MAGI WE CAN AGREE TO SAVE LIVES

Model Clinical Trial Agreement – Abbreviated & Obsolete
(Obtain Current & Complete Version at www.magiworld.org/standards)

Version 1.07 – January 5, 2006

This model agreement attempts to clearly, completely, concisely, consistently and correctly specify the duties and rights of each party to a clinical trial agreement. It is designed for Phase I-IV studies between one industry sponsor and one or more investigative sites. It is not intended for use in government-funded, investigator-initiated, registry or multi-sponsor studies, although much of it is applicable to such studies.

MAGI and its members disclaim any responsibility or liability from reliance on the information in this model agreement. The information in this model agreement is not legal or regulatory advice, may become outdated, and may or may not be applicable to specific situations. Consult with your legal or regulatory counsel, as appropriate.

Access, use and adaptation of the model agreement and commentary are restricted to MAGI members. MAGI members may access, use and adapt this model agreement and commentary in part or whole without fee or obligation to MAGI. MAGI and its members obtain a free license to any agreement language based on the MAGI model agreement. Any use of the model agreement or commentary in any contract or communication must state that MAGI is the source of the material. MAGI members may use the model agreement and commentary for instructional purposes in an educational setting. However, students who are not MAGI members may not use the model agreement and commentary outside of that educational setting.

Please suggest improvements and additions to the MAGI Model Clinical Trial Agreement and commentary such as clarifications, new alternatives and options, arguments pro and con, and regional legal and regulatory requirements. Send suggestions to magi@firstclinical.com.

Text	Optional Text & Commentary
Parties & Recitals	
_____ ("Sponsor"), a {form of entity} organized under the laws of {State}, _____ ("Site"), a {form of entity} organized under the laws of {State}, and _____ ("Investigator"), Site's {employee/contractor}, enter into this Agreement ("Agreement") whereby Sponsor engages Site and Investigator to conduct clinical research on _____ ("Study {Drug/Device/Biologic}") according to the provisions of this Agreement and Protocol _____. [1,2,3,4,5,6,7,8,9]	1. If Investigator is not a party to the Agreement, replace "_____ ("Site"), a {form of entity}, and _____ ("Investigator"), Site's {employee/ contractor}," with "_____ ("Site"), a {form of entity}, on behalf of itself and

_____ ("Investigator"), Site's employee.

2. If the Investigator, in essence, is the Site, the Investigator should be a Party to the Agreement. Otherwise, if the Investigator is an employee of the Site, he/she is bound to the Agreement by his/her employer's signature as Party to the Agreement. If, as an employee, he signs "read and understood", he avoids personal contract (but not tort) liability to the Sponsor, leaving the Site with any contract liability responsibility. If the Investigator is an independent contractor, he/she should sign as a Party to the Agreement because the Site may not have sufficient control over his actions to ensure that he complies with the contract, and to protect his/her own rights. If the Investigator is an owner or officer of the Site, he/she should sign in that capacity for the Site.
3. If the Investigator conducts the Study at a separate facility, e.g., a hospital, that facility may also be a party to this Agreement, or to separate Agreements with the Sponsor and Investigator.
4. List Protocol number and title.
5. Optionally, add: "In the absence of a separately-named Site, Investigator will have all Site responsibilities."
6. Optionally, add "_____ ("CRO"), a {form of entity}, will provide certain services delegated to it by Sponsor.
7. Optionally, add "_____ ("SMO"), a {form of entity}, will provide certain services delegated to it by Site.
8. Optionally, for non-profit sites, add:

"WHEREAS, Sponsor wants to enlist the assistance of Site to conduct the Study, and the Study is of mutual interest and benefit to Site and Sponsor, and will further the instructional and research objectives of Site in a manner consistent with its status as a nonprofit educational and health care institution;" This example reinforces the tax-exempt nature of the Study. Do not include recitals that should be terms in the body of the agreement, or that conflict with such terms. Recitals do not create legally-binding rights themselves, but they do provide a context for legal enforcement of agreements.

9. Many enterprises consist of numerous subsidiaries and affiliates. Verify that the other party to this Agreement has the ability to meet its obligations under this Agreement, e.g., pay its share of court awards. If appropriate, state its relationship to a parent or related entity with the necessary resources. The "Inc.", "Ltd, etc. in a party's name is important for correct identification.

1.0. Definitions

Affiliate. An organization controlled by, in control of, or under common control of one of the parties to this Agreement.

Agreement. This legally-binding agreement between the parties. [1]

Authorized Third-parties. People and organization that are contractually or legally obligated to protect Confidential Information and who have been informed of their obligations.

Confidential Information. Information as specified as confidential in Section 5.2. Confidential Information. Unless stated otherwise, "Confidential Information" is the other party's confidential information. [2]

1. The parties to the Agreement include:
a. The Site
b. The Sponsor or its CRO, acting as Sponsor's agent
c. The Investigator, unless prohibited by conflict-of-interest laws or acting entirely in his/her capacity as an employee of the Site
2. Alternative definition: Any proprietary information that either party provides to the other party in written or tangible

Court. A court of competent jurisdiction, regardless of its name. [3]

CRF (Case Report Form). The form, usually consisting of multiple pages, which Sponsor provides to Site for Subject data reporting.

CRO (Contract Research Organization). An entity, identified by name in the Agreement, that performs services such as site selection and monitoring, contract negotiation and data management for Sponsor; generally not an agent of the Sponsor, i.e., cannot legally obligate Sponsor in a contract.

CTA (Clinical Trial Agreement). This Agreement is an example of a CTA.

Day. Unless otherwise specified, a business day, without considering partial days.

Facility. The term "Facility" is not used in this Agreement. Instead, this Agreement uses the terms "Site" and "Location". In the U.S., a facility is a secondary location where the Site conducts the Study. In Europe, "Facility" is the term used for "Site".

Fee Schedule. As required by some IECs in Europe, the attachment to this Agreement showing the fees to Site and payment schedule.

GCP (Good Clinical Practice). Standards for the design, conduct, monitoring, auditing, recording, analysis and reporting of studies that provide assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of subjects are protected. In the U.S., the standards are set forth in the U.S. Code of Federal Regulations (CFR). In Europe, the standards are set forth in the International Conference on Harmonisation (ICH) E6 Guidelines for Good Clinical Practice. Studies may be governed by CFR, ICH or both standards.

IEC (Independent Ethics Committee). Outside the U.S., the ethics committee that reviews and approves or disapproves the Site's participation in the Study. IECs go by many names. They may be independent or affiliated with the Site.

Institution. The term "Institution" is not used in this Agreement. The term "Site" is used instead.

Intellectual Property. Inventions, ideas, discoveries, innovations, devices, data, mechanisms, substances, technologies, works, trade secrets, know-how, formulae and methods, including improvements, whether or not protectable by patent, copyright or other intellectual property rights.

Invention. Any Intellectual Property conceived, reduced to practice, made or developed, in whole or in part, by Site pursuant to its conduct of the Study or derived from Sponsor Confidential Information, that relates in any way to the form and designates as confidential when first disclosed.

3. Optionally, specify the name of the court. For example, claims against Tennessee state entities are adjudicated in the Tennessee Claims Commission.
4. Inventions that may be made during a clinical trial include new uses of the study drug, identification of metabolites or biomarkers of the study drug, methods for administering the study drug, dosing regimens, and drug combinations that include the study drug.
5. Optionally, include: **"**The definitions in ICH Guidance for Industry (E6) Good Clinical Practice: Consolidated Guidance, Glossary, are hereby incorporated by reference, to the extent that they do not conflict with the above definitions. Additionally, the definitions in the U.S. Department of Health and Human Services Public Health Service Grant Application (PHS 398) [PART II Supplemental Instructions for Preparing the Human Subjects Section of the Research Plan] are hereby incorporated by reference, to the extent that they do not conflict with the above definitions or the ICH definitions."
6. The MAGI Legal Glossary defines legal terms used in this Agreement.

Study {Drug/Device/Biologic}, including its administration or use, alone or in combination with any other drug or device, and any related assay.[4]

Inventor. A person who creates, in whole or in part, an Invention.

Investigator. The physician or other qualified person, identified by name in the Agreement as the Investigator, who is responsible for conduct of the Study at the Site. In the U.S., the Investigator signs and is listed in box 1 of Form FDA 1572.

IRB (Institutional Review Board). In the U.S., the ethics committee that reviews and approves or disapproves the Site's participation in the Study. IRBs go by many names. They may be independent or affiliated with the Site.

Location. An entity other than the Site with a physical location where the Study may also be conducted. In U.S. Investigational New Drug (IND) studies, Locations are listed in box 3 of Form FDA 1572.

Tangible Property. Biological samples, genomic data, x-rays, read-outs from equipment, photographs and other data not specified as Site Data or Sponsor Data.

Owner. The party that owns Confidential Information.

Paper. A paper, article, manuscript, report, article, poster, Internet posting, presentation slides, abstract, outline, video, instructional material, presentation (in the form of a written summary), or other disclosure of Study Results, in printed, electronic, oral or other form.

Personnel. Investigator, Subinvestigators and other Site employees and contractors who assist Investigator on the Study for the Site.

Protocol. The IRB/IEC-approved description of the Study, attached to this Agreement in Exhibit 2. Protocol, including any IRB/IEC-approved amendments. In U.S. IND studies, the Protocol is listed in box 7 of Form FDA 1572.

Recipient. The party to this agreement, including the Investigator, even if not a party, that receives Confidential Information from its Owner.

Results. The methods, data, analysis and conclusions of a Study.

Site. The entity that conducts the Study, identified by name in the Agreement as the Site. In U.S. IND studies, Site is listed in box 3 of Form FDA 1572 but may not be the only entity listed there. In Europe, a Site is normally called a "Facility", but this Agreement uses the term "Site".

Site Data. Source documents and subject medical records.

Site Indemnitees. Site, Investigator and their businesses, employees, officers, trustees, directors, IRB/IEC, privacy board, agents, subcontractors, partners, subsidiaries, parent and affiliates, if any.

SMO (Site Management Organization). An entity, identified by name in the Agreement, that performs one or more services such as business development, contract negotiation, and regulatory affairs for Site. SMO may be the payee in the Agreement.

Specimen. A biological sample, such as blood or tissue, from a Subject.

Sponsor. The responsible pharmaceutical, biotech, medical device, or other organization that contracts with the Site and/or Investigator to perform the Study. In U.S. IND studies, Sponsor is identified in box one of Form FDA 1571.

Sponsor Data. Completed Study Case Report Forms and Reports.

Sponsor Indemnitees. Sponsor and its employees, officers, trustees, directors, agents, subcontractors, partners, subsidiaries, parent and affiliates, if any.

Statement of Investigator. In the U.S., the equivalent of Form FDA 1572 for studies of medical devices under an FDA Investigational Device Exemption (IDE). U.S. 21 CFR Parts 812.43C 812.100 and 821.110 specify the requirements.

Study. The clinical research project identified by its title in the Agreement and described by the Protocol attached to the Agreement.

Study Device. The device that the Study investigates.

Study Drug. The experimental medication that the Study investigates.

Study Drug Materials. The experimental medication, comparator drugs, rescue drugs, other ancillary drugs, and placebos.

Subinvestigator. A physician or other qualified person who assists Investigator on the Study for the Site. In U.S. IND studies, Subinvestigators are identified in box 6 of Form FDA 1572.

Subject. A person who enrolls in the Study. In U.S. IDE studies, a Subject may be a person who contributes a specimen for use with a Study Device. (U.S. 21 CFR 812.3(p))

[5,6]

2. Study Governance

2.1. Protocol & Amendments

Sponsor will provide Site with a Protocol and supporting information necessary for Site to conduct the Study. The Protocol will be considered effective following its approval by Sponsor, IRB/IEC, Investigator, applicable Site authorities, and the FDA or other applicable regulatory authority. Site will conduct the Study in accordance with the Protocol. However, Site may deviate from the Protocol to protect Subject safety and welfare. Any such deviation will not constitute a failure to comply with the Protocol. Only the Sponsor may modify the protocol or add an addendum to the Study. Any modification or addendum to the Protocol must be approved by the IRB/IEC to become effective. If the IRB/IEC does not approve a modification within 20 days, Sponsor may terminate this Agreement. If IRB/IEC does not approve an addendum, Site will not perform that addendum.[1,2,3,4]

If, in Site's judgment, any modifications or addendums, collectively from the beginning of the Study at Site, increase Site's costs by more than __%, Sponsor will increase the Budget accordingly or Site may terminate this Agreement.[5]

1. Site authorities may include Contacts & Grants, Radiation Safety, Scientific Review, etc.
2. If Site or the IRB/IEC wants to modify the Protocol, it must ask the Sponsor to make the change.
3. An addendum is an additional sub-study that is added to strengthen the data or answer a question raised by the Study.
4. Optionally, add: "If IRB/IEC requires a modification to the Protocol during the Study, Site may terminate this Agreement if Sponsor does not approve the modification within 20 days."
5. A reasonable range of increase in costs is generally 0% to 5%.

2.2. Study {Drug/Device/Biologic} and Materials

Sponsor will provide to Site on a timely basis, without charge, the required quantities of properly-labeled Study {Drug/Device/Biologic} and other materials (e.g., CRFs) needed by Site to conduct the Study per the Protocol. Sponsor will also provide to Site any needed replacement Study {Drug Materials/Devices} and instructions for proper handling and storage.

Unless stated otherwise in writing by Sponsor, all such items are and will remain the sole property of Sponsor until administered or dispensed to Subjects during the course of the Study.

If Sponsor terminates this Agreement before completion of the Study, except to protect the safety and welfare of the Subjects, Sponsor will, free of charge, if requested by Site and permitted by law and regulations, {use its reasonable efforts to supply Site with sufficient Study Drug to complete the treatment of randomized Subjects/allow Subjects to keep Study Devices in their possession} as specified in the Protocol.

Sponsor warrants that:

a. It has obtained all necessary governmental and regulatory approvals to conduct the Study and provide the Study {Drug/Device/Biologic} including

1. "Quality" is not included in disclaimer because Sponsor should be able to warranty the quality of Study Drug under Good Manufacturing Practices.
2. In the U.S., the Magnuson-Moss Warranty Act requires that a statement of "No Warranties" on *consumer* products be distinctive from other text, so it is not applicable to this Agreement.
3. The FDA generally permits sponsors to charge investigators for investigational devices. Investigators usually pass this on to the subjects. The charge may not exceed the amount necessary to recover the costs of manufacture, research, development and handling of the investigational device (21 CFR 812.7(b)). The sponsor must justify the proposed

without limitation, all applicable FDA and IRB/IEC approvals; and that all approvals will be in full force and effect during the Study.

b. Study {Drug/Device/Biologic} has been manufactured and passed quality control tests in accordance with applicable regulations.

c. It has disclosed to Site and applicable government authorities all relevant, material information concerning the safety, use, efficacy and {drug/device/biologic} experience.

d. Use of the Study {Drug/Device/Biologic} for Study purposes will not infringe the rights, patent or otherwise, of any third-party.

e. Any hazardous material packaging provided by Sponsor meets regulatory requirements for Site's use according to the Protocol.

Without limiting Sponsor's obligations under Sections 9. Subject Injury and 10. Indemnification, Sponsor disclaims any other representations and warranties, written or oral, express or implied, with respect to the Study {Drug/Device/Biologic}, including any representation or warranty of performance, merchantability or fitness for a particular use or purpose.[1,2]

[3]

charges for the device in the IDE application, state the amount to be charged, and explain why the charge does not constitute commercialization (21 CFR 812.20(b)(8)).

2.3. Sponsor Monitoring

Sponsor will monitor Site according to the schedule in Exhibit 1. Budget. Sponsor monitors will be suitably qualified by training and experience. Site will ensure that Study records are ready for review prior to each visit. Visits will be at the mutual convenience of the Parties. [1,2,3,4]

1. Initial monitoring visit is typically within 2 to 3 weeks after first Subject enrollment so monitor can catch errors before they multiply.
2. Subsequent visits are typically 6 to 8 weeks apart, depending on the nature of the Study and volume of monitoring work.
3. Sites may want monitors to review case report forms before regulatory documents so payment is not delayed.
4. An additional monitoring visit may be scheduled prior to an audit or inspection.

2.4. Sponsor-supplied Equipment

Sponsor will provide to Site on a timely basis, without charge, the equipment specified in Exhibit 4. Unless stated otherwise in writing by Sponsor, all this equipment is and will remain the sole property of Sponsor. Sponsor will maintain

1. Delete this section if Sponsor does not supply any equipment.

this equipment. It will maintain property insurance on it. Site will use this equipment only for the Study or such other purposes as Sponsor may approve in writing. Site will return this Equipment, at Sponsor's cost, to Sponsor within 20 days after completion of the Study by Site or termination of this Agreement.[1,2]

2. If Sponsor operates equipment, add "Only Sponsor personnel will operate equipment."

2.5. CROs

Sponsor may delegate some of its Study responsibilities to one or more CROs. Site will cooperate with such CROs as if they were the Sponsor.[1,2]

1. Delete this section if Sponsor has no CROs.
2. Optionally, replace "Sponsor may delegate some of its Study responsibilities to one or more CROs." with "{Pursuant to CFR 21 Part 312.52,} Sponsor has delegated the following Study responsibilities to the following CROs: _____."

2.6. Audits

Auditor may audit Site's performance of the Study from time to time, but only if site monitoring is reasonably current. Sponsor will conduct audits during Site's regular business hours on mutually-agreeable dates. Site personnel will cooperate with auditors and make all Study records and materials available to them, subject to confidentiality and privacy restrictions. Sponsor will communicate any material findings to Site in an exit meeting or in writing within 48 hours, but will not share its internal audit report with Site. [1]

1. Site may want to include audit and inspection fees in the Study budget. Inspection fees are uncommon.

2.7. Inspections

Site will notify Sponsor within 2 days if any government or regulatory authority begins to conduct, or gives notice of its intent to conduct, an inspection pertaining to the Study. Site will provide Sponsor with copies of all pertinent written and electronic documents issued by the government or regulatory authority and any proposed response. Sponsor may review in advance and comment within 2 days on any responses that pertain to the Study. Such response will contain no false or misleading information with respect to the Study, the Study {Drug/Device/Biologic} or Sponsor. Site will also provide Sponsor with a copy of all written and electronic documents that pertain to the Study provided to the government or regulatory authority, subject to confidentiality and privacy restrictions. [1,2]

1. Sponsor may offer to assist Site in preparing for an inspection.
2. Sponsor may request to be present at an inspection. Regulatory authorities generally frown on its presence. Unless CTA provides otherwise, sponsor's presence is at Site's sole discretion. It may be useful for a sponsor representative to be on site in an advisory capacity during the inspection, but not participate directly in the inspection or communicate with the

inspector.

2.8. Other Sponsor Duties

Sponsor will comply with all applicable federal, state and local laws and regulations.(1) Sponsor will provide Site with a comprehensive and accurate Investigator's Brochure, especially with respect to information pertaining to the safety of the Study {Drug/Device/Biologic}. It will advise Site of all information for inclusion in the informed consent form that is material to a decision of potential or actual Subjects to participate or continue to participate in the Study. It will inform Site in a timely manner of new information pertaining to the safety of the Study {Drug/Device/Biologic}. It will inform Site in advance of any requirements beyond GCP. It will respond to Site questions and issues in a timely manner.

1. Optionally, add "and international guidelines and conventions". Some courts have recognized some guidelines and conventions as inherent to standard uses, customs and practices in clinical trials. See *Frakes* v. *Cardiology Consultants* (29 August 1997), Nashville 01-A-01-9702-CV-0069 (Tenn. C.A.), [1997] Tenn. App. LEXIS 597, online: LEXIS (Tennessee, APP) cited in Campbell, A., Glass, KC, "The Legal Status of Clinical and Ethics Policies, Codes and Guidelines in Medical Practice and Research" (2001) McGill L.J. 473. However, adding this language potentially exposes Sponsor to subject injury litigation claims.

3. Duties of Site & Investigator [1]

1. If Site does not conduct the Study according to the terms in this Section, it is in breach of contract. However, it is not contractually required to perform any activity not specified in this Section. If the terms are ambiguous, the Site's obligations may become the subject of dispute. To be unambiguous, a term must be clear as to who, what, where and how each activity is to be performed.

3.1. Conduct of Study; Protocol

Site will conduct the Study in a timely manner and in ~~strict~~ accordance with this Agreement and the Protocol, subject to deviations required to protect Subject safety, with notification to Sponsor within 3 days. The Protocol becomes effective upon IRB approval. Sponsor may modify the Protocol, effective upon notice to Site and IRB approval. Site may not modify the Protocol. It may, however, propose Protocol changes to Sponsor. It may also request exceptions to the Protocol, which must be approved by Sponsor and, when appropriate, by the IRB. If

1. Site may deviate from the Protocol for subject safety.
2. The percentage increase in cost that enables termination of the Agreement is negotiable, probably in the range of 0-10%.
3. Optionally, identify protocol name and

Sponsor changes the Protocol, Site may terminate Agreement if, (a) in Investigator's judgment, the changes have a negative impact on Subject safety or welfare, or (b) the cumulative protocol changes since Agreement was signed increase Site's cost or risk of conducting the Study by more than 2% and the parties are unable to agree on a revised Budget within 20 days. The Protocol in Exhibit 2 is incorporated in this Agreement by reference. [1,2,3,4]

number in this section.

4. An exception is a protocol deviation that the sponsor and sometimes the IRB approve in advance, e.g., waiver of an eligibility criterion.

3.2. GCP; Compliance with Laws and Regulations

Site will conduct the Study in conformance with generally accepted standards of good clinical practice and in accordance with all applicable federal, state and local laws and regulations. [1,2,3]

1. Optionally, Agreement may specify applicable laws, regulations (and guidances), such as:

a. Form FDA 1572 (or Statement of Investigator for device studies)

b. Regulations and guidances governing the conduct of clinical research and governing the protections of human subjects ("GCP") (21 C.F.R. § 50 and 21 C.F.R. § 312.50)

c. Federal Food Drug and Cosmetics Act, as amended

d. Health Insurance Portability and Accountability Act (HIPAA)

e. Regulations of the Centers for Medicare and Medicaid Services ("CMS")

f. Laws and regulations governing the purchase and sale of securities while in possession of material, non-public information about that company

g. Laws, rules and regulations regarding the federal anti-kickback statute (42 U.S.C. 1320a-7(b)), and (g) Limitation on Certain Physician Referrals, also referred to as the "Stark Law" (42 U.S.C. 1395nn)

h. International Conference on Harmonisation (ICH) guidelines

i. Declaration of Helsinki (specify version)

j. CIOMS International Ethical Guidelines

for Biomedical Research Involving Human Subjects (2002)

2. Specified laws and regulations must be applicable to Site's geographical location.
3. If Sponsor requires Site to comply with ICH, The Declaration of Helsinki, the Nuremburg Code, or any other requirements that do not have the force of law in the Site's country, specify the applicable version, if appropriate. Sponsor should monitor compliance to those requirements. Both parties should be prepared for those requirements to become an issue in any subject injury litigation.

3.3. Debarment & Disqualification

Site represents that neither it, nor to the best of its knowledge, after due inquiry, any of its investigators, employees, agents or other persons or entities (including their employees, partners, shareholders, members, subsidiaries and affiliates) providing services for the Study, has ever been debarred, disqualified, or banned from conducting clinical trials or is under investigation by any regulatory authority for debarment, disqualification or any similar regulatory action. Site will notify Sponsor within 15 days of any disqualification, debarment or other ban or investigation that comes to its attention. [1,2,3,4,5,6]

1. Sponsor's certification to the FDA may not include qualifying language such as "to the best of its knowledge." (http://www.fda.gov/cder/guidance/1700dft.pdf)
2. Sponsor may want to specify minimum requirements for the inquiry, e.g., reviewing information on government websites or asking persons to certify in writing that they have never been debarred.
3. Disqualified persons and entities may provide certain Study services, but with limitations.
4. It is essentially impossible for sponsors and sites, especially large ones, to ensure that all personnel, including non-employees, have not been debarred, disqualified, or otherwise banned, e.g., in a different state or country. A practical alternative is to say: "All study personnel will sign the delegation of authority log to

certify that they have not been debarred, disqualified, or banned from conducting clinical trials or are under investigation by any regulatory authority for debarment, disqualification, or any similar regulatory action. Site will initial all names to signify that they are not on the FDA debarment or disqualification lists."

5. Optionally, include other U.S. government sanctions such as FDA Restriction, FDA adequate Assurance, FDA Application Integrity Policy List (firms), Public Health Service Office of Research Integrity Administrative Action, and HHS Office of Inspector General Excluded Individuals & Entities (Medicare/Medicaid). Potential FDA sanctions may be indicated by a Warning Letter, Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE) Letter, Notice of Opportunity for Hearing (NOOH), and Presiding Officer Reports and Commissioner's Decisions in Clinical Investigator Disqualifications Proceedings.

3.4. Financial Disclosure

Site will ensure that, prior to their participation in the Study, Investigator and any Subinvestigators complete and return to Sponsor the Financial Disclosure Certification form provided by Sponsor. Investigator and any Subinvestigators will promptly notify Site and Sponsor of any required revision to their Financial Disclosure Certification during the term of this Agreement and for one year following completion of the Study. Upon Sponsor's written request following completion of the Study, Investigator and any Subinvestigators will provide an updated Financial Disclosure Certification form to Sponsor. [1,2,3]

1. Financial disclosure is legally required in U.S., but optional in many other countries.
2. In practice, updated Financial Disclosure Certification forms will generally flow from Investigator to Site to Sponsor.
3. E.U. law restricts transfer of personal information to many countries outside the E.U., including the U.S. In such case, obtain written consent to the transfer

from Investigator and any Subinvestigators.

3.5. Conflict of Interest

Site and Investigator (a) have no conflict of interest that would affect conduct of the Study, and (b) have received no offer by Sponsor or its related party of extra benefit for participation in the Study, including offers to family members. Site and Investigator will promptly notify Sponsor if any conflict of interest arises during the term of this Agreement. Site and Investigator will enter into no financial security transaction based on Study data or Results. [1,2]

1. This section is optional because it goes beyond the financial disclosures required by law in the previous section.
2. Optionally, add "Site has policies and procedures to discover, manage, report, and, where possible, eliminate conflicts of interest."

3.6. Investigator

Investigator will supervise the Study. [1] If Investigator cannot carry out his/her duties under this Agreement, or leaves Site, (or notifies Site that he/she is likely to leave), Site will notify Sponsor within 5 days. Site may nominate a replacement investigator. Sponsor, at its sole discretion, may approve or reject such replacement. If Sponsor rejects the proposed replacement, it may terminate this Agreement. Otherwise, Site and Sponsor will mutually determine whether the Study will continue at Site, move with Investigator to a different site, or move to another site with a different investigator. [2,3,4,5,6]

1. Optionally, specify Investigator's duties when supervising the Study.
2. Optionally, name Investigator in this section.
3. If Investigator is able to carry out his/her duties but wishes not to, the Termination section governs.
4. Optionally, add: "If Sponsor terminates Agreement, it may request Site's cooperation in transferring Subjects to another Site."
5. Optionally, add language that specifies what happens if parties cannot resolve future of study when Investigator leaves Site.
6. If the Investigator leaves the study, amend this Agreement with the signature of the replacement Investigator.

3.7. Subinvestigators and Other Personnel

Site will ensure that:

a. Adequate numbers of qualified Personnel are assigned to the Study to meet its obligations under this Agreement.
b. Subinvestigators and other Personnel have the necessary licenses and certifications, and are qualified by education, training and experience to perform their Study responsibilities.
c. Subinvestigators and Personnel perform their Study responsibilities and fulfill their obligations under this Agreement.
d. Subinvestigators and Personnel receive the necessary information and training.

Any Subinvestigator or other person or subcontractor working on the Study who is not employed by Site will execute a written agreement with Site obligating him/her to comply with confidentiality and other relevant terms and conditions of this Agreement. Site will notify Sponsor of proposed Subinvestigators; Sponsor may disapprove any proposed Subinvestigator within 5 days of notification. [1,2,3,4,5,6,7]

1. Sponsor may want to add: "e. there is at least one Subinvestigator." to cover for Investigator when he/she is unavailable.
2. Sponsor may want to provide the Subinvestigator Agreement template or approve its form.
3. Optional text: "Site will ensure that at least one Subinvestigator is prepared and qualified to fill in for Investigator in his/her temporary absence."
4. If Site is a HIPAA Covered Entity, Subinvestigators and other personnel not employed by Site must sign a HIPAA Business Associate agreement.
5. In the USA, submission of a Form FDA 1572 identifies a Subinvestigator and constitutes notification to the Sponsor.
6. Device studies use a Statement of Investigator instead of a 1572.

3.8. Delegation of Investigator Duties

Investigator will personally supervise the Study and may not delegate this duty. He/she may, however, delegate other duties to qualified personnel per protocol and regulatory requirements. Site may not replace Investigator or substantially reduce his/her role in the Study without Sponsor's prior written approval. If Investigator is to be absent from Site for more than ___ days, Site will designate a Subinvestigator to temporarily supervise the Study on the Investigator's behalf. Site will document this designation notify Sponsor of this designation prior to its commencement if possible, and certainly within three business days after its commencement. If Investigator is, or is to be, absent for more than ___ days, Sponsor may terminate Agreement if Site and Sponsor cannot agree on a replacement Investigator within that number of days. [1,2,3]

1. Temporary absence period generally ranges from a minimum of 0 to 21 days, with 7 to 14 days most common.
2. Maximum absence period generally ranges from 14 to 30 days before a replacement must be found.
3. Prior to signing Agreement, Site may notify Sponsor of anticipated Investigator absences, and Sponsor may approve such absences as an amendment to Agreement.

3.9. Facilities

Site will conduct Study only at facilities that are listed on its Form FDA 1572 and found to be adequate by Sponsor. Site will ensure that they remain adequate

1. Device studies use a Statement of Investigator instead of a 1572.

during the Study. Adequate facilities, at minimum, are safe, secure, hygienic, include adequately-maintained and calibrated equipment, and provide for secure and accessible storage of study materials and records. Sponsor may inspect facilities during monitoring visits. It may also, on mutually-agreeable dates during Site's normal business hours, inspect facilities to determine their continued adequacy. Site will notify Sponsor within 5 days of a significant detrimental change in its facilities' adequacy. [1,2,3,4,5]

2. Sponsor may want to add: "Site will conduct Study at a single location." Multiple locations make site monitoring and Study Drug/Device/Biologic management more difficult and time-consuming.
3. Sponsor may want to detail specific requirements, e.g., for specialized equipment required for the study. It may also want to specify requirements for a monitor workspace.
4. Although U.S. CFR 312.61 (Control of the investigational drug) does not require controlled storage of Study Drug Materials, most sponsors want double-lock security. U.S. CFR 312.69 (Handling of controlled substances) requires storage of controlled substances, e.g., narcotic study drugs, 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."
5. ICH Guidelines (5.18.4) require sponsor to ensure the adequacy of Site facilities. Site therefore cannot place unreasonable restrictions on sponsor inspections.

3.10. IRB/IEC

3.10.1. IRB/IEC Selection. Site will conduct Study with the initial and continuing approval of an IRB/IEC. If Site does not use the Sponsor-designated central IRB/IEC, it will notify Sponsor of its choice of IRB/IEC with documentation of compliance with 45 CFR 46, and/or 21 CFR Part 56, as appropriate. Site will not substitute IRB/IECs without written notification to the substituted IRB/IEC and Sponsor's prior written approval. [1,2,3]

3.10.2. Study Initiation. Site will initiate Study only after the IRB has approved the Study's protocol, informed consent form, and subject recruitment materials, as applicable, and Sponsor has received a copy of these approvals. Site will

1. A published roster or OHRP registration number is sufficient documentation of compliance, although all it really documents is the *existence* of the IRB.
2. Add, if appropriate, for central IRBs, one of the following texts:

   a. "Site will submit IRB application to the Sponsor for its review. Sponsor will review the application within 5 days. Site

obtain IRB and Sponsor approval of any protocol amendments before implementing such amendments, except when necessary to eliminate apparent immediate hazard(s) to the safety or welfare of Subjects, or when the change(s) involve only logistical or administrative aspects of the Study. It will discontinue the Study if it does not obtain any required periodic approvals. Site will notify Sponsor of any refusal of, withdrawal of, or suspension of IRB approval within 5 days of receiving such notification.

3.10.3. Compliance. Site will comply with government, IRB and Sponsor requirements to keep the IRB informed of progress of the Study, particularly with respect to serious adverse events, IND safety reports, and protocol violations affecting Subject eligibility or subject safety. Site will comply with the IRB's directives and inform Sponsor if any such directives vary from the Protocol.

will not submit the application to the IRB without the Sponsor's prior written approval."

b. "Site will submit IRB application to the Sponsor for its review. Sponsor will review the application within 5 days. Site will submit the application approved by the Sponsor to the IRB."

3. It may be appropriate to create separate versions of this section for local and central IRBs.

3.11. Study Documents

Site will prepare, maintain and retain complete, current, accurate, organized and legible Source Documents, Regulatory Documents, and other Study Documents. Site will submit CRFs, unless collected by Sponsor at Site Visits, within __ days following data collection for each page. Site will prepare and submit other documents required by the Protocol to the Sponsor within __ days. If Sponsor provides Site with source document templates, Sponsor has no responsibility for their design or contents.[1]

1. A range of 5 to 10 days is reasonable in most cases, unless the Study is exceptionally complex. Sponsors may want Sites to submit eCRFs and certain regulatory documents more quickly.

3.12. Reporting and Meetings

Upon the request of Sponsor, Site will submit oral and written progress reports. Upon the request of Sponsor, Site will meet with Sponsor at Site's location at mutually-convenient times. Site will submit to Sponsor a final report on the Study within {20/30/40} days of completion or earlier termination of the Study. [1]

1. Site may want to limit frequency of required written reports and meetings.

3.13. Record Retention & Destruction

Site will retain in a safe and secure location one copy of all printed and electronic data and reports resulting from the Study for the longer of (a) two years after the last marketing authorization for the Study Drug has been approved or Sponsor has discontinued research on the Study Drug or (b) such longer period as required by regulatory requirements. Sponsor will notify Site within 30 days after this retention requirement has expired. Sponsor will reimburse site for any subsequent storage costs plus management fee. When Site destroys records, it will do so in a manner that ensures that their confidentiality is protected. [1,2,3,4]

1. U.S. CFR §312.62. Other countries may have other record retention requirements.
2. Parties may agree that electronic records will be printed on paper for retention.
3. Sponsor may want to replace "for the longer of…" with "for __ years after termination of the Study."

4. Sites generally have no way to determine when the CFR §312.62 retention period ends, so a fixed period may be preferable, even if it is longer than the regulatory requirement.

3.14. Enrollment

Enrollment in Study is competitive. Site will use its reasonable efforts to enroll __ Subjects within the enrollment period of __ months after Study initiation. If Site enrolls fewer than __ Subjects within __ months after Site initiation, through no fault of Sponsor, Sponsor may close enrollment at Site. Sponsor may change the enrollment period at its sole discretion, upon __ days notice to Site. [1,2,3,4,5,6,7]

1. "Competitive enrollment" means sites can enroll additional subjects above their target; enrollment closes when the combined target enrollment is achieved.
2. Alternative language that is simpler:

a. Enrollment in Study is competitive. Sponsor expects about ___ sites to enroll ___ subjects by [date]. Sponsor may close enrollment at Site if Site is not enrolling or exceeds its share of Subjects.

b. Site will use its reasonable efforts to enroll __ Subjects. Sponsor may close enrollment at Site if Site is not on track to enroll this number of Subjects.

3. "Reasonable efforts" means that Site will give Study average priority and conduct it in a professional manner, with the due care and diligence that is customary in the industry. "Best efforts" means that Site will give Study top priority and conduct it in an exceptionally good manner.
4. The number of subjects to enroll may be stated as a minimum, maximum or exact number.
5. Stating an exact number requires a CTA amendment if the Site exceeds it. Changing an exact number requires IRB approval. A range is thus more flexible.
6. The enrollment period for the Study may

begin before a specific Site is initiated.

7. Sponsor should give Site adequate notice before closing enrollment so Site does not incur unnecessary costs or disappoint potential Subjects that are in the recruiting process. 7 to 14 days should be adequate.

3.15. Adverse Events

As soon as any Study Personnel concludes that a death, other Serious Adverse Event (SAE), Unexpected Adverse Event (UAE), or other event specified in the Protocol probably occurred during the Study, regardless of cause, Site will report the event within 24 hours to Sponsor, and follow-up with a written report of the event to Sponsor within 48 hours of concluding that such event probably occurred. Site will comply with other Sponsor and IRB reporting instructions. It will not delay the report because of incomplete information, which can be supplied later. Site will record other adverse events in the adverse event log. [1]

Site will not report adverse events directly to regulatory authorities, except (a) with 5-days prior notice to Sponsor, (b) to protect public safety and welfare, and (c) if Site believes Sponsor is not reporting adverse events according to regulatory requirements.[2]

Sites may discuss adverse events among themselves.

1. If Site reports verbally reports a probable event and later concludes that an event did not occur, it should so inform Sponsor and write a note to file.

3.16. Protocol Violations & Deviations

Site will notify Sponsor and IRB within three days after becoming aware of any material Protocol violation. It will record Protocol deviations in the Study records. To the extent possible, it will make its best efforts to quickly remedy violations and deviations. Sponsor will provide Site with a list of violations that it wants Site to report. [1]

1. The definitions of violations and deviations, and their reporting requirements, vary by sponsor and IRB, so Site may request guidance when classifying an event.

3.17. Informed Consent

Investigator will ensure that informed consent is obtained from Subjects prior to screening for, or participation in, the Study. Subject's dated signature on the current IRB-approved informed consent form will signify informed consent. [1] Both parties will ensure that the subject injury section of the informed consent form is consistent with Section 9. Subject Injury Claims. [2,3]

1. Although the Subject's dated signature constitutes informed consent for the purposes of this Agreement, Site is responsible for ensuring that Subject's consent is, in fact, informed and voluntary.

2. Sponsor, at minimum, should review and comment and on the informed consent form because it is the only party with sufficient information to determine if the informed consent form includes complete and accurate information about the Study {Drug/Device/Biologic}.
3. Sponsor may want to approve the informed consent form, but it may create a legal liability for the Sponsor if there is litigation due to Subject injury. On the other hand, if Sponsor does not approve the informed consent form, it may be liable to a claim of negligence. Are there any legal or regulatory citations or case law that explicitly hold Sponsor responsible for contents of the informed consent form?

3.18. Study {Drug/Device/Biologic}

Sponsor owns the Study {Drug/Device/Biologic}. It will provide the Study {Drug/Device/Biologic} to the Site at no cost. Site will verify to Sponsor receipt of the Study {Drug/Device/Biologic}. Site will store the Study {Drug and empty containers/Device} in a safe and securely-locked area per Protocol requirements. Site will maintain complete and accurate records on the receipt and disposition of Study {Drug and empty containers/Device}. Site will use {Drug/Device/Biologic} only for Study Purposes according to the Protocol. Site will not dispense expired Study {Drug/Device/Biologic} to Subjects. [1,2,3,4]

1. Return of Study {Drug/Device/Biologic} to Sponsor is covered in the “Return of Study Materials” section.
2. Sponsor may not require retention of empty Study Drug Materials containers.
3. Although it is not a regulatory requirement, Sponsor may want Study {Drug/Device/Biologic} stored in a locked cabinet in a locked room.
4. If Study Drug Materials are subject to Controlled Substances Act (See U.S. 21 CFR 312.69), replace “in a safe and securely-locked area.” with “in a securely locked, substantially-constructed cabinet, or other securely locked, substantially constructed enclosure.”

3.19. Specimens; Shipment of Hazardous Materials

Site provides Specimens to Sponsor "as is”. Site makes no representation or

1. IATA is an industry association. ICAO is a

warranty, express or implied, that Specimens are free from harmful biological or infectious agents or organisms and are otherwise merchantable or fit for a particular purpose or use. Sponsor assumes all risk of liability in connection with its use of Specimens. Any use of Specimens, whether such use occurs as part of or outside of the Study, shall be in accordance with the Protocol, the Informed Consent Form, the HIPAA authorization, and applicable law.

Site will ensure that only trained and certified Personnel prepare shipments of hazardous materials such as Specimens and dry ice. Site will package and ship Specimens and infectious substances in compliance with the requirements of the U.S. Department of Transportation (DOT), the International Civil Aviation Organization (ICAO), the Protocol and all other relevant laws and regulations. Sponsor will supply Site with necessary shipping materials that are compliant with DOT and ICAO requirements. [1,2]

regulatory authority.

2. U.S. Department of Transportation (DOT) requirements apply only to shipments originating or terminating in the U.S. Optionally, specify other relevant national requirements.

3.20. Electronic Data and Signatures

Site will submit Study data using the electronic system provided by the Sponsor. Sponsor warrants to Site that the system complies with U.S. 21 CFR Part 11 and HIPAA. Site will comply with Sponsor's instructions, U.S. 21 CFR Part 11, and HIPAA. Site will prevent unauthorized access to the data by maintaining physical security of the computers and ensuring that Personnel maintain the confidentiality of their passwords. Prior to using the system, Site will certify to the FDA that its electronic signatures are the legally binding equivalent of handwritten signatures. [1,2]

1. Use this section if Site employs eCRFs.
2. FDA Certification is required only once by the Site (not once per study).

3.21. Data Clarification Queries

Sponsor will make its best efforts to submit only legitimate data queries to Site. Site will respond within {3/5/10} days to Sponsor's timely queries. If Site is unable to resolve a query within this timeframe, it will instead respond with an explanation and expected date of resolution.[1,2]

1. Site may require more time to respond to queries in a complex study or if the query is about data collected months ago.
2. It is not customary, but Sponsor may want to charge Site if there is an excess of legitimate queries due to poor quality data submitted by Site (and/or give a bonus for clean data). Conversely, Site may want to charge Sponsor for responding to queries that are redundant or otherwise obviously non-legitimate. Legitimate or non-legitimate queries

should be defined.

3.22. Communication of Results to Subjects

Within 30 days after data lock, Sponsor will inform Site that it may break the Study blind and inform Subjects which treatment they received. Sponsor will inform Site of Study Results when the information is available to Sponsor. For a period of __ years after the Study, Sponsor will inform Site of observed Study Drug side effects so Site can inform Subjects.[1]

1. With device studies, sponsor is required to inform Site of device defects for the life of the device. There is no comparable regulatory requirement for drug studies.

3.23. Return of Study Materials

Within 30 days following the conclusion or premature termination of the Study or termination of this Agreement, Sponsor will instruct Site to return or destroy unused study materials, including Study {Drug/Device/Biologic}, devices, clinical supplies, CRFs and equipment furnished by Sponsor. Within 30 days thereafter, Site will comply with Sponsor's instructions. Sponsor will provide shipping materials and pay Site's out-of-pocket shipping costs. During the Study, Site may return unused materials to Sponsor with prior Sponsor approval.[1,2,3,4]

1. Sponsor may want to include destruction and/or return instructions in the Agreement, for example: "Within 30 days following the conclusion or premature termination of the Study or termination of this Agreement, Site will return unused Study {Drug/Device/Biologic} to Sponsor and destroy unused CRFs."
2. Site may want 45 or 60 days to return materials.
3. If Sponsor does not provide shipping materials, it should reimburse Site for the cost.
4. Site may want to return unused, bulky materials to Sponsor during a long study.

4. Compensation

4.1. Budget

Sponsor will pay Site in accordance with Exhibit A. Budget and this Section 4. Compensation.[1,2]

1. All compensation numbers should be in Exhibit A for flexibility and easy reference.
2. To avoid a possible subject injury litigation claim, disclose in the informed consent form that Investigator is receiving compensation to perform the Study.

4.2. Initial Payment

Within __ days after receiving {two/three} copies of this Agreement signed by Site and Investigator, Sponsor will make an initial, non-refundable payment to Site of $____. Subject to Section 4.13. Study Cancellation, Suspension or Early Termination, Sponsor will not provide any other compensation to Site for costs incurred prior to signing this Agreement. [1,2,3,4]

1. The initial payment is designed to cover one-time Site start-up costs such as preparation of regulatory documents and subject recruiting materials, training of Site personnel, and attendance at Study meetings. It may also include an estimated amount for subsequent costs such as Serious Adverse Event management and record retention. Alternatively, those costs can be specified in a separate section.
2. Sponsor may want to add additional conditions prior to the initial payment, such as receipt of satisfactory regulatory documents or IRB approval. Any such conditions should not substantially delay receipt of payments past the period when Site incurs the relevant costs.
3. Detail purposes of initial payment to document compliance with anti-kickback Sarbanes-Oxley laws.
4. If Site believes it is incurring too many costs prior to signing this Agreement, it may request Sponsor to agree in writing to reimburse a specified amount of the costs if Site does not participate in the study, regardless of the reason.

4.3. Advance Payment

Within __ days after receiving {two/three} copies of this Agreement signed by Site and Investigator, and documentation of IRB/IEC approval of the Study, Sponsor will make an advance, refundable payment to Site of $____. This advance payment will be applied to __% of amounts owed by Sponsor to Site until exhausted.[1,2]

1. The advance payment is designed to cover the cash-flow gap until Sponsor pays Site for visit-related activities. Before any visits occur, Sites can invest substantial time prescreening and identifying potential subjects.
2. Sponsor may want to add additional conditions prior to the advance payment,

such as receipt of satisfactory regulatory documents or IRB approval. Any such conditions should not substantially delay receipt of payments past the period when Site incurs the relevant costs.

4.4. IRB/IEC Fees

If the IRB/IEC is an independent body selected by Sponsor, that IRB/IEC will charge Sponsor for its services, and Site will not be liable for any fees. If the IRB/IEC is affiliated with Site or otherwise designated by Site, that IRB/IEC will charge Site for its services, and Sponsor will reimburse Site for its actual costs upon receipt of invoice from Site in an amount not to exceed $___ for initial review and approval, and an amount not to exceed $___ per year for renewals and other fees. Sponsor {has/does not have} responsibility to reimburse Site for initial fees if the IRB/IEC does not approve the Study.[1]

1. Optionally, replace "for initial review and approval, and an amount not to exceed $___ per year for renewals and other fees" with "for initial and continuing review and approval for __ years".

4.5. Subject Recruiting

Sponsor has provided Site with an initial recruiting budget to cover Site's third-party costs for design, production, media and postage for print, electronic, direct mail, and event Subject recruiting communications costs, direct and indirect, as specified in Exhibit A. Budget. Any Site request for additional recruiting funds will be accompanied by detailed documentation of funds expended to date.[1,2,3]

1. Direct recruiting includes, for example, radio ads. Indirect recruiting includes, for example, "dear physician" letters.
2. Optionally, replace this entire section with: "Sponsor will provide funds, as specified in Exhibit A. Budget, to reimburse Site for third-party costs for design, production, media and postage for print, electronic, direct mail, and event Subject recruiting communications, direct and indirect."
3. Optionally, replace this entire section with: "Sponsor will reimburse Site's third-party costs for design, production, media and postage for print, electronic, direct mail, and event Subject recruiting communications, direct and indirect. To obtain reimbursement, Site will submit invoices to Sponsor with a copy of supporting third-party invoices and a copy of the advertisement or other recruiting material. Recruiting materials

must be pre-approved by Sponsor and the IRB. The reimbursement will not include overhead and will not exceed the amount stated in Exhibit A. Budget, as amended."

4.6. Payment for Study Visits & Milestones

Sponsor will pay Site for completed Subject visits and milestones according to the Budget. A completed visit or milestone includes the proper completion of all Protocol activities and delivery to Sponsor of complete and accurate CRF data for that visit or milestone. Sponsor will not pay Site for incomplete visits or milestones (a) without Sponsor approval or (b) unless Subject leaves the Study. Site has sole responsibility for any extra costs or liabilities incurred by visits at a location not specified in the Form FDA 1572.[1]

1. Sponsors normally do not compensate Sites for travel costs, e.g., to satellite facilities or subject homes. Specify any such compensation in the budget.

4.7. Screen Failures

Sponsor will pay Site for visits prior to screen failure according to Exhibit 1. Budget. Site must obtain prior written authorization from Sponsor for additional screen failures or to rescreen a potential Subject.[1,2,3,4]

1. An alternative to "visits" is "completed activities". "Completed activities" makes sense if screening visits are commonly terminated prior to completing expensive activities. "Screening visits" is a poor term because it excludes prior visits. If "completed activities" is used, add: "Sponsor will not pay Site for activities conducted after Site obtained first screen-failure information for Subject."
2. The screen failure limit may be (a) number of screen failures, (b) screen failures as a percentage of enrolled subjects, or (c) total cost.
3. If there is no limit, replace "for up to __ potential Subjects. Site must obtain prior written authorization from Sponsor for additional screen failures." with "Site will make a good-faith effort to not screen potential Subjects who are not appropriate for the Study."
4. Sites often have difficulty tracking the number of screen failures vs. the

contractual limit, and requesting written authorization. Site should therefore report every screen failure to the Sponsor with a statement of the limit and an automatic request for an increase.

4.8. Incomplete Subjects

Sponsor will not pay Site for any activity conducted according to the Protocol:

a. after a Subject leaves the Study for legitimate reasons such as voluntary withdrawal or to protect the Subject's safety, except for early termination activities,
b. at the time and after a Subject becomes ineligible to continue in the Study because of a Protocol violation by Site,
c. that generated unusable data provided by Site to Sponsor that Sponsor cannot make usable, or
d. related to a Subject enrolled in the Study despite being ineligible for the Study, whom Site had good reason to know was ineligible.

If Sponsor has already made payment to Site, Site will refund such payment.

4.9. Third-party Costs

Unless stated otherwise in this Agreement, Site is responsible for all third-party costs it incurs during its conduct of the Study.[1]

1. Third-party costs include, for example, supplies, lab fees, and hospital charges for procedures.

4.10. Hold-back & Final Payment

Sponsor will hold __% of payments due to Site, except for pass-through costs specified as such in Exhibit A. Budget, until Site's completion of the Study{, not to exceed $____}. Sponsor will pay any open balance in a final payment to Site when (a) all required Subject visits have been completed, (b) Site has submitted all CRFs to Sponsor in a form suitable for use, (c) all data clarification queries have been resolved to Sponsor's satisfaction, (d) the Study close-out visit has been completed, (e) Sponsor has verified that all required regulatory documentation is complete, and (f) Site has returned all required equipment, drugs and other material to Sponsor.[1,2,3,4,5]

1. Hold-back is optional. Its purpose is to retain Site's cooperation until the final payment. If it exists, it should not be larger than 20%. If it is larger than Site's eventual profit or contribution from the Study, probably much less than 20%, it will create negative cash flow for the Site in and of itself.
2. If Sponsor includes pass-through costs such as subject stipends and third-party tests in the hold-back, the hold-back percentage should be reduced

accordingly.

3. Symmetry suggests that the hold-back be capped at the amount of the original advance payment.
4. The hold-back may be capped or smaller than normal for Sites with which the Sponsor has had positive experiences. It may also be divided into two pieces: half when the CRFs are all submitted and half when everything else is complete.
5. Sponsor should not delay payment because of an ongoing Site audit; it should just complete the audit in a timely manner. If the audit finds an important problem, it can dispute payment under the terms of the Agreement.

4.11. Change Orders & Unanticipated Costs

Sponsor will reimburse Site for cost increases due to protocol amendments, Sponsor instructions, and other reasonable unanticipated costs that it incurs during the Study. However, Sponsor's obligation to pay for out-of-scope services is limited to only those services Sponsor authorizes in advance.[1]

1. Exhibit 1. Budget assumes that Site will cover all costs not specified in the budget. There may, however, be costs that were not clear from the protocol and that would not be reasonable for Site to anticipate. Sponsor may change the Protocol, IRB or other requirements, causing Site to incur unanticipated costs. A local test facility may increase its fees. There may be a large number of complex SAEs.

4.12. Payment Schedule

Sponsor will pay Site for completed {procedures/visits/CRF pages ({submitted/collected})/Subjects/milestones/enrollment log} and reimbursable costs within {30/45/60} days after completion of billable event or receipt of proper invoice. Site will invoice Sponsor for _____. [1,2,3,4]

1. Optionally, replace entire section with "Sponsor will consolidate each {month's/quarter's} payments into one payment within {15/30/45} days after the end of that calendar {month/quarter}."
2. A calendar-quarter payment schedule is a cash-flow problem for sites, especially

if monitoring visits are infrequent or delayed.

3. Sites may want to add: "Sponsor will pay Site interest of 1-1/2% per month on payments that are late by more than two weeks."
4. Sites may instead want to add: "Site will pay Sponsor interest of 1-1/2% per month on advances that have not been charged against billable Study activities within 60-days of receipt. Sponsor will pay Site interest of 1-1/2% per month on billable activities not paid within 60 days of their completion, excluding any requirement for site monitor verifications."

4.13. Study Cancellation, Suspension or Early Termination

Sponsor may, subject to Section 12.3 Termination, cancel, suspend or terminate the Study, and notify Site of its decision. Site will immediately comply with Sponsor's instructions, subject to protecting Subject safety and welfare. Sponsor will pay Site for:

a. Study activities, partial or complete, that Site performed prior to receiving notice
b. Non-cancelable third-party obligations
c. Medically-necessary continuing care of Subjects
d. Reasonable costs incurred because of the cancellation, suspension or early termination, excluding lost profits[1]

1. If cancellation, suspension or termination is the fault of the Site, Sponsor may not want to pay some of these costs. It may, however, be difficult to determine fault, especially if there are multiple sites.

4.14. Charges to Third-Parties

Site will not seek or accept from Subjects or third-party payors compensation for any Study {Drug Material/Device}, procedure, test, treatment or other material or service provided or paid for by Sponsor. If a third-party payor refuses to reimburse fees covered under the National Coverage Decision and is refused, Sponsor will pay those fees, provided they are listed in Schedule A. Budget. Otherwise, Site is responsible. If either party represents that specific third-party reimbursement will be available, that party is responsible for those costs, if not reimbursed. Compensation under this Agreement is consistent with fees charged

1. In the United States, government third-party payors include Medicare, Medicaid, the Veterans Administration, and others. Private payors are principally insurance companies and managed care providers. Only Medicare and Medicaid are bound by the National Coverage Decision, but other third-party payors generally follow

for similar research in Site's geographical area, has been negotiated at arms-length, and is unrelated to the volume or value of any referrals or other business otherwise generated between Sponsor and Institution. [1,2,3,4,5,6,7,8]

its rules. The Veterans Administration is allowed to seek reimbursement from Medicare and Medicaid.

2. National Coverage Decision information is at http://www.cms.hhs.gov/coverage/8d2.asp.
3. Site may seek compensation for standard-of-care materials and services not provided or paid for by Sponsor. Medicare may reimburse for non-standard-of-care drugs and devices, with pre-approval.
4. Optionally, add "Site will inform subcontractors and affiliates associated with the Study that they are subject to this obligation."
5. Optionally, in U.S., replace "Site will not seek or accept from Subjects or third-party payors compensation for any Study drug, procedure, test, treatment or other material or service provided or paid for by Sponsor." with "Site will comply with the National Coverage Decision."
6. National Coverage Decision is applicable in the U.S.
7. Informed consent form may state that unreimbursed costs are charged to the Subject. Subject is not, however, legally bound by the informed consent form.
8. The "fair market value" sentence complies with anti-kickback laws in the U.S.

4.15. Payment Accounting & Discrepancies

With each payment, Sponsor will identify the Sponsor and Protocol number, and provide a detailed accounting of the items and amounts covered by that payment. Site must notify Sponsor of any payment discrepancy or other request for

1. Sponsor name may not be obvious from the check, especially if it is issued by a CRO.

additional payment within 20 days after receipt of final payment.[1]

4.16. Overpayment

If Sponsor has overpaid Site, it may deduct the amount of such overpayment from its next payment to Site. Otherwise, upon Sponsor's request, Site will refund any overpayment according to the payment terms in Section 4.13. Payment Terms.

4.17. Invoices

Any invoice to Sponsor must include an invoice number and identify the Sponsor name, Protocol number, and Investigator name. Submit invoices to the following person and address:[1,2]

1. This section is optional.
2. Include a telephone number and email address for follow-up.

4.18. Budget Adjustments

The Budget will not change during the initial {1/2/3} year period after execution of this Agreement. If the Study is not completed by the end of that period, Sponsor will adjust compensation to Site annually thereafter based on actual third-party charges and, in the U.S., on the increase in the U.S. City Average Medical Care Services Consumer Price Index from the middle of the initial period.[1,2,3]

1. This Section is optional. For studies shorter than 3 years, inflation is unlikely to be a significant problem. Note, however, that the budget can be revisited if the Study is extended.
2. Set the Budget for the initial period based on anticipated cost changes during that period.
3. The U.S. City Average Medical Care Services Consumer Price Index increased by 4.2% per year over the five years from 1999 to 2004. The index is available at data.bls.gov.

4.19. Contingent Fees

Site will invoice Sponsor with adequate documentation for any contingent fees specified in Exhibit A.[1]

1. Bonus and incentive fees, if any, may be included in this section. Bonus and incentive fees are problematic if they encourage Site to violate its regulatory and ethical obligations. Sponsor should obtain Site's approval before offering

bonus or incentive compensation directly to Study personnel because Sites may not want Sponsor to interfere with management priorities. Invoices are not required for bonus or incentive payments.

4.20. Payee

Site authorizes the single payee designated below to receive all of its payments under this Agreement. Site must inform Sponsor of the payee's taxpayer identification number before Sponsor can process the first payment. (See Exhibit A. Budget.) Payee:[1,2,3,4]

1. If Investigator is a party to this Agreement, replace "Site authorizes" with "Site and Investigator authorize".
2. Site may provide Taxpayer ID separately to Sponsor for confidentiality.
3. The allocation of payments between Site and Sponsor is their own private matter.
4. If the Payee is neither the Site nor the Investigator, Sponsor may want to review the relationship of the Payee to the Site and Investigator.

4.21 Taxes

Each party will pay its own taxes except as specified in Exhibit 1. Budget.

5. Confidential Information

5.1 Confidential Information

Sponsor's Confidential Information includes this Agreement and attached budget, the Protocol, Investigator's Brochure, Study reports and data, other information disclosed by Sponsor to Site, information generated by Site for Sponsor under this Agreement, Sponsor's other proprietary information of a technical, business or other nature, in any format, written{, verbal} or electronic, and derivatives thereof.[1,2]

Site and Investigator Confidential Information includes operating procedures, information about other studies, the identity of referring physicians, and other proprietary information of a technical, business or other nature, in any format, written {, verbal} or electronic, and derivatives thereof.[1]

This Section does not apply to information that:

1. There is no consensus between sponsors and sites as to whether information transmitted verbally, i.e., not in tangible form, should be treated as confidential. One compromise is that, for it to be treated as confidential, it must be "reduced to written form and transmitted within 30 days".
2. Some public entities in the U.S. must disclose at least summary information about all contracts.
3. If, for example, the Investigator

a. is in the public domain at the time of disclosure by Recipient to a third-party, through no breach of this Agreement by Recipient;
b. was lawfully in Recipient's possession prior to disclosure by Owner, as shown by written records;[3]
c. was lawfully disclosed to Recipient by a third-party that Recipient reasonably believed was not under an obligation to keep such information confidential;
d. is lawfully developed independently, as evidenced by contemporaneous written documentation;
e. is required to be disclosed by a government order, order by a court of competent jurisdiction, or other legal requirement;
f. is required from a Subject by a third-party payor;
g. is required to answer Subject's reasonable questions during the informed consent process; or
h. is required by Site, Investigator or third-party physician for medical treatment or counseling of Subjects.

originally developed and maintained as confidential an assessment tool, that tool would remain the confidential property of the Investigator. It would not become Sponsor Confidential Information. The confidentiality of that tool would be compromised unless this Agreement requires the Sponsor to protect it.

5.2. Confidentiality Obligations

During the term of this Agreement and __ years thereafter, Recipients will use Confidential Information only for the purposes set forth in this Agreement. Recipients will protect Confidential Information with at least the same care as they protect their own Confidential Information of a comparable nature, but in no event will they use less than reasonable care. They will disclose Confidential Information only to their personnel involved in conducting the Study, who are bound by a similar obligation of confidentiality, and have been informed of their obligations, and to Authorized Third-parties.[1,2,3,4]

The parties will make reasonable efforts to mark or otherwise identify their Confidential Information as confidential. However, unmarked information that a reasonable person would judge confidential will still be treated as Confidential Information. Any information marked or identified as confidential remains confidential even if subsequently disclosed to Recipient without such marking or identification.[5]

If a third-party discloses to Recipient what a reasonable person would consider the other party's Confidential Information, it will notify the Owner within 3 days and treat that information as confidential unless informed otherwise by the Owner.

If a Recipient discovers any loss or compromise of Confidential Information, it will notify the Owner within 3 days and cooperate with the Owner to mitigate the loss

1. 3 to 10 total years of confidentiality is common, and 5 to 7 years most common.
2. Sponsors often do not know how long they need to maintain confidentiality on drugs in development. Confidentiality in perpetuity requires Site to maintain this Agreement in perpetuity, which is not reasonable. If either party wants a very long confidentiality period that is unacceptable to the other party, this language may be acceptable to both parties: "In the one year period prior to expiration of this confidentiality obligation, either party may extend the period of confidentiality by an additional __ years."
3. This entire Section 5 is optional for large, Phase IV studies.
4. For example, Subinvestigators and

or compromise.

Upon termination or expiration of this Agreement and the request of the Owner, at Owner's expense, Recipient will destroy or return Confidential Information to Owner that it is not required to retain by law, regulation or other legal requirement.

A breach of this Section may cause irreparable damage that cannot be addressed adequately by money damages. In addition to any other remedies that may be available, the parties are therefore entitled to seek injunctive relief to prevent or restrain a breach of this Section, without having to post bond or other security.

referring physicians must sign a confidentiality agreement prior to seeing Sponsor's Confidential Information.

5. Optionally, delete this paragraph and replace definitions of Confidential Information (except for exclusions) with "Confidential Information includes information of a technical, business or other nature, in any format, written, electronic or verbal, that is marked by its Owner as confidential, and derivatives thereof." Sites may require that confidential information be marked "Confidential" because unmarked information imposes a difficult burden on the Site. On the other hand, is very difficult for the Sponsor to ensure that every confidential document and communication is marked. One failure to mark opens the barn door.

5.3. Disclosures

If a disclosure of Confidential Information is required by a government order, court of law, other legal requirement, Subject or third-party payor, Recipient will use its reasonable efforts to limit the disclosure and maintain the confidentiality of Confidential Information to the extent possible; and will notify the Owner immediately and, if possible, at least 5 days prior to the disclosure. In addition, Recipient will cooperate with any attempts by Owner to limit such disclosure by appropriate legal means.

This Section does not limit Site's disclosure rights under Sections 8. Publications & Presentations; 3.1.11. IRB/IEC, 3.3. Inspections & Audits; 4.14. Charges to Third-parties; or Section 14.2. Publicity and Use of Names. Nor does it limit Site or Investigator's right to immediately disclose Confidential Information to the extent necessary to protect the public from severe health hazards, or the protect the safety and welfare of Subjects, provided, however, that Site will notify Sponsor prior to making such disclosure and limit such disclosure to the extent feasible.

The full model agreement is available to MAGI members.