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Subject Injury Risk Management for Research Sites

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When a study subject has a serious health problem (or dies) during a clinical study, it is natural for the injured person (or the surviving relatives) to suspect that the study treatment is to blame. Assisting the subject with medical treatment addresses most issues, but legal action could ensue. Subject injury litigation is rare and court judgments are much rarer still, but even a successful defense is an expensive and punishing experience.

Health Insurance

Health insurance companies may or may not cover the cost of treating subject injuries. Check for an exclusion for costs incurred due to complications for an excluded service, i.e., routine clinical trial costs (unless required by state law). They may reimburse the cost but later demand a refund after an audit (and when the study sponsor is long gone).

Should they pay? On the one hand, their policy holder has suffered an injury, like any other. On the hand, why should insurance companies subsidize pharmaceutical and medical device companies? On the other hand, there is evidence that clinical research does not increase, and might even decrease, overall direct costs to insurance carriers. On the other hand, clinical research is often an "elective procedure" with unpredictable risks. On the other hand, clinical trials are needed to develop new treatments that keep people healthier, reducing insurance carrier costs or at least performing a valuable public service. On the other hand, study sponsors price new treatments without considering the contribution of insurance companies.

A related and perhaps more important question relates to the impact on the study subject. Claims resulting from study participation might contribute to premium increases or even cause them to hit their policy limits. If they subsequently, for example, lose their jobs, their medical record might make new coverage expensive and difficult to find.

Informed Consent Forms

Although it may not be obvious from reading many informed consent forms, their primary function is to inform potential study subjects. Another, presumably secondary, function is to help manage potential risks to the study site and sponsor. Well-informed subjects are less likely to bring legal action or successfully claim that they were deceived into enrolling in a study. Unfortunately, the risk management language can defeat the informational purpose of the document, opening the door to a claim that excessive legalese prevented informed consent. Exculpatory language saying that the site or sponsor is not responsible for injuries is prohibited. Medicare's notorious secondary payor rule seems like a cruel joke by the CMS gods.[1]

Medical Malpractice Insurance

Medical malpractice ("med mal") insurance protects physicians and healthcare organizations from patient injury claims resulting from "medical care" or "medical treatment."[2] The courts (for example, *Heinrich v. Sweet*, 62F. Supp.2d 282, 313 (D.Mass. 1999)) generally regard clinical research injuries as regular medical injuries, but clinical research is not necessarily medical care. People in clinical trials are not "patients"; they are "subjects," "volunteers" or

"participants." Some med mal policies specifically exclude clinical research or coverage for experimental or unapproved treatments. Others require the physician to apply for coverage for each study. It may be possible to purchase an "endorsement" that adds clinical trial coverage or purchase a separate clinical research policy.[3] If the policy is ambiguous about what it covers, obtaining written clarification could prove very useful, although ambiguity might be better than a clarification that clinical research is not covered. Regardless, most people would prefer not to pay their lawyers to argue the question in a court of law.

Clinical Trial Agreements

Clinical trial agreements typically include three sections related to injuries to study subjects: Subject Injury, Indemnification and Insurance. The Subject Injury section explains what constitutes a covered injury and who pays what if it occurs. The indemnification section explains the parties' obligations to each other in case a third party, usually an injured study subject, pursues legal action. The insurance section explains the site's and maybe the sponsor's insurance obligations. The first two sections are exceptionally complicated and beyond the scope of this article. Suffice it to say that they offer many opportunities for clever drafting; for example, an unrelated deviation from the protocol on Subject A may void indemnification against a claim by Subject B.[4]

MAGI's Model Clinical Trial Agreement includes this section on research site insurance:[5]

> **11.1. Site Insurance.** Site carries general liability insurance with limits of at least $_____ per occurrence and $_____ in the aggregate. It also carries medical malpractice insurance with limits of at least $_____ per occurrence and $_____ in the aggregate. Site's insurance (or comparable self-insurance) covers the Study, specifically covers the actions of investigators and other study personnel, and is not materially encumbered by existing claims. Site will maintain this coverage for the duration of this Agreement and, if the policy is claims-made, for {two to five} years thereafter. Site will provide certificates of insurance or evidence of self-insurance to Sponsor upon request. Site will notify Sponsor within 20 Days of any notice of cancellation or non-renewal of, or material change in, or claim against, its insurance coverage. Insurance carriers will have an AM Best rating of A-VII or better.

Required coverage limits are generally in the range of $1M/$2M to $2M/$6M. $1M/$3M is common. Clinical trial agreements often call for the site to provide the sponsor with a certificate of insurance. Insurance companies routinely provide certificates of insurance on the policyholder's request. Most policies are "on occurrence," which means they cover *incidents* that occur while the policy is in force, even after the policy terminates. In contrast, "claims made" policies cover *claims* made while the policy is in force.

Cross-Indemnification

Study sponsors have every right to protect themselves from incompetent and negligent investigators. Many study sponsors are thus fond of "cross-indemnification," whereby the investigator indemnifies the sponsor for harm caused by the investigator. Since the study sponsor normally indemnifies the site for injuries caused by the study drug or device and certain other causes, it seems reasonable for the site to indemnify the study sponsor for harms caused by *its* negligence. After all, what's good for the goose is good for the gander. Turn about is fair play.

Why shouldn't a guilty investigator indemnify an innocent sponsor? There are at least eight good reasons that may apply in certain circumstances:

- In most cases, the study subject would not have been injured in the absence of the study.

- Medical malpractice insurance seldom, if ever, covers costs associated with cross-indemnification.
- There may not be a guilty party, or one that deserves 100% of the responsibility. Indemnification defines who pays the defense costs until responsibility is apportioned at the end. Consider the scenario, for example, where the investigator has indemnified the sponsor, pays all the defense costs (which can easily exceed $1 million), and wins the case. The sponsor has no obligation to reimburse the investigator for part of those costs.
- The risk-reward profiles of the two parties are far from symmetrical: Pharmaceutical companies conduct clinical trials with the expectation that they will earn millions or billions of dollars in profit from a successfully marketed drug; investigators may earn only a few thousand dollars from a study, and they may quite possibly lose money.
- Pharmaceutical and device companies, once they are established, can spread their legal costs over a portfolio of products. Even with perfectly safe products, they expect a certain number of injury claims from an active clinical research program. They therefore buy insurance, or self-insure to cover the very small percentage of subjects who press expensive claims. In contrast, most investigators never see litigation from a study subject. The cost of clinical research insurance is prohibitive for many small sites.
- Some countries require study sponsors to buy subject injury insurance. They could do the same in U.S.[6]
- A single malpractice case can drive an investigator out of the research business, and can even destroy his or her medical practice or force personal bankruptcy. (A good malpractice insurance policy mitigates but does not eliminate these risks, and may not be renewed after a claim.)
- Government entities, such as state university hospitals, are legally prohibited from indemnifying sponsors. If sponsors are willing to do business with them on that basis, they can do the same for private-sector investigators.

One option is for the site to cross-indemnify the sponsor to the limit of its insurance coverage.

Other Potential Liabilities

Subjects do not need to suffer significant physical injury to claim damages. For example, the *Diaz v. Hillsborough County Hospital Authority* class action lawsuit was settled in 2003 with a payment of $3.8 million for "dignitary harm." Dignitary harm occurs when clinical trial subjects are not treated with respect for their personal rights. In the *Diaz* case, the plaintiffs alleged that they were induced by a very defective informed consent process to participate in clinical research that involved risky and painful procedures. Although this case remains an anomaly, the U.S. Supreme Court has stated that "No right is held more sacred or is more carefully guarded by the common law, than the right of every individual to the possession and control of his own person, free from all restraint or interference of another." (*Cruzan v. Director, Missouri Department of Health,* 497 U.S. 261, (1990))

Privacy violations, e.g., due to the release of genetic data, is a promising area for the plaintiff's bar. HIPAA violations are not covered by med mal insurance.

As in other potentially lucrative legal fields, such as regular medical malpractice, the clinical trial plaintiff's bar becomes more effective over time, learning from successes and failures, sharing documents, and setting precedents.

Commonsense Precautions

The author once reviewed the med mal policy for a 10-physican cardiology practice conducting diagnostic, pharmaceutical and surgical clinical trials. The policy specifically excluded coverage for clinical research.

Contracts and insurance are well and good, but good judgment is more important. Research sites can take the following steps to minimize the risk of subject injury claims:

- Understand your medical malpractice insurance. Secure adequate coverage. Obtain clarification from your carrier if the policy is ambiguous.
- Do not conduct studies that are likely to be associated with serious medical problems, especially if the study treatment will get blamed. In other words, stay away from acute diseases and fragile populations.
- Ensure that investigators and study coordinators understand and comply with the protocol and Good Clinical Practice, as well as normal medical care practices.
- Weigh the risks of the trial vs. the potential rewards. Cross-indemnification may be justified if the study budget is generous and the chance of subject injury is negligible.
- Read and understand the subject injury, indemnification and insurance sections of the clinical trial agreement. Negotiate as required. Consult with a qualified attorney, as appropriate.
- Comply with the spirit and law of informed consent. Demonstrate respect for study subjects and maintain good communications with them.
- Do not enroll high-risk study subjects, even in low-risk studies.
- Do not ignore injured subjects in the hope that they will just go away.
- Terminate the trial at your site if, in your professional judgment, the risk to the subjects outweighs the potential benefits.

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