

20 Protection of Human Research Subjects: From Compliance to Conscience

Greg Koski

How many people should we allow to be killed in human research trials? In 1995, Nicole Wan, a 19-year-old graduate student died at the University of Rochester from an overdose of lidocaine given to make her comfortable during bronchial alveolar lavage. The New York State Department of Health investigated and found that no safeguards were built into the protocol for the appropriate dose of lidocaine. No appropriate monitoring was conducted after the procedure was completed and she was sent out on her own. The Department found gross deficiencies in the entire process, with neglect of responsibilities by the investigators, the internal review board, and the institution.

There are, of course, other cases. We must ask ourselves why we have regulations being imposed on us in the first place. We must think about this when we complain about regulations and the government. When was the last time you saw a regulation to prohibit excessive contributions to valuable charities?

I spent about 30 years at a university as a basic, clinical investigator. I also worked in the research administration area, dealing with exactly the kinds of headaches and problems that these regulators impose on researchers. I have lived with them from both sides. And I know that you have to ask why the regulations are there.

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Why is there an enormous public focus and discussion about conflicts of interest in human research? Why are people demanding that our academic institutions shine lights into dark corners of their institutions where financial relationships exist that could compromise either the objectivity of the science or the well-being of the patients participating in the trials?

People are not talking about conflicts of interest because there is no problem. Consider the case of Jesse Gelsinger, an 18-year-old with a genetic disease who entered a trial in 1999, without full knowledge of what was going to be involved. He was not presented with information that might have been valuable in making a decision in concert with his family about whether or not to participate in the trial. There were gross deficiencies in the conduct of the trial, gross deficiencies in documentation of the data, and gross deficiencies in reporting requirements. And this was at one of our nation's premier academic centers and by one of our country's finest scientists (the acknowledged leader in the field).

Many people look to the death of Jesse Gelsinger as that line that defines where we had been and where we are now. As tragic as it is, and as painful as it is for the University of Pennsylvania and, especially, his family, to hear that story told over and over again, his death has done more to galvanize the necessary energy to address the problems that exist in this area than any other event that has occurred recently.

This case shows why we have to have regulations. Without regulations, we scientists and physicians have failed to make the commitments necessary to do what is appropriate to protect those we depend on to take part in our science, at least as far as human science goes.

Suppose we had a different world where everyone did the right thing all of the time. How would it be different? How could we get there? Wouldn't it be wonderful if the code of ethics described by Howard Schachman in Chapter 22 of this volume was actually followed by all the people who are members of that society?

The American Society of Gene Therapy (ASGT), after the Gelsinger affair, said, "We will not allow anyone in our organization to have an equity interest in a trial in which they are an investigator." I do not know how they are going to police that. I would hate to think that they would have to police that. I would hate to think that anybody who had an equity interest in a trial would have the poor judgment to actually participate as an investigator.

I do not yet know how many members of ASGT have been removed because they did a trial in which they had an equity interest. I would

like to believe that they all follow that guideline, just as I would like to believe that every investigator in this country adheres completely to the principles in the Belmont Report.¹ But they do not. We need to get to that place where they do. We need to get to that place where people truly embrace the notion that if you are going to experiment on your fellow humans, you must put their interests ahead of your own interests, whether financial, academic, or personal.

Protection of human subjects in research is not just an administrative process. It is not just an administrative burden. It is part of the science. It is part of what we do when we experiment on human beings, because we have a responsibility to put their interests first.

Why do we have regulations? In the 1960s, before we had regulations, people had procedures performed on them by the National Institutes of Health and the best academic centers across the country without being told that the procedures were life-threatening. That is why we have regulations. Right now we have a reactive, regulatory-based system, and that is unfortunate. We should move toward a different system, one that is proactive and performance-based.

That is what we are trying to do. We are trying to get scientists who do human research in this country to embrace the notion that the protection of subjects is inherent in what they do, not just an administrative burden. We need to build a system that promotes that, and we are trying to make that shift in the paradigm.

We are trying to do this in a way that achieves many important goals, not the least of which is simplifying the process that we have. I think everyone would endorse that. How can people do the right thing when they cannot figure out what it is? The system now is very complex, with many differences across many agencies and different systems.

We must achieve greater simplicity and uniformity. This is our mantra. We go all over the country saying this. With greater simplicity and uniformity, we can achieve the kinds of efficiencies and effectiveness of process that we need.

Jerry Kassirer recently published an article titled "Pseudoaccountability" in the *Annals of Internal Medicine*.² It reflects on the fact that in medicine in particular (the audience he is addressing) we have continued to develop systems, codes, and ethics that we expect people to adhere to. Sadly, they do not. So we have systems of pseudoaccountability, as he puts it.

We need to move to a system where we have true accountability in human research, because we have seen too many examples of lack of trust for too long. The list is very long.

When the Office for Protection from Research Risks (OPRR) made 20 site visits to our major academic centers, more than half of them had gross deficiencies in the process. A lot of that process is paperwork and compliance-based, but you know you have to do the paperwork. You made a commitment to the government as a recipient of funds that you will do the paperwork correctly. Many places have one half-time equivalent person dedicated to a process that supports over 2,500 ongoing human research protocols. This is not accountability or assurance. This is gross negligence. We have got to find ways to do better.

We are looking at getting rid of every ineffective regulation that we can so we can focus on a process that moves toward a smaller, more effective government. We have not passed a single regulation since I have been in office.

We will soon convene a brainstorming session that will bring together the stakeholders from the research community as well as people from government. We will look at every conceivable way that we can eliminate regulations that don't serve a valuable purpose. I personally, and my office, expect every one of the institutions, and every person involved in this process, to make a commitment similar to ours, that if you are going to do it, you are going to do it right.

In addition, the National Human Research Protections Advisory Committee of the OPRR is the first committee to work on an ongoing basis to bring public dialogue into the development of effective policies for the appropriate and responsible conduct of human research. We are directing all of our efforts toward making it easier for people to make the promise that they will do it right and to make it easier to enter into collaborative relationships to relieve some administrative burdens. We are redirecting the resources in the office toward support, outreach, education, and quality improvement. This is a very different approach from what was done in the past.

If we work together in a public-private partnership that establishes clear standards of excellence and clear expectations, we can get people to rise to this higher level of performance that is directed toward achieving our goals. If we use a minimized kind of government and work in partnership with those public processes such as certification and accreditation, I think we will have a system that is doing what it is supposed to do, a system that adds value rather than becomes a system of paperwork.

Compliance by itself does not do a thing to protect people. That is why you cannot get too worried about having every consent form dated just right. If we thought that dating consent forms properly was going to help protect people, that would be worth doing. But I do not believe that. I think an effective consent process is something that helps protect people. If we could get people to do an effective consent process, we probably would not have to focus so much on dating the consent forms correctly.

We have gotten to where we are through our own actions. We are going to have to work together now to get back to a place where reason prevails, and we are doing things for the right reasons rather than doing them because we have to.

Endnotes

1. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979.
2. Kassirer, Jerome P. "Pseudoaccountability." *Annals of Internal Medicine* 134, no. 7 (April 2001): 587-590.

