



Clinical Trial Research in Hospitals

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Executive Summary

Generally conducted in research hospitals, clinical trials allow patients to access treatments not yet available to the general public and provide access to healthcare otherwise not available due to cost or health insurance restrictions.

Clinical Trials play a vital role in modern healthcare. Required by the Food and Drug Administration (FDA), clinical trials help determine the safety and effectiveness of pharmaceutical drugs and medical devices before being marketed for mass consumption. Generally conducted in research hospitals, clinical trials allow patients to access treatments not yet available to the general public and provide access to healthcare otherwise not available due to cost or health insurance restrictions. While human biomedical or health related research can provide hope at times when none is thought to exist, it also increasingly is resulting in litigation against all or some of the parties connected to a study, including hospitals. This Advisen report sponsored by ACE explores the clinical trial liability exposures of hospitals, strategies for mitigating these exposures and frequent misconceptions regarding insurance coverage.

Introduction

Last year a leading research university suspended a clinical trial of a cancer treatment when it was discovered that the Oncologist leading the study had falsified his resume and had based the trials on spurious research results. A dozen plaintiffs filed a lawsuit naming the university and its administrators, researchers and physicians, alleging that they engaged in fraudulent and negligent behavior when they enrolled cancer patients in a clinical trial based on faulty data. The plaintiffs claimed that the flawed science “reduced the likelihood of surviving the cancer or the likelihood of experiencing a positive response to the chemotherapy regimen.”¹

Obviously, scandal is not a feature of most clinical trials, as it was in the first case cited above, but errors happen – sometimes with devastating consequences-- and the threat of a lawsuit is always present.

In another case, clinical trial subjects and subject representatives filed a lawsuit seeking actual and punitive damages as a result of a Phase I study of a cancer vaccine. The study enrolled patients with advanced stages of the disease who had been previously unresponsive to traditional therapies. According to reports, 94 subjects received the vaccine and 26 died during the course of the study. The plaintiffs sued the hospital, the principal investigator, the pharmaceutical sponsor, a top university official, the individual members of the Institutional Review Board (IRB), and a university bioethicist who consulted with the IRB.

These cases are just two examples of a clinical trial ending in a lawsuit. Things can go wrong, and when they do, the parties involved with conducting a study may find themselves in court. Obviously, scandal is not a feature of most clinical trials, as it was in the first case cited above, but errors happen – sometimes with devastating consequences-- and the threat of a lawsuit is always present.

Clinical trials are an important source of prestige for many hospitals, and provide vitally important benefits to the health and welfare of people everywhere. Clinical trials expose hospitals to potential liability, but in most cases decision-makers have concluded that the benefits justify the risks. “To help manage the risks a comprehensive clinical trial risk mitigation policy should be implemented by every hospital,” said Caroline Clouser, Executive Vice President, ACE USA Medical Risk. “This includes a review of the hospital’s insurance program to assure that full coverage for clinical trials is in place.”

It is important to note, approval of the clinical trial by a regulatory body such as the FDA, does not grant immunity to any of the parties involved when a problem occurs.

Testing unproven drugs or medical devices on humans inherently comes with risks. Though rare, injury and death sometimes results. Participants are routinely informed of the risks involved through the informed consent process, but informed consent does not necessarily confer immunity on a hospital or a physician. If trial participants are injured or believe they have been wronged due to participating in the study, they may sue some or all of the parties involved.

Lawsuits against hospitals arising from clinical trials also may be brought by one of the parties involved with the study such as the trial sponsor. Potential allegations include fraud, financial loss due to errors in executing a trial and damage to product or equipment.

The Roles of the Hospital in Clinical Trials

A risk mitigation policy that properly addresses a hospital's clinical trial exposures requires a thorough understanding of the roles and responsibilities a hospital can have in the clinical trial process. Each role potentially exposes the hospital to different liabilities and requires different risk management oversight.

Three roles are primarily involved with the execution of a clinical trial: the principal investigator (PI), the sponsor and the clinical research organization (CRO). Depending on the circumstances, a hospital can find itself in -- or partnering with a company in -- any of the three roles, each of which have unique exposures and specific regulatory guidelines. It is important to note, approval of the clinical trial by a regulatory body such as the FDA, does not grant immunity to any of the parties involved when a problem occurs.

Principal Investigator (PI)

The PI is responsible for overseeing the entire execution of a clinical trial. The PI's responsibilities include:²

- Submit trial protocol to the Institutional Review Board (IRB) for approval,
- Recruit trial participants,
- Develop the informed consent agreement,
- Follow the study protocol,
- Collect and analyze the study data, and
- Maintain ongoing communication with the IRB.

The PI is responsible for protecting the rights, safety, and welfare of the research participants by ensuring that the research is being conducted in an ethical manner and in accordance with all federal, state, and local laws, institutional policies and requirements of the IRB.³

A hospital itself does not function as a PI, but it often is the employer of the PI and provides the venue for a PI to carry out a clinical trial. As such, the potential liability of a hospital is closely tied to that of the PI.



Sponsor

A clinical research organization, also referred to as a contract research organization, is hired by the clinical trial sponsor to perform various services associated with the clinical research process.

The sponsor is a person or organization who initiates and is responsible for a clinical investigation. The general responsibilities of a sponsor include:⁴

- Selecting qualified investigators,
- Providing the investigators with the information they need to conduct an investigation properly,
- Ensuring proper monitoring of the investigation,
- Ensuring that the investigation is conducted in accordance with the general investigational plan and protocol's contained in the Investigational New Drug Application (IND),
- Maintaining an effective IND with respect to investigations, and,
- Ensuring that the FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the drug.

A sponsor is typically a pharmaceutical, medical device or biotechnology company, but a hospital can also be the sponsor of a clinical trial.

Clinical Research Organization (CRO)

A clinical research organization, also referred to as a contract research organization, is hired by the clinical trial sponsor to perform various services associated with the clinical research process. Examples of a CRO's responsibilities include monitoring data collected by the trial investigator, medical writing, regulatory support, investigator selection and qualification, clinical trial management and data analysis.⁵ CROs may be affiliated with a hospital, or they may be independent service providers. A hospital acting as a sponsor could be held liable under some circumstances for the errors or omissions of a CRO with which it contracted.

Institutional Review Boards (IRB)

Another important party in every clinical trial, and one that has the potential for producing significant liability exposures for a hospital, is the IRB. An IRB is a group formally designated to protect the rights, safety and well-being of humans involved in clinical trials.⁶ IRB's provide the study with checks and balances to assure patient safety and protect the parties involved with its execution from potential liability. The primary responsibility of an IRB is to review the trial protocol including:

- Study design,
- Scientific principles,
- Social and scientific significance,
- Protections,
- Qualifications of researchers,
- Adequacy of hospital resources,
- Ways to terminate study if necessary, and
- Safety measures

IRB members face potential liability if a trial goes awry with tragic consequences. If an IRB is affiliated with a specific hospital, it is likely that the hospital also will be named in a suit alleging negligence of the IRB. Even if the IRB members are not specifically named in a suit, a hospital may be held liable for their negligence. For example, in the milestone Canadian case, *Weiss v. Solomon*, one of the study participant's went into cardiac arrest while undergoing treatment as part of the study. Subsequently, the family sued the PI, the hospital and the physician that recommended participation in the trial. The court ultimately found both the PI and the hospital liable. The hospital's liability ultimately arose from the fact that the research committee (the Canadian term for an IRB) had approved a research protocol and consent form which was determined by the Court to be deficient.⁷

While bodily injury claims represent the most common type of suit, and certainly are the type that attracts the greatest amount of risk management scrutiny, they are not the only type of suit that can arise from clinical trials.

Types of Exposures

The PI, the Sponsor and the CRO all have very different roles in the clinical trial process, but all are potential targets for lawsuits, and often all are named in a suit. “Clinical trial litigation is commonly a consequence of injury to a trial participant, said Tristan Gabriel, Senior Vice President, ACE USA Life Sciences. “Allegations are often linked to informed consent issues.”

Clinical trial lawsuits can result from any number of allegations. Some of the more common allegations include.⁸

- Assault and Battery,
- Breach of the Right to Dignity,
- Clinical Negligence,
- Scientific Fraud, and
- Wrongful Death.

Gelsinger v. Trustees of the University of Pennsylvania is an often-cited example of a clinical trial bodily injury suit. In this case an eighteen year-old who had volunteered to participate in a corrective gene study died during the course of the study. As a result, the trustees of the university and two hospitals affiliated with the research, the investigators, the company that sponsored the research, the former medical school dean and a bioethicist, were all named as defendants on the basis of wrongful death, assault and battery linked to lack of informed consent, and common law fraud/misrepresentation linked to the informed consent process.⁹

While bodily injury claims represent the most common type of suit, and certainly are the type that attracts the greatest amount of risk management scrutiny, they are not the only type of suit that can arise from clinical trials. Other clinical trial exposures that people fail to realize and may not think about, but are still very important include:

- Property damage to equipment or spoilage of materials,
- Financial loss due to a delay in the trial or other issues that cause it to have to be redone,
- Criminal fines and penalties for marketing practices such as sanctions for noncompliance with federal and state regulations related to promotion,
- Civil/criminal penalties related to Medicaid/Medicare fraud,
- Fraud involving misrepresentation of defective drugs and products, and
- Foreign exposures for clinical trials conducted entirely or in part overseas.

Insurance Coverage Needs

Risk managers often assume that a hospital professional liability (HPL) policy provides full protection against liability as a result of an incident resulting from its professional services or those of its physicians during a clinical trial. However, this is not always the case, which is why a careful review of the policy terms and conditions is essential to assure the hospital has the appropriate coverage and identify coverage gaps and restrictions. A separate product/clinical trials liability policy may be needed.

For example, the definition of “professional services” in the HPL policy should be reviewed to determine whether those services include the professional services the hospital is undertaking in the clinical trial. Additionally, the policy definition of a patient should be reviewed to determine if it includes test subjects.

According to David Shuey, Willis Life Sciences Practice Leader, “Hospitals also should consider property insurance for damage to equipment and products, the policy should also include coverage for spoilage. Errors and Omissions (E&O) insurance is also essential to cover ‘financial damages’ if the hospital fails to comply with the clinical trial agreement, incur delay in execution, or make an error in conducting the trial which requires a repeat of efforts.”

While insurance provides hospitals with peace of mind protection and is essential, the best hospitals take pride in preventing lawsuits from occurring in the first place.

Risk Management

While insurance provides hospitals with peace of mind protection and is essential, the best hospitals take pride in preventing lawsuits from occurring in the first place. To achieve this, a hospital clinical trial risk mitigation policy should be developed and properly executed. Some elements of a risk mitigation policy include identifying the types of clinical trials, identifying the role the hospital is playing, selecting a qualified principal investigator, executing a clinical trial agreement (CTA), ensuring compliance with HIPAA and monitoring adverse events.

Type of Clinical Trial and Role Being Played

The first step in any clinical trial risk mitigation policy should be to gain a clear understanding of what type of trial(s) is occurring at its facilities and what role the hospital is playing. As previously mentioned each of the various roles – PI, Sponsor, and CRO – creates different exposures for a hospital and require a different risk management approach.

Clinical Trial Initiated and Sponsored by a Pharmaceutical, Medical Device or Biotechnology Firm: In order for a product to become FDA approved and be recommended for mass consumption, pharmaceutical, medical device and biotechnology firms must first sponsor a human clinical trial to determine the effectiveness and safety of the product. These commercially sponsored trials are frequently conducted in a hospital setting with one of the hospitals physicians acting as the trials Principal Investigator (PI). In this arrangement, the trial sponsor (e.g. Drug, Device or Biotechnology Company) will be responsible for any liability as a result of the product being tested and the hospital and/or the PI will be responsible for any liability as a result of negligence in administering the trial (malpractice).¹⁰ The respective roles and liabilities of the various parties are defined in a contract, the Clinical Trial Agreement (see below), before a trial begins.

Commercial Clinical Trial Initiated by Principal Investigator: Often drugs are identified as potentially being effective in treating diseases other than what they were initially designed for. For example, it may be believed that a drug commonly used for breast cancer may also be effective in treating ovarian cancer. In these circumstances, a hospital physician may approach the drug, device or biotechnology company about a clinical trial partnership. Under this scenario, the hospital physician becomes the PI and will often look outside of their facility to recruit trial subjects as well as look to a CRO for assistance in administering the study.

In this arrangement, the hospital and the PI are the trial sponsors and therefore should seek indemnification from the drug or device company for claims arising from the product. CROs will often then seek indemnification from the hospital for liability arising out of the trial. A standard HPL policy will typically protect against allegations of malpractice by the trial participant, unless the participant is not a patient of the hospital which would then require a separate products/clinical trials policy.

Clinical Trial Initiated by the Hospital: Some hospitals may be involved with scientific research to discover cures to specific diseases. If a hospital has developed a drug or device that it would like to take to clinical trial, the hospital and PI become the trial sponsor and therefore do not have a commercial drug or device company to seek indemnification from. In this situation a standard HPL policy typically will not provide protection for the exposures as a result of the sponsoring. If this is the case a hospital should purchase a separate products/clinical trials policy.¹¹

Before engaging in any of the above, the hospital, its legal counsel and insurance broker should thoroughly review any contracts with trial sponsors, CROs or anyone else involved.

Selecting a Qualified Principle Investigator

PI's must be able to comprehend the science behind the trial and have the clinical training and expertise to manage any side effects and potential adverse events.

As the leader of the research team, PI's are the first line of defense in assuring that the clinical trial is conducted responsibly and in accordance with the study protocol. PI's must be able to comprehend the science behind the trial and have the clinical training and expertise to manage any side effects and potential adverse events. For this reason it is of the utmost importance that the qualifications and training of the PI be thoroughly reviewed and the review process is documented. If the PI conducting the trial is found not to have the proper qualifications and training, it opens the door to potential liability. The lawsuit discussed at the top of this report, in which a researcher falsified his resume, is a clear example of this exposure.

Other circumstances that can result in legal recourse that must be thoroughly reviewed and addressed are the relationship of the PI and the trial sponsor and the relationship of the PI and the test subjects. If it is found that an incentive will be paid to the PI by the sponsor if the trial is a success this creates a conflict of interest that could result in significant liability. Additionally, if the test subjects and the PI have an existing relationship, the patient may be more apt to seek legal recourse if the trial does not achieve the expected results or results in an adverse event.

Clinical Trial Agreement (CTA)

After the clinical trial PI has been selected and before the trial is underway, a contractual relationship between the hospital/PI and the sponsor called a clinical trial agreement (CTA) should be initiated. The CTA is a legally binding agreement that details the roles and responsibilities between the parties. CTA's are essential because they allocate risk, responsibility, financial support and obligations.¹² For this reason the insurance and indemnification clauses in the CTA should be reviewed by the hospital's risk management and legal department as well as by their insurance broker.

Other Risk Management Considerations

NOTES:

¹ Jennifer Couzin-Frankel, *Science Insider*, "Flawed Cancer Trial at Duke Sparks Lawsuit", (September 9, 2011)

² National Cancer Institute, "Including Clinical Trials in Your Practice: An Overview", <http://training.cancer.gov/includingclinicaltrials/util/print/includingclinicaltrials.pdf>

³ Partners Human Research Committee, "Principal Investigator's Responsibilities", http://healthcare.partners.org/phsirr/PI_Responsibilities.htm

⁴ Centerwatch, "Roles and Responsibilities in Clinical Trials", http://www.centerwatch.com/pdfs/s11604_ch4.pdf

⁵ Emissary, "Definitions of Clinical Research Terminology: Contract Research Organization", <http://www.emissary.com/Definitions/contract-research-organization-definition.html>

⁶ Pharmaceutical Product Development (PPD), "Institutional review Board's (IRB's) role in Clinical Trials", (2009), <http://www.ppd.com/investigators/irb.htm?print=t>

⁷ Randi Zlotnik Shaul, Shelly Berenbaum and Megan Evans, *BMC Medical Ethics*, "Legal liabilities in research: early lesson from North America", (June 2005), <http://www.biomedcentral.com/1472-6939/6/4/>

⁸ "Clinical Trial Lawsuit: Legal Representation When You are Injured by a Clinical Trial" http://www.pritzkerlaw.com/Clinical_Trial_Lawsuits/

⁹ *Gelsinger v. Trustees of the University of Pennsylvania* (Phila. Cnty. Ct. of C.P. filed September 18, 2000), Sherman, Silverstein, Kohl, Rose and Podolsky Law Offices. Accessed May 24, 2005 [<http://www.sskrplaw.com/links/healthcare2.html>]

¹⁰ David Shuey & Frank Castro, Willis, LifeLines, "Research and Development in the Hospital Setting", (May 2012), http://www.willis.com/documents/publications/Life_Sciences/LifeLines_May_2012_Research_in_Hosp.pdf

¹¹ David Shuey & Frank Castro, Willis, LifeLines, "Research and Development in the Hospital Setting", (May 2012), http://www.willis.com/documents/publications/Life_Sciences/LifeLines_May_2012_Research_in_Hosp.pdf

¹² Nancy J Stark, CDG Whitepapers, "Clinical Trial Agreements", (September 2011), http://clinicaldevice.typepad.com/cdg_whitepapers/2011/09/clinical-trial-agreements.html

- **HIPAA:** Finding qualified participants for clinical trials is often a challenge. However challenging it may be, though, when searching disease registries and other databases for qualified participants, the same rules apply with regards to the privacy of patient health information (PHI). Sponsors, PIs and anyone else involved with the study may neither use nor disclose protected health information for research purposes without advance patient consent. HIPAA requirements must be followed.
- **Informed Consent:** Trial participants should be informed about what exactly will occur during the trial so that they can make an informed decision about whether or not to participate. Trial participants then confirm their agreement to participate through a written consent form. This document should be produced by the creators of the study and it should be reviewed and approved by the IRB. Failure to do so will open the door to potential liability.
- **Monitor Adverse Events:** Standard clinical trial practice requires PI's to monitor and report serious adverse events to trial sponsors. Research staff must be taught how to properly collect and report data. Failure to do so can result in liability.

Conclusion

Performing clinical trials on human subjects is necessary for healthcare innovation and progress. Strictly regulated to ensure the wellbeing of the study participants, the very concept nonetheless denotes a degree of inherent risk. While the risk is real, it does not mean that litigation and potential financial loss are imminent. According to Ms. Clouser, "Hospitals with a clear understanding of their clinical trial exposures and that have developed a strategy that is both proactive in preventing losses and comprehensive in covering them through a well-designed insurance program can feel confident about moving forward with vital research."

This Special Report was written by Josh Bradford, Associate Editor, Advisen Ltd. and sponsored by ACE.