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Treatment Reimbursement in Informed Consent Forms and Clinical Trial Agreements

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The U.S. Code of Federal Regulations (45 CFR 46.116(b)(3)) requires that informed consent forms disclose "any additional costs to the subject that may result from participation in the research." This regulation almost certainly requires disclosure of costs that result from an injury to the subject. Non-compliance with this regulation may invalidate the subject's informed consent, thereby creating the potential for further liability. It is thus incumbent on all parties involved in drafting, approving, delivering and explaining the informed consent form to provide a clear disclosure of these potential costs, and then comply with the terms of that disclosure if a subject is injured during a study.

It is beyond the scope of this article, but note that the regulation does not define the term "costs". Thus, it does not limit the disclosure to the out-of-pocket cost of medical treatment or even monetary costs. Further, 45 CFR 46.116 prohibits the use of exculpatory language to exclude such costs.

If a subject is injured during the course of a clinical trial, he/she may be eligible for reimbursement of his/her cost of medical treatment. Two documents set forth the terms for this reimbursement:

- The investigator's signature on an informed consent form (ICF) documents the obligations ("duty of care") of the investigator and his/her employer – the site – to the subject. In contrast, the subject's signature documents only his/her intentions. The site's obligations are legally enforceable, while the subject's intentions are not. The typical ICF discusses reimbursement in a relatively brief and simple manner so as to be understandable to subjects with no legal training and perhaps limited reading ability.
- The clinical trial agreement (CTA) is a legally-binding contract between the research site and the study sponsor. It sets forth their respective responsibilities for reimbursing injured subjects for medical treatment. The subject injury section of the CTA may discuss reimbursement in great detail, including numerous conditions and exceptions. It may also be ambiguous, leaving the parties' responsibilities unclear. (Large claims, typically for death or serious physical injury, are typically governed by the indemnification section of CTAs and are outside the scope of this article.)

ICFs resemble contracts because the site and subject agree in writing to exchange value for value. They may create contractual obligations for the site and perhaps the sponsor. For example, in York v. Jones (717 F. Supp. 421, 425 (E.D. Va. 1989)), a Virginia court held that the informed consent form contractually bound a research site to transfer a study subject's fertilized eggs to a hospital of her choosing.

However, their status as contracts – subject to enforcement under contract law – is not a settled legal question because the subject is not obligated to perform. For example, it is unimaginable for a site to bring a claim under contract law to force a subject to comply with the study protocol. However, tort law permits one party to recover damages for injuries caused by the negligence of another party. The presence of negligence – one party's failure

to exercise ordinary care for the safety and well-being of another party – then becomes an important question.

The study sponsor may draft the ICF and require its approval of any changes. However, study sponsors are not legally bound "parties" to the informed consent form. Thus, any statement ("representation") in the ICF that the sponsor will reimburse the subject for medical treatment of a study injury is only an indirect obligation that must be enforced through tort (non-contract) vs. contract law.

Most CTAs have a "third-party beneficiary" clause. This clause says that, regardless of the CTA's contents, it does not create any rights for third-parties such as study subjects. If a subject is injured, the site has no right to enforce the sponsor's reimbursement obligations unless the subject files a legal claim against the site.

Thus, because the site stands between the subject and the sponsor, no document directly obligates the sponsor to reimburse the subject. The ICF may say that the sponsor will reimburse the subject, but the sponsor is not legally bound by the ICF. The CTA may provide for the same reimbursement, but the subject is not a party to the contract, so obtains no rights. For the subject to enforce a claim against a sponsor, he/she must thus demonstrate in court that an obligation exists in the form of an implied contract or a duty of non-negligence. Because the investigator – the site's representative – signed the ICF, it is generally easier for the subject to enforce a monetary claim against the site than against the sponsor.

In general, the courts have ruled that ICFs do not create a legal obligation by the sponsor to the subject. (For example, see Abney, et. al v. Amgen, Inc.; slip opinion decided March 29, 2006; US Court of Appeals, 6th Circuit; No: 05-6132) Sponsors may, however, find that even the most carefully-crafted CTA does not provide the protection they expect.

In at least one case, Dahl vs. Hem Pharmaceuticals Corp., 7 F.3d 1399 (9th Cir. 1993), held that an informed consent form is a contract between subject and sponsor. In this case, the court required the sponsor to comply with the ICF and provide study drug for one year after the study in return for the subject's completion of the study. In this case, the subject could not bring the claim against the site because the sponsor was the party holding the study drug.

The courts may apply "agency," a third legal theory, to hold the sponsor liable if, in practice, the investigator acted as the sponsor's agent, despite contrary language in the CTA. Such a finding requires that the investigator or site acted under the control of the sponsor. For example, if sponsor personnel trained, supervised and directed the investigator in the conduct of the surgical procedure that injured the subject, the courts may find that the investigator acted as the sponsor's agent, even though the CTA stated that such actions do not constitute control. If the sponsor writes the ICF and requires the investigator to use the ICF without alteration, a similar argument could be made, especially if the injury is caused by a side effect known to the sponsor but not disclosed – or emphasized – in the ICF or investigator's brochure.

As a practical matter, if a subject has a legitimate claim, the sponsor is likely to provide reimbursement. In the context of a $10 million study budget, a few thousand dollars to make a potentially big headache go away is a minor cost of doing business. Given the sponsor's key role in the study and drafting of the ICF and CTA, a tort claim by the subject against the sponsor has a good chance of succeeding, but not without an expenditure of time and legal expense that may outweigh the value of any eventual award.

ICF vs. CTA Conflicts

If the site represents in the ICF that the sponsor will reimburse under broad conditions but the CTA sets forth narrower conditions, the site is obligated by its representation to provide the reimbursement out of its own pocket.

If the injury is caused by the site's negligence, misconduct or noncompliance with the protocol, reimbursement should be the site's responsibility. Other exceptions or silences in the CTA that should not be the site's responsibility include:

- The site did not notify the sponsor of the injury prior to the subject incurring medical expenses.
- The subject obtained treatment that was not standard-of-care.
- The site did not obtain prior approval from the sponsor before providing medical treatment.
- The injury exacerbated a pre-existing condition but did not create a new condition.
- The injury was psychological rather than physical.
- The charges for the treatment were higher than the sponsor considers reasonable and customary.
- The injury was caused by the performance of a procedure, not administration of the study drug.
- The subject obtained diagnostic tests, not "treatment"; further, these tests may have indicated no injury occurred.
- The subject incurred costs ancillary to treatment, e.g., chartering a jet from a foreign country to obtain proper emergency treatment.
- The subject's insurance company refused to reimburse the cost of treatment, or initially reimbursed the cost and then reversed its decision later.
- The subject caused or contributed to the injury by not following instructions.
- The injury was indirect, e.g., the study drug caused the subject to faint while driving a vehicle.
- The term "injury" was not defined in the ICF and the subject interpreted it to include any damage, harm, loss, injustice or violation of rights.

In each of these situations, although the site did nothing wrong, the sponsor avoids responsibility, leaving the site to reimburse the subject or dispute the matter with the subject. The sponsor may decide to provide reimbursement without the contractual obligation, but only at its own discretion.

The Solution

There are four ways to reconcile the ICF with the CTA:

- Exceptions can be added to the ICF, at the risk of complicating the document.
- Exceptions can be removed from the CTA.
- The CTA can say that the sponsor is responsible for reimbursement according to the terms of the ICF, which is attached as an exhibit to the CTA.
- The CTA can say that study subjects are third-party beneficiaries of the subject injury section.

As long as the ICF grants the subject broader rights than does the CTA, the site is potentially assuming responsibilities that rightfully belong to the sponsor. On the other

hand, as a practical matter, the exceptions in the CTA may not provide any protection to the sponsor. It is thus in both parties' interests to resolve potential conflicts before they occur.

Disclaimer

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