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Health Law

Wright v. Fred Hutchinson Cancer Center: Maintaining Patient and Public Trust in Clinical Research

An ethical case explores a lawsuit against Fred Hutchinson Cancer Center of Seattle by patients who claimed they were not told of the full risks associated with a clinical trial they participated in.

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Fred Hutchinson Cancer Research Center is the largest and most successful bone marrow transplant center in the world and receives more funding from the National Institute of Health (NIH) than any other independent US research institute. In the 1980s the center conducted a series of clinical trials using T-cell depletion in an effort to prevent graft-versus-host-disease (GVHD), a major cause of death in bone marrow transplant patients. Several of the patients enrolled in the trials died. After an inflammatory series of articles about the clinical trials in *The Seattle Times* [1], several families of patients who had participated in T-cell depletion clinical trials sued the center [2]. The patients' families claimed that clinical investigators at the center did not disclose to the patients that the experimental GVHD treatment was known to cause bone marrow treatment rejection, that they did not disclose relevant information to the Institutional Review Board (IRB) and intimidated the IRB in contravention of federal regulations, and that investigators had a financial interest in the outcome of the trial due to their ownership of stock in the company supplying materials for the trial.

Depositions taken from individuals involved in the trials and expert physicians who objectively reviewed the case and testified to its merits revealed that there were lengthy, detailed, and documented discussions with patients and their families that described the potential risks and benefits of the clinical trials, that there was extensive opportunity for patients and their families to ask questions and discuss alternatives and concerns about the trials, and that the written consent forms allowed patients to make informed choices about their treatment and trial participation. Further, the chairman of the IRB that had approved the trials indicated that the clinical trials were reviewed, assessed, and approved independently and without obstruction or intimidation by the trial investigators. Finally, although the company that granted a license to use several monoclonal antibodies for the trials was co-founded by one of the investigators and several physicians at the center owned stock in the company, the company did not sell or have plans to sell any of the antibodies for the clinical trials treatment, and they did not seek patent protection for the antibodies or their use.

The patients' families made the following legal claims:

- the set of federal regulations that define research requirements for informed consent in clinical trials, known as the Common Rule [3] was violated [4] and under the Civil Rights Act of 1983 families could sue for damages.
- the families were third-party beneficiaries to the contract between the center and the Department of Health and Human Services, which disburses federal grant funds on the condition that the research fulfills federal regulatory IRB criteria for ethical research conduct; and
- the families had their US constitutional due process rights under the 14th Amendment violated when the Center interfered with the IRB procedures because adequate research procedures had not been in place and the patients had suffered harm.They claimed that US acceptance of the Nuremberg Code (which describes the special need

> for safeguards for human experimentation), Declaration of Helsinki (which discusses the disclosure standards for informed consent), and Belmont Report (which describes the inadequacy of medical malpractice standards to ensure informed consent in clinical trials and the need for additional safeguards), all indicated US acceptance of such a standard in due process jurisprudence.

Disposition: Wright v Fred Hutchinson Cancer Center

The US district court for the Western District of Washington dismissed all of the patients' family claims, holding for the center and granting the center's motion for judgment in its favor.

At the outset, the court noted the standard for granting the center's motion:

> The Court…accepts as true the allegations of the plaintiffs'…and views them in the light most favorable to the plaintiffs. [Defendant's] motion[s]…will not be granted unless it "appears beyond doubt that the plaintiff can prove no set of facts in support of [its] claim which would entitle [it] to relief."

The court first noted that there is no private right of action for violations of regulations such as the Common Rule for informed consent in clinical trials because such breaches are not deemed violations of a "federal right" as defined by law. Next, it noted that there was no legal support for a private civil rights claim because neither statute nor legislation has defined a right of action for Common Rule regulatory violation.

Next, the court disagreed with the families' claim to third-party beneficiary status. The court held that parties that may benefit from a government contract are not generally assumed to be true third-party beneficiaries; that is, they do not have standing to enforce an agreement between parties in a governmental contract unless there is a specified and clear intent noted in the agreement or by the authorizing statute that defines the agreement. In this case, the parties were not intended under the agreement or any authorizing law to have these kinds of enforceable rights, and hence the families could not legally support their claim.

Lastly, the court addressed the 14th Amendment Constitutional claim and held that the families' due process rights were not violated. Under the 14th Amendment of the US Constitution, citizens are entitled to have adequate due process. This means that the government must have adequate procedures to protect the individual, but flawless implementation of the procedures is not required. However, if harm occurs due to imperfect procedure application, the state must provide an adequate post-deprivation remedy. The traditional state tort system is usually considered an adequate post-deprivation remedy. Because the families had access to adequate procedures—a standard IRB process—and had access to post-deprivation tort remedies, the court concluded that there was no due process violation.

The court later dismissed the patients' families' claims as well as their motions for reconsideration.

Commentary

The patients in any clinical trial have the fundamental right to assess and determine the extent of their participation through adequate informed consent. Under the AMA *Code of Ethics* Opinion 8.08, patients have the absolute right to self-decision regarding treatment modalities, and such self-decision can only be effectively expressed if they have all material information regarding treatment [5]. It is therefore the physician's duty to present the medical facts and circumstances in a manner that the patient can understand and to make clinical recommendations that are consistent with sound medical practice [6].

In the case of clinical trials, the obligation extends further. The AMA *Code* indicates that, when experimental, the "clinical investigation…[must be] part of a systematic program competently designed, under acceptable standards of scientific research, to produce data which are scientifically valid and significant" [7]. As part of this obligation, physicians are also required to indicate any potential or actual conflicts of interest in the outcomes of the trial: "any material ties to companies whose products they are investigating, including: financial ties, participation in educational activities supported by the companies, participation in other research projects funded by the companies, consulting arrangements, and any other ties" must be disclosed [7].

In this case, physicians at the Fred Hutchinson Cancer Center appear to have attempted to fully inform the patients about the potential risks and benefits associated with the GVHD T-cell depletion trials. Renowned, neutral experts in both clinical trials and clinical medical ethics appeared to agree that the extensive discussions and documentation were well within the bounds of acceptability for disclosure and offered adequate opportunity for patient concerns to be raised. Indeed, the extent of discussion and documentation presented in deposition was exemplary for clinical trials research, at least with regard to the scientific nature of the trials.

Although this court decided that the extent or relationship of physicians in the clinical trials to corporate interests did not need to be disclosed under federal rules, it can be argued from an ethical perspective that the relationship between the investigators and the company that supplied monoclonal antibodies should have been disclosed to all patients clearly and early. One of the investigators had co-founded the company and others owned stock in it. Transparency is the hallmark of trust, and it may have been that patient families, upon discovering these relationships, were understandably skeptical of official explanations. In particular, the lack of full and frank disclosure may have led to an increased reliance by the patients and their families upon the depiction by newspaper accounts such as in the *Seattle Times* and elsewhere, rather than by explanations the center or the physician investigators themselves provided.

Clinical trials with extensive informed consent have the potential to benefit the patients who engage in them as well as the present and future society. Any health care providers who seek to participate, and have their patients participate, in clinical trials must rigorously adhere to the *Code of Ethics* principles both in letter and in spirit. Indeed, physicians must avoid both actual impropriety as well as the appearance of impropriety. Only by doing so will patient and provider trust—the foundation of the therapeutic relationship—be maintained, and a partnership between the two promoted that will result in optimal outcomes for the patient today and in the future.

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