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Clinical Trial Agreement Considerations For Investigators

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Key: "Principal Investigator" (PI) can include investigator(s) and all co/sub-investigators; "Institution" or "study site" refers to the organization where study/trial is conducted; and "Sponsor" can include a pharmaceutical/device/biologic company, CRO, SMO, vendor, university, or hospital which owns the study/study protocol/study data/study product.

Section of Clinical Trial Agreement & Goals:

Introductory Paragraph(s): The goal is a clear and accurate statement of who the parties are and their role (sponsor/contract research organization (CRO)/investigator/study site....). It should be clear from the introductory paragraph/first page who owns the study data (work product of the study), who is receiving study data and what the study data will be used for. An effective date is normally found in the introductory paragraph. Backdating (to put a date on a document that is earlier than the actual date of its writing or signing) of the agreement may not be permitted.

1. Study Protocol: The full and official protocol title (identical to the full and official protocol title submitted to the Institutional Review Board (IRB)) should be listed in the agreement and the protocol may be considered part of the agreement by reference or attached to the agreement as an exhibit/addendum. Investigators should remember that the protocol title in the agreement must match the protocol title submitted to the IRB and the protocol title referenced in the informed consent form.

2. Principal Investigator: A statement identifying the principal investigator (PI) by full name and whether the PI is an institution employee. Where the PI is not an institution employee

the PI should evaluate whether they are conducting the study as an employee of another organization and whether their employer should be referenced in the agreement.

3. Institutional Review Board (IRB) Approval: A statement that such information appropriate for IRB review will be given to the IRB. The IRB must be permitted to make all of its decisions independently and without the approval of the sponsor. Sponsor does not have the right to approve or disapprove the IRB's decisions (though sponsor is free to terminate the study and agreement if sponsor disagrees with the IRB). IRB records are generally owned by the institution. Institution will retain the original IRB records and will allow sponsor to audit/make copies of such records. For additional information on IRB review see:
http://www.access.gpo.gov/nara/cfr/waisidx_08/21cfr50_08.html;
http://www.access.gpo.gov/nara/cfr/waisidx_08/21cfr56_08.html;
http://www.access.gpo.gov/nara/cfr/waisidx_07/45cfr46_07.html.

4. Compliance with Laws: A statement that all parties (sponsor, CRO, vendor, university, institution…) will comply with applicable law.

5. Patient Enrollment: A statement that the investigator shall use reasonable efforts to recruit subjects who meet the eligibility requirements; but not "best" or "absolute" efforts; which are higher standards. A statement that the sponsor acknowledges that subject enrollment is contingent upon the availability of eligible subjects. There cannot be quotas with regard to subject enrollment/retention which would be a conflict of interest.

6. Informing Sponsor: Institution should allow reporting to the sponsor as required by law or regulation but should be critical of reporting obligations that surpass what is required by law or regulation. Reporting obligations must be reasonable and practical for the institution's department(s) conducting the research.

7. Confidential Information: Most institutions will not warrant or represent the appropriateness of sponsor's future use or transfer of study data (since institution did not create the study) and will have no practical control over what sponsor does with the data (except such restrictions set forth in the agreement). Institution must retain at least one archival copy of sponsor's confidential information (e.g.: study protocol, investigator brochure, written instructions to PI & staff, case report forms and study data). Institution must have records that the study occurred at Institution and the content of the occurrence. Institution cannot return all study documentation, forms, records and information relating to the study at the end of the study or upon early termination.

Where institution is a hospital, institution should require the sponsor to maintain the confidentiality of patients, even those patients not involved in the study. Institution should require the sponsor to protect and maintain the confidentiality of all patient or subject medical records as well as all individually identifiable subject information. Institution should require the sponsor not to use individually identifiable subject information except for purposes of the study, or as required by law or regulation. Institution should ask the sponsor not to contact a study subject for non-study purposes except with the subject's written consent. The investigator must assure that any statement in the informed consent form which suggests that the sponsor will maintain study subject confidentiality is supported by the terms of the agreement.

Where institution is a "covered entity" under HIPAA and cannot agree with either the sponsor or investigator on a HIPAA issue once the study begins (e.g.: whether the Authorization should be

updated with new information), institution must have the right to terminate the agreement. Institution must, in coordination with their IRB/Ethics Committee, be able to disclose confidential information (including sponsor's confidential information, adverse events and study data) to the study subject in order to protect the health, safety or welfare of the study subject or where such information is relevant to the study subject's willingness to continue participation in the study.

8. Compensation: The agreement must clearly and precisely state all payment amounts and the payment schedule. All compensation should be described in the agreement or an exhibit/addendum to the agreement.

9. Termination: Institution should not agree to perform non-compensated work after the effective date of termination. It should be within institution's sole discretion whether institution will transfer the study and study subjects to another study site upon termination since this is operationally burdensome and may present additional risk to institution. Institution should not continue study protocol implementation for the purpose of creating study data after termination of the agreement (though institution may continue some protocol activity where the health and safety of the study subject requires such action).

10. Conflict of Interest: When conducting research at Banner Health investigators should be aware of the following policy: "Research Conflict of Interest - Disclosure, Review & Management"; see: http://policiesandprocedures.bhs.bannerhealth.com/Docs/Banner%20Facilities/2008/06/Research%20Conflict%20of%20Interest%205-14-08.9163.2.doc.

11. Amendment: All amendments must be in writing, approved and signed by all parties prior to becoming effective. The sponsor should not be permitted to unilaterally amend the agreement, the protocol or the study budget. Backdating of the amendment may not be permitted.

12. Indemnification: The sponsor should indemnify, defend and hold harmless institution and the investigator for lawsuits, actions and claims which arise out of the study, implementation of the study protocol (including sponsor's written instructions), the study drug, device or biologic, the sponsor's use/disclosure of study subject information, or Sponsor's handling, use or subsequent transfers of study subject biological materials (where applicable).

Institution should not agree to exclusions/exceptions to sponsor's indemnification obligation that are so broad and so many that the indemnification is effectively useless. In general, many institutions will not indemnify a sponsor for a study where the institution does not also own the study, study protocol, study data, or object under study.

13. Governing Law: Many institutions require the contract to be interpreted according to the law where the institution's hospital/facility is located.

14. Insurance: Sponsors should have adequate insurance based on the nature of the study and the potential risk. Institutions will generally not add sponsors to institution's insurance policy as an additional insured.

15. Use of Name: Institutions generally do not want the sponsor to use institution's name, symbol or picture without institution's written permission (examples of prohibited uses include: sales, promotion of a product or advertising). Sponsor should be permitted to use institution's

name and other information as required by applicable law or regulation (e.g.: FDA submission materials).

16. Term: Institution should require a clear effective date of the agreement which matches the start date of the study. Again, backdating of the agreement may not be permitted. The end date may be a calendar date or "upon completion of the study" and in the latter, the act that constitutes completion of the study should be identified in the agreement. The term of the agreement should be the true/realistic performance period of the entire study at institution.

17. Publications: Institution should be permitted to publish the study data though some reasonable delays may be accommodated. Institutions are critical of the absolute right of the sponsor to prohibit publication or long delays of publication. Anything beyond 12 months is considered a lengthy delay. If an investigator intends to publish the investigator should assure the scope and timing of their publication is consistent with the terms and conditions of the agreement. The investigator must assure that the agreement is consistent with the intended publisher's rules and requirements (see ICMJE standards as an example: http://www.icmje.org).

18. Warranties (Use of Study Results): Institutions will not generally agree to certain warranties, express or implied, concerning the results of the study, merchantability, or fitness for a particular purpose of such results. Institutions do not want to be liable for any direct, consequential, or other damages suffered by sponsor or any others as a result of the study.

19. Subject Medical Care Reimbursement: Where the subject is injured as a result of the study and their insurance does not pay for such injury/needed medical care (or the subject does not have insurance) institutions want the sponsor to pay for such care. Patients are not often willing to absorb such expenses and most institutions do not want to absorb such expenses. Since it is the sponsor's protocol which caused the injury and the sponsor stands to benefit from the study data, it is generally fair for the sponsor to pay for such medical care. Investigators should remember that subjects may obtain medical care from healthcare providers other than investigator or institution (unrelated hospitals, urgent care centers...) and the agreement should require sponsor to pay for such care. The sponsor should pay for study subject medical care where institution is prohibited from billing for such care.

20. Signature Lines: A party who has obligations under the agreement should sign the agreement. In general, sponsor should sign the agreement. Many institutions will object to vague, unclear or non-legally enforceable statements of representative capacity from organizations claiming to sign on behalf of sponsor.

21. Exhibits & Addendums: All exhibits and addendums referenced in the agreement should be attached to the draft agreement (except for the study protocol which may be referenced rather than attached (e.g.: "the study protocol is made part of this Agreement by reference")).

For questions regarding this educational/discussion document please call the System Contracts Specialist assigned to Banner Health Research Administration (602) 747-9704