Insurance in Clinical Trials

Clinical trial insurance is intended to compensate patient-volunteers ("volunteers") in a clinical trial (or their dependents) for death or injury arising out of their participation in the trial. This article is intended to provide basic information about clinical trial and associated liability insurance covers and some of the factors you may wish to discuss with your insurance broker and legal advisors, when arranging insurance for clinical trials.

"Even with excellent protocol design and thorough preclinical research, exposure to an investigational product in a clinical trial presents bodily injury risk to participants and, through legal proceedings and judgements, financial and reputational risk to all trial-stakeholders. Such risks, while unavoidable, can be mitigated or transferred through a well-designed insurance program."[1]

Clinical trial insurance can be provided on 2 different response bases: legal-liability or "no-fault". Whether you need cover on a legal-liability or a no-fault basis will be predicated by the relevant guidelines/regulations/legislation of the country where the trial will be conducted. If cover is provided on a legal-liability basis, the policy will include an operating clause where an allegation of negligence will have to be proved before the policy will respond to compensate the volunteer.

In certain jurisdictions (for example, in South Africa) the local guidelines require that clinical trial insurance must be compliant with the Association of British Pharmaceutical Industries ("the ABPI") Guidelines for Compensation for Trial Participants. This will mean that the clinical trial policy and certificate must specify compensation for trial-related injuries on a "no-fault" basis in addition to providing cover for legal liability arising out of the clinical trial.

Cover under a no-fault policy is intended to provide compensation to the volunteer, when, on a balance of probabilities, the injury they have suffered can be attributed to the administration of a medicinal product under a trial or any clinical intervention or procedure provided for by the protocol that would not have occurred but for the inclusion of the volunteer in the trial[2]. Cover would therefore include adverse events which occur, even where the study has been conducted according to the protocol and would include both expected/known and unexpected adverse drug reactions. Cover will also include adverse reactions which result from procedures which are required by a clinical trial, for example if there are complications which arise from a lumbar puncture.

Who are the key-stakeholders in clinical trials?

The key-stakeholders in a clinical trial would generally include institutions where the trials are to be conducted, the clinical investigators, contract research organisations ("CRO's"), sponsor, institutional review boards ("IRBs")/ethics committees and volunteers.

What is not covered by clinical trial insurance?

Adverse events which constitute disease progression, HIV-transmission, oncological and teratogenic complications of the drugs included in the study, are generally not covered. This could prove problematic. For example, the ABPI's guidelines indicate that, *"compensation should be paid to a child injured in utero through the participation of the subject's mother in a clinical trial as if the child were a patient-volunteer with the full benefit of these Guidelines..."*[3]

Clinical trial insurance arranged in respect of a specific trial, will generally only cover claims made within the period of insurance (period that the trail is conducted and extended reporting period as reflected on the policy certificate), unless arrangements have been made to extend the policy. A policy may need to be extended, if for example, it appears that the trial will take longer to complete than initially anticipated. Once the extend-reporting period has ended, no claims can be made against the trial-specific policy (as opposed to an annually renewable clinical trial insurance policy where cover may still be available).

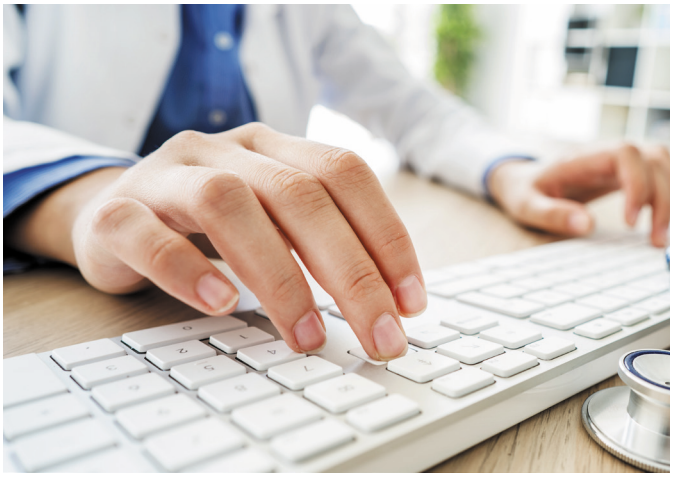
Who should take out the clinical trial insurance?

Regard needs to be had to the applicable regulations/guidelines in the country where the trial will be conducted. In most countries the sponsor of the study, investigator or the patent holder of the medication, is responsible for obtaining the insurance and they will be the policyholder or "Insured" under the policy.

Indemnity to others/additional insured's provisions

In certain instances, the sponsor/investigator may wish to extend cover under the policy to include other stakeholders, for example:

- It would be reasonable for a clinical investigator to expect indemnification where they are sued by a volunteer for injuries sustained during the trial, where the clinical investigator has diligently followed the protocol designed by the sponsor, and
- A CRO, who acts as the local legal representative for a sponsor outside the country where the trial is conducted, is likewise reasonably entitled to expect indemnification from the sponsor for liability arising out of assuming that responsibility.[1]



You will need to make your insurance broker aware of any additional persons/entities that you would like the policy to cover, especially if you as a sponsor have agreed to contractual indemnification of those parties. However, a sponsor should be careful to ensure that their policy is not exhausted covering claims where other parties are in fact legally liable, for example, where a CRO fails to prevent serious regulatory non-compliance.[1]

Clinical investigators and CRO's should nevertheless ensure that they have their own liability insurance cover in place, as they may incur liability which is not covered under the clinical trial policy.

Documentation required for insurers to quote on clinical trial insurance

Usually you will need to complete a comprehensive proposal form providing full details of the trial, including for example:

- Name/Address of proposed policyholder (usually the Sponsor)
- Name/Address of any additional insured/s that need to be covered under the policy, for example the ethics' committee and in some instances the clinical research organization and the clinical investigators,
- Study title,
- Trial phase,
- Protocol number,
- Approximate number of subjects and trial centers,
- Start date, and
- Anticipated end date.

Insurers will also require:

- A copy of the informed consent form proposed, and
- A copy of the trial protocol.

Multi-national clinical trials

When arranging cover for multi-national clinical trials, you should discuss the following with your insurance broker:

- An annually renewable master clinical trial policy, obtained in the Sponsor's country ("The Master Policy"), to be dovetailed with cover provided by,
- Local insurance policies issued by insurers that are licensed to provide cover in the countries where the trial will be conducted ("local policies").

Differences in conditions insurance ("DIC") can be arranged on the Master Policy to respond to claims which would be covered under the Master Policy but which are excluded under the local policies. For example, the local policy may exclude cover for non-economic damages claimed by a volunteer, for pain and suffering, or loss of amenities of life, but such claims could be covered by a DIC provision in the Master Policy.

Differences in limits insurance ("DIL") can likewise be arranged on the Master Policy to respond to claims where the amount claimed exceeds the limit of cover provided under the local policy.

Sponsors may elect to obtain a global policy in their country of origin to cover all the trials that they are conducting at multiple sites in different countries and decide not to obtain local policies. However, they should bear in mind that:

- Cover arranged under a global master policy may not comply with local regulations and guidelines, especially if the master policy provides cover on a legal liability basis only and the local guidelines require cover on a "no-fault" basis.

In certain territories:

- Compulsory terms and conditions apply, for example in

France, a 10-year extended reporting period is required after a trial has been completed.[7]

- Prescribed minimum limits of cover per trial or per volunteer, may be prescribed.
- Insurers may only be able or willing to issue policies for a certain number of years.
- Where a trial will be conducted over a longer period, the local insurers may require reinsurance treaty approval before they are able to provide cover.
- Regulations may require that local insurance be obtained; local policies may have the additional benefit of being responsive to local market practice.
- You may receive a policy document which is not in English and needs to be translated.
- Different guidelines applicable in those territories will require cover which will meet the compensation requirements set out in those guidelines.
- Goudsmit, recommends that the Master Policy contain a collectability provision which provides that the Master Policy will respond to pay an insured claim, where that claim has proved uncollectible under the local policy.[1]

Other considerations when arranging clinical trial insurance

- What do the guidelines that you need to comply with, say with regard to the extended reporting period? An extending reporting period allows you to continue to report claims which arise after the trial has ended. For example, in terms of the ABPI, a 3-year extended reporting period is required (where many policies may only provide for a 30-day period).
- Will the policy respond to claims where the patient alleges that they have suffered harm as the result of negligence in the research or development of the medicinal product under trial?
- Will the policy respond to cover claims arising out of products' liability in territories where strict liability is imposed on manufacturers for injuries arising out of defective products?
- Will the policy respond to cover claims which arise out of the administration of other licensed medicinal products to the volunteer for the purposes of comparison with the product under trial?
- Will the policy respond to cover claims made by volunteers who have received a placebo during the trial, for failure of the investigator to provide a therapeutic benefit to the volunteer?
- Will the policy respond to cover liability arising out of treatment extended beyond the end of the trial at the instigation of the investigator, or does such liability need to be covered under the investigator's own medical malpractice insurance policy? "*The use of unlicensed products beyond the trial period is wholly the responsibility of the treating doctor and in this regard, attention is drawn to the advice provided to doctors in MAL 30 concerning the desirability of doctors notifying their protection society [or medical malpractice insurer], of their use of unlicensed products.*"[4]

- Will the policy exclude cover where the adverse reaction causing the volunteer's injury was foreseeable or where the volunteer has freely consented to participate in the trial and they have been informed in advance of the possible adverse reactions?

- Where cover will not be provided under the clinical trial insurance policy arranged, has complimentary liability cover been arranged?

- Does the informed consent document provide adequate details of what the volunteer will and will not be compensated for?

Other liability insurance covers which may be required

Especially where it may not be self-evident that you/your company are involved in conducting clinical trials, it is advisable to review your liability insurance policies with your insurance broker to ensure that the relevant policies will extend to include cover for liability claims arising out of trials. Otherwise, you may find that a claim is rejected on the basis that involvement in clinical trials is an exclusion under the policy in question, or the Insurers were not notified of your involvement in clinical trials and they deem this to be a failure to declare all material information to them. Depending on your role in a clinical trial and the nature of the trial, you may need to establish:

1. If you are a clinical investigator: whether your medical malpractice insurance will cover you for claims arising out of the trial. The clinical trial insurance arranged may not extend to include cover for alleged medical malpractice of the clinical investigator. In some instances, special cover may need to be arranged as claims arising out of clinical trials may be a specific exclusion under your normal medical malpractice insurance policy. For example, a clinical investigator could face claims of medical malpractice arising out of:

   a. Failure to follow the protocol: incorrect dosage or timing of dosage,
   b. Incorrect administration of trial product,
   c. Failure to deal adequately with an adverse reaction.

2. If you are an institution where the trial will take place: whether your medical malpractice insurance will cover you for claims made against you or your employees, which arise out of clinical trials.

3. If you are an institution where the trial will be conducted: whether your public liability insurance extends to cover liability arising out of clinical trials, for example, where a volunteer falls on a wet floor and breaks their hip.

4. Whether your current cyber-liability insurance arrangements will extend to include liability for data-privacy breach arising out of the trial or any other cyber-liability event (denial of service attacks, ransomware, hacking, viruses) given the confidential nature of the information that will be processed, including volunteers' personal data. Clinical trial cover is unlikely to respond to claims arising out of cyber-liability.

5. Whether your liability insurance (whether under the clinical trial insurance or a separate policy) will cover legal defence costs for alleged criminal breaches of statutory laws in the country where the trial is being conducted. Often cover under liability policies for statutory defence costs is sub-limited so

you will need to establish whether the cover limit offered, is sufficient.

6. If you are a contract research organisation: whether the limits in place that you have under your professional indemnity insurance are adequate to your potential exposure. Does your contract include any limitation of your liability arising out of the trial? If a sponsor or other party were to sue you, alleging that your negligence, for example in incorrectly capturing data or failing to uncover fraud perpetrated by the clinical investigators, will mean that a trial has to be redone, what is your potential liability?

7. Whether you need to arrange cover for occupational HIV exposure.

8. Whether there is any potential directors' and officers' liability exposure which may arise out of a trial and if so whether your existing cover will extend to cover claims arising out of clinical trials.

9. Whether pollution liability insurance is required.

REFERENCE

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