

# Heading Off a Clinical Trial Liability Lawsuit

Jill Wadlund

Sponsors can take positive steps toward limiting their exposure to liability suits, even in these days of increasing litigation.

**F**or years, clinical trials have been largely sheltered from the liability lawsuit crisis that has plagued other industries.

That is changing.

In the past few years, litigation against the clinical trials industry has increased sharply. Several cases, such as those against Fred Hutchinson Cancer Research Center (Seattle, WA) and the University of Oklahoma Health Sciences Center, attracted national media attention and are well known throughout the clinical trials community.

The best known suit was filed against the University of Pennsylvania by the family of Jesse Gelsinger, an 18-year-old man who died after participating in a 1999 gene therapy trial. It later emerged that the investigator running the trial had a majority interest in a biotech company that stood to make millions if the experiments were successful. Although some of those financial interests were disclosed to the family, serious questions were raised about whether Gelsinger received unbiased medical information.

Cases like this can no longer be considered isolated incidents. Although a few cases receive a great deal of publicity, a number of others are not generally publicized.

The targets of litigation are often the clinical investigators and research institutions that conducted the trials. Yet the companies that sponsor trials are also at risk when something goes wrong. Pharmaceutical companies must take aggressive steps to make sure the clinical trials they sponsor are above reproach and

to guard against even the appearance of conflicts of interest.

Failing to uphold rigorous standards for their clinical trials, sponsor companies may expose themselves to the threat of costly litigation. Clinical trials liability insurance can help protect pharmaceutical companies from some of the expenses associated with a liability lawsuit. But companies with poor risk management practices may experience difficulty obtaining such insurance, and/or may have to pay more for less protection. The more steps sponsor companies take toward a best practice approach to conducting clinical trials, the more favorable their insurance program may be, and the less likely they are to find themselves involved in a lawsuit.

Beyond the threat of litigation, pharmaceutical companies need to consider additional business risks, which include the potential for regulatory sanctions, civil penalties, and criminal prosecution. Additionally, the public's perception of clinical trial safety has deteriorated. That may cause sponsor companies to have even greater difficulty in finding willing participants. Problems in recruiting trial subjects can lead to delays in getting a product to market and bad press about a trial can harm the reputation of the sponsor company. Such problems can also raise questions about data integrity and even about the overall quality of the sponsor company's research and development efforts.

### Beyond FDA compliance

Pharmaceutical companies that want to head off these types of business risks, as well as the threat of litigation, cannot simply rest content by complying with the U.S. Food and Drug Administration's rules and regulations. It might be best to consider FDA regulations the minimum requirement.

If a company is not in compliance with the FDA regulations, it may have lost its case before it even begins. Mere compliance with the regulations, however, will not be enough to protect a company in a court of law, where it is often judged against the industry's best practices and standards. Companies may want to consider going beyond FDA regulations. For instance, the FDA does not require formal training for investigators, but pharmaceutical companies may require that all investigators have proof of formal training in clinical research.

To protect themselves from liability, pharmaceutical companies must take a close look at

- the financial interest of the investigators and their research team.
- the qualifications of principal investigators and institutional review boards.
- the ethics of subject recruitment techniques.
- the informed consent process.
- trial monitoring.

### Financial interest

To avoid potential conflicts of interest, sponsor companies should closely examine their ties to their investigators.

Certainly, investigators should be paid for their time and service. But the potential for conflict arises when companies compensate investigators by giving them a financial stake in the product's success. This is not uncommon, but any time a clinical investigator has a financial stake in a product's success, it raises serious ethical questions. Plaintiffs' attorneys may treat such an

arrangement like a smoking gun, claiming that it provides investigators with a motive for unethical behavior. Most people in clinical trials are good and conscientious, but few can endure the kind of scrutiny that defendants face in liability suits.

For this reason, sponsors would be wise to disclose more information than that required by FDA regulations requiring them to inform subjects of any potential conflict. Any financial

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ties between an investigator and the sponsor company should be disclosed to participants as part of the informed consent process. It may not be necessary to state the exact amount of the investigator's financial interest, but the fact that the investigator has a stake should be disclosed.

Even then, it is risky for an investigator to have an equity stake in the company sponsoring the trial. Such relationships raise questions not only about participants' safety, but also about the integrity of the trial data, and that can have long-term consequences for the product. When there is an equity interest on the part of the clinical investigator, the sponsor may want to use a data safety monitoring committee—an independent body that monitors the study and the data integrity.

### PI qualifications

Companies also should consider extensively screening the qualifications of principal investigators (PIs) to ensure that they have had formal training in conducting clinical trials. This is not the type of training a typical physician receives in medical school. Doctors without research training may be very good practitioners, but may not be properly prepared to take charge of a clinical trial. Some academic institutions offer such training, and sponsor companies may want to consider requiring this.

### IRB qualifications

Clinical trials in the United States are approved and reviewed by institutional review boards (IRBs). Those bodies, which are usually composed of physicians, scientists, and lay people, review study protocols and consent documents to ensure that the participants' rights are protected, and that the study does not present an undue or unnecessary risk to subjects (21 CFR 56). But not all IRBs are equal.

About 80,000 trials were conducted last year and many IRBs struggle to keep up with the workload. As a result, some critics claim that protocols developed by well-regarded doctors and professors at some major institutions are essentially rubber-stamped by the IRBs. Other IRBs may be rendered ineffective by the mix of personalities on the board, with lay people intimidated by strong personalities in the medical community. We have found that most of our clients do not see screening IRBs as

an obvious step to take. Yet, it is a risk management best practice for drug companies.

One step sponsor companies may wish to take to deal with such issues is to prequalify IRBs. Sponsor companies should try to determine whether the members of an IRB are qualified to be on the board (21 CFR 56.107). They might also be able to learn whether the board has enough time to review all of the study protocols on its agenda. Ideally, companies will choose investigators whose IRBs are working toward accreditation.

It is often in the sponsor's long-term best interest to seek out an IRB that meets these standards. Sponsors want IRBs to approve their studies, but if the IRB does not do its job properly and something goes wrong, the sponsor company may be sued—and it is the sponsor that is likely to bear the brunt of the litigation and business disruption.

### Subject recruitment

Sponsor companies must take care that participants do not feel pressured to participate in their clinical trials. Recruiters must avoid making overblown promises or understating the risk and the experimental nature of trials in advertisements and national



Sponsors that give investigators a financial stake in a product's success can create a conflict of interest.

databases. They also must be aware of the potential for monetary reimbursement to be coercive. Researchers may compensate trial participants for their time and for travel expenses. But the compensation must be a fair reflection of the subjects' expenses and the inconvenience of participation.

Some companies pay clinical investigators a bonus for enrolling a certain number of subjects by a certain date. This has the potential to create an incentive for investigators to deviate from protocol requirements. Investigators can be offered bonuses, but the incentive should be equally weighted to protocol compliance.

### Informed consent

Before being enrolled in a clinical trial, human subjects must sign a consent document that details the nature of the study and the risks involved. A survey conducted by CenterWatch revealed that 30% of participants did not understand that their study could carry additional risks and discomforts, and 70%

didn't know what questions to ask at the outset of the informed consent process. One way companies can protect themselves is through careful preparation of the consent document and extensive investigator training on the consent process.

The consent document must be easy to read and understand. The industry standard for consent documents is that they be written at or below an eighth grade reading level. Most important is that the potential subject be able to comprehend the information in the document. Writing readable consent documents, which often must explain complex medical issues, at grade levels that low is challenging. But the sponsor and investigators should treat this task as important rather than leave it to the institutional review board to make necessary adjustments. In fact, sponsors should review any changes that IRBs make to consent documents to ensure that no critical information has been deleted and that the readability and comprehension levels of the documents have not been corrupted.

Sometimes the principal investigator delegates the responsibility for conducting the informed consent process to other members of the research team. If the PI intends to delegate that responsibility, then the applicable research staff should be evaluated for the skills needed to perform this function. Researchers should never simply give the consent document to participants to read and sign. They should have face-to-face discussions with them and answer any of their questions. After reviewing the consent document with the participants, some investigators test potential subjects to see how much of it they understood. When a subject demonstrates a failure to grasp the critical points, the researchers should discuss those issues with them again until they do understand.

### Monitoring

It is important that companies make sure the trials they sponsor are well monitored. The primary purposes of monitoring is to ensure the protection of human subjects, evaluate the research team's compliance with the study protocol, and assess compliance with good clinical practice. Pharmaceutical companies should require comprehensive formal training of clinical research associates (CRAs) to ensure effective clinical trial monitoring.

We too often hear about training that is largely "learn as you go" with little supervision from experienced staff members. Even when companies have formal training programs, they often cover only the basics and fail to provide the in-depth preparation needed to operate at ideal performance levels. New training programs are being developed all the time, and the industry supports professional certifications in clinical research. Sponsor companies should encourage their CRAs to pursue training and certification.

### Litigation an ongoing trend

Some pharmaceutical companies may see the trend toward litigation as a short-term phenomenon. Given the growing number of clinical trials and the growing level of interest in this type of litigation by plaintiff law firms, this is most likely an ongoing trend.

Clinical trials liability insurance can help to offset some—but not all—of the cost associated with an event that leads to an expensive liability lawsuit. Insurance company underwriters are

likely to ask questions about many of the issues mentioned here when a pharmaceutical company's insurance program comes up for renewal. Companies who follow industry best practices will be likely to receive better terms and pricing for their future insurance coverages. Insurance companies that specialize in this type of coverage often provide risk management services to assist companies in pursuing best practice performance levels.

Observing best practice procedures may offer more than the opportunity for a better insurance program. Sponsor companies may experience greater success in enrolling subjects when they have a reputation for superior clinical trial safety efforts. In addi-

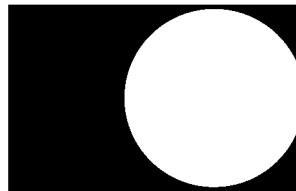
tion, investors are likely to place greater importance on the way companies manage these exposures. Ultimately, they could favor those pharmaceutical companies that demonstrate superior research processes and integrity.

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