



**RISK
MANAGEMENT
SERIES**

Participation in Clinical Research Involving Human Subjects

This advisory is the third in a series of advisories addressing risk management issues for health centers. This advisory discusses certain legal issues that a health center should address before undertaking to conduct and/or participate in biomedical research¹ and/or clinical studies involving human subjects.² In addition, this advisory sets forth recommended elements of a standard policy designed to provide safeguards for health centers that decide to participate in biomedical research activities involving health center patients as subjects.

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GROWING CONCERN

The biotechnology “explosion” which has occurred over the last decade and the concomitant public debate over ethical and other implications generated by new fields of research, such as gene therapy, have markedly increased public (and governmental) awareness regarding such research and the extent to which mechanisms regulating such research protect human subjects.

Two trends in biomedical research appear to be responsible for growing public concern and heightened regulatory scrutiny.

1. The marked growth in research funding by large private corporations has raised concern regarding conflicts of interest and other ethical issues.
2. Biomedical research is no longer exclusively within the purview of

- 1 Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. 45 C.F.R. § 46.102.
- 2 This memorandum does not address a health center’s potential liability to participants in the study in the event that they are harmed as a result of participation.

academic medical centers.³ Rather, research is conducted by an increasingly varied number of providers including small community clinics, physician practices and community hospitals, thus enhancing the immediacy and tangibility of research-related issues to most communities.

There also appears to be an increasingly blurry distinction between publicly-funded research and private industry-funded research.⁴ The result has led to increased scrutiny of clinical research protocols by Congress and Federal regulators (including the DHHS Office of Inspector General), as well as a reconsideration of the regulatory review system itself.⁵ One effect of this enhanced scrutiny was the well-publicized suspensions of clinical research at several prestigious medical institutions.

The performance of biomedical research (including research conducted at a federally-funded health center) using human subjects is a highly-regulated field at both the Federal and State level. The corner-

stone of the Federal regulatory scheme is the requirement that all Federally-supported biomedical research proposals which intend to use human subjects must first be reviewed and approved by an Institutional Review Board (“IRB”) so as to assure that such research protocols and procedures offer sufficient patient protections. Furthermore, both Federal and State law establish significant procedural protections for patients, particularly focused on obtaining the informed consent of patients prior to their participation in a biomedical research study.

FEDERAL LAW

Federal statute, 42 USC §289, requires that any entity applying for a grant from the Department of Health & Human Services (“DHHS”) to support biomedical research involving human subjects must provide assurances to DHHS that the applicant has established an

IRB to review such research proposals. Federal regulations codified at 45 CFR Part 46 titled the “Basic HHS Policy for the Protection of Human Research Subjects”, are known as the “Common Rule”. Similar regulations have been promulgated by seventeen (17) different Federal departments and agencies, including the Food and Drug Administration (“FDA”).⁶ The FDA oversees all research related to the products it regulates, regardless of whether the research is federally or privately funded.

Federal regulations require that each institution that engages in federally-supported research using human subjects must provide a written Assurance of Compliance describing the procedures for assuring compliance with the relevant DHHS regulations.⁷ According to guidance set forth by the Office of Human Research Protection (“OHRP”) (previously known as the Office for Protection and Research Risks (“OPRR”)), an administrative unit within DHHS, an institution is considered to be engaged in research when its facilities or staff intervene or interact with living individuals for research purposes, or when the institution obtains or uses the private information of identifiable individuals in the conduct of the research.

OHRP has released internal guidance regarding which specific activities it considers an “engagement” with respect to institutions which are involved in research, but are not the recipient of the Federal research funds.⁸ However, the legal principles guiding the OHRP’s distinction of engagement versus non-

3 Barnes, M., Krauss, S. Conflicts of Interest in Human Research: Risks and Pitfalls of “Easy Money” in Research Funding, BNA Health Law Reporter, Vol. 9, No. 35, p. 1378 (Aug. 31, 2000).

4 As a practical matter, virtually all institutions that conduct both federally-funded research and privately-funded research voluntarily opt to extend the Common Rule protections to privately-funded research. See Testimony on Protection of Human Research Subjects by Dr. Gary B. Ellis, Director, Office of Protection from Research Risks; Senate Committee on Government Affairs, March 12, 1996. Two reasons appear to support this practice: (1) institutions need only establish only one process/standard for reviewing all research; and (2) to the extent the Federal requirements implicitly establish the legal standard of duty/care for conducting such research, applying this standard to all research minimizes an institution’s risk of liability under a negligence theory.

5 See Protecting Human Research Subjects: Status of Recommendations, DHHS Office of Inspector General, April 2000.

6 See 21 CFR Parts 50 and 56.

7 See 45 CFR §46.103(a).

8 See Attached OPRR Internal memo regarding Engagement of Institutions in Research, January 26, 1999. <http://ohrp/osophs.dhhs.gov/humansubjects/assurance/engage.htm>

engagement activities is not clearly evident. Accordingly, whether directly receiving research support or indirectly (*i.e.*, as subcontractors to supported institutions), health centers may be required to file an Assurance of Compliance. If the health center is uncertain, it may find it helpful to communicate directly with the OHRP for an opinion as to whether the health center must submit its own Assurance of Compliance, or whether its activities are covered by the Assurance of Compliance submitted by principal institution.

In addition, the Health Resources and Services Administration (“HRSA”) has also released internal guidance regarding its requirements and understandings of the applicable Federal “Common Rule” regulations and their applicability to research activities involving human subjects which is supported by HRSA grants, contracts or cooperative agreements or under the authority of any HRSA program.⁹

Institutional Review Boards

Federal regulations require that all Federally-supported biomedical research proposals which intend to use human subjects must first be reviewed and approved by an IRB. The role of the IRB is to objectively review and monitor the conduct of biomedical research in order to ensure sufficient patient protections in major areas of concern including, but not limited to, confidentiality of patient information, the informed consent process, explanation of the

foreseeable and unforeseeable risks and potential benefits, and the availability of alternative treatments.

Health centers typically become participants in biomedical research through the solicitation of health center physicians and/or other practitioners by third party researchers associated with universities, hospitals and/or private research organizations. Frequently, universities, hospitals and private research organizations have established IRBs, which, in most cases, have reviewed and approved the relevant research proposal prior to solicitation of the health center. However, in some cases, health centers may have practitioners who have developed research proposals independently. In such situations, a health center may find itself in the position of having to create and operate its own IRB.

The requirements for IRBs are set forth in 45 CFR Part 46. Sections 45 CFR §46.107 through §46.115 contain detailed guidelines and requirements for the composition and operation of IRBs, including minimum requirements for IRB membership, which are designed to ensure that IRB members have sufficiently diverse backgrounds, experience, and expertise to promote complete and objective review of proposed research.¹⁰ The primary IRB composition requirements (paraphrased here) are as follows:

- ◆ An IRB should have at least five members of varying backgrounds;

- ◆ IRB members should possess the professional competence necessary to review specific scientific research activities and to ascertain the acceptability of proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice;
- ◆ If an IRB regularly reviews research involving a vulnerable category of subjects (such as children, prisoners, pregnant women, or the disabled), the IRB should consider inclusion of one or more individuals experienced in working with those subjects;
- ◆ Every nondiscriminatory effort must be made to ensure that an IRB does not consist entirely of men (or entirely of women); no selection to the IRB may be made on the basis of gender. In addition, an IRB may not consist entirely of members of one profession;
- ◆ An IRB should include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas;
- ◆ Each IRB must include at least one member who is not otherwise affiliated with the institution and who is not a member of the immediate family of a person who is affiliated with the institution;

⁹ See HRSA Policy Circular No. 96-05, Protection of Participants in HRSA Research Programs.

¹⁰ See 45 CFR §46.107

- ◆ An IRB may not allow a member to participate (except to provide information required by the IRB) in the review of any project in which such member has a conflicting interest; and
- ◆ An IRB may invite individuals with competence in relevant areas specific to the proposed research to assist in a review, but these individuals may not participate in voting.

Informed Consent

The other facet of the Federal regulatory scheme governing biomedical research is the emphasis on ensuring a stringent informed consent process. Specifically, Section 45 CFR §46.116 requires that informed consent be obtained only under circumstances providing a subject with sufficient opportunity to consider the information provided, while minimizing any possible coercion or undue influence.¹¹ The specific information required by this regulation must be conveyed in a precise, forthright manner whenever possible. In addition, information must be provided in a language understandable to the subject.

Elements of Informed Consent Under Federal Law

Section §46.116(a) requires that the following information be conveyed to the subject:

- ◆ A statement that the study involves research; an explanation of the purposes of the research and the expected duration of the subject's participation; a detailed description of the procedures to be followed; and identification of any procedures which are experimental;
- ◆ A description of any reasonably foreseeable risks or discomforts to the subject;
- ◆ A description of any benefits to the subject (or to others) which may reasonably be expected from the research;
- ◆ A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- ◆ A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
- ◆ For research involving more than minimal risk¹², an explanation as to whether any compensation or any medical treatments are

available if injury occurs and, if so, what they consist of, or where further information may be obtained;

- ◆ An explanation of whom to contact for answers to questions about the research and the research subject's rights, and whom to contact in the event of research-related injury; and
- ◆ A statement that participation is voluntary; refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled; and that the subject may discontinue participation at any time without penalty or loss of benefits.
- ◆ In addition, §46.116(b) contains additional elements for informed consent that must be conveyed to the subject if determined appropriate by the IRB. These elements include:
 - ◆ A statement that the particular treatment or procedure may involve risks to the subject (or embryo or fetus), which are currently unforeseeable;
 - ◆ Anticipated circumstances under which the subject's participation may be terminated without regard to the subject's consent;
 - ◆ Any additional costs to the subject that may result from participation in the research;
 - ◆ The consequences of the subject's decision to withdraw from the research and procedures for the orderly termination of participation by the subject;

11 Federal law requires specific additional protections for subjects who represent vulnerable populations. Specifically, these populations include children, prisoners, pregnant women, and fetuses.

12 "Minimal risk" as defined at 45 CFR §46.102(i) means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

- ◆ A statement that significant new findings developed during the course of the research, which finding may affect the subject's willingness to continue participation, will be provided to the subject;
- ◆ The approximate number of subjects involved in the study.

Federal regulations allow an IRB to approve consent procedures that alter or eliminate one or more of these requirements in limited, discrete situations to the extent appropriate and necessary.¹³ For example, 45 CFR §46.116(d) allows an IRB to modify/waive requirements if:

- ◆ The research involves no more than minimal risk;
- ◆ The waiver/modification will not adversely affect the subjects' rights or welfare;
- ◆ The research could practicably be performed without the modification/waiver; and
- ◆ The subjects will be provided with pertinent information whenever appropriate.

ADDITIONAL FEDERAL CONSIDERATIONS

Health Insurance Portability and Accountability Act ("HIPAA")

Effective April 14, 2003, the regulations implementing HIPAA contain "administrative simplification" provisions, which among other things, establish detailed requirements for use of protected, individually identifiable health information ("PHI") in research involving human subjects or their PHI.¹⁴ The general rule is that a "covered entity" (defined to include health providers like health centers) can only use or disclose PHI for research purposes with a subject's (patient's) authorization.¹⁵ The limited exceptions (which are each subject to additional, specific

requirements) to this general rule are if: (i) an IRB (or similar "privacy board") approves a waiver of such authorization in limited circumstances;¹⁶ or (ii) the PHI is disclosed for research on decedents¹⁷ or for review for purposes preparatory to research (i.e., to prepare a research protocol or similar research-related purpose).¹⁸ In addition, HIPAA requirements do not apply to de-identified health information.¹⁹

In most research situations involving human subjects, health centers should expect that a HIPAA authorization for research will be required in addition to the informed consent required by the Common Rule and/or State law.²⁰ It should be noted that the HIPAA regulations allow a covered entity to condition research-related treatment on a subject signing an authorization for use or disclosure of PHI. See 45 C.F.R. §164.508(b)(4)(i). Moreover, this authorization for research-related treatment may be combined with

13 45 CFR §46.116(c) and (d).

14 This analysis is based on the Privacy Standards originally published in the Federal Register on December 28, 2000 (65 Fed. Reg. 82462), and as proposed to be modified by the Notice of Proposed Rulemaking ("NPRM") published on March 27, 2002 (67 Fed. Reg. 14776).

15 Please note that the HIPAA regulations establish different requirements for "authorizations" as opposed to "consents."

16 See 45 C.F.R. §164.512(i)(1)(i).

17 To satisfy this exception, a researcher must document the death of the individual and represent that the use of the deceased individual's PHI will be used solely for research purposes and is necessary to the research purposes. See 45 C.F.R. §164.512(i)(1)(iii).

18 See 45 C.F.R. §164.512(i)(1)(ii).

19 See 45 C.F.R. §164.501, . §164.514(b) . We note that meeting the requirements necessary to qualify as de-identified information is a very difficult task, although proposed amendments set forth in the most recent HPRM may make the process slightly easier.

20 We note that patient consents to use PHI in research activities prior to April 14, 2003 will be "grandfathered" under the HIPAA regulations. However, an authorization will be required for future uses/disclosures of PHI after April 14, 2003.

either the patient's consent to participate in the research, the patient's general consent to use/disclose PHI for treatment, payment and health operation purposes required by HIPAA²¹, or the covered entity's notice of its privacy practices which should help ease the administrative burden in these situations. See 45 C.F.R. §§164.508(b)(3)(i); 164.508(f)(2).

An authorization for use/disclosure of PHI for research purposes must be written in plain language and include the following elements:

- ◆ The PHI to be disclosed must be described and identified in a specific/meaningful fashion;
- ◆ The extent to which PHI will be disclosed for treatment, payment or health care operations;
- ◆ The purpose(s) of each requested use/disclosure;

The specific identification of persons/entities (or class of persons/entities) authorized to make the requested use/disclosure;

The specific identification of persons/entities (or class of persons/entities) authorized to whom the requested use/disclosure may be made;

The expiration date/event of the authorization (which should be related to the purpose of the authorization);²²

- ◆ A statement and explanation of the patient's right to revoke the authorization in writing at any time, as well as an explanation of the exceptions to this right to revoke;
- ◆ A statement that information used/disclosed may be subject to redisclosure by a recipient and may be no longer protected;
- ◆ The patient's signature and date;
- ◆ A statement that the patient may inspect or copy the applicable PHI;
- ◆ A statement that the patient may refuse to sign the authorization; and
- ◆ A description of any direct or indirect remuneration the covered entity (*i.e.*, the health center) will receive from a third party arising from the use/disclosure of PHI.
- ◆ A patient should be provided with a copy of the authorization. See 45 C.F.R. §164.508(c), (d), (f)(1).

Other aspects of the HIPAA regulations including, but not limited to, the requirement to use or disclose PHI to the extent minimally necessary, as well as the obligation to catalog and make available to patients upon request an accounting of all disclosures of PHI to third parties, will also apply to research activities. This adds to the administrative burden of conducting research. The analysis for deciding what PHI is "minimally necessary" should be guided by the research protocol identifying the purposes and information required for a particular research project.

Excess Compensation

As mentioned above, funding for research using human subjects is increasingly being provided by private entities (*i.e.*, pharmaceutical and biotechnology companies) and such funding frequently includes substantial financial incentives to the individual researchers and/or institutions in order to ensure participation. However, such financial compensation can be legally problematic to the extent it exceeds the reasonable costs and/or value of the researcher's (and/or institution's) participation.

The federal Anti-Kickback Statute, which is codified at 42 U.S.C. § 1320(a)-7b(b), prohibits arrangements in which remuneration is exchanged for referrals or the purchasing or leasing of goods, services or equipment paid for in whole or in part by a federal health care program. Specifically, the statute prohibits any person or entity from knowingly or willfully soliciting or receiving (or offering or paying)

21 We note that the most recent NPRM would make consent for these purposes optional; however, an authorization (whether or not combined with a "consent" for treatment) to use/disclose for research purposes would still be required.

22 We note that the most recent NPRM states that "the end of the research study" (or similar language) is sufficient if authorization is for use/disclosure of PHI for research, and that "none" (or similar language) is sufficient if PHI is to be used/disclosed for creation or maintenance of a research database or repository.

remuneration directly or indirectly in cash or in kind in return for such referrals, purchases or leases. Violations of this statute occur even if the intent to induce referrals (or the purchase of goods or services) is only one of several reasons for the arrangement. Remuneration is interpreted expansively to encompass anything of value exchanged for referrals, including monetary savings through the use of discounts, rebates and free goods and/or services.

As applied in the clinical research context, a kickback violation may occur if the financial compensation from research sponsors is intended to induce researchers and/or institutions to either make referrals (*i.e.*, patient prescriptions) or purchase goods or services (*e.g.*, pharmaceuticals) from the sponsor, and the goods or services are paid by a Federal health care program. Remuneration, in the clinical research context, may be inferred if researchers/institutions receive compensation that is:

1. Unjustifiable in light of the amount or scope of work required;
2. For activities (*e.g.*, travel, speaking honoraria) which have questionable relation to the research being performed; or
3. For research projects with questionable scientific value.²³

23 Barnes and Krauss, *supra* note 5 at 1380-81.

24 See 42 CFR §1001.952.

25 Barnes and Krauss, *supra* note 5 at 1380-81.

26 *Id.* at 1382.

LEGAL CONSIDERATIONS

Compensation Arrangements

- ◆ As a matter of precaution, health centers involved in clinical research should establish systems to ensure that any compensation (in whatever form) received by either the health center or the researcher, is justifiable and proportionate to the research activities to be performed.
- ◆ Health centers might also consider establishing compensation limits (either from individual sponsors or for particular types of compensation) and/or requiring administrative approval for the acceptance of particular types of compensation (*e.g.*, travel, honoraria).
- ◆ Moreover, while there is no specific regulatory “safe harbor” for clinical research compensation arrangements, it is advisable in negotiating such compensation arrangements to adhere to the key aspects of the Anti-Kickback safe harbors.²⁴ In particular, compensation should be consistent with fair market value for the research services provided and should not vary based upon volume or value of referrals (or purchased good or services) to the sponsor. Avoid compensation mechanisms such as enrollment bonuses, which are based on the number of subjects enrolled by the researcher or institution.²⁵ Such bonuses raise

the additional concern that researchers may be so financially motivated as to ignore the imperatives of securing full informed consent from human subjects.

Unspent Research Funds

Health centers should also establish policies that address unspent research funds or compensation, *i.e.*, “residual funds”. The existence of residual funds may imply that the compensation was either excessive or, if the research sponsor is a health care-related provider or pharmaceutical company, was meant to induce referrals or the purchase of goods or services prohibited by the Anti-Kickback statute. In particular, such policies should prohibit individual researchers from personally benefiting from residual funds consistent with the Internal Revenue Service rules applicable to charitable organizations, which prohibit the assets of a health center from inuring to the private benefit of its employees.²⁶

Financial Disclosures/Conflicts of Interest

The Public Health Service (“PHS”), the National Science Foundation (“NSF”) and FDA have each promulgated rules and/or regulations designed to address potential financial conflicts of interest. PHS regulations (42 CFR §50.601 *et. seq.*) are applicable to researchers and institutions that accept grant funds for research from PHS agencies, which include the National Institutes of Health (“NIH”). In particular,

funded institutions are required to manage conflicts of interest, which includes imposing a duty on all research investigators to disclose “Significant Financial Interests”.²⁷ NSF and the FDA have established similar disclosure requirements, albeit with differences regarding the scope of application, the threshold amounts which trigger reporting duties and which particular research institutions or investigators are specifically required to report such conflicts.²⁸

Federal Tort Claims Act Coverage of Research Activities

Pursuant to Section 224 of the Public Health Service Act, health centers that are Section 330 grantees are eligible to be “deemed” covered under the Federal Tort Claims Act (“FTCA”), thereby allowing such health centers to eschew purchasing malpractice insurance. However, FTCA coverage applies only to the acts and omissions of employees (and certain contracted clinicians) of such covered entities²⁹ which occur within the grantee’s scope of project. Accordingly, if a health center wishes to assure that clinical research activities are covered under FTCA, health centers should take affirmative steps to ensure that such activities are: (i) within the health center’s approved scope of project³⁰; and (ii) within the individual researcher(s) scope of employment (or the con-

tract for services if such person is an independent contractor)³¹. In addition, FTCA coverage, with a few specific exceptions, covers only services provided to health center patients. If research activities are conducted “outside” a health center’s scope of project, professional liability insurance should be acquired to cover such activities.

BPHC has issued very limited guidance regarding the specific issue of FTCA coverage for clinical research activities conducted at a health center.³² Specifically, in the form of questions and answers, BPHC answered a hypothetical question regarding FTCA coverage for a health center clinician involved in a study comparing two pharmacotherapy strategies to control hypertension using health center patients. The question specifically noted that the clinician would not be using experimental drugs. BPHC stated that such clinical research activity would be covered,

but only for health center patients being treated by the clinician as “part of the protocol.” However, the answer did not include a rationale for why the proposed research activity would be covered, *i.e.*, was it covered because it did not include experimental drugs, or because controlling hypertension is within a primary care clinician’s scope of employment. Therefore, the most that can be extrapolated from this guidance is that clinical research activities are not per se barred from FTCA coverage. Accordingly, it may be advisable to request a determination of coverage from BPHC before proceeding with research activities.³³

27 The general threshold for a Significant Financial Interest is aggregated payments in excess of \$10,000.00 (or more than a 5% ownership interest). See 42 CFR §50.603.

28 See 21 CFR Part 54; NSF Grant Policy Manual. Also See Barnes and Krauss, *supra* note 5 at 1384-86, for a summary of PHS, NSF and FDA financial disclosure and conflict of interest obligations.

29 In addition to health center employees, FTCA covers licensed contractors working full-time (i.e. on average, 32 1/2 hours per week) or part-time providers in fields of family practice, general internal medicine, general pediatrics or obstetrics and gynecology. See Bureau of Primary Health Care (“BPHC”) Policy Information Notice (“PIN”) 99-08, Health Centers and the Federal Tort Claims Act, p. 3.

30 A health center’s scope of project is defined by the health services and delivery sites identified in the health center’s approved grant application. FTCA coverage for new health services and/or delivery sites is dependent upon BPHC approval of a change in scope. See BPHC PIN 2000-04 for policies related to scope of project.

31 An individual’s scope of employment is generally determined by the terms of such individual’s employment agreement and written job description, which should identify what types of services such individual will provide and where those services will be delivered.

32 See BPHC Program Assistance Letter (“PAL”) 99-15, p. 5.

33 See BPHC PIN 99-08, p.4.

STATE LAW

State law frequently establishes additional requirements for obtaining informed consent and/or maintaining the confidentiality of patient information (*e.g.*, patient “bill of rights” statutes) as opposed to creating an independent system of IRB-type oversight. As a general rule, Federal laws and regulations preempt similar state laws to the extent they are inconsistent (unless a specific provision of the Federal law states otherwise). However, the Part 46 “Common Rule” regulations specifically state that these rules do not affect State or local laws which provide additional protection for human subjects.³⁴ This means that the Federal regulations represent the minimum, “baseline” standards. Any State law which requires more than these “baseline” standards must be complied with as well.

KEY ELEMENTS FOR A STANDARD HEALTH CENTER POLICY

From a liability perspective, it is critical that the senior managers of a health center obtain and verify relevant documentation and evaluate whether the benefits of research participation (for the health center, its personnel, and, most importantly,

its patients) are worth the legal, financial and professional risks (*e.g.*, loss of license) associated with non-compliance with an approved research protocol and/or bad outcomes. Assuming that the health center’s management approves the conduct of research at its site in cases where the health center is not the principal research institution, the health center should enter into a formal written agreement setting forth (with specificity) the respective duties and liabilities of each party.

Step 1: Documentation

Any employee (or contractor) of a health center who desires to participate in or conduct biomedical research using human subjects on health center premises or with patients of the health center should be required to obtain written authorization from the medical director, executive director and/or other appropriate officer(s) of the health center. In order to decide whether or not to provide such authorization, the appropriate officer(s) should require the following information:

- ◆ Documentation that the proposed research project has been reviewed and approved by a qualified IRB in compliance with relevant Federal and State law or, conversely, documentation that such review and approval is unnecessary under applicable law;

- ◆ A copy of the protocol for the proposed research project; and,
- ◆ A copy of the protocol to be used for obtaining informed consent from participating patients and any forms to be used to obtain that consent.

Obtaining the aforementioned documentation is critical to assessing the potential risks of proceeding. For example, experimental drug research protocols frequently address, in substantial detail, drug amounts, application directions³⁵ and/or restrictions, and usage restrictions. Noncompliance with any one of these specific directives, whether intentional or unintentional, could generate a substantial risk of malpractice or other legal risk which may or may not be covered by insurance or FTCA.

Step 2: Consideration of Additional Factors

Upon the submission of the documentation described above, the relevant corporate officers (*e.g.*, medical and/or executive director) should have discretion to consider additional factors prior to authorizing the employee and/or contractor’s participation in the proposed research. Such additional factors may include, but are not limited to:

- ◆ Compliance and/or consistency with the health center’s mission and values;
- ◆ Patient privacy and safety considerations;

34 45 CFR §46.101(f).

35 The level of risk would likely be increased if such protocols require patients to self-administer drugs.

- ◆ The benefits of participation, *e.g.*, potential patient benefit, improved provider/staff morale and education;
- ◆ The potential revenue to be generated from the primary research institution;
- ◆ Direct and indirect financial costs associated with participation;
- ◆ The positive effects regarding the development of relationships/affiliations with influential third parties;
- ◆ Professional liability insurance/FTCA coverage considerations;
- ◆ Potential interference in an employee's (and/or contractor's) ability to perform his/her regular duties; and
- ◆ Potential legal exposure to the health center corporation.
- ◆ the expectations and duties of the health center, its employees and contractors, and the duties of the research institution;
- ◆ the anticipated timetable for the research project;
- ◆ necessary or appropriate provisions regarding the maintenance of confidentiality of patient information under Federal and State law, including the final "HIPAA" regulations, informed consent and other requirements subject to the Assurance of Compliance;
- ◆ the anticipated time commitments of the employee and/or contractor participants; and
- ◆ appropriate (*i.e.*, fair market value) compensation for direct and/or indirect financial costs incurred by the health center in performing the research.
- ◆ agree to indemnify the health center, its directors and employees for all claims or actions arising from the sponsoring institution's involvement.

Moreover, a health center should take affirmative steps to assure itself that research activities to be conducted at the health center site (whether or not by health center staff) are covered by the health center insurance coverage (whether private or FTCA) or, alternatively, that the health center is a named insured with respect to the primary institution's insurance coverage for the relevant research activities.

In addition, health centers should take appropriate affirmative steps to ensure that the agreement ensures that all medical and/or other sensitive information regarding patients participating in clinical research will be held confidential by the parties in accordance with applicable Federal and State statutes and/or regulations, as well as in accordance with health center policies and procedures.

In addition, health centers should insist that the primary research institution/sponsor:

- ◆ provide an assurance (as well as notification of any potential future action) that the institution/sponsor has not been debarred or suspended by DHHS or otherwise the subject of any adverse governmental/regulatory action, including Federal, State, local government or an applicable licensing/accreditation agency; and

Step 3: The Written Agreement

Upon obtaining authorization from the designated corporate officers, but prior to initiating the research project at the health center, the health center should enter into a written agreement with the research institution responsible for directing or conducting the approved research project. The agreement should set forth:

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