Testimony
Before the
United States Senate
Health Education Labor and Pensions
Committee
Protecting Human Subjects in Research:
Are Current Safeguards Adequate?

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I am Cherlynn Mathias a Registered Nurse currently working as the Manager of the Clinical Research Department at Harris Methodist Fort Worth, a large community hospital in Texas. However, today I am here to testify about my experiences as a study coordinator at the University of Oklahoma.

I was hired in June of 1999 and almost immediately I realized that ineligible subjects were being enrolled into the Melanoma Clinical Trial that Dr. J. Michael McGee was conducting. The trial had actually opened three years before my employment. When I asked about the subjects being ineligible, I was told that McGee as the Principal Investigator, (clinical researcher) could enroll whomever he wished and that the conduct of the study was his responsibility. In late July, Dr. McGee requested that I build a database, which contained endpoints not described in his study design. The purpose of the database was to gather statistics for publication and also for an upcoming medical conference in which McGee was scheduled to speak. The building of the database required me to do a retrospective chart review of all the melanoma vaccine patients. In the course of doing the chart reviews, I discovered that several patients had been allowed to self inject the vaccine. The patients who were self-injecting were storing the vaccine at home in their refrigerators. Not only was I surprised by this finding because of the obvious concern for drug accountability record keeping and storage of the experimental drug in an unsecured environment, but also I was concerned about patient safety. The Vaccine Protocol called for the drug to be stored at the temperature of liquid nitrogen. I wondered if the vaccine was stable at the higher temperatures? Also the patients were at risk for drug reactions that might be serious and life threatening, such as anaphylactic reactions. It was obvious that adverse event monitoring was lacking.

In July after discovering that a monitoring plan had never been developed, I was able to convince Dr. McGee to travel to another clinical site. The site was an Oncologist office in Springfield, Missouri. We discovered that the drug was being kept in the refrigerator freezer, which was located in the staff lounge. Once again the drug was not being stored at the proper temperatures and the drug was being subjected to a freeze thaw cycle. Nor was the drug in a secure location. In fact there was not any temperature monitoring occurring at all. Institutional Review Boards, IRB's, are the gatekeepers for the safety and well fare of the human subject, as mandated by the federal regulations. However we found out that the Oncologist had never sought local IRB approval, although he himself was an IRB member.

In October I discovered that the current version of the protocol had never been submitted to the IRB, although it had been in use for seven months. However, the OU IRB had approved a change in the inform consent, which new title and contact information included St. John's Medical Center. This is significant because the study was never submitted to the St. John's IRB, even though St. John's IRB chair was also a member of the OU IRB and he was present when the change was voted on.

I informed McGee that we were using an unapproved version of the protocol and inform consent. He was surprised and disbelieved the information. After a discussion he agreed that I should contact the OU IRB administrator.

The administrator met with Dr. McGee and I in late October. He gave us some bad advice. He said that the IRB was not concerned about monitoring, or study design issues. He also said that the problems concerning the other sites and their approval was none of the IRB's business, but rather a FDA matter. He instructed us to write protocol amendments that he would get approved to cover us retrospectively.

In November protocol amendments were submitted to the IRB. They included a change to allow patients to self-inject, increase the size of the trial, change the statistical power, addition of a second drug GM-CSF, and other modifications to the protocol that were already ongoing. These are but a few examples that patient's safety and welfare were compromised as mandated by the federal regulations.

I continued to be concerned about the trial. I had already started staying late and reading everything I could find on the FDA website concerning Good Clinical Practices, Good Manufacturing Practices, and Good Laboratory Practices. The more I read the more alarmed I became. I started asking questions about the manufacturing process and became convinced that the lab was out of compliance as well. Many of the required safety testing for new lots of vaccine had never been completed. Plus the vaccine was not being manufactured in a sterile environment. Dr. McGee continued to increase enrollment.

Soon thereafter I started following the chain of command within the medical college and sounding the alarm for what I saw as serious non-

compliance with the federal regulations that were put in place to protect human subjects. Eventually this led me all the way to the top of the medical college. By the time I blew the whistle in June of 2000 the University had formed a committee that included the Dean of the Medical College; the Director of the Office of Research; the IRB Chair; the Lab Director; Dr. McGee; Our Department Chair and myself. The committee was engaged in acts of cover-up instead of promptly reporting as required by the federal regulations.

What led me to contact the Office of Human Research Protections? It was the pledge that I took when I became a registered nurse, that I would be a patient advocate. I was haunted by many images, but particularly one image continued to eat at me. It was the inform consent process. By now I knew that it had been coercive to promise subjects that the melanoma vaccine offered hope of a cure.

Adverse events reporting were practically non-existent. Unfortunelty, this sad situation of not reporting adverse events is the same across the nation as was found by a study conducted by the University of Maryland School of Medicine, Dr. Adil Shamoo.

Today the University had adopted many positive changes in the way research is conducted. The President of OU is David Boren. I believe in David Boren. In my opinion he is one of Oklahoma's greatest assets. The University is in the process of implementing a model compliance program and David Boren; the president of OU is committed to doing so.

One of the changes is he has put in place is greater protections for whistle blowers. I am a graduate of OU and actually in my own way I love the University.

Now that I have moved from an academic medical center to a community setting, I have recognized a new set of inadequacies in the system. It is common practice for physicians in private practice to select potential participants from their own patient databases. The inform consent process in such instances needs to be more carefully monitored. In such circumstances the relationship and role between patient and doctor; researcher and participant becomes convoluted. Participants too often are mislead concerning possible benefits and risks. Many physicians who have experienced a loss of revenue due to the restructuring of health care are using the monies paid for research as a way to supplement income.

Conflicts of interest do not escape even those at the lowest level in research operations, the research staff. I like many of my peers, job performance is predominately gauged on the number of participants enrolled and not necessarily on the quality of these data. I believe the pressure on the research staff to meet enrollment quotas puts the inform consent process at jeopardy.

Another threat to the research process and human subject protections is the lack of adequately trained research personnel. Individuals are frequently given the tasks of study coordination without

proper training. Investigators often know even less than the research staff about the expectations involved in research implementation. Certification by all those involved in research would certainly be of benefit. I strongly urge you to pass such legislation and I believe the concern for the American Public's safety should mandate it.

I also urge you to pass legislation that allows the regulators to fine individual investigators and to increase the budget that would allow for more oversight. The regulators are hamstrung when it comes to enforcement. We must give them the tools to hold individuals accountable for their actions.

Lastly, an organization which I recently joined, CIRCARE, Citizens for the Responsible Conduct In Research, is predominately troubled by the fact that federal guidelines do not apply to privately funded research (except for drug applications to the Food and Drug Administration (FDA)), thus creating a two-tiered system of human subject research standards and safeguards. I urge you to pass legislation that would require all research to be subject to the jurisdiction of FDA and OHRP; therefore, I appeal to you for the passage of the National Human Research Protection Act.