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Liability Risks Hamper Clinical Trials

Coherent, dependable scheme is needed to protect all participants.

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CLINICAL TRIALS, the testing of new medical treatments on humans, are often spoken of as an important source of new treatments for disease, but they are also an important alternative source of healthcare for many thousands of patients.

Many illnesses have approved treatments that are of little or no benefit at all. Other illnesses may have robust treatment regimens, but such treatments may not be effective for a large cross section of patients. In other cases, a treatment may exist, but the cost may be prohibitive for many patients or their insurance or Medicare or Medicaid may not cover it.

For any of these patients, enrollment in a clinical trial may provide the possibility of receiving either customary care for their illness, referred to as "standard of care" treatment, or a possible new treatment or, in some cases, a combination of both.

Participation in clinical trials always carries some risk to the patient's health. While rare, in some cases administration of a new treatment regimen, drug or biologic or use of an investigational device may even result in injury or death.

Disclosure of known potential risks is made to potential trial participants through the informed consent process, resulting in execution of a form that has been reviewed and approved by an institutional review board or, outside the United States, an ethics committee, a group formed to review the trial and protect the rights and health of the trial participants.

While the current clinical trial scheme in the United States requires sponsors of trials to provide potential participants disclosure as to known potential risks of participating, there is no coherent and dependable scheme in this country for the protection of patients, hospitals and sponsors against the costs posed by clinical trial injury.

Covering Financial Risks

Such injury can be a substantial financial risk for all of the parties involved.

For the patient, injury from participation in a clinical trial may be serious or even result in death. Certain injuries require long-term care and, in few cases, lifelong care.

For the doctor and hospital, there are related risks. The treatment and care related to clinical trial injuries can be expensive. Doctors and hospitals generally rely on the trial's sponsor to maintain insurance that will cover the cost of patient injury and death. That said, insurance may not cover all the costs and will certainly not insulate the doctor and hospital from suits and other actions.

Similarly, indemnifications and carefully crafted informed consents are of only limited value when determining liability for the cost of treatment. Even if a sponsor accepts full responsibility, there is no assurance that the sponsor, particularly a start-up company, has the financial wherewithal to cover long-term treatment costs that might arise or will even be around to pay for long-term care.

Few clinical trial sponsors realize that their insurance does not always cover all of the costs for treatment of clinical trial injury. Even a large sophisticated company often will not understand the terms of coverage spelled out in its insurance policies.

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The company may not realize that a clinical trial insurance policy does not cover all the risks posed by a clinical trial, including in some cases the costs for the treatment of clinical trial injury, and that a sponsor often must come out of pocket to pay such costs even if it has already covered a high retention (deductible).

Coverage under some policies will not even kick in until an injured patient threatens to bring a suit, perhaps creating a perverse incentive for a sponsor to consider withholding payment for treatment in the hope that a suit will be brought.

When a hospital successfully adds language to its clinical trial agreement that requires a sponsor to maintain insurance that covers all of the potential liabilities arising in connection with a trial, it is possible that very little has been achieved. This sort of language requires insurance that will never be written by any U.S. insurer. So, the hospital may be taking false comfort in its belief that the sponsor and its insurer have such insurance and the sponsor (and not the hospital) will take care of everything.

Europe Does a Better Job

While the United States lacks a no-fault insurance system that protects persons participating in clinical trials, many European countries have implemented such systems. Several have taken the lead in finding new ways to protect clinical trial participants and, thereby, offer more predictability to the sponsors, hospitals and doctors conducting the clinical trial. Following are two examples.

As in the United States, in the U.K. there is no legal obligation for sponsors to purchase clinical trials insurance. That said, in practice U.K. sponsors generally purchase insurance for their trials.

The Association of the British Pharmaceutical Industry (ABPI) is a trade organization that draws participation from a large percentage of the companies manufacturing and selling pharmaceuticals in the U.K. ABPI brings together industry and governmental and regulatory authorities in a uniquely productive manner and has taken two notable actions that help to combat the confusion and contentiousness that usually permeates discussions as to how to pay for patient injury.

First, it has promulgated Clinical Trial Compensation Guidelines for use by all its members and by national health trust facilities. Second, the ABPI has issued a standard form of clinical trial agreement and indemnities for use by its members and national health trust facilities.

As it turns out, the forms have been generally accepted by nearly all sponsors of trials in the U.K. and are also generally insisted upon by all national health hospitals and research facilities. The forms are notable in that they are unusually fair to both the sponsor and the hospital, so very little negotiation is usually required. In practice, the U.K. contracting process is fairly straightforward and, if handled properly, the legal issues and process can become secondary to the clinical work being performed, as it should be.

Germany has made efforts to manage more carefully the risk posed by the uncertainties of insurance. First, Germany requires all sponsors to maintain clinical trial insurance for each trial, which includes minimum coverages for each trial participant, with an overall maximum for each trial.

The limits required by the German government are high, in response to which Pharmapool was created. Pharmapool includes an association of over 100 German insurers who help to cover the risks that a single insurer may not be able to cover. Pharmapool sets the rates and coverages that create a layer of reinsurance that helps to ensure that the costs for treatment of patient injury is covered.

Generally, premiums are paid up front, thus ensuring that monies are available if needed. Risk is further managed by requiring insurers to use ethics committees that are located closest to the clinical trial site, so the sponsor or hospital cannot be tempted to "cherry pick" its ethics committee. Such broad-based pooling of risk makes good sense for clinical trials.

While Germany has attempted to tackle insurance and coverage issues, it has not been able to standardize its clinical contracting forms and processes. Germany's

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laws requiring compensation to inventors of intellectual property have been a stumbling block to contract standardization.

German hospitals each seem to have their own form of agreement and there is widespread confusion as to what is required in the intellectual property ownership, assignment and compensation provisions. So, while a patient may be well protected in Germany, the contracting process can still be painful and tedious, thus slowing the clinical trials process and increasing its cost.

Help From U.S. Regulators?

So, in light of the many reforms throughout Europe, what are the U.S. regulators of clinical trials doing to help clarify how payment for clinical trial injury is to be allocated and paid?

The answer to that question is, when cast in the most generous light, unclear. To understand where we are now, it is best to look at a quick history on this topic.

On June 7, 2000, in a press release, the White House announced that "…President Clinton issued an Executive Memorandum directing Medicare to revise its payment policy and immediately begin to explicitly reimburse providers for the cost of routine patient care associated with participation in clinical trials, and to take additional action to promote the participation of Medicare beneficiaries in clinical trials for all diseases."

Until June of this year, 10 years later, the Centers for Medicare & Medicaid Services (CMS) had issued no binding regulations that clearly state whether hospitals can seek reimbursement for the treatment of clinical trial injury. In fact, most of their guidance worked to muddy the waters on this subject.

Most hospital administrators and general counsel referred to a 2004 CMS letter from Gerald Walters, Director of the Financial Services Group, Office of Financial Management, to Holley Lutz of Gardner, Carton & Douglas. In that letter, Mr. Walters asserts that any agreement by a trial sponsor to pay for medically necessary services related to injuries received as a result of participation in a clinical trial constitutes a demonstration of the primary payment responsibility of the sponsor.

He concludes that if Medicare or Medicaid have reimbursed for any of the costs of treatment for which there is another party with primary payment responsibility, the party with primary payment responsibility is statutorily obligated to reimburse Medicare.

Mr. Walters' letter gained quite a bit of popularity over the ensuing seven years, though it was not clear to anyone what (if any) force it may have. In the absence of any definitive guidance from CMS, most hospital attorneys pulled out a copy of the letter as their basis for rejecting any request by sponsors to seek Medicare reimbursement for relevant treatment costs, despite the fact there was nothing that made such a request inappropriate.

It was also a position that seemed to run counter to the Clinton executive memorandum above, especially when contrasted with the following statement from the press release concerning the executive memorandum:

> This week, the Health Care Financing Administration (HCFA) will inform all claims processing contractors that Medicare will immediately begin to reimburse for the routine patient care costs *as well as costs due to medical complications associated with participation in a clinical trial, removing this barrier to participation*. (Emphasis added.)

In a CMS Alert dated May 26, 2010, CMS provided its first official guidance as to payment for clinical trial injury. In the Alert, it dodged key issues and stated that it considers reductions in charges or the provision of value to a Medicare beneficiary who "…has sought or may seek medical treatment as a consequence of the underlying incident giving rise to the risk…." to possibly be self-insurance or liability insurance, which may or may not need to be reported pursuant to Section 111 requirements.

Unfortunately, the long-awaited CMS Alert leaves many questions unanswered. It provides no framework for sponsors and hospitals to agree on a definitive procedure for such payments and, worse yet, it appears to perpetuate the decades of uncertainty that the Clinton executive memorandum attempted to eliminate.

It is therefore to be expected that hospitals will continue to refuse to seek reimbursement for Medicare and Medicaid for the costs of treating clinical trial injury and, therefore, that the beneficiaries of Medicare and Medicaid will continue to be foreclosed from certain healthcare opportunities.

Contracting Amid Confusion

The discussion around payment for treatment of clinical trial injury has led to a patchwork of contract provisions and contracting styles and, as is inevitable, confusion and inefficiency for all parties participating in clinical trials.

For instance, if a sponsor desires to conduct a Phase 2 clinical trial with 20 clinical sites, the sites will likely be composed of some blend of large institutions and smaller hospitals or hospital systems and, depending on the indication, private medical practices.

A prudent sponsor would plan for lots of comments and significant negotiations on the clinical trial agreement with large institutions, while the smaller hospitals or hospital systems would likely offer fewer comments and require less negotiation depending, of course, on how active their inside counsel were in these types of transactions. Finally, the sponsor would expect almost no comments from medical practice sites.

In the 20 clinical trial agreements that the sponsor will need to execute with clinical sites and principal investigators, it is likely that, even despite efforts to "standardize" its approach to the treatment of and payment for patient injury, only a few of the agreements would read the same on the indemnification, patient injury and insurance provisions, while the majority will have provisions that take different approaches on these topics.

This is a system that requires time and effort. Sponsors and clinical sites and principal investigators often spar on the contents of the clinical trial agreement and, in the end, the patient may be the loser if the parties spend their time and money trying to push risk to the other party, while neglecting to agree specifically how trial injuries will be treated and the treatment paid for.

The Unfortunate Result

Enrollment in U.S. studies is notoriously low when considered as a percentage-of-potential-patients basis.

A recent GAO report analyzing clinical trials stated that in 2008, 40 percent to 65 percent of clinical trials of U.S. FDA-regulated products were conducted outside the United States. Patients would be more apt to enroll in a study if they had assurance that their injuries would be treated without cost to them, even if the injury requires long-term care and even if the company providing the experimental treatment goes belly up.

The uncertainty and inefficiency of the U.S. system can also work as a deterrent for non-U.S. sponsors.

While many foreign sponsors recognize that the United States is a key market for the sales of pharmaceuticals and devices, and that an FDA approval is something that will be useful and respected in many other jurisdictions, some are not willing to navigate the unknown risks posed to sponsors of U.S. clinical trials. This can be especially concerning for sponsors who would like to test treatments during which patients may die, such as treatments for certain late-stage cancers.

Often foreign sponsors view U.S. clinical trials as a "bet the farm" move, believing they could be exposing their entire company to U.S.-style judgments as they are aware the insurance may or may not cover their actual losses.

The end game for all sponsors, academic institutions, hospitals and investigators is to improve public health and to increase their ability to offer to their patients treatments that address their symptoms, help them manage their ailments and treat/cure their diseases. A sensible, coherent approach to the treatment of patient injury and payment for treatment of patient injury could go a long way in furtherance of that goal.

Suggested Improvements

Our system of treatment and payment for treatment could greatly benefit from a few simple improvements.

First, the obligations of each party participating in the trial need to be spelled out clearly. Sponsors need to provide insurance, hospitals need to be required to treat or obtain treatment for patient injury, investigators need to oversee the process, and insurers and CMS need to decide (or be told) what their role will be.

Second, sponsors need to be offered insurance that covers all the primary risks of clinical trials.

Third, the clinical trial agreement contracting process and documentation needs to be standardized. It would be best if key obligations were not subject to regular re-negotiation in each new clinical trial agreement.

Fourth, all of the foregoing is useless without standardizing the cost for treating a study subject. Predictability of cost is key to covering the costs of treatment and ensuring enough money has been set aside to protect the patient.

Finally, if the United States would like to earn world respect for our own standards for the treatment of clinical trial injuries, we should consider requiring for all sponsors conducting trials in this country employ the same protections in every country in which the trial is being conducted.

These reforms are the sort of change that could bring more participants into clinical trials and more sponsors to our country with new and innovative treatments.