CLINICAL TRIALS: RISKS, REASONS AND THE RESPONSE

Who or what do we think of when we hear the term "clinical trials"? For some, the topic elicits thoughts of life sciences – small biotech firms and big pharma in pursuit of the next wonder drug. Others think about clinical trials from the perspective of a healthcare provider – independent research sites offering experimental drugs/devices under a FDA study. In all apparations, clinical trials test the unknown on human subjects...a risky proposition. The fact is, there are several organizations participating in a clinical trial and each plays a different roles with their own unique liability exposure.

The insurance industry has had a mediocre performance in offering insurance instruments that clearly identify potential risks and seamlessly insure the exposures to each of these entities. This article will summarize the exposures to loss, identify the gaps in traditional insurance and propose a solution to simplify risk transfer.

As you know, a clinical trial studies the effects and efficacy of new drugs, devices or treatments on human subjects. A great deal of research occurs in the *pre-clinical* stage to warrant any testing of patients. In order to assess and monitor the safety of a clinical trial, several parties must coordinate services and share information. First and foremost, the Food and Drug Administration (FDA) approves or disapproves any proposed research from becoming a clinical trial. Once the FDA approves a trial, a host of parties come together for the wellbeing of the human subjects.

Trial sponsors, contract research organizations, ethics committees and investigators are the four major categories of organizations responsible for executing a trial's well-defined protocols and procedures. Each entity has a unique responsibility that exposures it to litigation when injuries/errors occur.

Trial Sponsors	*The FDA defines the trial sponsor as the "responsible party." The sponsor is a person/entity who initiates a clinical investigation, but who does not actually conduct the investigation. The responsible party can also be a "sponsor-investigator" - an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to a subject.*	**Potential Lawsuits**	• failing to develop safe protocols • failing to respond to the health of patient subjects • possessing improper financial interest or conflict of interest between sponsor and principle investigators • failing to respond to Black Box warnings in a timely fashion • intentionally or unintentionally failing to accurately compile data • failing to report negative outcomes

Trial sponsors can be "Big Pharma", a small biotech firm, a university hospital or a private psychiatrist. No matter *who* the trial sponsor might be, they are often the responsible party during a clinical trial. "Responsible party" is the term used in Title VIII of the Food and Drug Administration Amendments Act of 2007 to refer to the entity or individual who is responsible for registering a clinical investigation and submitting trial information to the Clinical Trial Registry Data Bank.[1] Most clinical trials and their trial sponsors have an exposure to product liability. Trial sponsors typically purchase a coverage that can address product liability, clinical trial liability and medical expense coverage under one policy. As the responsible party it is imperative that the trial sponsor has insurance/risk management practices to avoid loss arising out of the actions of the investigators and other parties.

Contract Research Organizations (CROs)	*A CRO is a person/entity sharing one or more of the obligations of a sponsor. These independent contractors can design protocol, select patent population, monitor investigations, evaluate reports, and prepare materials to be submitted to the Food and Drug Administration.*	**Potential Lawsuits**	• failure to monitor patient subject health • failure to comply with protocols set by trial sponsor • failure to respond to Black Box warning in a timely fashion • improperly recruiting patients • failing to accurately compile data

CROs buy E&O insurance with some coverage nuances. Large CROs have a broad scope of service that can include contract manufacturing of the trial drug/product, Phase I medical services, patient recruiting and regulatory services. Most CROs buy E&O insurance that includes a Products/Completed Operations component and almost all cover the vicarious liability from bodily injury caused by the sponsor or investigator. Only the CROs that offer medical services through their employees buy medical professional liability. Forms designed for CROs are perhaps the most comprehensive because they must be flexible enough to address suits made by patient subjects, trial sponsors and investigators.

[1] www.clinicaltrials.gov, Elaboration of the Definition of Responsible Party and Applicable Clinical Trials

Investigators - Hospitals	*These facilities often operate as independent research sites with direct patient contact. Hospitals are increasingly being used for Phase I studies and some large teaching hospitals operate as sponsor-investigators developing the protocols under review. Often times hospitals develop their own institutional review boards.*	**Potential Lawsuits**	• providing negligent medical professional services • failing to comply with trial protocols • inaccurately collecting or remitting data • improperly recruiting patients • failing to report negative outcomes
Investigators - Physicians	*Individual physicians act as principal investigators: someone conducting a clinical investigation. More specifically a person under whose immediate direction the drug is administered or dispensed to a subject.*	**Potential Lawsuits**	• providing negligent medical professional services • failing to comply with trial protocols • inaccurately collecting or remitting data • improperly recruiting patients • "therapeutic misconception" – implying the subject is receiving a therapy when other actions/reactions are being studied

Investigators, the healthcare providers in the trial, are often asked to provide evidence of medical malpractice or medical professional liability insurance. Investigators' greatest risk during a trial is to inflict bodily injury to a test subject. Unfortunately, trial sponsors and the CROs who identify and engage the investigators, fail to ask the investigators for evidence of *Clinical Researchers E&O* insurance. If an investigator has a rogue employee who falsifies data, a medical malpractice policy does not respond. If an investigator fails to follow the trial protocols, the data can be deemed useless and the trial must be performed again. In this scenario, a medical professional liability policy will not pay to make the sponsor whole to recoup its fees or grants. Clinical Researchers E&O responds to the financial loss litigation that is most likely to be brought by the trial sponsor or its CRO. Sadly, there are a handful of carriers that provide a policy form that covers both the bodily injury (malpractice) and financial loss arising out of a clinical trial.

Ethics Commitees	*These boards are composed of at least five members that include scientists, doctors, and lay people. They review and approve clinical trials taking place within their jurisdiction before the trials can begin. An institutional review board is the most common type of ethics committee (EC). Another type of EC is a data safety monitoring board.*	**Potential Lawsuits**	• failuring to conduct meaningful, continued review of patient subjects' health • failing to disclose conflicts of interests between EC members and sponsors

Instituional ethic committees assume they have adequate coverage in place under their academic or medical institution's liability program. Commercial institutional review boards (IRBs), for-profit ethics committees, typically buy low limits of liability. IRBs perform an oversight role that can lead to litigation from test subjects. Cases such as *Grimes v. Kennedy Krieger*, *Robertson v. McGee* and *Gelsinger v. University of Pennsylvania* set the foundation for defining the duties and responsibilities of the IRB to the patient subjects. When you consider the potential exposure to loss associated with the previously mentioned lawsuits, it is concerning to imagine an IRB only purchasing $1M in professional liability insurance.

More recently, the Anil Potti cases associated with Duke University and its IRB should have companies revisit the idea of adequate insurance (Note: the FDA audit found "no significant deficiencies" in the conduct of Duke's IRB).

Professional liability policies that insure IRBs are typically generic E&O policies that do not clearly list and acknowledge the expected responsibilities of the IRB. A policy that does not define their professional services is a recipe for a claims dispute.

As noted earlier, the exposure to litigation varies with the types of services/responsibilities. Recent publicized cases have been associated with HC providers falsifying data as well as big pharmaceutical firms accused of not disclosing all adverse events during trials. These cases imply professional liability, product liability and possible criminal prosecution. The insurance coverage afforded to the sponsors, CROs, investigators and ethic committees must be tailored to their unique exposure. Because of the contractual connections between the various parties, it is imperative for all entites to have a robust risk management program that includes an understanding of their coverage as well as the coverage of their sponsors/vendors.

Unfortunately, very few trial sponsors and their CROs have implemented best practices to verify adequate insurance from investigators and IRBs. Simlarly, investigators rarely assess the sponsors' financial solvency and insurance protection for the medical injuries of patient subjects. With so many parties involved in a single trial, it is surprising that the insurance industry has not found a streamlined solution to consolidate and transfer this risk. By looking at construction project underwriters, we may have found the solution.

With so many parties involved in a single trial, it is surprising that the insurance industry has not found a streamlined solution to consolidate and transfer this risk.

A wrap-up policy, sometimes called an owner controlled insurance program (OCIP) or a contractor controlled insurance program (CCIP), is a single insurance contract that names all of the construction participants on a given "project". The wrap-up policy allows the project owner or construction manager to consolidate all insureds, including subcontractors, onto one policy and eliminate the risk of uninsured/underinsured vendors for general liability, products/completed operations and/or workers' compensation. The concept removes any finger-pointing between carriers because most injuries during the project are covered by one insurer.

As clinical research underwriters, we have embraced the wrap-up concept and applied it to clinical trials coverage. The "project owner" is the trial sponsor; the "construction manager" is the contract research organization. The "subcontractors" are the independent research sites and any other vendor associated with the trial for whose services the sponsor/CRO can be held vicariously liable.

Insurance under a sponsor controlled insurance program (SCIP) or a CRO controlled insurance program (CRCIP) is a blended professional and general liability policy. Coverage includes commercial general liability, products/ completed operations, professional liability, 1st party rework coverage, medical expense and regulatory (Form 482/483) expense coverage. The professional liability responds to the medical professional services provided by research sites as well as the medical and non-medical professional services provided by the CRO, IRB and sites. By broadening the traditional coverage, the insurance responds to most bodily injury, financial injury and property damage arising out of the trial, regardless of the negligent party. The following table recaps some of the current coverage gaps and the solution provided under a controlled insurance program.

Current Coverage Inadequacies	SCIP/CRIP Solution
Research Sites purchase cover for bodily injury, but not covered for financial losses	Coverage applies to the cost of rework from errors made by an independent research site.
Review Boards and Research Sites dictate their tail coverage for medical malpractice and they typically buy low limits resulting in an insurance deficit for bodily injury	Sponsor or CRO maintans the policy, thus, they control coverage for prior acts associated with trials. Sponsor or CRO has ability to buy a block of limit to ensure adequate limits are in place for bodily injury.
Fragmented Claims Handling	Sites have ability to quickly report patient subjects' injuries. No fingerpointing to identify the responsible party….a unified front before plaintiffs.

We should also note that a safer environment is another benefit by an OCIP program. A consistent emphasis on patient safety is another part of the SCIP/CRCIP value proposition. Small sites with limited experience in trials are able to have access to educational modules developed by industry experts. Coverage, claims and risk management become a seamless solution for a major trial.

Trial sponsors, contract research organizations, ethics committees and investigators each have specific responsibilities while carrying out a clinical trial. Insurance coverage for the various parties is fragmented with gaps in coverage and claims disputes a common occurrence. The concept of the sponsor (or CRO) controlled insurance program brings a comfort in knowing that all participants are adequately protected. For a single trial or multiple trials, a controlled program's uniform coverage, joint defense and risk services is the single solution approach that the clinical research industry needs and deserves.