 to six months in prison and $415,000 in financial penalties. The scientific foundation for multimodal analgesia was shattered.

Remediation

When the fraud was discovered, Dr. Reuben's colleagues (including the author) expressed shock and disbelief:

- He could not have done this! We trusted him as a physician, as a colleague. He is a nice person!
- How is something like this even accomplished? Someone had to know!

We thought we were following all the regulations. We thought we had all of the institutional checks and balances in place. We thought our standard operating procedures (SOPs) were sufficient. We thought our culture of teamwork and transparency meant all activities were visible. We thought we were operating under the highest possible ethical standards. We thought all of our colleagues had impeccable integrity. We thought wrong.

As it turned out, Dr. Reuben conducted two types of clinical research: industry-sponsored and investigator-initiated. He conducted his industry-sponsored trials normally, with IRB approvals, study coordinators, site monitors, etc. However, he conducted his investigator-initiated studies entirely on his own. (His investigator-initiated trials were industry-funded with grant payments made directly to him personally.) He never informed the local IRB of the studies; instead, he altered an old IRB approval stamp on his "new" study to secure publication in journals. He told his study coordinators that they had their hands full with industry-sponsored studies. As a result, it took BMC over 10 years to connect the dots from publications to imaginary studies.

Dr. Reuben's departure meant our remediation work was just getting started. The imaginary studies were already closed, but we had to pull apart the tangle of sponsors, staff, subjects, documentation, co-authors and journals to determine who, if anyone, may have had

knowledge or been involved. Once it was determined that Dr. Reuben perpetrated this deception alone, rebuilding an effective research process was the hard part. The FDA inspection was a great incentive. Each department implemented a preliminary protocol review process, requiring departmental sign-off before advancing to IRB submission. IRB forms and processes changed. We implemented new software for IRB submissions and review management. We updated job descriptions. We updated all the SOPs.

We had to make sure nothing like this could ever happen again. The IRB is now meticulous in its review and courageous in asking questions and, when appropriate, saying "no." It looks at:

- WHO is conducting the research? Is the principal investigator qualified by training and experience to conduct research?
- WHAT is being researched? Is it based on solid science? Will the results make a difference?
- WHERE is research being conducted? Are the facilities adequate?
- WHEN is research being conducted? Is the time required to do the research available to the investigator and staff?
- WHY is research being conducted? Is there compensation for the research?
- HOW is the research being conducted? Are the SOPs adequate and are they being followed?

Now, we submit every protocol to Sponsored Programs Administration (SPA), which manages a registry of all research, no matter the type or size of study, even retrospective chart reviews and nursing research. If there is a question about the legitimacy or status of a study, a request is made to SPA and/or the IRB to check the study registry and/or IRB number.

BMC's Research Integrity and Education (RIE) Program now ensures the integrity of human subjects research.

The RIE Program requires CITI training for all persons involved in any form of human or animal research. It also provides internal education to investigators, staff and patients involved in research. Monthly clinical research staff meetings provide informational updates. Larger educational research topics (Grand Rounds) are scheduled throughout the year, as speakers are available.

In 2006, the REI Program established an internal audit program to assess compliance with federal, state, local and institutional laws, regulations and policies and identify areas for improvement, but audits were not performed on a routine basis. Now, at minimum, we review at least one protocol for every investigator at least once per year. Audits include assessing the accuracy and completeness of IRB and investigator files, confirming adherence to federal, state regulations, IRB and institutional requirements, and reviewing staff training records.

In 2010, the REI Program obtained accreditation from the Association for the Accreditation of Human Research Protection Programs (AAHRPP). This accreditation demonstrates our commitment to human subject protection and continuous quality improvement. Preparing for accreditation requires a comprehensive review and updating of SOPs. (Although Dr. Reuben did not harm any imaginary subjects, it was not due to IRB oversight.)

The new process seems cumbersome, but people are adjusting and some requirements are gradually relaxing. We no longer have the luxury of just hoping for the best.

Will these steps absolutely guarantee that another BMC physician will never publish articles based on imaginary studies or commit a different type of fraud? No, outright fraud can be difficult to detect because it is so unexpected. However, our new systems make it much more difficult. In addition, anti-fraud vigilance is now embedded in our culture.

Conclusion

We never imagined a trusted colleagues could commit fraud for years right under our noses. It couldn't happen here! But, it did! We thought we had the appropriate policies and procedures in place. We had SOPs that met the regulatory requirements. We thought we were vigilant. Obviously, our protections were inadequate. We hope our new protections will help us meet the challenge but we have the humility to know we can never rest.

You are now on notice: Fraud or other misconduct might be occurring in your organization at this very moment. How do you really know it's not?

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References

1. Wikipedia, http://en.wikipedia.org/wiki/Scott_Reuben

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