

Conducting Clinical Trials Without Ending Up on Trial

Research, by definition, involves risks. It is up to everyone involved - sponsor, investigator, and staff - to try to minimize those risks for subjects. Failure to do so often prompts legal action. The targets of litigation are typically investigators and clinical institutions. However, sponsors, institutional review boards (IRBs)/research ethics committees (RECs), and even patent holders of medical devices are increasingly being named in lawsuits. Because the number of malpractice lawsuits is increasing and the amounts of awards have skyrocketed, it is important that investigators recognize the sources of risk and how to protect themselves through careful and ethical conduct of clinical trials. In this chapter you will learn about some of the legal risks of conducting clinical trials and how to avoid such problems.

Types of Litigation

There are several types of injury that can arise in clinical trials that investigators should be aware of so that they can avoid them. These injuries are outlined below:

Battery: Battery is intentional and unlawful bodily contact on another person without that person's consent. While most often associated with criminal behavior, in the context of a clinical trial, a battery claim can arise if a patient was enrolled in a study without proper informed consent, and thus, procedures were performed or drugs given to the patient without his/her permission. Battery can result in both compensatory (direct compensation for loss, injury, or harm) and punitive (extra awards to deter further similar action or act as punishment) damages.

Negligence: Negligence is when a defendant (ie, principal investigator) owed the plaintiff (ie, subject) a legal duty of care, and the defendant breached that duty by failing to perform in accordance with that level of care, resulting in an injury. In a clinical trial, this could mean that a research subject was supplied inadequate information (incomplete consent) about the risks of a particular procedure by the investigator (or member of the investigation team, such as the clinical trial coordinator). If the subject had received all of the information he or she may not have chosen to participate, so the investigator was negligent in supplying the appropriate information. Another, and perhaps more recognizable example, would be a surgical procedure not being performed using sterile instruments. Negligence awards are generally compensatory but may be punitive if "gross" negligence is determined.

Strict liability: Strict liability involves the sale of a product that is defective and is unreasonably dangerous to the user. An example related to clinical trials would be failure to give proper warning to subjects about the experimental nature of the investigational drug.

Fraud: Fraud is the deliberate attempt to cover up, mislead, or deceive another. The obvious clinical trial example is an investigator who falsifies data. A less clear example is a nurse who makes an error during a blood draw but does not tell anyone. Fraud has also been committed if a clinical trials coordinator signs an informed consent form in place of a legitimate witness. Insurance fraud occurs if managed care is charged for medications or procedures associated with the clinical trial. Fraud can have grave consequences, including putting patients' lives at risk if a drug comes to market based on false data that is actually associated with either serious adverse events or little efficacy.

Breach of the right to be treated with dignity: This type of tort (damage, injury, or a wrongful act) is based on the Nuremberg Code and Declaration of Helsinki, and basically means that subjects have the right to be treated with respect and to make their own decisions regarding their person. An example related to clinical trials is the subject who has been told by the investigator that he or she will most

likely receive the active compound, when the chance is really 50:50. Although cases involving the dignity of the research subjects are rare, the courts have been recently seeing more cases.

Violation of anti-kickback statutes: Similar to insurance fraud, United States investigators can be in violation of anti-kickback statutes if they charge a federal healthcare program (Medicare, Medicaid) for services or agents for which they have been remunerated by a sponsor or grant. This is a felony and taken seriously by the government.

Sources of Risk

You may think that you are immune from making some of the mistakes listed earlier, but no one is perfect. Emotions and individual experiences motivate actions, which may not always be exemplary. Some common sources of risk are described in the following section.

Conflicts of interest are one of the greatest reasons that investigators compromise their research efforts. Investigators who have a financial stake in the outcome of a study may make decisions that are not in the best interest of an individual patient. For example, a sponsor who pays a bonus for early enrollment of patients may encourage investigators to enroll subjects who may not be appropriate for the study. Similarly, subjects who are overly compensated for their participation may lie about side effects in an attempt to stay in the study and continue to be paid. Conflicts of interest can also arise when investigators enroll their own patients into clinical trials because the goals of patient care and clinical trials are often different.

Good practitioners are not always good investigators, and formal training on conducting clinical trials is not routinely offered in medical school. Thus, violations may occur as a result of ignorance, but nevertheless, the harm to the patient and the trial can be severe. Furthermore, the suitability of the site may not be appropriate for the study, which could put subjects and the research in jeopardy. For example, insufficient staff may result in errors in the collection and recording of data, leading to fraud, or in the care of subjects, leading to the potential for battery or negligence. Even having a room that is too small for equipment involved in the study could lead to injury to subjects.

Although most of the burden of properly run clinical trials falls on investigators, the performance of the IRB/REC may expose an institution to litigation. Heavy workloads may prohibit careful review of trials, and it has been suggested that protocols developed by well-respected physicians and professors at major institutions may be approved without careful review. Also, the lay members of the committee may feel intimidated by the healthcare professional members, and, thus, may not express their reservations about a popular study. However, a less-than-careful protocol review by an IRB/REC does not excuse an investigator who recognizes deficiencies in a particular clinical study in which he or she is participating.

Providing Protection

All clinical research contracts and documents should be vetted by an experienced attorney who understands the issues involved with conducting clinical research, including indemnification, intellectual property rights, and timelines of payments. In the university setting, this duty is usually handled by a grants and contracts office that has experience negotiating for the best interests of you and the institution. If you do not have access to such an office it is advised that you hire an experienced attorney to assist you.

As an investigator, you are at risk of litigation from errors of the study sponsor; at the same time, the

sponsor is at risk of litigation from mistakes you or your staff may make. To protect each party from liability created by the other, a mutual indemnification by the sponsor and the institution is generally included in the clinical trial agreement. This mutual indemnity protects each party from the cost of defending a lawsuit resulting from the fault of the other party. For example, a sponsor could not be sued if an injury to a subject was the result of an investigator not following the protocol. Investigators with sufficient bargaining power may sometimes persuade a sponsor to remove the investigator's indemnity altogether, leaving the investigator liable only to the patient for the investigator's actions or omissions.

Another form of protection is clinical trial liability insurance. Institutions generally require investigators to carry this type of insurance, which may be paid for by the sponsor or be paid out of pocket by the investigator. The cost of these policies varies widely depending on the type of research, number of subjects, the phase of the clinical trial, and past experience conducting clinical trials, among other factors. Most standard malpractice insurance policies exclude clinical research, and thus, it is important to have special insurance in place before engaging in any research endeavors.

Conclusions

Although avoiding the potential for litigation seems obvious, it is often the subtle transgressions that garner the most attention. The overriding imperative of all parties (eg, investigator and staff, sponsor, institution) involved in conducting clinical trials should be the protection of the human subjects. However, even the most ethically run studies may encounter mistakes that result in injury, and thus, before agreeing to participate in a given trial, you should review and negotiate the scope of the indemnity clause and at a minimum, research the cost and availability of insurance riders covering clinical trials. The consequences of any litigation reach beyond (sometimes significant) financial losses. All of the time spent investigating the new agent or device may be wasted; the institution or clinic could be stripped of federal funding; all research trials, and not just the one from which the allegation originated, could be halted; and reputations can be permanently ruined. Thus, think carefully before agreeing to the next attractive protocol that passes your desk.

Resources

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