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Clinical trial contracts: Confidentiality matters

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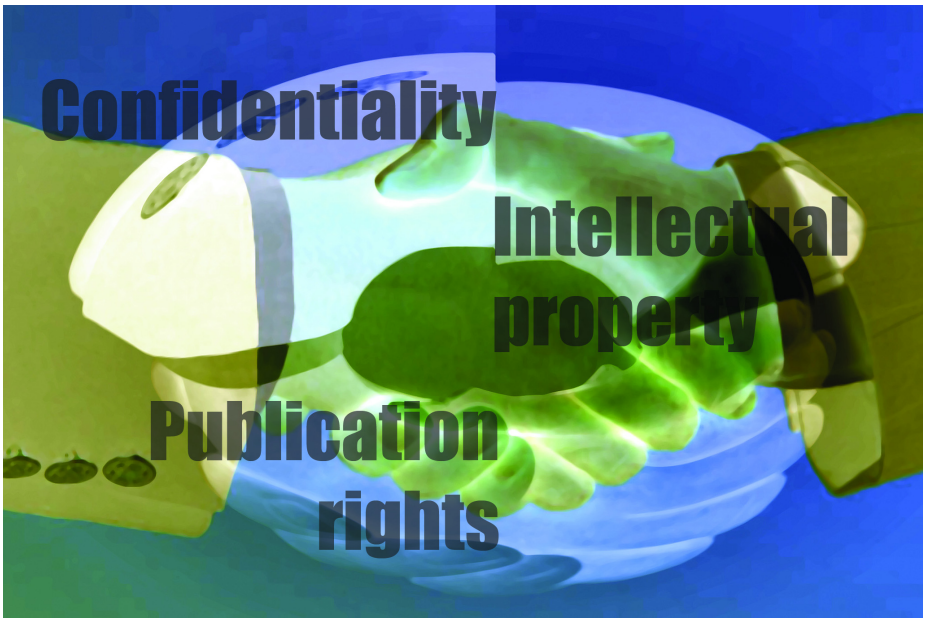
In this, the first of a three-part series on the legal aspects of negotiating clinical trial agreements from the sponsor's perspective, **Katherine R Leibowitz** focuses on the key issues of confidentiality, intellectual property and publication rights



KEYWORDS: Clinical trial agreements; Confidentiality; Intellectual property; Publication rights

Sponsors of clinical trials generally devote substantial resources to regulatory compliance, while often glossing over the business relationships embodied in the clinical trial agreement. The agreement is signed by the sponsor, the institution and the PI, and enshrines these parties' rights and obligations. Although clinical trials are conducted under regulatory frameworks, they have become big business, and the sponsor should approach negotiation of the clinical trial agreement as a business necessity.

This article describes three of the most difficult business issues encountered by sponsors when negotiating clinical trial agreements, specifically confidentiality, intellectual property (IP) and publication rights. It proposes solutions designed to minimise the time and energy spent negotiating. Two follow-up articles will address commercial issues such as financial interests, risk allocation and data protection, which tend to be less controversial, but are equally important to the sponsor. This article is written from the perspective of the sponsor, whose interests will often diverge from those of the institution and the principal investigator (PI).

Confidential information

In the sponsor's perfect world, all information relating to the trial would be treated as confidential until the medicine in question received US FDA or EU approval. This would help keep the fruits of the trial safe from the sponsor's competitors, who might otherwise benefit unfairly from the sponsor's considerable investment of time and money. It could also make damage control easier, should the necessity for such action arise.

The most controversial type of confidential information is research results – the sponsor's desire to keep a tight lid on the trial is directly at odds with the research institution's view that it has a mandate to publish

However, universities and large private medical centres will not agree to confidentiality obligations that place unacceptable limitations on their academic freedom, or interfere with their mandate to promote research and the public welfare. They believe that in a perfect world no information resulting from a trial would be confidential, with the institution and the PI freely sharing and publishing everything discovered.

Since both the value of the sponsor's investment and the scope of the institution's and PI's publication rights derive from the definition of confidential information, this definition should be worked out carefully.

Clinical trial agreements proposed by institutions often split the definition of confidential information into two categories: everything the sponsor provides is confidential, while everything the institution and PI develop during the trial is not confidential. Under this scenario, the medicine and the protocol would be confidential. Patient medical records, case report forms (CRFs) and other reports required by the protocol would not be.

This definition fails to protect the sponsor's commercial interests, because the institution and PI can share all information collected or created during the trial with any third party, including a competitor of the sponsor or the general public. It also fails to protect the sponsor's proprietary interests in any IP arising from the trial. However, if the sponsor pushes hard enough, institutions and PIs will often agree to a more sponsor-favourable definition of confidential information.

Some clinical trial agreements provided

by sponsors make everything relating to the trial or the medicine confidential. Even if this expansive definition survives the institution's review process, the institution, PI and sponsor probably do not share the same views on what is confidential and what can be published. An all-encompassing definition of confidential information might leave the institution and PI with nothing to publish. When pressed, many sponsors will readily agree that they do not intend to exercise such draconian oversight over the institution's and PI's publication rights. However, some sponsors do want complete control over what information can be published about the trial, although they will rarely obtain this. Either way, by failing clearly to agree what information is confidential, the parties are setting themselves up for disappointment, a strained working relationship and possibly a legal dispute.

To facilitate negotiations, the sponsor may want to break down the definition of confidential information, which in some agreements is referred to as proprietary information, into the following four categories:

- **Terms and conditions of the clinical trial agreement.** If this is important to the sponsor, the institution and PI will typically agree to treat the agreement as confidential information.
- **Information disclosed by or on behalf of the sponsor to the institution and investigator.** This includes the medicine and related technical information, the protocol, and IP the sponsor had before the trial started. The sponsor should think this through carefully. For example, the sponsor may also wish to include data from animal studies, and any other pre-existing information that it considers proprietary and for which it wishes to claim trade secret status. Once again, the institution and PI will typically accept this second category.
- **Miscellaneous information relating to the regulatory side of the trial**. This information includes the regulatory status of the medicine, communications with the FDA, European Medicines Agency or national drug regulatory agency and correspondence with institutional review boards (ethics committees in the EU) and data safety monitoring boards. This category may also include the number of research subjects enrolled in the trial at any given time. Consideration of miscellaneous matters enables the parties to move away from the all-or-nothing definitions of confidential information typically offered by each side. Institutions and PIs will usually agree here, as they have no need to disclose or publish the information in question.
- **Research results.** Inevitably this is the most controversial category, as the sponsor's desire to keep a tight lid on the trial is directly at odds with the institution's view that it has a mandate to publish (see Box below). There are legal and practical distinctions between source records, such as X-rays or patient charts, and reports produced pursuant to the protocol, such as CRFs. The institution and PI have a legitimate need to use data contained in source records in their scholarly publications and research. Without these data, they would have nothing to publish. The sponsor has an equally compelling need to prevent full-scale disclosure of trial data to competitors or the general public.

The underlying source data should not be included in the definition of confidential information, since they normally include materials such as X-rays, CT scans and patient medical records, the confidentiality of which is governed by the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and US state law or, in Europe, EU privacy data protection legislation. Restrictions on use of the source records are more properly negotiated, if at all, in the publications provision (see Box).

As regards research results that are not protected by relevant privacy laws, such as CRFs and other reports required by the protocol that do not include individually identifiable health information, the sponsor has the same commercial motivations to keep these confidential, and the institution and PI have the same concern about encroachment on their publication rights. However, most institutions and investigators will agree when pressed that they have no intention of

Establishing the rights to publication

From the institution's and investigator's perspective, the publications provision may be the most critical right they will obtain from the sponsor. If the parties have reached open and informed agreement on the definition of confidential information and on the allocation of IP ownership, addressing publication rights is relatively simple, with the exception of one thorny issue: a 'dump' of trial data to the sponsor's competitors or to the general public.

Typically, the sponsor grants the institution and the PI the right to engage in publications, presentations and other public disclosures regarding their activities under the clinical trial agreement, subject to a limited right of prior review for the sponsor. Note that 'publications' should extend to oral presentations and other public disclosures, as all disclosures could be equally damaging to the sponsor's interests. The sponsor's prior review normally extends for at least 30 days before the submission of any proposed publication and consists of two rights: (1) the sponsor can require the institution and/or PI to redact sponsor-confidential information from the proposed publication, (2) the sponsor can require the institution and/or PI to delay publication for an additional period, typically 60 to 90 days, so that the sponsor can seek patent protection.

If the trial is a multicentre study, the sponsor has an interest in coordinating the results from all trial sites into a single publication. Typically, the clinical trial agreement will require each institution and PI to defer any independent publication until after release of the multicentre publication. To protect the institution and PI from unreasonable delay, it is standard for the sponsor to permit site-specific independent publication if the multi-centre publication has not been released within a year of the trial's completion. If the trial site is a small doctor's office or a clinic, or if the institution will serve as a coordinating centre for the trial, the sponsor may be able to demand greater control over publications.

A literal reading of the publications clause might permit the institution and PI to disclose so much trial data as to constitute a data dump to the sponsor's competitors or the general public. To address this, some sponsors permit the publication of trial data only in summary form, although this approach generally does not sit well with institutions or PIs. Another solution starts with the parties acknowledging that the sponsor does not intend to leave the institution and PI with nothing to publish, and that the institution and PI do not intend to engage in a data dump to the sponsor's competitors. The clinical trial agreement itself could provide that the institution and PI will not reveal trial results to any third parties in greater detail than has been disclosed in scientific journals and other non-commercial publications.

Sponsors should not underestimate the prestige factor for institutions that agree to serve as trial sites and can thereby offer patients access to a new medicine. The institution and PI should be prohibited from engaging in interviews or other media contacts, including TV and internet, about the trial or the medicine, without the sponsor's consent. The sponsor should insist on this provision, in order to avoid violating regulations relating to the promotion of medicines under investigation.

publishing actual CRFs or other reports. Rather, they need the free and unfettered ability to engage in scholarly publications based on the data collected during the trial.

One compromise is to include these items in the definition of confidential information and to clarify in the publications clause that the sponsor cannot require the institution and PI to remove them from their proposed publications. This way, the information is generally afforded confidential treatment, but can be disclosed by the institution and PI under the publications provision. Sponsors should also consider whether they want investigators to present early trial results at medical meetings and whether such presentation would be only with the sponsor's prior approval, and these matters should be reflected in both the confidentiality and publications provisions.

Resist marking requirements

The more specific the sponsor can be about the information it wants kept confidential, the less the likelihood of the institution or PI disclosing such data. Some clinical trial agreements offered by institutions require the sponsor to mark as 'confidential' or 'proprietary' all information that it wants kept confidential. The sponsor should strongly resist a marking requirement as too onerous and also too risky, since valuable confidential information is likely to be inadvertently not marked.

If the institution will not compromise on the marking requirement, then the sponsor should insist on the insertion of language stating that certain enumerated types of information will be considered confidential regardless of whether they are actually marked, such as the protocol, technical information about the medicine and correspondence with the FDA. In this case, the sponsor should also institute rigorous procedures for appropriately marking information.

Intellectual property ownership

Many sponsors do not realise that as a matter of law, the creator of IP, or in some cases the creator's employer, owns the IP it creates unless it transfers ownership to a third party in writing. Therefore, the institution and/or PI will retain ownership of any IP they develop during the trial, unless they expressly assign ownership to the sponsor. This means that, for example, if the institution and/or investigators were to develop new dosing or a new indication for the sponsor's medicine, the sponsor would not own these developments or enhancements unless the parties had agreed to this.

Under IP law, if the institution and/or investigators develop new dosing or a new indication for a sponsor's medicine, the sponsor does not own these developments or enhancements unless ownership has been expressly assigned to the sponsor

Although it has often become customary for sponsors to own the IP arising from their trials, many institutions' clinical trial agreements either fail to include an IP assignment provision or include a very limited assignment. Institutions are accustomed to entering into sponsored research agreements, where ownership of IP typically remains with the institution and PI. Moreover, many universities have policies that require them to retain ownership of the IP they create. Sponsors should persevere on this issue because, when pressed, institutions and PIs will usually assign the IP that the sponsor is likely to need. The four types of IP rights are discussed below: patent, copyright, trade secret and trademark.

Patents and non-patentable inventions. A patent is an exclusive right to prevent others from making, using, selling, offering for sale and importing the goods or services covered by the patent claim. Patents are costly to obtain and by the time the clinical trial begins the sponsor has invested hundreds of thousands of dollars developing and testing its product. Patent protection is perhaps the most powerful form of IP protection available to sponsors, because if, for example, the sponsor were to patent its medicine, it could prevent competitors from making and selling similar medicines that infringe upon the patent for the life of the patent.

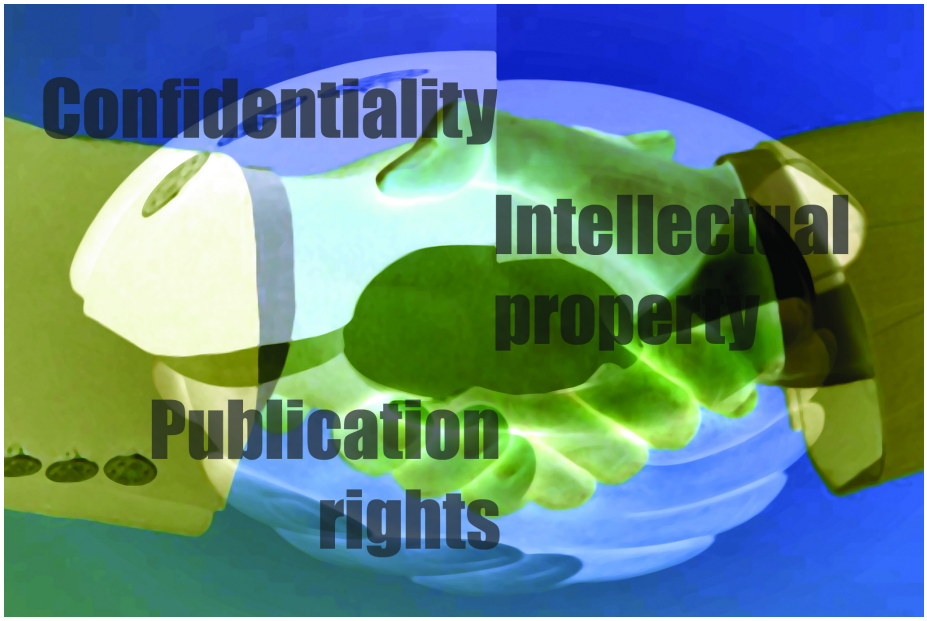
Many institutions' clinical trial agreements do not include an assignment of inventions – including discoveries, improvements, know-how, processes, ideas, compositions of matter and other terms that are typically the subject of patent licences – by the institution and PI to the sponsor. Some agreements include a limited assignment of inventions that are derived entirely from the protocol or the sponsor's proprietary materials. Other institutions postpone the issue, stating in their agreements that the parties will determine patent ownership at the time a patentable invention is created. It is common for institutions to try to limit the scope of assignment to inventions that are patentable, thereby excluding inventions that are not patentable.

From the sponsor's viewpoint, but for its sponsorship neither the institution nor the PI would have access to the medicine or funding to conduct the research using the sponsor's materials and confidential information. Therefore, the sponsor has a legitimate claim to ownership of the inventions arising from the clinical trial. The sponsor's clinical trial agreement will include both patentable and non-patentable inventions, because it is not possible to determine whether something is patentable until patent protection is sought.

As a compromise, the parties can generally agree upon (1) an assignment by the institution and PI to the sponsor of all inventions, whether or not patentable, arising from their performance of obligations under the clinical trial agreement or otherwise relating to the sponsor's confidential information, (2) an acknowledgement by the sponsor that the institution and PI retain ownership of all inventions from the trial that relate solely to research methods or documentation techniques. This compromise reflects a fair allocation of invention ownership. Although these negotiations can be difficult, sponsors should firmly resist any attempt by the institution or PI to retain any broader scope of invention ownership.

Copyright. The owner of a copyright has the exclusive right to copy, modify, distribute, perform and display the work of authorship. As with patents, in the absence of a written assignment to the sponsor, ownership of the copyright in a work will reside with the author or the author's employer. Reports written during the clinical trial, such as CRFs, may be eligible for copyright protection, but the raw data contained in these reports would not.

As with patents, institutions' clinical trial agreements rarely include an assignment of copyrights to the sponsor. However, a sponsor should not be restricted in its ability to use, copy or distribute the written materials prepared by the institution and/or PI pursuant to the protocol. The institution and PI should therefore be pressed to assign to the sponsor all copyrightable works created by them in the performance of their obligations under the clinical trial agreement. This copyright assignment should not extend to publications of the institution or



PI. In addition, the institution and PI will often reserve the right to use copyrighted materials and inventions for education and research purposes.

Trade secret. A trade secret is a creature of US state law. It is information that (1) the owner makes reasonable efforts to keep confidential, (2) is not generally known and (3) affords the owner a competitive advantage. State trade secret laws protect the owner from unauthorised use and disclosure of his or her trade secret. Clinical trial agreements typically do not include a separate provision for trade secrets, but the confidentiality provision can afford trade secret protection to certain sponsor-provided information.

The sponsor's medicine, technical information relating to the medicine, the protocol and other information provided by the sponsor to the institution or PI may qualify for trade secret protection and should therefore be included in the definition of confidential information.

To protect its investment in the medicine and the trial, the sponsor may wish to treat all inventions and research results arising from the trial as trade secrets by including them in the definition of confidential information. While institutions and PIs will generally agree to assign ownership of inventions and research results arising from the trial to the sponsor, they will almost universally refuse to grant trade secret protection, because this would interfere with their publication rights.

The standard publications provision allows the sponsor to require the institution and/or PI to remove sponsor-confidential information from proposed publications. Securing trade secret protection for inventions by including them in the definition of confidential information would give the sponsor the ability to force the institution and PI to remove inventions from any proposed publication. Instead, institutions and PIs will give the sponsor the standard publication right of being able to require them to delay a proposed publication so that the sponsor can seek patent protection. Institutions and PIs will normally insist on the right to publish research results, thereby precluding trade secret protection, even though they may otherwise agree to limited confidentiality – undertaking, for example, not to share research results with competitors.

Occasionally, the sponsor may succeed in obtaining trade secret protection for inventions and/or research results arising from the trial, particularly from small institutions or private hospitals, but care should be taken to confirm that the parties are clear about the impact this has on publication rights.

Trademark. A trademark is an exclusive right to use a word, name or symbol to indicate the origin, quality and ownership of a product, and to distinguish it from the products of a third party. As with trade secrets, clinical trial agreements typically do not have a separate provision for trademarks. Institutions' clinical trial agreements will often prohibit the sponsor from using the names of the institution and PI and any trademarks of the institution in connection with sponsor publications about the trial or the medicine. Similarly, sponsors' clinical trial agreements will often prohibit the institution and PI from using the sponsor's name and trademarks for any purposes. Despite this prohibition, the institution and PI will typically assume that they can use the sponsor's name in their publications; therefore, the parties should make sure the publications clause is clear on this point.

Some sponsors may want to disclose the name of the institution and/or PI at trade shows or in scientific journals or other publications relating to the trial. It is important to clarify whether the parties may use each other's trademarks, as each may have reasons to want to refer to, or to prohibit references to, each other's names in public disclosures.

Pre-existing IP and assignments

Clinical trial agreements regularly include a provision stating that each party will retain ownership of the IP that it brings to the trial. This is non-controversial, yet worth reciting in the clinical trial agreement in order to make clear that the IP ownership transfers in the clinical trial agreement do not affect a party's pre-existing IP.

When obtaining assignments of IP rights, the sponsor should understand that an assignment by the institution will not necessarily include IP created by the PI. For this reason, it is critical that the sponsor obtains written assignments of IP rights from both the institution and the PI.

Parties other than the institution and the PI – such as co-investigators, staff physicians, residents, interns, independent study coordinators and CROs – may be involved in the creation of IP during the trial. These ancillary parties, or their employers, will own the IP they develop during the trial, unless they are subject to executed written assignments. The sponsor should ensure that the IP assignments by the institution and PI will bind the ancillary personnel. Where appropriate, the sponsor should itself obtain written assignments from other ancillary parties. GCPj

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•***Next month:*** *Katherine R Leibowitz will look at the issues around managing financial interests and risk allocation.*

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