

PLAINTIFF'S ATTORNEY SPEAKS OUT ON CLINICAL TRIAL CONDUCT

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The Monthly Bulletin recently interviewed attorney Alan Milstein to seek his views regarding the conduct of clinical trials today. Milstein, a partner at Sherman, Silverstein, Kohl, Rose & Podolsky, P.A., in Pennsauken, N.J., has served as the plaintiff's attorney in several high-profile lawsuits against institutions conducting clinical trials. He represented the family of Jesse Gelsinger, an 18-year-old patient who died from complications related to a gene therapy trial conducted at the University of Pennsylvania.

Milstein also serves as an adjunct professor at Temple University's Beasley School of Law, where he received his law degree in 1983. He has a master's degree in American Studies from the University of Kansas and an undergraduate degree from the University of Maryland.

Q: Several of your complaints against research institutions or investigators refer to "financial interest[s]" that the defendant investigators allegedly hold in companies that are sponsoring clinical trials. What steps should institutions, investigators and institutional review board (IRB) members take to minimize conflicts of interest in clinical research? Would clear and up-front disclosure of these interests to patients prior to their enrollment solve this problem?

Milstein: Absolutely not. Disclosure is not the answer to conflicts of interest. You have to eliminate conflicts of interest. You cannot manage them; they must be eliminated so that the investigators and the institutions have no material, financial incentives with respect to the research that they're conducting. Disclosure does not solve that problem.

Q: In a recent Harris survey of roughly 2,000 adults, only about 25 percent of respondents said they were "very confident" that clinical trial participants "are treated as patients, not as guinea pigs" and only 20 percent said they were "very confident" that patients "[a]re not recruited just so that the doctors and hospitals involved can make more money" (see "Majority of Americans Find Clinical Trial Participation Risky, Recent Survey Finds," April 2002, p. 3). What should companies and researchers do to give the public greater confidence in the way clinical trials are conducted?

Milstein: Well, I think an essential part of that is to get the money influence out of these trials, so that's certainly one medial measure. Secondly, there needs to be a greater emphasis on the informed consent process - not simply relying on the document, but the process - to make sure that subjects understand the nature and purpose of the experiment and the risks and benefits of their participation. And, there needs to be effective oversight of the clinical trial process both by the IRB system, which at present is overworked and overburdened, and by the governmental regulatory agencies, such as [the Office of Human Research Protections (OHRP)] and the FDA.

Q: In several of the complaints your firm has filed, one particularly controversial cause of action has been the charge that defendants in these suits breached the right of

subjects “to be treated with dignity” as enunciated in the Nuremberg Code and the Declaration of Helsinki. Could you explain this further?

Milstein: In virtually every claim we’ve brought, we have sought what we call dignity damages; such a claim is not new. The control group [participants] in the case arising out of the Tuskegee Syphilis Study received damages in the ultimate settlement, which could only be for their dignitary harm. These damages compensate a subject who was unwittingly part of an unethical experiment. So that is one subset of the dignity claims.

In some of the cases that we have brought involving state actors, we have sought to claim a constitutional right analogous to the right to bodily integrity and we’ve called that the right to essential human dignity. This phrase comes out of Justice [William] Brennan’s dissent in the case involving involuntary LSD experiments conducted on soldiers. [*Editor’s note:* Milstein is referring to *U.S. v. Stanley*, 107 S. Ct. 3054 (1987), in which the U.S. Army “secretly administered doses” of LSD on four separate occasions to James B. Stanley, a soldier who “volunteered ... to test the effectiveness of protective clothing and equipment as defenses against chemical warfare.” The majority of the U.S. Supreme Court overturned an appellate court ruling that would have allowed Stanley to file suit against the government under the Federal Torts Claim Act for the problems he subsequently experienced. In a dissenting opinion, Brennan emphasized the need for researchers to obtain “voluntary consent” from their subjects and insisted that “[s]oldiers ought not be asked to defend a Constitution indifferent to their essential human dignity.”]

In essence, that claim says that like the right to bodily integrity - which has long been held to be a constitutional right - there is within the liberty interest of the 14th Amendment a constitutional right to be free from state-sponsored unethical human experiments.

It’s been somewhat misinterpreted by the press to say [dignity damages] come out of Nuremberg or ... the Helsinki Declaration. I’m well aware that neither Nuremberg nor Helsinki establishes the law of the land. But what we have argued is that both Nuremberg and Helsinki are reflections of what we as society deem [to be] essential human rights. I don’t think anybody would question that in any civilized society the state should not be able to conduct experiments on its citizens without voluntary, full and complete informed consent.

Q: Your firm recently filed suit on behalf of the widow of a man involved in an artificial heart clinical trial (*Quinn v. Abiomed*, Court of Common Pleas, Philadelphia County, No. 001524). One aspect of that suit that has garnered significant attention is your decision to name a patient advocate as a defendant. In the complaint, the advocate, a physician, is alleged to have committed malpractice and negligence by failing to “advocate for the Quinns” by not asking sufficient questions of the investigators and by failing to fully explain to the Quinns the “risks and limited benefits” associated with Mr. Quinn’s participation in the artificial heart trials. Could you explain why you chose to name the patient advocate?

Milstein: It was a critical part of the claims for which the Quinns had sought redress. I'm a strong supporter of the patient advocate system. I believe that these advocates are important [in] ensuring that clinical trials are conducted ethically. But when [you] are a patient advocate, that involves some serious responsibilities. And with any kind of responsibility comes potential liability.

Q: Could other participants in the clinical research process, such as clinical research coordinators or monitors employed by sponsors and investigating institutions, also be deemed to have committed malpractice or negligence using the same types of arguments made in *Quinn* or in *Robertson v. McGee* (U.S. District Court for the Northern District of Oklahoma, Case No. 01CV00GOH(M)), in which the bioethicist who advised the IRB was named as a defendant because he allegedly failed "to exercise reasonable care under all of the circumstances, in accordance with accepted bioethical practices?"

Milstein: Absolutely. Anybody who has the responsibility to protect human subjects is potentially liable in a situation where that protection has broken down, where the subject has been left unprotected. People have said how novel and unique these theories are. I don't think they're very novel at all. If you have a duty to an individual and you breach that duty and, as a result, that individual suffers damage, then there is liability. That is the essence of our tort system.

Q: In many cases, patients enroll in clinical trials on the advice of their personal physicians. What steps can primary care physicians or others who recommend enrollment to patients take to ensure that trials are being conducted ethically and in full compliance with Department of Health and Human Services regulations?

Milstein: There certainly needs to be more on the Web. There needs to be some kind of central database [or] central Web site that participants can go to.

Physicians [shouldn't] recommend that patients [enroll in] clinical trials unless they know if it's in the patient's best interest to participate. I think ... when patients go to doctors and consult with them about these issues, patients listen to and rely on the advice of the doctor.

Q: In *Robertson v. McGee*, the complaint filed by your firm states that a nurse and study coordinator at the University of Oklahoma reported her concerns to the OHRP because the principal investigator and the other defendants failed to remedy problems with the way the trial was being conducted or to report "safety violations" to the FDA. According to at least one press account, the nurse became an "outcast" in the medical community.

What recommendations would you make to coordinators, monitors or other staff who become concerned that their employer is failing to comply with federal regulations but may lack the authority to change what is going on at their institution?

Milstein: I think it's critical that anybody in an institution that sees unethical conduct become a whistleblower and report the misconduct to the proper authorities. That is what the system requires if it is to succeed. Everybody involved in this area - including me - believes that medical and scientific research is essential [and] that medical advancements are essential to the human condition. But these advancements must only come through ethical experiments. If we as a society are going to enjoy the benefits of such research, we need to be confident that those on the front lines ensure that such experiments are conducted ethically.

Q: The FDA's Center for Devices and Radiological Health (CDRH) recently announced the first disqualification of a clinical investigator for allegedly violating investigational device exemption regulations (see "Device Clinical Investigator Disqualification Is First for CDRH," November 2002, p.1). Is there a particular therapeutic area - biologics, devices, drugs - where you believe investigators and institutions should be subject to more FDA/OHRP oversight?

Milstein: I think that anybody involved in human subject research should be subject to serious and thorough OHRP and FDA oversight. Unfortunately, there is so much research going on that it is impossible for those agencies to conduct adequate oversight. But I wouldn't differentiate the need for such oversight in, for instance, device experiments as opposed to pharmaceutical experiments.

If there's one area [adequate oversight is], lacking it's the area of surgical experimentation. ... A lot of surgeons don't believe that when they conduct research on a new technique or procedure, that [such] research requires IRB approval just like any other experiment.

Q: In June 2002, the Pharmaceutical Research and Manufacturers of America (PhRMA) published a voluntary code for companies conducting clinical research (see "PhRMA Spells Out Appropriate Clinical Trial Conduct," August 2002, p.1). If sponsors and investigators followed the principles enunciated in PhRMA's voluntary guidance, would fewer problems with clinical trials result?

Milstein: I don't see anything in those guidelines that are different than the regulations in 45 C.F.R. Part 46, the Common Rule [see <http://ohrp.osophs.dhhs.gov/polasur.htm>], or in the Belmont Report [see ¶840] or in the other bodies of law that are supposed to govern the conduct of human experiments. What needs to happen is that investigators follow those regulations and guidelines and that the government enforce [them].

Q: Some private or nonprofit organizations, including the Association for the Accreditation of Human Research Protection and the National Committee for Quality Assurance have developed voluntary accreditation programs for institutions conducting clinical research (see related story, p.1). Supporters believe that voluntary accreditation programs like these help to "restore public trust" in the clinical research process. Are they correct?

Milstein: I don't think voluntary accreditation is the answer. I think it should be mandatory. But even mandatory accreditation isn't necessarily the answer. Does anyone doubt that the University of Pennsylvania or Johns Hopkins would have been fully accredited at the times when Jesse Gelsinger or [24-year-old lab technician] Ellen Roche died in human experiments conducted at those institutions? So I don't think accreditation is the answer, but I would certainly favor mandatory accreditation [by the OHRP] as opposed to voluntary [accreditation].

[*Editor's note:* Complaints filed by Milstein's law firm related to clinical research issues are available online at <http://www.sskrplaw.com>.]