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A Safety Net

Insurance has responded to changes in the clinical trials landscape and has evolved in many ways to perform in a crisis

Hanna Beaumont at La Playa

Clinical trials liability (CTL) insurance will always have at its heart 'putting it right' for the patient or participant undergoing the trial if something goes wrong. However, trial insurance has many other interwoven strands, of which you may not be aware.

High-profile media coverage of clinical trials disasters such as the 2006 'Elephant Men' trial at Northwick Park and the Rennes incident in 2016 lingers long in the mind of the public, but, in truth, clinical trials have an excellent safety record.

Human volunteers are protected with a framework of risk management, including rigorous controls and procedures, but discovery will always involve risk and, where mitigation reaches its limits, insurance must provide a safety net.

Alongside regulation and operational controls, a well-designed and robust insurance programme must be in place to provide financial compensation for participants – and financial protection for the research organisations conducting these trials.

The universe of clinical trials is changing, as new non-pharmaceutical products come into the market with clinical application – from apps to medical robotics. New EU regulation is soon to change the landscape in terms of insurance.

CTL Insurance

Clinical trials carry obvious risk – for the patients or subjects and also for other stakeholders in the process who may incur substantial liabilities if things go awry. CTL insurance is a vital piece of the risk mitigation jigsaw and, in many territories, a legal requirement. Available from specialist insurers (such as CFC, Chubb, CNA, QBE, and Lloyd's of London) and accessible through an expert broker, CTL insurance provides cover for:

Negligent Harm
Harm caused as a result of alleged negligence, lack of due diligence, lack of care, breach of duty of care, or an act of carelessness towards a participant in a research project.

Case Study: Elephant Men Trial 2006
Within an hour of receiving the trial drug, six volunteers had been rushed to intensive care and were fighting for their lives, with soaring temperatures, organ failure, and some of their bodies swelled so severely that they became known in newspapers around the world as the 'Elephant Men'. The report focussed on dosage and testing schedules.

Non-Negligent Harm
This is harm with no specifically identified cause, but likely to have arisen from the participant taking part in the research study. The policy wording works in accordance with compensation guidelines for the regulator in each territory.

Case Study: Adverse Reaction
A participant had an adverse reaction while partaking in a clinical trial and was hospitalised for four days. Their medical expenses following the incident were covered under the policy's compensation cover, and the insurer helped facilitate the continuation of the trial with minimal interruption.

Underwriters will build the cover and the rating around:

The Protocol Document
This includes details of:

- The drug or device: Information about the API (in the case of a drug or vaccine) or, in the case of a device, its intended scope and purpose. Which phase of trial has been reached – 1, 2, 3, or 4? Is it invasive or non-invasive?
- Country of the trial site(s)
- The schedule for the tests or procedures and details about dosages involved and the length of the study

- The informed consent documents (describing the purpose of the study, the risks, and potential side effects of participation and its duration/procedures)

Trial Participant Information
This is the number and nature of trial subjects – are they healthy volunteers, pregnant women, sick children, or patients with an existing condition? Insurers will pay particular attention to trials involving vulnerable groups such as children or women of child-bearing age.

The Indemnity Limit
The level of indemnity limit required for liability insurance will affect the premium.

Details of the CRO
Underwriters need the details of the CRO, the clinical investigator, or organisation responsible for the conduct of the trial. What is their experience? What is the average number of trials conducted per annum? Are there any previous adverse events noted?

The underwriter will also want to know about the following:

Clinical Trial Management Practices
Insurers will query evaluation and risk assessment processes, safety and ethics in the protocol, peer review, accreditation, monitoring of SOPs, and documentation management.

Informed Consent Controls
The CRO will need to share how consent documents are developed and prepared, legal reviews, readability of documents, and processes for ensuring understanding prior to sign off.

Risk Management
How would an adverse event be dealt with – what crisis management planning is in place? Is there any previous history of cessation of trials? How will the trial meet Good Clinical Practice standards?

Trial managers should be ready to provide plenty of information to the insurer – liaising closely with the broker partner. The better prepared, the more quickly the insurer can make the call on underwriting risks.

In terms of rating (cost per £ of liability/risk), clinical trials insurance has become cheaper over the years, reflecting the high standards of care and regulation and, hence, profitability of the risk from an underwriting perspective.

Who Should Buy the CTL Insurance?

The sponsor(s) (whose details appear on the protocol) of the trial arranges the insurance. This may be a biotechnology company, pharma business, or institutional research organisations such as hospitals, universities, research institutes, charities, and even disease advocacy organisations.

How Insurance Is Evolving

These days, clinical trials are not just about drug development (the development of a new chemical entity). They may involve the clinical testing of a new medical device or surgical procedure. As the liabilities change, so too has the insurance evolved, offering additional lines of cover around risks and liabilities arising from contracts between trial parties (eg, withheld fees). Policy (or multi-trial programme) periods have shifted to cover the whole length of the trial as opposed to an annual policy, which has to be renewed every year mid-trial.

Case Study: Software Error
A software developer created a platform to upload data from medical imaging devices for use in a clinical trial. The platform enabled access to records across multiple trial sites. During the course of a change order update, an error was introduced into the code.

The developer resolved the issue, but multiple images had to be retaken as a result of the coding error. The insurer was able to negotiate a favourable settlement before the issue went legal to prevent any further costs. In fact, the professional indemnity cover sold alongside the CTL policy footed the bill.

Similarly, as society becomes more litigious, disputes and breaches of contract can trigger costly lawsuits requiring insurance protection. Insurance can also provide financial protection from trial-related risks such as:

- Reputational damage, which covers the cost of a PR agency to mitigate damage and crisis-manage communications
- Contractual liabilities
- Contamination and stock deterioration
- Loss in transit

Case Study: Reputational Damage
A trial sponsor attracted negative press following reported problems with a clinical trial in Australia. Trial participants reported severe nausea following first-in-man trial of immunotherapy cancer treatment, and relatives reported the issues to a local newspaper.

The sponsor used a PR firm to handle communications and press releases and to coordinate communications with the trial host site. Costs were covered under the brand protection clause in their insurance. Meanwhile, the patients were treated for nausea and the dosage reduced, resulting in continuation of the study with minimal expense incurred.

The Impact of New EU Regulation

New EU regulation due in 2019 will affect the limit of cover stipulated and the way the insurance is structured. For trials

Case Study: Contractual Liabilities
A trial sponsor took issue with delays with recruitment and trial progress and threatened to issue proceedings against the CRO alleging breach of contract. The insurer identified that the sponsor's position appeared to be motivated by sizeable unpaid fees owed to the CRO, and the matter was settled with the CRO offering to waive a portion of the unpaid fees. The policy covered the shortfall to the CRO.

Case Study: Contamination and Stock Deterioration
A drug discovery company's drug was being held at a third-party clinical services company for relabelling. The drug was relabelled and released in batches as the trial progressed, but, with the final batch, a number of vials were flagged as contaminated. Investigations meant delays of three months – the costs of which were covered under business interruption insurance.

conducted in conjunction with the UK's NHS, an overall limit of at least £5 million is commonly required, whereas in Germany, the limit is stipulated as a quantum per trial subject.

The latest EU Regulation on clinical trials on medicinal products for human use will require sponsors to publish results of trials on a centralised database that will be available to the public. EU member states will be required to establish an insurance guarantee system, making CTL a compulsory class of insurance or setting up a national insurance pool. However, clinical trials that are "low intervention clinical trials" (as defined) will not be subject to this requirement.

The current Clinical Trials Directive requires sufficient funding to be available to provide indemnity if trial subjects receive bodily injury, and insurance provides this. For European community countries, the requirements depend on the practical implementation of the *European Commission Clinical Trials Directive (2003/94/EC)* and the country-specific regulations. Requirements differ between countries (and occasionally, in practice, between different ethics committees in different regions of the same country).

Conducting Trials Overseas

Overseas trials may require insurance certificates and paperwork in the local language. Examples are:

- US: A company may opt to trial in the US to create documentation, publication, and recognition to support the case when seeking FDA approval. The cover can be placed via a local broker if they have access to an insurer with global capabilities – higher levels of cover are likely to be needed due to the litigious culture in the US
- Germany: Germany is generally a more regulated environment – and insurance cover is based on the number of trial participants (referred to as 'patients' and not 'data research subjects')

Structuring Insurance

If a company has a specialist life sciences policy, the package policy can be extended to include CTL, or one can buy standalone CTL cover. The former means money can be saved by spreading the risk. However, some ethics committees require insurance to be structured differently – standalone or per participant. Either way, it is important that CTL is carefully dovetailed with a broader insurance portfolio to ensure every base is covered, without expensive duplications.

A CTL policy commonly lasts the duration of trial, usually with a maximum of five years plus an extended reporting period. It is important that the wider insurance programme is also set up well, with good IT security around personally identifiable information (eg, data held for correspondence purposes) and a robust cyber insurance policy. Talk to a broker about the bigger picture of the business risk and how the trials dovetail with other activities and exposures.

Selecting a CTL Insurance Broker

Look for a broker with:

- Genuine life sciences expertise in-house
- Speed of response – how quickly do they get back to an initial enquiry?
- Foreign and domestic capability
- Understanding of country-specific requirements

Good management of clinical trials should be based on a genuine partnership with an insurance adviser and a culture of openness, trust, and understanding.

Acknowledgments
Our thanks to CFC Underwriting for their contributions to case study material.

About the author

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