

JOURNAL OF CLINICAL RESEARCH BEST PRACTICES

Vol. 2, No. 1, January 2006

"Can You Handle the Truth?"

Clinical Trial Agreement Trivia

By Norman M. Goldfarb

Clinical trial agreements are a complex blend of business, law and regulation. In the process of coordinating development of the Model Agreement Group Initiative (MAGI) Model Clinical Trial Agreement (CTA), numerous fine points surfaced, often of great consequence. Some of these points became the basis for the following 27 trivia questions, originally published in MAGI News. If you already know the answers to these questions, you know CTAs. If not, read the answers those follow so you can impress your friends and stymie your negotiation partners.

Clinical Trial Agreement Trivia Questions

Patient vs. Subject (MAGI 1)

What are the differences between "Patients", "Subjects", "Volunteers" and "Participants"?

Representations & Warranties (MAGI 2.2)

Montana Pharmaceuticals requires Asian Research to represent and warrant that no government agency in any country has ever sanctioned any member of the proposed international study team. Asian Research has not performed a thorough investigation in every country in the world, so a sanction may exist somewhere. It wants the study, so has decided to represent or warrant this statement, but not both. Which should it choose?

Records Destruction (MAGI 3.1.14)

U.S. 21 CFR §312.62, in simplified terms, requires retention of study records for (a) two years after the FDA approves the study drug, or (b) two years after investigation of the study drug has ended. How do investigators know when the retention period has expired?

Secure Drug Storage (MAGI 3.1.19)

What are the U.S. regulatory requirements for secure storage of investigational drugs?

GCP; Compliance with Laws and Regulations (MAGI 3.2)

Amazon Pharmaceuticals has sent Bangkok Research a clinical trial agreement for clinical study. In the boilerplate section, the choice of jurisdiction and governing law is Brazil. The agreement also requires that Bangkok Research comply with all applicable laws and regulations, including those of Brazil, where Amazon Pharmaceuticals is headquartered. Since Bangkok Research is located in Thailand, not Brazil, would it be obligated to comply with Brazilian regulations that may conflict with Thai requirements?

Initial Payment (MAGI 4.2)

Urgent Pharmaceuticals has invited Dr. Jones to participate in a clinical research study. It is pressing her to complete the regulatory documents and submit the study to her local IRB. It has invited her and her study coordinator to attend an investigator meeting. Dr. Jones is looking forward to participating in the study, but there are some open issues with the clinical trial agreement that may take some time to resolve, assuming they can be resolved at all. Because of manufacturing "glitch," it is also unclear when the study drug will be available. Preparing the documentation and submitting it for IRB review, paying the IRB's fee, and attending the investigator meeting with her study coordinator will cost Dr. Jones thousands of dollars in out-of-pocket and opportunity costs. Should Dr. Jones invest the time and money to move forward with the study, or should she wait until the open questions are resolved?

Close-out (MAGI 4.3)

A site has submitted all CRF pages and resolved all open data queries. However, the sponsor has indefinitely postponed the closeout visit until it can replace the site monitor, who has been transferred to another study. When can the site expect receipt of the final (hold-back) payment?

Debt Collection (MAGI 4.8.)

An investigative site subcontracts with a radiology center to perform MRI scans on subjects in a clinical trial. The radiology center performs the scans. The site declares bankruptcy before paying the radiology center. Can the radiology center obtain payment from the subjects? Can it obtain payment from the sponsor?

HIPAA (MAGI 6.1)

A site monitor from a sponsor is reviewing source documents. He learns from a signed Informed Consent Form that a friend, who is subject, has an embarrassing disease. The site monitor tells the subject's employer, who legitimately fires the subject. Was HIPAA violated? If so, by whom? Who is liable for the disclosure?

Publication (MAGI 8.5)

Dr. Marcia Key, a professor at Opinion University, is an investigator on a study for Leader Pharmaceuticals. She writes a paper based on the study that "raises questions" about the safety of the study drug. She submits the paper to Leader Pharmaceuticals for pre-submission review. Leader Pharmaceuticals informs Dr. Key that she may not submit the paper because it discloses Leader Pharmaceuticals' confidential information. Dr. Key responds that the confidential information is required to support the paper's conclusions. Third-party experts agree and the parties are unable to compromise on an acceptable text. Assuming the clinical trial agreement gave Dr. Key standard publication rights, will Leader Pharmaceuticals be able to obtain a temporary restraining order and then an injunction against publication of the paper?

Subject Injury (MAGI 9)

Pharma Pharma drafts an informed consent form that Research Research, a private research site, uses in a clinical study. Subject Subject is injured due to participation in the study, but fault for the injury cannot be determined. The informed consent form says that the sponsor

will pay the subject's uninsured medical costs. However, according to the clinical trial agreement, Pharma Pharma does not have to pay for medical treatment because it did not receive timely notice from Research Research of the injury. The sponsor and the site are in the same legal jurisdiction and have equivalent financial resources, insurance, legal representation, etc. Subject Subject wants to use the responsibility for payment statement in its lawsuit. It can only afford to sue one party. Who should he sue?

Negligence (MAGI 10)

What is the difference between "negligence" and "gross negligence"?

IRB Indemnification (MAGI 10)

Does the sponsor's indemnification cover IRB members?

Hold Harmless (MAGI 10)

Paranoid Pharmaceuticals asks Shaky Investigations for cross-indemnification. Shaky refuses. Paranoid offers to accept Shaky's hold-harmless instead. Should Shaky accept Paranoid's offer?

Hired Auto (MAGI 10, 11)

A study subject needs a concomitant medication to continue in a study. The study coordinator, on his own time, borrows a car to transport a study subject to a pharmacy so the subject can purchase the medication. On the way back, the coordinator crashes the car into another car. The employee is aware of a company policy against transporting study subjects in personal automobiles. The owner of the other car sues for damages. Who pays?

Fall from Table (MAGI 10, 11)

A subject is sitting on an exam table for a blood-draw required by a study. He falls off the table and is injured. Who pays?

Diagnostic Insurance (MAGI 11)

A study subject complains of chest pains. The site performs a series of expensive diagnostic tests, with negative results. The subject doesn't want his insurance billed because he believes his anxiety about the study caused the chest pains. Who pays for the tests?

Sponsor Insurance (MAGI 11.2)

Gyood Research is conducting a study for Spicy Pharmaceuticals on an implantable device for the treatment of dyspepsia. The device is "reactivated" with a normal pill. Three upper endoscopies are required: (1) as part of the screening procedure, (2) during the implantation process, and (3) one-month later, just prior to taking the pill. A subject contacts Gyood Research validly claiming an injury due to one of the endoscopies, but does not specify which endoscopy. Spicy Pharmaceuticals has indemnified Gyood Research for injuries due to study procedures. All of the endoscopies were performed properly, so there is no question of negligence or malpractice. Spicy Pharmaceuticals has products liability insurance for the clinical trial. Will it cover the subject's claim?

Effective Date (MAGI 12.1)

Nebraska Research is conducting a study for Florida Pharmaceuticals. Florida Pharmaceuticals' final, close-out payment is late. Before calling to demand payment, Nebraska Research reviews its copy of the clinical trial agreement. It discovers two copies of the agreement, signed by Florida Pharmaceuticals but not by Nebraska Research. Apparently, it never signed and returned a copy of the agreement to Florida Pharmaceuticals. Is Florida Pharmaceuticals responsible for payment?

Termination (MAGI 12.3)

LHTB Research is conducting an oncology study for Midnight Pharmaceuticals. The study requires a course of twelve treatments over a one year period. The life expectancy of untreated subjects is three months. Subjects receive the experimental drug, or the standard-of-care treatment with a life expectancy of six months. After LHTB Research has treated all the subjects for three months, Midnight Pharmaceutical's new financing falls through, the company declares bankruptcy, enters into liquidation proceedings, and all the employees except the lawyers and accountants are dismissed. What is LHTB Research's obligation to continue treating the subjects?

Survival (MAGI 12.5)

What is the most important clause to include in the survival clause?

Jurisdiction (MAGI 14.1)

A sponsor in Iowa wants to sue a site in Ohio for non-performance due to defective CRFs. The CTA is silent on jurisdiction. Will the case be tried in Iowa or Ohio?

Governing Law (MAGI 14.1)

How does Ohio = Montana + Maryland + Pennsylvania?

Entire Agreement; Modifications (MAGI 14.3)

Joan I. Samiable, MD recently reviewed her clinical trial agreement with Friendly Pharmaceuticals. She discovered the following discrepancies between the agreement and reality: (a) Her name was misspelled "Joan L. Samiable", (b) the cap on subject enrollment did not reflect an agreed increase from six to ten, and (c) an amendment to the protocol was not described. Which of these discrepancies require a formal written amendment to the agreement?

Severability (MAGI 14.11)

ST Research, a research site in the state of Remorse, is unhappy with the clinical trial agreement it signed with FTF Pharmaceuticals. It tells FTF Pharmaceuticals that it wants out of the contract, but FTF Pharmaceuticals insists that it perform, and points out a clause in the agreement that calls for significant penalties for non-performance. ST Research asks its attorneys to find loopholes in the agreement that would allow it to escape its obligations.

The attorneys find nothing obvious, but there are several defects in the contract: (a) ST Research's state of incorporation is incorrect, (b) the limitation of liability clause is not printed in bold and all caps, as required by Remorse state law, (c) there is a conflict of law issue in the subject privacy provision, and (d) the publication rights section endangers ST

Research's non-profit status. ST Research decides to terminate the agreement as legally unenforceable in the state of Remorse. On what grounds can FTF Pharmaceuticals dispute the termination?

Signatures

Cambridge Research and Boston Bio are negotiating a clinical trial agreement. Their representatives have signed that they "agree" with the contents of the agreement. The investigator, Dr. Marblehead, has been asked to sign that he has "read and understood" the agreement. If he signs on the "read and understood" dotted line, how are his rights and obligations different than if he had signed that he "agreed"?

Signatures

Timonics Biotech is running out of time to find a key opinion leader for its pivotal trial for Punctuate, a potential breakthrough in the treatment of punctuality disorders. Dr. Justin Thyme is interested, but wants to discuss the study with his colleagues at Circe University prior to their attendance at the annual meeting of the Association of Time Perception, the first meeting of the Association in over seven years. As Chairman of the Circe Psychiatry Department, Dr. Thyme signs the confidentiality agreement on behalf of the University, so he can share information about the study with his colleagues. (Normally, he would sign just for himself.) Timonics Biotech sends him the protocol and investigator's brochure to read on the plane. As a legal clerk at Timonics Biotech is filing the confidentiality agreement, she wonders if Dr. Thyme actually has signatory authority for Circe University. If not, Dr. Thyme's colleagues will be legally free to discuss the study at the meeting with attendees from competitors of Timonics Biotech. At this point, it is impractical for Timonics Biotech to obtain separate confidentiality agreements from all of Dr. Thyme's colleagues.

Clinical Trial Agreement Trivia Questions

Patient vs. Subject (MAGI 1)

Physicians provide medical care to "Patients," e.g., to cure their illnesses. If medical care is provided in a clinical trial, it is incidental to the trial's main purpose of creating knowledge about the study treatment. A remarkably high percentage of clinical trial Subjects, even in studies with a placebo control, have the "therapeutic misconception" that the purpose of the trial is medical care.

People who participate in clinical trials are not "Patients." They are "Subjects", "Volunteers" or "Participants." Although all of these terms are much more accurate than "Patient," none of them are ideal. The term "Subject" carries a negative guinea pig connotation, although guinea pigs are not asked for their informed consent and investigators have minimal obligations for the safety and welfare of guinea pigs. The term "Volunteer" emphasizes that the person is a willing participant in the trial. On the other hand, it may influence the person to place altruism ahead of his/her own best interests. The term "participant" is fairly neutral, but implies a passive "warm body" role, which should not be the case.

Representations & Warranties (MAGI 2.2)

A representation is a statement that something, usually in the past or present, is true. A warranty is a statement that the warrantor will stand behind something, which may or may

not be true. To a non-lawyer, representations and warranties have subtle but significant legal differences. Asian Research should, of course, neither represent nor warrant something that it does not know to be true. It can, however, represent that something is true based on its current knowledge and understanding. It can limit the representation to current countries of employment. It can tell Montana Research, outside of the CTA, what efforts it made to determine the truth of the statement. It can offer to perform a more thorough investigation at Montana Research's cost. If Montana Research insists on its original requirement, it should not be conducting research overseas.

Records Destruction (MAGI 3.1.14)

Few, if any, CTAs obligate the Sponsor to inform the Investigator when the retention period expires. It's impractical to put the burden on the Investigator. Here are two alternatives to address the problem:

Sponsor will notify Investigator within 30 days after 21 CFR §312.62 records retention requirements expire, or compensate Investigator \$___/month/box plus interest at ___%/month for continued storage.

Investigator will retain study records for ___ years after Study closeout. Investigator may then notify Sponsor in writing of planned Study records destruction. If Sponsor does not request an extension in writing within 30 days, Investigator may destroy the Study records.

Secure Drug Storage (MAGI 3.1.19)

U.S. CFR 312.69 (Handling of controlled substances) requires storage of controlled substances, e.g., narcotics, in "a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited to prevent theft or diversion into illegal channels of distribution." U.S. CFR 312.61 (Control of the investigational drug), which applies to regular study drugs, says nothing about controlled storage, only controlled issuance.

Regardless of the absence of a regulatory requirement, most sponsors want double-lock security and most sites provide it. The moral of the story is "Don't rely on the regulations in a CTA without reading them."

GCP; Compliance with Laws and Regulations (MAGI 3.2)

International law is a morass, so this answer is subject to possible laws and treaties that may apply to this situation in Brazil, Thailand or any other country. In general, however, the choice of jurisdiction and law provision governs how contract disputes will be adjudicated, not which regulations the site must follow. Specifying Brazilian regulations for Bangkok Research to follow does not create a regulatory obligation enforceable in Thailand because Thailand has its own regulations. However, if Bangkok Research violates Brazilian regulations and the Brazilian authorities notice, there may be regulatory sanctions in Brazil. In addition, by signing the agreement, Bangkok Research accepts a binding contractual obligation to be adjudicated in Brazilian courts under Brazilian law. Any judgment could be enforced in Brazil, and may be enforceable in Thailand, depending on the relevant laws and treaties. If a subject is injured in the study and sues for damages, he/she can cite Bangkok Research's obligations under the agreement, including compliance with Brazilian regulations.

These issues can be avoided if the agreement just leaves it at "all applicable laws and regulations". However, if Bangkok Research does not comply with certain Brazilian laws and regulations, the Brazilian authorities may not accept its data. In this case, Amazon Pharmaceuticals should specify exactly which laws and regulations Bangkok Research must

follow and provide a certified translation into a language acceptable to Bangkok Research. As usual, Bangkok Research should not sign any agreement if it does not understand all the ramifications.

Initial Payment (MAGI 4.2)

If the study is cancelled because the drug could not be manufactured, Urgent Pharmaceuticals may cover the IRB fee, and possibly the study coordinator's salary for the wasted time. It will probably not cover the revenue Dr. Jones lost by attending the investigator meeting. If it perceives that Dr. Jones is being "unreasonable" in the contract negotiations, it may not reimburse any of her costs. Dr. Jones has a business decision to make, which depends on many factors. The decision will be easier if Urgent Pharmaceuticals agrees in writing that it will reimburse a specified amount of the costs she incurs and does not participate in the study, regardless of the reason. Urgent Pharmaceuticals thus has its own business decision to make.

Close-out (MAGI 4.3)

If the CTA requires only CRF submission and data query resolution for the hold-back payment, the final payment is due now. If completion of the study by the site is required, payment is postponed indefinitely. Since the delay is the sponsor's responsibility, it may be willing to make a partial payment. If the CTA requires "timely" or "best efforts" completion of the closeout visit, payment should not be delayed. If "completion of the study" is required, without specifying the site or defining "completion," final payment may be delayed for years, at the sponsor's discretion.

Debt Collection (MAGI 4.8.)

The subjects probably never accepted financial responsibility for the scans, so they do not have to pay. The informed consent form is probably fairly specific on this point. The sponsor accepted financial responsibility in the clinical trial agreement, although not directly with the radiology center. Receipts from the sponsor go into the site's receivership account. The radiology center becomes a creditor.

HIPAA (MAGI 6.1)

HIPAA was not violated, because the sponsor is not a Covered Entity or a Business Associate of the Covered Entity (the site). The subject presumably signed a HIPAA Authorization that disclosed the possibility of disclosure by entities such as sponsors. The sponsor may have a contractual obligation of confidentiality to the site outside of HIPAA. Subject could claim damages from the site and the sponsor. Sponsor would probably be liable if a contractual obligation existed. Otherwise, site may be liable for negligence in not obtaining sponsor's contractual commitment. Indemnification clauses generally do not cover unauthorized disclosures of subject's private information. If the subject signed an agreement with his employer to disclose this health condition because its absence is a condition of employment, there may be no damages.

Publication (MAGI 8.5)

Standard publication rights in clinical trial agreements with academic institutions permit investigators to publish papers based on study results, even if the paper does not support the sponsor's commercial interests. On the other hand, because sponsors have the legitimate right to protect their confidential information, most CTAs explicitly prohibit

investigators from disclosing the sponsor's confidential information. The rights of the two parties thus conflict. The court may or may not grant a temporary restraining order, depending on its judgment of the intent of the parties as evidenced in the CTA and the relative importance of the conflicting rights. If the court does not grant a temporary restraining order and Dr. Key proceeds to publish the paper, Leader Pharmaceuticals can sue her and the University for breach of contract and possibly win a very large settlement. Dr. Key would have been better off if the CTA had explicitly permitted her to disclose the sponsor's confidential information if required (a) for a scientific publication or (b) to protect public safety and welfare.

Subject Injury (MAGI 9)

The informed consent form says that Pharma Pharma is obligated to pay, but Research Research cannot obligate Pharma Pharma by giving the informed consent form to Subject Subject. The CTA probably says that it does not create any third-party beneficiary rights, which helps protect Pharma Pharma. The informed consent form says nothing about any payment obligation by Research Research. However, by representing in the informed consent form that Pharma Pharma would pay Subject Subject for uninsured medical costs, Research Research accepted responsibility for that payment. Subject Subject can still sue Pharma Pharma under tort (non-contract) law, on the grounds, perhaps, that Pharma Pharma approved the informed consent form. Subject Subject should therefore sue Research Research. Research Research and Pharma Pharma can then sort out between themselves who ultimately pays the legal costs and any judgment.

Negligence (MAGI 10)

Negligence is the failure to exercise a reasonable degree of care under the circumstances, resulting in an unintended injury to another party. Gross negligence is an extremely careless act or omission that is willful or constitutes reckless disregard for the consequences to the safety or property of another. Negligence is much likelier to occur and much easier to prove than gross negligence.

IRB Indemnification (MAGI 10)

Indemnification agreements generally cover the institution. The IRB is considered to be a part of the institution and is thus covered. There is no question that employee members would be included. Unaffiliated members should confirm that they are covered by the institution's policies and insurance for their good faith committee activity. The Sponsor's indemnification of the Site probably does not cover an independent (e.g., central) IRB. The IRB may have its own insurance, or may obtain separate indemnification from the Sponsor and/or the Site.

Hold Harmless (MAGI 10)

Cross-indemnification (indemnification by the site of the sponsor) is anathema to most investigative sites, so the question is whether hold-harmless is any better. Shaky may want to accept Paranoid's offer, depending on the specific hold-harmless language and governing law. Of all contract legal terms we have encountered so far, "hold harmless" is the most confusing. To start with, its interpretation varies by jurisdiction. Based on several discussions with attorneys, it appears that "hold harmless" means that if a study subject sues Shaky and wins damages, Shaky will not turn around and sue Paranoid. The "hold harmless provision", however, may include many or all of the features of indemnification.

Hired Auto (MAGI 10, 11)

If the company has "hired and non-owned auto" insurance, the company's insurer probably pays. If not, the company probably pays because the trip related to company business, although it can argue that the employee violated company policy, so should be liable. If no one but the owner of the other car has insurance, his auto insurance probably pays under the "uninsured motorist" clause. The sponsor probably has no liability, but may be sued anyway.

Fall from Table (MAGI 10, 11)

If he fell off the table because of his own negligence, his medical insurance pays for treatment and he does not recover any other damages. If he fell off the table because the table malfunctioned, the physician's general liability policy or the table manufacturer's product liability policy probably pays. If he fell off the table because he fainted or while the nurse was helping him adjust his position, the physician's general liability or medical malpractice policy probably pays. If the sponsor has agreed to pay for all adverse events associated with the study, then the sponsor pays any costs not covered by his insurance. If the sponsor has agreed to pay only for adverse events associated with administration of the study drug, then the sponsor probably pays if the drug was administered immediately prior to the blood draw. (Note the frequent use of the word "probably.")

Diagnostic Insurance (MAGI 11)

Sponsors generally do not agree in the CTA to pay for negative diagnostic tests. Here is some language that would cover this situation:

"If medical testing is required to confirm the existence of an illness or injury that may, in the Investigator's judgment, be related to Subject's participation in the Study, Sponsor will reimburse the cost of such testing, provided Investigator makes a good-faith effort to obtain advance written authorization by Sponsor."

Sponsor Insurance (MAGI 11.2)

Medical product companies carry product liabilities insurance. Assuming clinical trial coverage is included in the policy, the insurance covers injuries caused by the study drug or device, but usually not procedures. The following exceptions may apply: If the sponsor's device is used to perform the procedure, it is probably covered. Device implantation and explantation procedures may be covered. The sponsor may be able to obtain coverage for sites for other procedures at an additional cost.

Effective Date (MAGI 12.1)

A payment obligation requires the existence of an agreement between the parties. The existence of an agreement requires an offer by one party, acceptance by the other, and an exchange of considerations, e.g., payments for services. Clinical trial agreements generally require acceptance in writing, but, in the absence of signatures, a court will determine whether a contract exists based on the actions of the parties. In this case, an offer was made, consideration was provided by both parties, but acceptance was not completed in writing. However, performance under the agreement indicates acceptance. Payment for that performance indicates that Florida Pharmaceuticals believes that a valid contract exists, but Florida Pharmaceuticals could argue that the payments were made in error. Assuming Florida Pharmaceuticals received case report forms, a court could determine that an

agreement does exist, or at least that Florida Pharmaceuticals is entitled to payment for the benefit it received.

If Nebraska Research HAD NOT performed work on the study, and Florida Pharmaceuticals had not made any payments, Florida Pharmaceuticals could withdraw its offer and the contract would not come into being. If Nebraska Research HAD performed work on the study, but not communicated that fact to Florida Pharmaceuticals, Florida Pharmaceuticals probably can withdraw its offer. Note that some states do not recognize oral agreements, so verbal communications may not be binding. If the parties go ahead and execute the agreement in writing, they cannot back-date it. Rather, they should modify the agreement, describing the circumstances, and with an effective date prior to any work performed.

Termination (MAGI 12.3)

There are two types of bankruptcy: reorganization and liquidation. In a reorganization, the business continues to operate, but under the supervision of a judge for the benefit of the creditors rather than shareholders. The judge may or may not consider it in the interests of the creditors to continue the study. Midnight Pharmaceuticals, however, is in liquidation, and the bankruptcy judge is expeditiously winding up the company's affairs for the benefit of the creditors.

Midnight Pharmaceuticals has a legal obligation to its creditors under bankruptcy law, but it has no legal obligation to the subjects or to the FDA under Form 1571. It probably has an ethical obligation to supply available drug to the subjects and pay for their continued treatment, but bankruptcy law trumps research ethics.

Unless a third-party quickly steps in to purchase the rights to the study drug and continue the study, there is no sponsor, no IND-holder, no FDA-required supervision of the study, and no product liability insurance. Therefore, unless LHTB Research assumes Midnight Pharmaceuticals' responsibilities, it cannot continue with the study. It may choose to offer subjects treatment with the standard-of-care drug, but is probably not obligated to incur the expense.

It is very unlikely that the informed consent form discusses this scenario in the required statement of risks or the description of circumstances under which the investigator may terminate subject participation in the study. Subjects could thus sue the investigator and sponsor to continue the treatments. Subjects that are at increased risk of death would probably obtain a sympathetic hearing in court, regardless of the legal merits of their case. The court may require LHTB Research to continue treatment with the standard-of-care drug, with the opportunity to bill the subject's insurance company, if any, and LHTB Research's bankruptcy administrator for the fees.

If it had been LHTB Research that declared bankruptcy, its bankruptcy judge would decide whether it wants to continue with the study. The clinical trial agreement usually gives both parties the right to terminate the agreement if the other party enters bankruptcy. If LHTB Research's conduct of the study would be compromised by its bankruptcy, Midnight Pharmaceuticals would probably want to move LHTB Research's subjects to another site, if possible.

Survival (MAGI 12.5)

The survival clause specifies which sections of the agreement continue in force after the agreement terminates or expires. Sites, for example, want to ensure that Sponsors pay any open invoices. Technically, the most important clause in the survival clause is the survival clause itself. Although a court would likely hold that a survival provision is implied for

certain sections of the contract, the time and expense to obtain a court ruling may be prohibitive.

Jurisdiction (MAGI 14.1)

The sponsor can file the case in either jurisdiction. If the sponsor files in its home jurisdiction of Iowa, the site may contest jurisdiction. The court in Iowa will decide jurisdiction based on numerous factors, including the location of the parties and where the failure to perform occurred. If the cause of action is based on defective CRFs, jurisdiction may be decided based on whether the contract requires the CRFs to be provided to a CRA at the site or delivered by fax or over the Internet to the sponsor's location. If the site counter-sues on various grounds such as failure to pay, the jurisdiction question gets more complicated. The judge presiding over the case has full discretion to accept or reject jurisdiction and one of the parties may be baffled by his/her decision.

Governing Law (MAGI 14.1)

Maryland's statute of limitations on contract litigation of 15 years equals the sum of Montana's 8 years plus Maryland's 4 years + Pennsylvania's 3 years. The best solution for governing law for CTAs within the United States is usually leaving the clause silent, but it will matter in the unlikely event of litigation.

Entire Agreement; Modifications (MAGI 14.3)

Most agreements say something like "any modification to this Agreement must be in writing and signed by all parties." However, non-substantive errors, such as typos that have no contractual implications can be ignored, corrected informally, or corrected in the next amendment. If, for example, the investigator's name is misspelled, the sponsor can type the correct name on payment checks without breaching the contract. The change in the subject recruitment cap is material, so definitely requires a formal amendment. If the protocol is attached to the agreement either physically or by reference, amendments to the protocol require formal amendments to the agreement. To avoid the paperwork, the agreement can say: "IRB-approved changes to the Protocol are incorporated by reference into this Agreement, subject to agreement on any budget modifications."

Severability (MAGI 14.11)

Fortunately for FTF Pharmaceuticals, the agreement includes a well-written severability clause. Most severability clauses allow defective language to be deleted from a contract without affecting the rest of the contract. However, if the contract legally cannot be performed without the deleted provision, the contract can be terminated. In this case, however, the severability clause requires the parties to negotiate in good faith to repair the defects, so ST Research cannot escape its contractual obligations.

Signatures

Cambridge Research and Boston Bio are "Parties" to the agreement. Dr. Marblehead would not be a Party. If Dr. Marblehead is an employee of Cambridge Research, he is bound to the terms of the contract by his employer's signature. Any claims involving Dr. Marblehead would go through Cambridge Research.

If Dr. Marblehead is an independent contractor, Boston Bio should obtain Dr. Marblehead's signature as a Party to the Agreement because Cambridge Research may not have sufficient

control over his actions to ensure that he complies with the contract. If he is not a Party to the Agreement, Dr. Marblehead probably cannot win a breach of contract claim against Boston Bio and vice versa.

If there is a dispute, Dr. Marblehead may say he read, understood but did NOT agree to the contract. As an employee, he would be bound by his employer's signature anyway. If he is an independent contractor, Boston Bio could file a tort (non-contract) claim that it relied on his silence under the legal doctrine of estoppel.

Regardless, it would be helpful if the Agreement specifies the sections to which Dr. Marblehead should pay particular attention.

Signatures

Even though Dr. Thyme said he could sign the confidentiality agreement on behalf of Circe University, Timonics Biotech's rights under the confidentiality agreement are subject to a court's determination of whether, after reasonable diligence, it had reasonable cause to take his word for it. In this case, Timonics Biotech made no attempts to verify his authority, for example by calling someone in the Circe University Clinical Trials Office. Based on previous experience, it should have known that few universities give signatory power to department chairs in such matters. Further, if Timonics Biotech had visited the Circe University Clinical Trials Office webpage, it may have noticed that Dr. Thyme's name was not on a list of people authorized to sign contracts on the University's behalf.

Fortunately for Timonics Biotech, by the time Dr. Thyme arrived at the meeting, the punctuality branch of the association has already finished their business and departed, while the procrastination branch had not yet arrived. Timonics Biotech was thus able to fax Dr. Thyme a binding confidentiality agreement signed by the Circe University Director of Clinical Research before any harm was done.

Norman M. Goldfarb is Managing Partner of First Clinical Research, a provider of a clinical research best practices consulting, training, implementation and research services. Contact him at (650) 465-0119 or ngoldfarb@firstclinical.com.