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Western Institutional Review Board

A Guide for Researchers

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The purpose of this guide is to provide you with information about WIRB's processes and clinical research issues. WIRB will from time to time amend or update the guide. WIRB will strive to keep the guide current, but cannot warrant its accuracy. The material provided is intended for informational purposes only, and should not be used as a substitute for legal and/or regulatory advice or opinions. For questions regarding legal interpretation, contact an attorney admitted to the bar in your state.

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1. Introduction

Western Institutional Review Board (WIRB) is pleased to provide this handbook of information about using WIRB as your IRB. The information is intended to provide practical guidance about submission questions, IRB review and oversight, and other topics that may be of interest to you and your research staff. Please use the information in any way that will serve to assist your research efforts as we join together in protection of the human research subject.

2. History of WIRB

The Western Institutional Review Board (WIRB) was established in 1968 to provide human subject protection for endocrinology research conducted by Dr. Angela Bowen. The Board later reviewed a variety of research for other investigators in the local community, and Dr. Bowen incorporated WIRB in 1977.

With the introduction of the research regulations in 1981 came an increased need for independent IRB review services. In response, WIRB established the current for-profit structure, enabling it to serve an expanded clientele throughout the local community and across the United States.

WIRB first offered institutional IRB services in 1996. With the changing regulatory environment of the late nineties, WIRB extended its institutional services to several large university IRBs and other local IRBs. WIRB provides services to a growing number of institutions, while continuing to serve independent researchers around the world.

WIRB has developed over the years and added services to meet researcher and subject needs. Subjects who call WIRB are able to reach a live operator any time of the day, any day of the week; and a WIRB staff physician is always on call for inquiries from subjects or physicians regarding significant safety concerns or emergencies.

The Applied Research Ethics National Association established the Council for Certification of IRB Professionals (CCIP) in 1999 to advance the quality of human subject protection programs through a voluntary certification program initiated in 2000. A WIRB staff member was part of the first group to be recognized by CCIP as Certified IRB Professional (CIP), and more than 40 WIRB employees have since been certified.

In late 2001, WIRB implemented an electronic document storage system, to provide the Board and staff with easy access to IRB records. In early 2003, after several years of development, WIRB implemented a validated electronic workflow and database system, allowing the staff to provide a higher level of support to the Board.

In 2003, WIRB was the first independent IRB to be accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). In 2006 and again in 2009, AAHRPP renewed WIRB's accreditation status.

WIRB strives to respond to the evolving needs of the global research community and has provided services internationally since 1986.

In response to Canada's revised research review requirements, WIRB established a panel to review research conducted in Canada. The Panel, composed primarily of Canadian nationals, held its first review meeting in October 2001.

Today WIRB provides review services for more than 400 organizations (academic centers, hospitals, networks and in-house biotech research), as well as for individual investigators in all 50 states and internationally. WIRB has worked with all major pharmaceutical and device manufacturers, CROs, and the biotech industry. In 2007, WIRB started having daily meetings to review investigator submissions and started a panel devoted to Phase 1 dedicated units.

In 2007, WIRB launched a web portal that allows WIRB's clients to track their submissions, view the review history and download regulatory documents. In 2009, WIRB began to offer "smart" online versions of many WIRB submission forms.

3. Regulations Affecting Clinical Research, Including HIPAA

A. The Regulatory Framework Within Which WIRB Functions

WIRB is registered with FDA/OHRP. WIRB's IRB registration number is IRB00000533, and WIRB's parent organization number is IORG0000432.

WIRB reviews many types of human subject research, including clinical research, behavioral research, and epidemiological research, in the United States and internationally. WIRB reviews research in accordance with three primary standards, as well as other regulatory standards, when appropriate:

- the Food and Drug Administration (FDA) Regulations on research with human beings (21 CFR 50 and 56), and
- the Health and Human Services (HHS) Regulations on research with human beings (45 CFR 46 Subparts A, B, C, and D),
- the International Conference on Harmonization (ICH) "Guidance for Industry—E6 Good Clinical Practice: Consolidated Guideline."

The FDA regulations apply to clinical investigations conducted on medical products under FDA jurisdiction that will be marketed in the United States; principally drugs, devices and biologics.

The HHS regulations apply to research that is funded by HHS and other agencies that have adopted "the Common Rule," represented at 45 CFR 46, Subpart A. Institutions that receive federal funding for research must obtain an "assurance," a formal agreement with the government in which the institution promises to take prescribed steps for the protection of human subjects. Usually, the type of assurance will be a Federalwide Assurance (FWA) from the Office for Human Research Protections (OHRP). However, for some research, other types of

assurances may be used. If you have questions about obtaining an assurance, see the section of this investigator handbook entitled “Special Considerations for Federally Funded Research,” consult the OHRP web site, or contact WIRB’s Client Services at 1-800-562-4789 or clientservices@wirb.com.

The International Conference on Harmonization (ICH) is an international standard for drug approval that has been adopted as either law or guidance in many countries (EU, Canada, Japan and the United States). In the United States, FDA has adopted it as guidance. ICH is similar to the FDA drug and IRB regulations, but has a few stricter standards.

WIRB has established written procedures that ensure that research approved by WIRB meets these three primary standards. However, WIRB may vary from the requirements of one of the three standards when it is not applicable. For instance, we will allow the investigator to vary from the ICH requirement that the subject receive a signed consent form for an HHS-regulated behavioral interview study conducted in a setting where a signed copy of the consent form represents an unacceptable risk of breach of confidentiality for the subject.

In addition, WIRB reviews research funded by the Department of Defense, the Department of Education and other federal agencies, as well as research that will be submitted to the Environmental Protection Agency.

B. HIPAA

WIRB also provides services under the Privacy Rule (45 CFR Parts 160 and 164 of the Health Insurance Portability and Accountability Act of 1996). WIRB will review requests for waivers of authorization and partial waivers of authorization for covered entities upon request (WIRB forms for requesting review of partial and full waivers of authorization are available on the Download Forms page of www.wirb.com). WIRB will also review authorization language upon the request of a covered entity. If the authorization language is embedded in the research consent document, then the IRB must review it. If the authorization language is separate from the research consent document, then the covered entity may determine whether or not to submit the language for IRB review. WIRB will review separate authorization documents upon request.

C. Expedited Review

WIRB does not use the expedited review process for the initial review of research. All initial review of research, even for those categories of research which fit the expedited categories, are reviewed at a convened meeting. WIRB does use the expedited review process for changes in research. In accordance with FDA guidance in the September 1998 Information Sheets, entitled “Continuing Review After Study Approval,” WIRB reviews only minor changes in research through expedited review.

WIRB also ensures that changes in research that are approved through the expedited review process meet the OHRP standard of not materially changing the risk/benefit ratio (OPRR Institutional Review Board Guidebook, 1993).

4. Conflicts of Interest

WIRB considers that the most important step in managing potential conflicts of interest lies in appropriate disclosure, and this begins with the investigator's disclosure to a sponsor and the IRB of financial holdings, relationships, and other interests that might constitute a conflict of interest for the researcher as an investigator. When the researcher is a member of an institution, disclosure of potential conflicts to the appropriate institutional committee or office is also required.

In order to comply with the Department of Health and Human Services (HHS) guidance entitled "Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection," WIRB has established a policy for reviewing financial conflicts of interest of investigators, research staff and institutions. WIRB initial review submission forms contain a section for reporting of financial conflicts of interest.

The investigator or study staff will be considered to have a financial conflict of interest if the investigator, investigator's immediate family, the study staff, or the study staff's family

1. Has a financial interest in the research with value that cannot be readily determined (for example, stock that is not publicly traded);
2. Has a financial interest in the research with value that exceeds \$10,000 other than payments for conducting the trial as outlined in the clinical trials agreement;
3. Has a financial interest in the research with value that exceeds 5% ownership;
4. Has received or will receive compensation with value that may be affected by the outcome of the study;
5. Has a proprietary interest in the research, such as a patent, trademark, copyright, or licensing agreement;
6. Has received or will receive payments other than payment for the conduct of clinical research from the sponsor that exceed \$10,000 in the last 365 days;
7. Is an employee of the agency or company sponsoring the research;
8. Is on the board of directors of the sponsor;
9. Has a financial interest that requires disclosure to the sponsor or funding source; or
10. Has any other financial interest that the investigator believes may interfere with his or her ability to protect subjects.

Diversified mutual funds or similar instruments in which the shareholder has no control over the equities held by the fund are not considered to present a conflict of interest.

A financial conflict of interest is not intrinsically wrong. Rather, the purpose of analyzing a financial conflict of interest is to determine when the interest offers incentive to the investigators or other party to breach a duty to subjects or to society, and to determine how to address the conflict of interest. As individuals vary in their personal integrity, and as the WIRB Board generally does not know investigators and other parties intimately enough to judge their integrity, WIRB uses two reasonable-person standards for analysis:

- First, the Board considers whether the financial conflict of interest could challenge the integrity of a reasonable individual.
- Second, the Board considers whether the financial conflict of interest would appear to a reasonable member of the general public to be a conflict that could challenge the integrity of the conflicted party.

Using these reasonable person standards, the Board considers the following factors in its analysis of the reported conflict of interest:

- Amount of Risk

The degree of risk and discomfort faced by subjects in research varies greatly. In high-risk studies, such as those involving the use of a medical device in invasive surgery, a conflict of interest could greatly affect the risks faced by subjects. In a study involving the analysis of human tissue, the risks to the subjects are generally limited to confidentiality issues.

- Effect of the Conflict of Interest on Subjective Decision-Making

The participation of the party with the conflict of interest could affect subjective decision-making, both consciously and subconsciously, and thus influence the conflicted party's judgment and behavior. Subjective decisions that could be influenced by a conflict include the design of the research, choosing which subjects to enroll, clinical care provided to the subjects, use of subjects' confidential medical information, data collection and analysis, adverse event reporting, and the presentation of research findings.

- Amount of Interaction Between the Conflicted Party and the Subjects

Many of the concerns about the conflicted party's decisions will be lessened if the conflicted party does not interact directly with subjects. For example, in many tissue studies the conflicted investigator simply receives waste samples from a surgery facility, and has no contact with the subjects. On the other hand, in a similar study the investigator may also perform the surgery, in which case the concerns over the effect of the conflict are greater.

- Other Parties Involved in Overseeing the Conflict of Interest

Often, there are other parties besides the IRB involved in the oversight of conflicts of research.

- Large institutions will often have a separate conflict of interest committee. (The standards for these committees are highly variable. WIRB has agreed not to lessen the protections put in place by an institutional conflict of interest committee, but WIRB also reserves the right to impose additional oversight.)
- For FDA-regulated studies, the FDA will be providing a scientific review of the research results.

- NIH does detailed reviews of research proposals in advance, and inquires about conflicts of interest at certain procedural steps.
- Some institutions have assigned subject advocates who sit in on the consent process.

The Board will consider the role and oversight of these and other such parties.

- Training in Conflict of Interest

The investigator or other conflicted party may have participated in training on the ethical analysis of conflict of interest and, therefore, may be more aware of the ethical issues and in need of less oversight.

- Nature of the Interest, and Relationship to the Research

The interest may be one in which large change is possible based on the outcomes of the study under review. An equity interest in a start-up company could be drastically affected by the research results, whereas stock in a large pharmaceutical company is not as likely to be affected. Is it a single site study or a multi-center study? The ability of the investigator or other conflicted party to affect the financial interest varies greatly in these different situations.

- Unique Investigator or Institution Qualifications to Conduct the Research

Occasionally, the investigator or institution is uniquely qualified to conduct the research. For instance, the investigational article may be a surgical device that has been developed by a surgeon who specializes in a surgical technique that only he/she conducts.

Possible Board Actions:

The following are actions the Board may take regarding conflicts of interest:

- A finding that the conflict of interest is not likely to jeopardize subject safety or bias the investigator's decision-making and does not require further action.
- A finding that disclosure of the conflict to subjects or others is necessary.
- A finding that controls on the conflict need to be put into place, such as limiting the role of the investigator with a conflict of interest.
- A finding that the conflict is unacceptable, and must be eliminated in order for the research to proceed.
- Other.

5. The Informed Consent Process

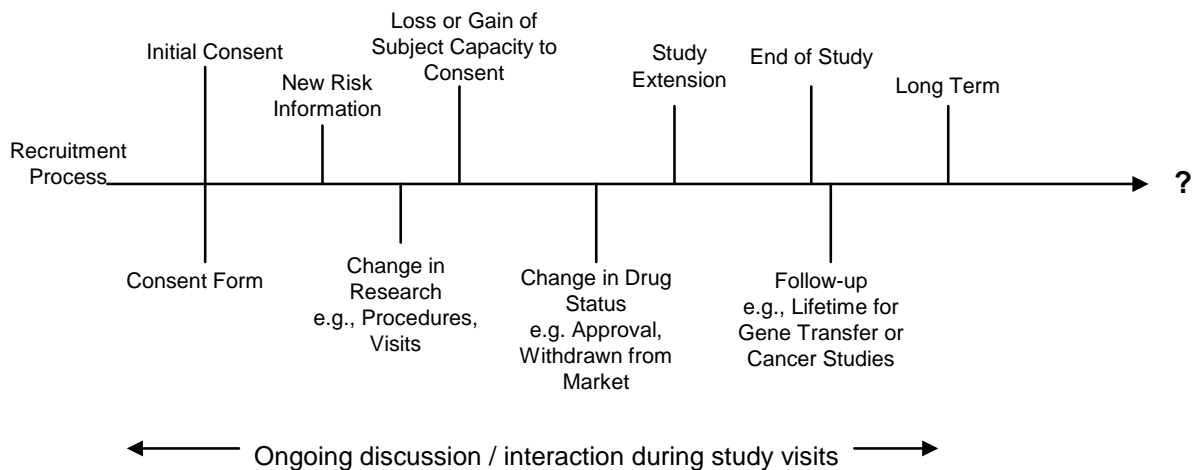
The informed consent process is central to the ethical conduct of research. It is an on-going conversation between the human research subject and the researchers that begins before consent is given and continues until the end of the subject's involvement in the research (see consent

process diagram, below). There are various tools for the investigator to use to optimize this conversation, but the most important feature of informed consent is the investigator commitment to the process.

A. Goals of the informed consent process

- Give the subject **information** about the research
- Make sure the subject has **time** to consider all options
- Answer all of the subject's **questions** before the decision is made
- Make sure that all information is **understood** by the subject
- Obtain the subject's voluntary informed **consent** to participate
- **Continue to inform** the subject throughout the research study
- **Continue to re-affirm subject consent** to participate throughout the research study

B. Consent Process Diagram



C. Tools an investigator might use to assist the informed consent process

- Consent Form -- also called Informed Consent Form (ICF), Informed Consent Document (ICD) or Patient Consent Form (PCF)*
- Pamphlets or other reading materials*
- Internet information*
- Instruction sheets*
- Audio-visual presentations*
- Charts or diagrams*
- Discussions
- Consultation with others

* *These items require IRB review before use.*

D. Investigator responsibilities in regard to informed consent

- Obtain consent before initiating study-specific procedures.
- Provide a **quiet, comfortable, and private setting** for the informed consent process whenever possible.
- **Explain** the consent process to the subject.
- Make sure the subject has **time to consider** all options; allow subject to take the form home before signing (whenever possible).
- Consider the **subject's reading abilities**. Check to make sure WIRB has not disallowed subjects unable to read. If enrollment of limited or non-readers is allowed, involve an impartial witness in the informed consent process.
- **Answer all questions.**
- To the extent possible, make sure the subject **understands enough information** about the research study to give informed consent.
- To the extent possible, make sure the subject can consent **free from coercion or other undue influence**.
- Since the informed consent process continues throughout the subject's participation in the study, **consent should be informally verified on a continuing basis**.
- **Significant new information** must be given to the subject, and continuing consent documented in some way; for example, new risk information presented to the subject in an addendum to be signed by subjects who agree to continue to participate.

E. Issues to consider during the consent process

- Was the subject alert and, in your opinion, able to read and understand the language in the consent form?
- If the subject was unable to read the consent form, and limited or non-readers were allowed to participate, did you have an impartial witness present for the entire process? (An impartial witness is someone with adequate reading ability who is independent of the trial, who cannot be unfairly influenced by people involved in the trial, who attends the informed consent process while the consent form is being read to the subject, who reads the informed consent form and any other written information supplied to the subject, and who is willing to attest to this by signing the consent form.)
- If the subject is not fluent in English, was an approved translation of the consent form provided in the primary language of the subject? Was there also a bilingual translator present to assist with the informed consent process? Note: a translator alone is not considered adequate.
- Was the subject under any pressure (for example, family pressure, lack of medical insurance) to participate in the research? Was this discussed?
- Did the subject take time to carefully read the consent form, or read it along with you?
- Were the risks as set forth in the consent form carefully explained to the subject?

- Are there any other risks or concerns not stated in the consent form and were these explained to the subject?
- Was the subject asked if he or she had any questions about the study?
 - Did the subject have any questions or concerns?
 - Were the subject's questions answered?
 - Was the subject satisfied with the answer(s) they were provided?
- Did the person conducting the consent discussion check for subject understanding by asking some basic questions about the research? Did the responses reflect adequate understanding?
- Did the subject express a clear decision to proceed with the study?
- Was the consent form signed by the person who conducted the informed consent discussion?
- Was the consent form signed by a witness (if required)?
- Was the consent form signed by the Principal Investigator (if required)?
- If a Legally Authorized Representative is allowed to sign for the subject, were additional concerns about the subject's understanding and assent considered and addressed?

F. Consent by Legally Authorized Representatives

The laws regulating who can consent for *adults* who lack the capacity to consent for themselves are defined at the state level and vary from state to state. Persons who can consent for adults who lack the capacity to personally provide informed consent are known as Legally Authorized Representatives (LARs). See 45 CFR 46.102(c) and 21 CFR 50.3(l). Such trials, unless an exception is justified, should be conducted in individuals having a disease or condition for which the investigational product is intended.

WIRB's initial review submission forms solicit information about plans for use of LARs from investigators who plan to enroll adults who lack the capacity to consent for themselves. Sites should be able to explain how they determine which individuals meet the criteria for being a Legally Authorized Representative (LAR) under their state/provincial and local law. WIRB can provide a copy of the relevant statutes for your state upon request; however, advice from your legal counsel is strongly recommended. Sites should also be able to explain the process they use for verifying that an individual is qualified to serve as an LAR.

If the site's state/provincial/local laws regarding Legally Authorized Representatives are difficult to interpret, the sites may provide the Board with a letter from legal counsel which includes a statement such as the following: "The individuals who are authorized under state law to consent on behalf of a prospective subject to that subject's participation in the procedures involved in this research protocol are _____."

G. Consent by Subjects Who Cannot Physically Sign the Consent Form (due to physical impairment)

WIRB does not require a Legally Authorized Representative to provide consent for subjects who are *cognitively* capable of consenting, but *physically* unable (for example, due to paralysis). In those cases, obtaining consent from the subject with the assistance of a witness is usually sufficient. WIRB can provide additional guidance for these situations upon request.

H. Assent

When a subject may not be able to legally consent to research participation, a Legally Authorized Representative provides the consent for the subject. However, WIRB usually also requires that subjects who are not able to consent for themselves assent to participation if possible. "Assent" means a subject's affirmative agreement to participate in research. An investigator should not interpret a subject's failure to object as "assent" unless the subject has also affirmatively agreed to be in the research.

Assent is usually required for research involving *underage subjects* and research involving *adults with diminished capacity*. Assessing an adult's capacity to consent may be somewhat difficult, depending on the subject's medical/mental condition and the requirements of the protocol. If the investigator anticipates that some subjects may be able to consent while others may not, the investigator should establish a process to assess capacity.

Whenever there is doubt about capacity, the subject is best protected by involving a Legally Authorized Representative who knows the subject and is willing and able to participate in the informed consent process with the potential subject.

Assent is not a legally binding action, but within research ethics it is used to signify the agreement of the potential subject to participate in the research. WIRB will usually indicate which subjects' assent must be obtained and the method by which assent is to be obtained. The usual direction is as follows:

- Assent is not required for subjects 6 years and younger
- Verbal assent is required for subjects ages 7 through 14 years using the assent section below and the information sheet for children.
- Verbal assent is required for subjects ages 15 through 17 years using the Assent section below and the information sheet for adolescents (the reference to "17 years old" is modified by the Board when the local age of majority is not 18).
- Adults, assent is required, when the adult is capable, using the assent section in the Consent form.

ASSENT SECTION:

Statement of person conducting assent discussion:

1. I have explained all aspects of the research to the subject to the best of his or her ability to understand.
2. I have answered all the questions of the subject relating to this research.
3. The subject agrees to be in the research.
4. I believe the subject’s decision to enroll is voluntary.
5. The study doctor and study staff agree to respect the subject’s physical or emotional dissent at any time during this research when that dissent pertains to anything being done solely for the purpose of this research.

Signature of Person Conducting
Assent Discussion

Date

Statement of Parent or Guardian:

My child appears to understand the research to the best of his or her ability and has agreed to participate.

Signature of Parent or Guardian

Date

These instructions are modified by the Board when needed, to reflect the Board’s assessment of subject condition and the potential risks and benefits facing the subject.

In order to assent, a subject must have at least a basic understanding of what might be asked of them in the research and what might happen. The information sheet should present this in simple wording and format.

The additional challenges an investigator faces in the assent process depend on the level of understanding the subject may be able to achieve. This will vary with each individual potential subject. An investigator may be able to obtain information about the subject’s ability to understand from the person providing consent.

Recognition of the potential for unintended “coercion or undue influence” or “intimidation” is essential for the assent process. The person obtaining assent must take extra care to minimize these aspects of the communication between subject and researcher. At times this may mean having a different individual conduct the assent process in order to optimize the communication.

WIRB initial review submission forms ask sites if they plan to enroll **wards of the state**. Federal regulation 45 CFR §46.409 outlines special requirements for the involvement of wards in research. Sites that plan to enroll wards may be required to provide a plan for appointing an advocate for each subject.

I. The Consent Form

The primary informed consent tool that involves both the researcher and the IRB is the consent form. This document is used in all research for which there is no approved waiver of consent. Thus, most research will involve use of an IRB-approved consent form.

An approved consent form must comply with several regulatory requirements:

- The required elements (as defined by the regulations) must be appropriately included.
- The content of the consent form must be understandable to a non-scientist.
- No waiver of rights or other exculpatory wording may be present or appear to be present in the consent form.

Satisfying the above requirements presents a joint challenge to the IRB and the investigator. In order to obtain WIRB approval of a consent form, the investigator may opt to do one, or a combination, of the following:

- Submit a *sponsor template* consent form for review (for multicenter studies, the sponsor template has often already been submitted to WIRB and reviewed)
- Submit an *investigator-written* consent form for review
- Request WIRB write the consent form

i. Some general guidelines for writing a consent form

Consent templates and/or outlines are available from WIRB, as well as from some NIH groups such as NCI, and other sources. See [Appendix 1](#) for a sample *Consent Template*. Consent templates provide a framework and structure upon which to build a consent form.

- Consent forms should be written in simple, non-technical language for readers of a seventh-grade reading level who may not have taken science courses in school.
- Use the term “subject” rather than “patient” (the term “participant” may be used in some behavioral research).
- Avoid statements that suggest any waiver of subject rights or release from liability of the investigator or sponsor.
- Avoid use of “I understand” or “you understand” language as this may imply a level of understanding that is not present, and may discourage questions,
- Write all of the consent form except the consent section in the second person (“you are asked to”) rather than first person or third person.
- The consent section should be written in first person (“I consent to...”).
- Avoid wording that is, or may seem to be, coercive or overly reassuring to a potential subject.
- Do not make claims of safety or efficacy for investigational articles or procedures.
- Try to avoid the use of the terms “treatment,” “therapy” or “therapeutic” (because these words may imply effectiveness).

ii. Consent form elements

The following is a list of the usual elements of a consent form (*including elements required by 21 CFR § 50.25; 45 CFR § 46.116; E 6 GCP 4.8.10*).

Introductory Information and Purpose

- Explain the research study and the expected duration of subject participation, and include the approximate number of subjects involved in the study.
- Reassure readers that it is appropriate to ask questions, and that they may take the form home for consideration (if appropriate for the given research).
- State clearly that the study is research.
- State the status of the test article based on the country where the research is being conducted; for example, in the U.S., drugs are “*approved*,” vaccines are “*licensed*,” and devices are “*cleared*” or “*approved for marketing*,” otherwise they should be designated as “*investigational*.”
- State the purpose(s) of the research; for example, drug protocols usually test for safety, tolerability and effectiveness.
- State why the person is being asked to participate in the study; for example, “You are being asked to participate in this study because you have been diagnosed with...”

Description of Study/Procedures

- Describe the visits and procedures (in agreement with the protocol), indicating which procedures are experimental.
- Briefly describe the study’s design; for example, “This is a dose escalation study. As subjects participating in the study tolerate a specific dose level, the new subjects entering the study will be given a higher dose of the study drug.”
- Explain the method used for determining if subjects will receive study drug or placebo, the method for assigning them to a group, and explain the chance of assignment to each group in the study.
- State the number of visits.
- Explain the length of study participation.
- Explain what happens at the visits. It is not necessary to list the procedures visit-by-visit, as detailed descriptions can result in an unnecessarily long consent form.
- Outline any additional participation requirements such as contraception requirements or prohibited activities.

Risks and Discomforts

- Describe any reasonably foreseeable risks and discomforts to the subject. Risks and discomforts must be stated in non-technical, layperson’s language.
- Provide the risks related to all drugs required by the protocol, including rescue medications, over-the-counter analgesics, and approved control group drugs.
- Include the possibility of allergic reactions and that serious allergic reactions can be life-threatening.
- Describe the risks and discomforts of invasive or unusual procedures, including protocol-required biopsies.
- Describe the risks and discomforts of blood draws, if subjects will have blood drawn.
- Include a statement explaining that there may be risks of participation and side effects which are still unknown.

- Whether known or unknown, explain the risks to women who are pregnant or who become pregnant during the study.
- Include a statement that unknown risks and discomforts are possible; if appropriate, include unknown risks to an embryo or fetus if a subject (or a subject's partner) is or becomes pregnant.
- Where applicable, include the risk that the subject's condition may worsen while they are in the study (whether assigned to active drug or placebo).
- If the study drug will be taken home and there is no childproof packaging or warning labeling, include a warning to keep it out of reach of children, or others who may not be able to read or understand the label.

Expected Benefits

- Describe any possible benefits to the subject or others; indicate that benefits are not guaranteed.
- If statements regarding direct benefits of participation are included, they should be qualified as "possible" or that they "may" occur.
- Receipt of procedures and study items may be listed as benefits to the subject, but not in conjunction with their being "free" or at "reduced cost," as these statements imply a form of payment and thus should not be categorized as "benefits." The FDA Information Sheet "Guidance for Institutional Review Boards and Clinical Investigators" (1998) states, "Payment to research subjects for participation in studies is not considered a benefit, it is a recruitment incentive." Forms of payment may be referenced elsewhere in, but not listed as a benefit of participation.

Alternatives

- Describe appropriate alternative treatments or procedures, if available.
- List several alternatives to participation if they exist; alternatives may include alternative drugs or therapy, palliative care, hospice care, etc.
- The consent form may say, "Your study doctor will discuss these with you."
- The section on alternatives should include a brief summary of the risks and benefits of the alternatives.

Costs

- Describe any known or anticipated costs to the subject.
- State who is responsible for the costs of the study-related items such as medications, procedures, device, visits, hospitalization and treatment for possible side effects.
- Indicate which procedures and items will be provided at no charge.
- If insurance will be billed for anything, include information about possible costs to the subject or their insurance. If anything is being billed to insurance, discuss what happens if the insurance does not pay.

Payment for Participation

- Describe the planned prorated payment for participation, if any.
- Any money or other incentive of monetary value should be listed in this section rather than the benefit section.

- If subjects are to be paid, state specifically for which visits subjects will receive payment and when such payment will be made; for example, “payment will be made at the end of each study visit,” “payment will be made at the end of the last study visit” or “payment will be made within one month after the last study visit.” Be as specific as possible to minimize confusion. Consider whether any aspects of the total amount or the proration plan may be coercive or unduly persuasive (WIRB does not routinely allow more than half the total payment to be assigned to the last visit). The Board may require revision of the payment or payment schedule.

HIPAA Authorization or Confidentiality:

Describe the limits on confidentiality of information in this section.

Prior to HIPAA, the section on confidentiality was often titled “Confidentiality,” but is now usually titled “Authorization To Use And Disclose Information For Research Purposes” and includes more information for the subject as outlined by the HIPAA regulations. Some sites (e.g., those outside the U.S.) are not bound by the Privacy Rule and may opt to include only the confidentiality information required by the sponsor, 21 CFR 50 and 56 and/or 45 CFR 46. Some covered entities also opt to use a stand-alone authorization and exclude authorization language from their consent forms.

The authorization section presents the information required by the federal regulations regarding patient privacy rights. WIRB has developed standard template wording for the authorization section that identifies the parties who can use and disclose the PHI as well as the parties to whom the PHI may be disclosed. It also includes the following required information:

- A meaningful description of the PHI, which can be edited for each study.
- A description of each purpose for the use and disclosure.
- Information about the subject’s rights related to the authorization (California, Illinois, Indiana, Washington and Wisconsin state laws require an expiration date).
- Information about the expiration of the authorization.
- Instructions on how to revoke the authorization.
- A statement about what may happen if the authorization is not signed.
- A warning that once information has been released, it may no longer be covered by the Privacy Rule and may be released again without further authorization.

WIRB also ensures that the authorization section is modified as needed based upon local law; for example, authorizations for California sites are placed at the end of the consent form with their own signature lines and in 14 point font.

Compensation for Injury

- Outline the plans for compensation and/or medical treatment for research-related injury or illness, including who will be responsible for the costs.
- Explain what will happen if the subject gets injured. Explain how they will get treatment.
- Clearly state who will pay for treatment if the subject is harmed.
- Address what will happen if the subject’s insurance is billed for the treatment, but refuses to pay.

WIRB requires that the clinical trials agreement (CTA) between the sponsor and the investigator (or investigator's institution) and the approved consent form do not conflict with each other regarding the compensation for injury. For example, if your CTA indicates that expenses for treatment of research related injury will be paid, the consent form must state this as well. Before submitting a request for review of a new research project to WIRB, please consider what method you will use to ensure that no subjects are enrolled unless the CTA and the WIRB-approved consent form are in agreement. WIRB accepts a variety of plans, for example:

- The research is minimal risk research for which compensation for injury language in the consent form is not necessary.
- There is no CTA for the research.
- The research is funded by a government agency (such as NIH) that does not offer compensation for injury.
- Upon receipt of WIRB approval documents, the investigator will check the CTA against the WIRB-approved consent form and resolve any conflicts via a request for a consent form modification to WIRB and/or a modified CTA before enrolling subjects.
- The sponsor or CRO may agree to review the WIRB-approved consent document and resolve any conflicts via a request for a consent form modification to WIRB and/or a modified CTA before authorizing enrollment at this site. **WIRB requires the name and signature of the sponsor or CRO representative, or written correspondence from the sponsor or CRO indicating who will take this responsibility.**
- The PI's hospital, university or medical center has a contract with WIRB for IRB services, and it has an established process for ensuring that the compensation for injury language in the CTA and in the consent form do not conflict.
- The PI's hospital, university or medical center has an established process for ensuring that the compensation for injury language in the CTA and in the consent form do not conflict. (Submitters must provide a description of the process.)
- Sites may also submit plans that differ from any of the plans outlined above.

Questions

Regulations require that a contact be provided for each of the following types of questions.

- Questions about the research.
- Questions about research-related injury or illness (the Board prefers a physician be listed as the contact for injury or illness) or study problems.
- Questions about their rights as research subjects (list WIRB and, if desired, a local or institution IRB contact).

Voluntary Participation/Withdrawal

- State that the subject's participation is voluntary and that a subject may withdraw at any time for any reason.
- State that the subject's decision not to participate or to withdraw from the research early will involve no penalty or loss of benefits to which the subject is otherwise entitled.
- State that the subject's participation may be ended by the study doctor or sponsor at any time for any reason without the subject's consent. Include any specific reasons cited in the protocol. General reasons may also be included. *Please note:* the FDA may stop the research, but will not stop the participation of an individual subject.

- Include information on any risks involved with withdrawing early; for example, the need to taper the study drug, obtain follow-up, be placed on standard medication, etc.
- Indicate that subjects who withdraw after the start of the study may be asked to return for a final visit and final study procedures, and must return the study drug.

Other

- Explain that significant new information that may be related to the subject's willingness to remain in the research will be provided to the subject.
- Identify the source of funding for the research.
- Disclose conflicts of interest (financial and otherwise).
- State that the subject will receive a copy of the signed and dated consent form.

Consent

This section changes to first person for emphasis; for example, "I voluntarily agree..." or "I have..."

- Include a statement of the subject's consent to participate, as well as an authorization to release medical (or research, as appropriate) records to the parties in the HIPAA authorization (or confidentiality) section, if applicable; and a statement that the subject is not giving up any legal rights by signing the consent form.
- Include a statement that the subject has read the information in the consent form or had it read to her/him (as appropriate); however, don't include statements which imply a level of comprehension, such as "I understand..."
- Include a statement that the subject's questions have been answered.

Signatures and Dates

- Include appropriate signature and date lines for consent as applicable.
- Include a space for the person conducting the informed consent discussion to sign (required by ICH).
- Provide a line for the investigator to sign if desired by researcher or sponsor; however, this is not a WIRB requirement.

iii. Assent Forms

When an adult subject is not able to legally consent to participate in the research, a Legally Authorized Representative (LAR) provides the consent for the subject. For children, parents or guardians provide consent for minor children. However, WIRB usually also requires that both incapable adults and children assent to participation if possible.

Assent requires that subjects have at least a basic understanding of what might be asked of them, and what might happen. WIRB recommends providing a simple assent information sheet that explains the research to older children and adolescents.

Template Assent Information Sheets for Children and for Adolescents are included in [Appendix 2](#) and [Appendix 3](#), respectively.

iv. Improving the Readability of a Consent Form or Assent Information Sheet

- Decrease sentence length.
- Limit each sentence to one thought or topic. Avoid run-on sentences.
- Use simpler words (select words with fewer syllables).
- Use common words. Remove technical jargon and medical terms.
- In discussing risks, use the symptoms the subject might experience rather than just the medical terms for the problem.
- Use short, simple paragraphs.
- Use correct basic grammar and form.

When evaluating a proposed word or phrase, consider whether a reader with no college education, no science courses, and little or no exposure to the medical professions would easily understand it. Most words or concepts can be explained in simple language.

When drafting a consent form, frequently ask “Does the reader need this information in order to make an informed decision?” Avoid including excess technical information that would only confuse or intimidate a reader.

v. Special Considerations for Gene Transfer (Gene Therapy) Consent Forms

The following is based on Appendix M (NIH Guidelines for Research Involving Recombinant DNA Molecules, April 2002).

Word Choice in Gene Transfer Consent Forms:

Use the term “gene *transfer*” instead of “gene *therapy*.” Replacing the term “therapy” with “transfer,” helps diminish any implication of effectiveness.

Use “agent” instead of “drug” or “medicine” to refer to the investigational gene transfer product.

Try to avoid the use of the terms “treatment,” “therapy” or “therapeutic” (because these words may imply effectiveness). The following are some suggested techniques for avoiding extensive use of the term “treatment”:

- Substitute the word “dosing,” or “group” for “treatment”:
 - “If you are assigned to ~~Treatment group~~ Treatment group A, ...”
 - “At the end of the ~~treatment dosing~~ treatment dosing phase, ...”
 - “~~Treatment Dosing~~ Treatment Dosing in the study will stop ...”
- Delete the word “treatment”:
 - “Subjects may receive up to 12 cycles of ~~treatment~~ if there is ...”
- Substitute the name of the agent:
 - “If you receive ~~treatment with~~ ABC 123,”
 - “...effects of ~~your treatment~~ ABC 123 and/or chemotherapy on ...”
- Address the increased possibility of **loss of confidentiality** because of media and public focus on the research.

Example: Research studies involving gene transfer have received a great deal of attention from the media. Although every effort will be made to protect your

identity and that of your family, this attention may result in a greater risk than usual that information concerning your study participation will appear publicly without your consent.

Additional Consent Form Elements for Gene Transfer Consents:

- Inform subjects that an **autopsy will be requested if the subject dies**.
Example: In the event of your death, an autopsy will be requested. It would be done to provide additional information about the research. Your family, and your “legally authorized representatives” have the right to refuse the autopsy even if you sign this consent form.

Additional Risk Information Considerations for Gene Transfer Consents:

Consider the special characteristics of the gene and vector involved and discuss common and/or unknown risks:

- Where will the agent end up in the body?
- How long will the agent be in the body?
- Can it be transmitted to others (*horizontal transmission* to those in contact with the subject, or *vertical transmission*, to offspring via egg or sperm)?
- Is there a risk of leukemia (with retroviral type gene transfer vectors) or other types of cancers or conditions (for example with angiogenesis-type agents)?
- Are there special precautions which must be taken because of these risks?

J. Certificates of Confidentiality

For some types of research, the Board may direct an investigator to obtain a certificate of confidentiality. A Certificate of Confidentiality helps researchers protect the privacy of human research participants enrolled in biomedical, behavioral, clinical and other forms of sensitive research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant.

Investigators might consider applying for a certificate for research involving subject populations peculiarly prone to face legal or social harm by another’s discovery of their private, confidential, or protected information that can be exploited legally. For example, research that involves subjects involved in illegal, stigmatized, or embarrassing behavior; subjects with illegal status (alien, child runaway, AWOL, etc.); and subjects with a stigmatized disease (HIV, alcoholism, mental illness, etc.) might have additional protection if a certificate of confidentiality has been obtained.

Frequently asked questions about certificates of confidentiality are available on the NIH web site here: <http://grants.nih.gov/grants/policy/coc/faqs.htm> and OHRP has posted guidance here: <http://www.hhs.gov/ohrp/humansubjects/guidance/certconf>. Instructions for applying for a certificate are available here http://grants.nih.gov/grants/policy/coc/appl_extramural.htm, but NIH is not the only source for one, as several federal agencies issue certificates.

K. Pregnant Partner Consent

Many protocols now include instructions for investigators to collect data on the outcome of pregnancies that occur in partners of male subjects. WIRB follows 45 CFR 46, which defines research as use of private, identifiable information for research purposes. Since investigators would be obtaining private information from the pregnant partner and infant, the partner would be a subject in the research. Investigators must obtain consent from the pregnant partner before any data collection can occur, and WIRB requires a consent form to be submitted for these subjects if a pregnancy occurs.

If plans for obtaining consent from the pregnant partner (or a request for a consent waiver) are not submitted at initial review, the Board may approve the research, but send a letter reminding the investigator and sponsor that pregnant partners and their infants cannot be followed-up until WIRB approves a consent plan for them. Please note that no action is necessary until such time as a pregnancy occurs.

A sample consent form template for obtaining consent from partners who become pregnant and for collecting data about their infants is available in [Appendix 4](#) of this document and on the Download Forms page of www.wirb.com. The template consent form cannot be used without WIRB approval.

6. Working With WIRB for IRB Review – An Overview

The Western Institutional Review Board is composed of several individual review panels. Each WIRB panel consists of nine standing members and designated alternates.

Panel Structure and Schedule

Monday:	Panels 1, 7 & 14
Tuesday:	Panels 2 & 5
Wednesday:	Panels 3, 11 & 14
Thursday:	Panels 4, 12, 10 (bi-weekly) & 13
Friday:	Panels 6, 8 & 14
Investigator Focused Meetings – Daily	

New protocols are assigned to panels based on both the specialty required to review the protocol and on the next available panel meeting. The upper right corner of the WIRB Certificate of Approval displays the panel assignment.

Once a protocol is assigned to a particular panel, all subsequent reviews for that protocol (new investigators, changes in research and continuing review) are carried out by that panel. Reviews for investigators at Canadian locations are assigned to the WIRB Canadian panel; therefore, a protocol taking place in both the United States and Canada can be assigned to both a U.S. panel and the Canadian panel.

WIRB's Internet tracking system, available at www.wirb.com, can be used to track the status of a submission, including when it has been scheduled for board.

Users who create a WIRBNet account, can access expanded tracking information and can download review documents from the site. Click on the yellow WIRBNet Login button on the home screen of www.wirb.com to set up an account.

To learn more about accessing research review details on WIRB's web site, WIRB's panel structure, or to determine the panel assignment of a particular protocol, call Client Services at (360) 252-2500 or e-mail clientservices@wirb.com.

7. Submitting Documents for WIRB Review

A “smart” online form is available for most WIRB submissions (such as initial review, change in research, unanticipated problems). The “smart form” submission is generally a shorter process because it dynamically omits questions that are not relevant, based on the answers you provide about the research. It also features a safe and secure process for uploading your submission documents, and provides general guidance about what type of documentation is required for various types of review requests. Click the “WIRBNet Login” button on www.wirb.com to set up an account.

Users who complete their submission online receive an e-mailed confirmation that WIRB has received the submission. It includes a reference number that will facilitate discussions of the submission with WIRB staff. The confirmation e-mail also serves as an official WIRB acknowledgement of receipt.

8. Materials required for initial review

The following is a general list of items required by WIRB to begin the review process for a research study.

A. Items required for all initial review requests

**Materials marked with an asterisk may be omitted if WIRB is already in receipt of a current version. This may include a WIRB-approved consent form for a previously approved protocol, as well as recruitment and other subject materials.*

- **WIRB Submission Form** WIRB offers three versions of its initial review submission form. Investigators participating in multi-center protocols that have already been reviewed by WIRB may fill out a shorter version called “**Investigator Submission Form for Multi-Center Protocols.**” Investigators submitting protocols that have not been previously reviewed by WIRB must complete the full length Initial Review Submission Form. Sponsors and CROs seeking pre-approval of their research can use the version titled “Initial Review Submission Form For Sponsors and CROs.” WIRB recommends submitters provide typewritten answers rather than handwritten answers to avoid errors and delays resulting from legibility problems. An annotated version of the full length forms is also available on the web site with additional instructions for answering the questions in the form.

- **Protocol***
- **Current professional license** for Principal Investigator, showing the expiration date* (Federal Regulations do not recognize Co-Principal Investigators; therefore, if two PIs plan to share oversight of a single study, the Board requires a completed submission form for each investigator and holds each individually responsible for the conduct of the entire study. Canadian regulations do not allow for approval of Co-Principal investigators of any kind.)
- **Curriculum Vitae (CV)** for Principal Investigator and each Sub-Investigator*
- **Consent form***
- **Other materials to be provided to the subjects** which are not included in the protocol, such as advertisements, questionnaires, subject diaries, etc.* (Any commercially available validated instruments cited in the protocol that are used without modification are not listed individually on the Certificate of Approval; however, approval of the protocol does extend to the uses of such industry standard forms as described in the approved protocol.)

i. For drugs, biologics and food supplements

Provide a copy of each of the following:

- **Investigator’s Drug Brochure***
- **Background Information for Food Supplements***
- **FDA Form 1572** (if applicable)
- **Canadian Qualified Investigator Undertaking Form** (Canadian sites)
- **Documentation from sponsor or FDA verifying the IND (Investigational New Drug) number if one is required for the research.* If an IND is not required, provide the reason why in writing.**
- **For gene transfer studies subject to RAC review, please submit the RAC correspondence, Appendix M responses, and Institutional Biosafety Committee (IBC) approval and minutes (if available). If the IBC review has yet to occur, please provide a date for the intended review and contact information for your NIH-OBA registered IBC. WIRB can provide IBC oversight; see the WIRB Services tab at www.wirb.com.**

ii. If a DEVICE study, provide device manual and ONE of the following:

- **FDA Letter** granting the Investigational Device Exemption (IDE);* (unredacted) OR
- **Letter from sponsor** stating that the study is a non-significant risk device study;* (unredacted) OR
- **Letter explaining why the investigation is exempt** from the IDE requirements under 21 CFR § 812.2(c) or otherwise exempt. *

B. Suggested Guidelines for Writing a Research Protocol

If you will be drafting a protocol for submission to WIRB, the following guidelines will help you to include the necessary elements.

i. Cover Sheet

- Display protocol title, protocol identifying number, and date. Amendments should be numbered and dated.
- Display the name and address of both the sponsor and the medical monitor (if someone other than the sponsor).
- Display the name and title of the investigator responsible for conducting the research, and the address and telephone number(s) of the research site(s).

ii. Purpose of the study and background

- **Purpose of the study:** State the specific scientific objective(s) (aims) of the research.
- **Background:** Provide background material which supports the purpose of the research, and which is detailed enough to allow someone who is not an expert in the field to understand the context of the question, and the study design. References may be cited in the Background section.

iii. Criteria For Subject Selection

- **Number of subjects:** State the total number of subjects expected to participate. For multi-center protocols, this should include both the overall total and the number of subjects to be enrolled at each site.
- **Gender of Subjects.** Describe the intended gender distribution of the subjects. If there are any gender-based enrollment restrictions, explain the nature of the restriction(s) and provide justification. Equitable inclusion of both men and women in research is important to ensure that both receive a proportionate share of the benefits of research and that neither bears a disproportionate burden. Therefore, subjects of both genders should be included in the research unless there are appropriate medical or scientific reasons for excluding them. Women of childbearing potential may not be routinely excluded from participating in research; however, pregnant women should be excluded unless there is clear justification why they should be included. A clear statement whether pregnant women are included or excluded is also required, along with the justification.
- **Age of Subjects.** State the age range of the subjects. Provide the rationale for selecting this age range. Participation of adult subjects in research should not be age-restricted unless there is scientific or medical justification. Check the age of majority in the jurisdiction where the study is to be conducted and whether special considerations apply to research with minors. Additional restrictions may apply to research involving minors.
- **Racial and Ethnic Origin.** Describe the intended racial and ethnic distribution of the subjects. If there are any enrollment restrictions based upon race or ethnic origin, explain the nature of the restrictions and provide justification. Within the

limitations imposed by the population of the study site(s), research should include sufficient enrollment of persons of diverse racial/ethnic backgrounds to ensure that the benefits and burdens of research participation are distributed in an equitable manner.

- **Inclusion Criteria.** List the inclusion criteria. These should be based on the scientific rationale and safety considerations, and should define who will be eligible as a subject.
- **Exclusion Criteria.** List the exclusion criteria. These should be scientifically valid and help further define the subject population. Subjects at particular risk from the study interventions or procedures should be excluded. Be sure to account for warnings, precautions, and contraindications listed in current product labeling.
- **Vulnerable Subjects.** If vulnerable subjects (e.g., those with limited autonomy or those in subordinate hierarchical positions) are included, justify their inclusion. Children, pregnant women, nursing home residents or other institutionalized persons, students, employees, fetuses, prisoners, and persons with decisional incapacity are examples of vulnerable subjects who may be in need of greater protection. Additional restrictions or requirements may apply to research involving vulnerable subjects.

iv. Methods and Procedures

- **Methods and Procedures.** Summarize the research design and sequentially identify all procedures to be used to accomplish the specific aims of the project. Clearly identify and distinguish procedures that are considered experimental, procedures that are performed exclusively for research purposes (including “extra” routine tests), and procedures that would occur regardless of the research (i.e., standard of care). Point out any procedures, situations, or materials that may be hazardous, and the precautions to be exercised to maintain subject safety.
- **Data Analysis and Data Monitoring.** Describe the statistical or analytical methods to be used. For all studies involving greater than minimal risk, describe how the data will be monitored to ensure the safety of the subjects. For research involving intervention that entails potential serious risk to subjects, compares blinded treatments over a long time period, or which may call for “stopping rules” for certain endpoints, a data monitoring committee may be required to protect the safety or welfare of subjects. A detailed description of its operation (e.g., membership, function, frequency of review, stopping rules) should be included.
- **Data Storage and Confidentiality.** Describe where the research data will be stored during and after the study and how it will be secured. The investigator must take necessary steps to maintain confidentiality of data. This includes coding data and choosing an appropriate and secure data storage mechanism preventing unauthorized access to data. State who will have access to the data and how the data will be used. If data with subject identifiers will be released, specify the person(s) or agency to whom the information will be released and the purpose of the release (e.g., routine verification of case report forms).

- **Transition from Research Participation.** If applicable, describe how subjects terminating their participation in the research will be returned to their usual care (e.g., taper study medication and resume usual medication, return to primary care provider).

v. Risk/Benefit Assessment

(a determination as to the risks and benefits of the research to subjects is the responsibility of the IRB; however, the following information is still required in the submitted protocol)

- **Risk Category.** State the risk that the research presents as one of the following: Minimal, or Greater than Minimal. Minimal Risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. A risk is a potential harm associated with the research that a reasonable person would likely consider injurious.
- **Potential Risk.** Describe the potential risks associated with the study. Risks are not only physical, but can be psychological, sociological, economic, or legal. Risks include any specific toxicities noted in the investigator's brochure. If possible, estimate the probability that a given harm may occur and state its potential reversibility.
- **Protection Against Risks.** Describe how the study design will prevent or minimize any potential risks or discomfort. Potential risks and discomforts must be minimized to the greatest extent possible such as by subject monitoring, appropriate subject withdrawal criteria and follow-up.
- **Potential Benefits to the Subjects.** Describe potential medical benefit(s), if any, for subjects participating in the research. If there are no anticipated benefits, this should be stated.
- **Alternatives to Participation.** This section should include a description of alternative therapies or courses of action which are available should the subject elect not to participate in the study.

vi. Subject Identification, Recruitment And Consent/Assent

- **Method of Subject Identification and Recruitment.** Describe how prospective subjects will be identified and recruited. The identification and recruitment of subjects must protect privacy and be free of undue influence. Recruitment of an investigator's own students, employees and patients is considered coercive in most circumstances. The steps taken to minimize undue influence must be included if these individuals are to be enrolled as subjects.
- **Process of Consent.** Describe or list everyone who is authorized to obtain consent and how the process of informed consent will be structured to be conducive to rational and thoughtful decision making by the subject (or subject's legally authorized representative) without any element of coercion or undue influence. If used, 'Auditor/Witness' roles would be described in this section.
- **Subject Capacity.** If not all subjects will have the capacity to give informed consent, describe how capacity will be assessed and by whom. Describe the

anticipated degree of impairment relative to their ability to consent to participate in research. Research with persons who have diminished capacity is allowed only for minimal risk or direct benefit studies.

- **Subject/Representative Comprehension.** All investigators have a legal and ethical obligation to ensure that prospective subjects or subjects' representatives have sufficient knowledge and comprehension of the information represented by the elements of informed consent to enable them to make an informed and enlightened decision whether or not to participate or allow participation in research. In this section, describe how it will be determined that the subject or subject's authorized representative understood the information presented. This section should clearly document that the investigator has an adequate plan in place to assure an acceptable level of comprehension before consent is obtained. If children or decisionally impaired adults will be subjects, this section should also include a specific plan to assess comprehension during assent (the subject's agreement).
- **Debriefing Procedures.** In psychological studies where any information will be purposely withheld from the subject, state the information to be withheld, justify this non-disclosure, and describe the post-study debriefing of the subject.
- **Consent Forms.** Consult IRB consent form guidelines for specific sections required for consent documents. [See 21 CFR 50.25 available on the FDA website, or the FDA guidance at <http://www.fda.gov/oc/ohrt/irbs/informedconsent.html>]
- **Documentation of Consent.** The PI is responsible for ensuring that valid consent is obtained and documented for all subjects. If not already addressed above (see Process of Consent section), specifically describe how consent will be documented and how and where documentation will be stored.
- **Costs to the Subject.** Describe and justify any costs that the subject will incur as a result of participating in the study. This section should clarify who (e.g., sponsor, grant, subject) will pay for procedures associated with the study or necessary follow-up. Normally, subjects should not have to pay for research procedures that do not provide direct benefit. No charge may be made to subjects for costs covered by another entity. Subjects may not be charged for investigational drugs without the written permission of the FDA.
- **Payment for Participation.** Describe any reimbursements or payments (e.g., cash, coupons or gift certificates, academic credit) that the subjects will receive for participation. List the prerequisite condition(s) that must be fulfilled by subjects to receive these payments. The amount must be justified and not constitute undue inducement of the subject to participate in the research or to continue beyond where they would have otherwise withdrawn. To protect the subject's right to withdraw without penalty, the IRB requires a prorated system for financial payments. In most circumstances, no more than 50% of the total payment may be withheld till the end of the study. Payments should accrue as the study progresses and subjects do not have to complete the entire study to be eligible to receive a payment.

C. Requirements for Human Subject Protection Training

WIRB requires investigators to verify on the initial review submission form and each Continuing Review Report form that each member of the research team has successfully completed training in human research subject protection. *Your institution may have additional training requirements, please check with your institutional official.* Please note that HIPAA training or prior research experience alone does not satisfy this requirement for training in human subject protection. WIRB's expectation is that training include topics such as ethical principles related to human subject protections, federal regulations for protection of human subjects, and Good Clinical Practice.

When standard of care therapy is part of the research, WIRB only requires this training of staff members who are involved in the consent process, recording of data, submission of unanticipated problem reports or other procedures specific to the research.

WIRB accepts training completed in a variety of formats (such as online modules, live seminars, college courses, self-study texts that provide CEU or CME credit) and from a variety of sources (such as government entities, non-profit institutions, professional organizations, and commercial businesses). A list of potential sources, including web-based tutorials and books, is available at www.wirb.com or by contacting WIRB's Client Services.

Physicians and their teams who request approval of use of a humanitarian use device or treatment use of a investigational product are not required to complete human subject protection training.

D. Suggested Guidelines for Evaluating Staff Levels at the Site

WIRB's **initial review submission forms** ask for information about staffing levels at the site. WIRB evaluates site staffing levels based on a variety of criteria.

At a minimum, all clinical sites should have the following:

- Enough trained investigators and staff to administer the protocol without deviations that impact subject safety or data integrity.
- Enough trained investigators and staff to ensure there is sufficient time available for staff to interact with the subjects as much as is necessary for good clinical care.
- Enough trained investigators and staff to provide coverage for emergencies.

In addition, the Board considers what level of staffing would be required to execute the protocol. For example:

- How many subjects are already enrolled and what is the predicted rate of accrual?
- How many visits are required by the protocol?
- What type of visits are required and will the subject need to see the investigator at each visit?
- Are the required procedures complex or lengthy?
- Does the administration of the study drug require supervision or extensive instruction?

- Are the subjects generally healthy, seriously ill, or suffering from multiple conditions?
- Is the disease involved acute or unpredictable?
- Are the side effects of the intervention expected to be numerous or serious?
- Are the subjects considered vulnerable?

The particular composition and expertise of the study staff also is a consideration:

- Does the investigator have experience in conducting research? (This variable can affect overall management of the research staff and functions.)
- Are the staff members experienced in conducting research? Are they skilled at maintaining accurate and complete study records?
- Do the investigator and staff have experience with the type of treatment in the protocol?
- Does the site have other ongoing protocols?

For example, the Board might determine that an experienced research coordinator can administer 3 to 5 drug protocols that require weekly or biweekly visits of ½ hour to 2 hours and enrollment of 5 to 15 subjects. However, if the site's ratio amounted to 7-10 of these studies per experienced coordinator, the Board might table the research and recommend the site adjust the staffing levels. The Board would also expect to see at least one physician sub-investigator appointed to provide back-up for the PI.

Different types of protocols, however, require different levels of staff time and expertise. Because of their narrow inclusion criteria, oncology protocols normally don't rapidly accrue subjects, and because they are often carried out by groups of oncology specialists, the Board might tolerate a high protocol-to-staff ratio. In these cases, the Board's focus might shift from the number of staff, to the ability of a large staff to successfully coordinate a subject's care and execute the study plan.

In the case of a non-treatment protocol, the question of staff levels may not be important.

E. Compensation to Investigators for the Conduct of Research

Financial compensation to investigators should be at fair market value for the procedures and services provided. WIRB will review "bonus payments" and other compensation to investigators that is not directly tied to payment for study procedures or services on a case-by-case basis. (AMA Code of Medical Ethics Policy #E-8.0315)

F. Special considerations for Drug Research: Do you need an IND?

WIRB's **initial review submission forms** ask for information about an IND. As a general rule, WIRB requires that a sponsor or investigator obtain an IND from FDA for clinical investigations involving drugs or dietary supplements. However, if the investigation uses a marketed drug, the sponsor or investigator may propose that the investigation is exempt from an IND under 21 CFR § 312.2(b), which states:

- (b) Exemptions. (1) The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of this part if all the following apply:
- (i) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
 - (ii) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
 - (iii) The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
 - (iv) The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50; and
 - (v) The investigation is conducted in compliance with the requirements of Sec. 312.7 [regarding marketing and promotion].

Criteria (i), (ii), and (v) are under the control of the investigator and/or sponsor, and WIRB holds the investigator and/or sponsor responsible for complying with those criteria. Criterion (iv) is satisfied by the fact that the study has been reviewed by WIRB.

WIRB will consider whether the conditions for (iii) are met, and send a letter to the investigator addressing that item.

For clinical investigations using a dietary supplement, WIRB will require that the sponsor or investigator obtain an IND if the protocol is designed to provide information on a health claim. However, WIRB will accept a written statement from FDA that an IND is not necessary for a given clinical investigation of a dietary supplement.

G. Special considerations for Device Research

The FDA regulations establish additional requirements on the part of the IRB for the review of studies using medical devices. Before reviewing research involving a device (or devices), the Board must identify and evaluate the regulatory status of the device(s) (such as determining whether the device study qualifies as a Non-Significant Risk (NSR) Device study, a Significant Risk (SR) Device study, or whether the research use of the device is exempt from the IDE regulations).

If you believe the device is NSR and the Board agrees, then the Board may go on to review the research. However, if the Board disagrees, and finds the study to be SR, and there is no IDE assigned, it will provide the investigator and, if appropriate, the sponsor, with its finding. The sponsor is responsible for notifying the FDA of the Board's SR determination. The Board will not review the research until the sponsor provides written proof that either the FDA has granted an IDE to the sponsor or that the FDA disagrees with the Board's SR determination and has

determined that the device is NSR. If the FDA has not responded to the IDE application, as described in FDA 21 CFR § 812.30, this proof may consist of a letter showing that an IDE application was submitted at least 30 days prior to the date on which the submission was forwarded to WIRB.

If the research is SR, provide WIRB with proof of the IDE number at the time of submission. The Board will automatically consider the research to be SR. In most cases, submitters should ensure WIRB receives a copy of the IDE letter that has not been redacted. Redacted IDE letters generally do not provide sufficient information for the Board.

Note: If the subject must undergo a medical procedure as a part of the study, and that medical procedure is not one which the subject would otherwise undergo as part of standard medical care, the Board must consider the risks associated with the procedure as well as the use of the device. If potential harm to subjects could be life-threatening, could result in permanent impairment of body function, or permanent damage to body structure, the device should be considered SR.

H. Special considerations for Behavioral Research

WIRB reviews behavioral research. Behavioral research is non-clinical research, and oftentimes is qualitative rather than quantitative. When submitting behavioral research, provide a detailed protocol, a description of the protections of confidentiality that will be used, and a description of the consent process. Also, if deception is involved, the submission must also include a description of the information to be withheld, a justification for the non-disclosure, a description of potential psychological or other risks to subjects resulting from the deception, and the process for post-study disclosure of the deception and debriefing of the subjects, including provisions for psychological counseling or other follow-up which may be needed.

I. Special considerations for Federally Funded Research

i. Grants

For federally funded research, WIRB must review a complete copy of the grant application. There is an exception to this requirement for multi-site research; the requirement for IRB review of the grant applies only to the awardee institution. The grant generally need not be reviewed by the IRBs (including WIRB) at non-awardee institutions participating in the multi-site research; however, there may be situations or certain types of research in which the Board may require the complete grant as part of its review for an investigator at a non-awardee institution.

ii. FWAs

When an institution (a legal entity) receives federal funding for research, the institution usually must obtain an assurance as required under section 45 CFR § 46.103 of the Common Rule. Each separate legal entity that is engaged in the research must obtain an assurance. For research funded by agencies that are part of the Department of Health and Human Services (HHS), this will usually be a Federalwide Assurance (FWA) obtained from the Office for Human Research Protections (OHRP). Those agencies outside of HHS that have adopted the Common Rule may

accept a Federalwide assurance, or may use a different assurance mechanism. OHRP provides guidance on when an institution is engaged in research at <http://www.dhhs.gov/ohrp/humansubjects/guidance/engage08.html>.

Prior to the Board's review of federally funded research, the following requirements must be met:

- 1) As described in the OHRP guidance entitled "Engagement of Institutions in Research," a Federalwide Assurance (FWA) must be filed for all sites engaged in federally funded research.
The guidance is available at <http://www.hhs.gov/ohrp/humansubjects/assurance/engage.htm>. The FWA form is posted on the OHRP website. You can access this form at http://www.hhs.gov/ohrp/assurances/assurances_index.html#domestic. Provide WIRB with a copy of the HHS-approved FWA application.
- 2) An IRB Authorization Agreement must be completed. See [appendix 5](#) for a sample pre-filled authorization agreement in which WIRB is listed as Institution A. Complete the Institution B sections of the form.
- 3) WIRB requires that Investigator Training Certificates must be on file with WIRB prior to WIRB review of the research. The investigator and key personnel must complete the NIH training ("Protecting Human Research Participants") at <http://phrp.nihtraining.com/users/login.php>, or an equivalent course. "Key personnel" are all individuals responsible for the design and conduct of the study. **Modules 1, 2 and 3 of the OHRP training modules must be completed by the Signatory Official (on the FWA) and the Human Protections Administrator (primary contact).** The OHRP training can be found at <http://137.187.172.153/CBTs/Assurance/login.asp>.

At the time of initial review of the protocol, the Board also participates in a teleconference with a member of the research staff at the site. The attendee in this teleconference is typically the study coordinator or another full-time employee who can answer basic questions about the research facilities, subject recruitment, consent processes, and community attitudes toward research.

Additional information about FWAs and IRB review of federally funded research can be found on the OHRP website at <http://www.hhs.gov/ohrp/>.

Contact WIRB's Client Services for clarification or assistance regarding these requirements.

J. Special considerations for multi-center studies

Each individual submission for a multi-center study must be accompanied by a completed WIRB initial review submission form. We recommend using the "smart" online form available via the WIRBNet Login button on wirb.com. The "smart form" submission is generally a shorter process because it dynamically omits questions that are not relevant, based on the answers you provide about the research.

If you aren't able to use the "smart" online form to submit, submission forms are available on the WIRB website at www.wirb.com or can be requested from Client Services by calling 1-800-562-4789 or e-mailing clientservices@wirb.com. WIRB offers three versions of its initial review submission form. Investigators participating in multi-center protocols which have already been reviewed by WIRB may fill out a shorter version called **Investigator Submission Form for Multi-Center Protocols**. Investigators submitting protocols that have not been previously reviewed by WIRB must complete the full length **Initial Review Submission Form**. Sponsors and CROs who desire pre-review of the protocol and subject materials, may use the version called **Initial Review Submission Form for Sponsors and CROs**.

Any site submission lacking a complete submission form, FDA form 1572 (when applicable), current CV and license, or proof of a current medical license (when applicable) will not be scheduled for review until the missing information is submitted. Depending on the type of research, additional information may also be required. Contact WIRB Client Services for information about submission requirements for specific types of research.

The Sponsor or CRO contact will receive copies of the reviewed documents sent to investigators, unless otherwise requested in writing.

i. Consent forms for multi-center research

Once the Board has reviewed and approved a consent form for a multi-center protocol, submitting sites may request the previously-approved version of the form. **Opting to use the previously-approved version can significantly reduce the processing time, and result in more rapid receipt of approval documents.** Sites request use of the previously-approved form on the submission form. Investigators who choose to use the previously-approved consent form should not include a consent form with their submitted materials; WIRB will generate a consent form for the PI by incorporating any institutionally-required language and the site-specific information such as payment information, locations, etc. into the previously-approved consent.

Site-specific information which must be provided on the WIRB submission form includes:

- All **telephone numbers** for the consent form, including a 24-hour number for emergencies (for research that is greater than minimal risk) .
- **Payment for participation** information. Indicate either "no payment" or provide a statement explaining the payment plan as you would like it to appear in the consent form (amounts, visits not paid, when payment will be made). Please double-check your math, and please submit to us the exact wording you would like to have used. Misunderstandings concerning the subject payment plan are a major source of corrections and subject complaints. Also, please be sure your payment plans agree with the sponsor's preferences, if any.

To determine if a previously approved consent form is available for a particular protocol, contact Client Services at 1-800-562-4789.

ii. Impact of changes

Investigators choosing not to use a previously approved or template consent form will experience delays in the review process while their unique consent forms are prepared for Board review.

Additional delays may occur if the Board has questions about the consent form or if the investigator does not accept Board-required changes to the submitted consent form.

iii. National ad campaigns / Advertisements for all investigators

Sponsors and CROs will benefit from submitting **advertising and other recruitment materials** with the initial review submission, as later submissions incur a fee for review. Audio and video recordings must be accompanied by the script. Please submit the script for review before the advertisement is recorded, so that any board-directed changes can be reflected in the recording.

Advertisements which will be used by some or all participating investigators should be identified as such in the cover letter or submission form. Identifying shared advertisements as such will help ensure consistent review of materials for all participating sites. For best results, when submitting subject recruitment materials or other subject materials (diaries, questionnaires, etc.) that have been previously reviewed by WIRB, state in the cover letter that the items have been previously reviewed by WIRB. Board support staff will provide the Board with information about the previous Board review, so that the previous decision of the Board can be taken into account when the additional materials are reviewed.

iv. Approvable submissions

WIRB can assist sponsors and CROs during the planning stages of a multi-center study by pre-reviewing the protocol and subject materials, including a template (or “master”) consent form. The fee for initial review applies.

If the Board finds the research as reviewed acceptable (“approvable”), the submitter is issued a letter documenting the Board’s determination, a redlined template consent form indicating the Board’s changes, and appropriate documentation of the review of the other subject materials submitted. It is important to note, however, that no Certificate of Approval (COA) is issued, and the research cannot go forward until appropriate documentation for an investigator has been received and reviewed by the Board, and a COA has been issued for that investigator.

The following is a general list of items needed by WIRB to conduct an approvable review:

- WIRB initial review submission form for Approvables: “**Initial Review Submission Form for Sponsors and CROs**”
- Protocol
- Template Consent form
- Other written materials to be provided to the subjects that are not included in the protocol, such as questionnaires, subject diaries, etc.

If a **drug/biologic** or food supplement study, provide a copy of the following:

- Investigator’s Drug Brochure
- Background Information for Food Supplements

If a **device** study, provide ONE of the following:

- FDA Letter granting the Investigational Device Exemption (IDE) for the proposed use (please do not provide a *redacted* copy); OR

- Letter from sponsor stating that the study is a non-significant risk device study (please do not provide a *redacted* copy); OR
- Letter explaining why the investigation is exempt from the IDE requirements under 21 CFR 812.2(c) or otherwise exempt.

Following Board review for approvable status, individual investigators may be submitted.

- Sites that plan to use the approvable template language should not include a consent form document with their submitted review materials, and should answer “Yes” to the question on the initial review submission form which asks “For **multi-center studies**, it is likely a consent form for this protocol has already been approved by WIRB. If available, would you like to use it?” WIRB will use the submitted information from each site to add site-specific information (such as telephone numbers, payment for participation, etc.) to the consent form template found approvable by the Board.
- When WIRB receives a submission from a site in Canada and the research was found approvable by a U.S. panel, the submission is reviewed by WIRB’s Canadian panel, which reviews and modifies consent forms according to Health Canada regulations. Language in consent forms approved by the Canadian panel may differ from the language in the approvable consent form produced by a WIRB U.S. panel.

Sponsors of research involving multiple Canadian locations may benefit from requesting an “approvable” review by WIRB’s Canadian panel prior to submitting Canadian investigators for review.

- When WIRB receives a submission from an investigator at an institution, WIRB may modify the language in the approvable consent form to conform to the institution’s requirements.

If WIRB does not receive an investigator submission within 10 months of the original review, WIRB will inquire if the sponsor plans to submit any sites. If the sponsor indicates they plan to submit more sites, WIRB will keep the protocol open. If the sponsor indicates they do not plan to submit sites after all, or if WIRB does not receive a response to the inquiry, the protocol will be closed (in the event that WIRB receives an investigator submission for the protocol, WIRB will schedule a new review of the research; initial review fees apply).

K. Special considerations for international research

i. Canadian researchers

The WIRB Canadian Panel is located in Vancouver, Canada. Its membership is compliant with the requirements outlined in the Division 5 regulations of Health Canada. This panel is able to review research for Canadian sites that do not need to use their own local research ethics board. For more information about the WIRB Canadian Panel, please call Client Services at 800-562-4789 or the WIRB Canadian office in Vancouver at 604-872-5030.

ii. Countries requiring dual IRB review

When WIRB reviews research in other countries, it obtains information on local laws and local attitudes, and welcomes the help of investigators and sponsors in obtaining this information. WIRB prefers that in international research there be a local IRB or other review committee that oversees the research in addition to WIRB, in order to help ensure that the research is culturally acceptable. However, WIRB is willing to consider international research in which there is no local IRB as long as dual IRB review is not required by local law and WIRB is able to receive adequate information about the cultural acceptability of the research. Usually this is accomplished through the participation of someone knowledgeable about the culture in the convened board meeting.

iii. Consent form considerations for non-English speaking countries

When WIRB enters into a dual IRB agreement with another IRB to oversee the research, all changes to the consent form will be subject to approval by both IRBs. When the WIRB-approved consent form is translated by the other IRB, WIRB will not routinely conduct its own verification of the translation (as is customary for translations for studies conducted in the U.S. and Canada) unless the circumstances warrant it. Translated versions of the consent form are not required to display a WIRB approval stamp and sites are not required to adhere to the statement on the second page of the Certificate of Approval which says “Provide non-English speaking subjects with a certified translation of the approved consent form in the subject's first language. The translation must be approved by WIRB.”

L. Special considerations for investigators at institutions

In addition to meeting the requirements of WIRB, an investigator at an institution may be subject to local institutional requirements. Institutional investigators should check with their local research office to determine what requirements, if any, must be fulfilled prior to submitting research to WIRB. Such issues as pre-review by internal committees, use of template consent form language, and approval/submission through a central office should be addressed with your local institutional officials.

M. Special considerations for subjects who do not speak English

All consent forms and other subject materials must be in a language easily understood by the subject, and all translations must be approved by WIRB. WIRB provides translations services for WIRB-approved sites only.

If you are enrolling non-English speaking subjects, you must have plans for conducting the consent discussion in the language understandable to the subject, and for ongoing communication with the subject throughout the research and in case of emergency. The WIRB initial review submission form solicits information about plans for ensuring adequate communication. Sites may, for example, ensure at least one member of the research team is fluent in the language, and that research staff member(s) will be available during emergencies; or ensure the research team has 24-hour access to a translation service with sufficient medical expertise to discuss the research.

If a non-English speaking subject may receive benefit from study participation, and that benefit is not available outside of the study, under very restricted circumstances WIRB may allow an ad hoc oral translation of the consent form if time or financial restraints affect the subject's safety. Please request WIRB review of these situations.

i. WIRB-Arranged Translations:

Translations requested on the submission form are sent to a qualified translator **after the English materials are finalized and sent to the site**. This timeline ensures the materials sent for translation are the final version.

If a research study is approved without a translated consent form and a non-English speaking subject later qualifies for enrollment, the site can obtain a translated version of the consent form for use in consenting the subject by submitting a request to the WIRB Translations Department. The request should identify the Sponsor, Sponsor Protocol Number, Investigator and the language requested. The subject cannot be enrolled until they have received the WIRB-approved translated consent. If WIRB is asked to provide a price quote for the translation, the translation process will not begin until WIRB receives authorization to proceed.

WIRB bills an administrative fee for translation services in addition to the translator's fee. The bill is sent to the party requesting the translation or their designee (WIRB requires written confirmation that the designee will accept the invoice). Sites who subsequently request the same translation are billed only the administrative fee, unless their consent form includes site-specific changes that require additional translation.

WIRB suggests that before sites request a translation, they check with their sponsor to determine if the sponsor already has made a translation or arrangements for translation, and if not, if the sponsor is willing to pay for a WIRB translation.

ii. Sponsor/CRO/Site Translations:

The **WIRB-approved version** of the consent form or other materials may be translated and submitted to the Board along with a certification statement signed by the translator that identifies the specific translated documents and attests to the translator's fluency and the accuracy of the translation from English to the target language (see sample format below). The translation must correspond to the WIRB approved version of the material; therefore, a translation of the sponsor template consent form or materials is not acceptable.

If the translation is acceptable, the approval date will be affixed by WIRB staff and an approved copy sent to the site.

Other documents (e.g., subject diaries, subject instructions) need to be legible (faxed copies often are not legible) and accompanied by a translator certification statement.

Sample Certification Statement:

CERTIFICATION

I hereby certify that I am fluent in English and [name of language] and that I have, to the best of my knowledge and belief, made a true and complete translation from English to [name of language] of the WIRB approved [name of document; e.g., Research Subject Information and Consent Form, advertisement] for [sponsor / protocol number], [WIRB protocol number] this _____ day of _____, [*month / year*].

(Signature of Translator)

Name of Certification (*ATA, DSHS, other*) _____
Certificate No. _____

N. Special considerations for enrollment of wards of the state

WIRB initial review submission forms ask sites if they plan to enroll **wards of the state**. Federal regulation 45 CFR §46.409 outlines special requirements for the involvement of wards in research. Sites that plan to enroll wards may be required to provide a plan for appointing an advocate for each subject.

9. The review process

A. Board Actions

The Board may take a variety of actions upon review of a submission.

i. Approve

When the Board takes an “approve” action on new research (or a change in research), it is accepting oversight (or continued oversight) of the research and allowing the research to go forward as approved.

When the approval is based on Board-required consent form modifications, the investigator will be provided with a finalized consent form with the required modifications incorporated by WIRB staff. When the approval is based on Board-required modifications to other materials, the investigator is responsible for incorporating the changes prior to using the materials. Such modifications will be indicated on the items or in a letter.

Approval is usually communicated to the investigator by a Certificate of Approval (COA).

Upon approval of a new study, the following are prepared and sent to the PI, Sponsor or CRO, SMO, and institution (as applicable):

A Certificate of Approval

A copy of the Board-approved consent form (when applicable), ready for use.

Depending on the type and extent of the Board's changes, a redline of the changes to the consent form. Redlines annotated with legend codes are accompanied by the legend "Reasons for Change."

Explanatory letters, if directed by Board or otherwise necessary. Letters are used to communicate special Board determinations, requirements, or other necessary information.

ii. Approve in Principle

An "Approve in Principle" action is only used when a federal funding agency requires IRB approval before grant monies can be released, and the investigator does not have the funding to complete the research proposal until the grant monies are released. The Board takes this action if it appears the research will be acceptable when the proposal is completed. The Board's determination is communicated by letter (no Certificate of Approval issued), and does not grant approval for initiation of activities involving human subjects. Upon completion of the research proposal, the protocol, consent form, and other required elements must be submitted to WIRB and approved before activities involving human subjects can begin.

iii. Approvable

An "approvable" determination indicates the research as reviewed is acceptable to the Board. For new research found "approvable," the research cannot go forward until the Board approves an investigator. Consent forms and subject materials found approvable by the Board may be subsequently modified by the Board.

When the Board takes an "approvable" action on an audio or video script, a recording of the script cannot be used until a final version has been reviewed and approved by the Board (i.e., the audio or video recording).

An "approvable" action is communicated to the submitter by letter. (A COA is not issued for approvable studies and scripts, and an approval stamp is not affixed to "approvable" consent documents.) If a script is found "Approvable As Modified," the final audio-video product must contain the modifications made by the Board.

iv. Disapprove

When the Board takes a "disapprove" action on new research, it is rejecting oversight of the project as submitted, and the research is not allowed to go forward.

When the Board takes a "disapprove" action on a change in research, the change cannot be implemented, and the Board expects the research will continue as previously approved.

Disapproval may occur for a variety of reasons, most of which involve subject safety and/or scientific validity. Disapproval is communicated to the investigator by letter, in which the reasons for disapproval are explained.

Reconsideration of a disapproval may be requested and is taken to the same panel which voted the disapproval. Additional information may be provided to the Board for its consideration. The investigator may appear before the Board in person or via teleconference, if desired.

v. Table (“Defer” in Canada)

The Board takes a “table” action to remove an item from Board consideration at a scheduled meeting and obtain additional information or clarification. Staff and/or Board members follow up as directed with the investigator or sponsor to address the reasons for tabling the item. Staff prepare the item and reschedule it for the Board to complete its review. A tabled item is brought back to the same panel that tabled it. Additional information may be provided to the Board for its consideration. The investigator may appear before the Board in person or via teleconferencing, if desired.

Some of the common reasons for Board tabling an item are discussed below:

- **Incomplete submissions and inaccurate information.** If answers on the WIRB submission form are left blank, the answers don’t make sense, or they conflict with the protocol, the Board is unable to make an appropriate decision and may table the item to request further information. We recommend using the “smart” online form available via the WIRBNet Login button on wirb.com to avoid accidental omissions; the smart form does not allow you to move on if a required field has been left blank.
- **Protocol allows legally authorized representatives (LARs) to consent for subjects when not ethically appropriate.** Sometimes protocols contain standard language stating that the subject or their LAR may consent to research, even when the research can be ethically conducted using only capable subjects who are able to consent for themselves. The Board bases its decision on the basic ethical principle that research studies should only enroll subjects who do not have full mental capacity when the study cannot be conducted in any other way, unless there is a significant prospect of direct benefit to those subjects that is not otherwise available. Please make sure that your protocol does not unnecessarily include incapable adult subjects.
- **Not all members of the research team have completed training in human subjects protection.** WIRB requires that all investigators and their research staff complete human subject protection training prior to submitting to WIRB. (HIPAA training alone is not sufficient.) More information about available training in human subject protection is available here: http://www.wirb.com/content/foot_wirb_training_resources.aspx. Since treatment use INDs and treatment use IDEs (as defined at 21 CFR 312.34 or 21 CFR 812.36) are not “research” in the usual sense, physicians requesting approval of single-patient treatment use INDs and IDEs are generally exempted from this requirement.
- **Local law requirements are not met or prevent conduct of the research.** The Board may table a submission when specific local law requirements are not met. For example, there are requirements that must be met when a study conducted in New Jersey involves incapable adults. If the additional requirements are not met, the Board must table the study. The WIRB Initial Review Submission Form contains extra instruction for investigators in those states that have additional regulatory requirements that need to be fulfilled prior to Board approval.

- **IND or IDE issues.** One of WIRB’s requirements is that IND and IDE requirements are satisfied. Some submissions received by WIRB need an IDE or IND and do not have one. For more information on IDE and IND requirements, please see http://www.wirb.com/content/sponsor_cro.aspx.
- **Emergency plans or hospital privileges not sufficient.** The WIRB Initial Review Submission form asks for information about the facility to be used in an emergency and whether the PI or sub-investigator have staff privileges at the facility. If the answer is no, WIRB requires a plan be submitted that describes how subjects will be referred for hospitalization, contact information for a physician that has agreed to attend to these patients and a description of what measures will be used to assure communication between the investigator and the attending physician.
- **Risks to subjects outweigh benefits.** The Board provides a letter outlining the reasons why the risk to benefit ratio was determined to be unacceptable.
- **Scientific validity is lacking.** The Board provides a letter outlining the reasons why it determined that the research lacked scientific validity.
- **Justice issues.** Board will consider whether groups are inappropriately included (such as pregnant women, mentally incapable persons and children) or are inappropriately excluded (like women or minorities) from the research.
- **Consent issues.**
 - **Consent in emergent setting.** In emergent settings, subjects have limited time and are often impaired in their ability to make informed decisions about participating in research. The Board gives special consideration to the consent process when it will take place in an emergency setting and requires that an acceptable process be in place for obtaining consent. WIRB’s initial review submission form requests detailed information about the consent process in emergent settings.
 - **The process for obtaining consent over the Internet or telephone is not sufficiently explained.** WIRB must be assured that the elements of consent required by the regulations are still addressed and that security and privacy concerns are addressed.
 - **Request for waiver of consent or waiver of documentation of consent not adequately justified.** There are certain regulatory requirements that need to be met for waivers of consent and waivers of documentation of consent to be acceptable in research. WIRB has specific forms used to collect information about waivers of that will help the Board determine if the waiver is appropriate. More information about the requirements for waivers can be found at http://www.wirb.com/content/foot_wirb_faq.aspx.
 - **Consent of secondary subjects is not addressed.** When the project proposes the collection of information about an individual from someone else (for example, medical information about an identifiable relative of the subject) without direct contact with the individual, that individual may be considered a “secondary subject” and consent (or a waiver of consent) for that individual needs to be considered. For more information, please see the OHRP guidance available online here: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.102>.

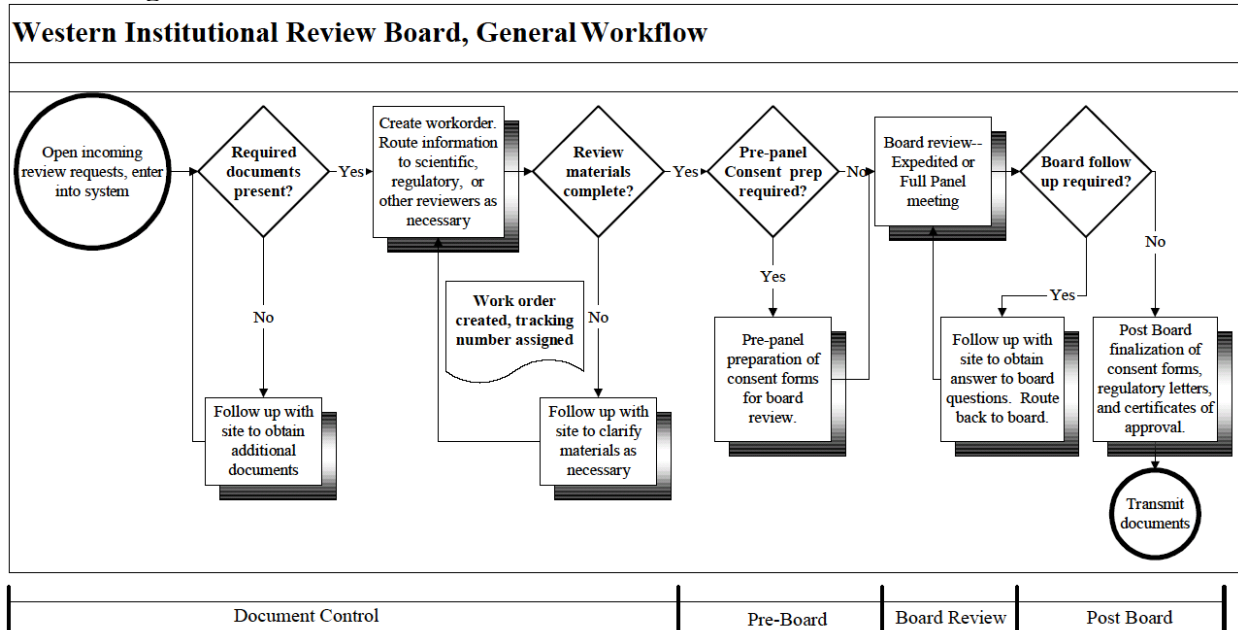
- **Recruitment issues insufficiently addressed or not addressed.** The most common issues the Board encounters with subject recruitment methods are outlined below:
 - Screening scripts that do not contain the required information, or are not accompanied by the WIRB Screening Procedures Information Form. WIRB’s screening requirements are outlined at the end of its Screening Procedures Information Form.
 - Cold calls. As a general principle, when potential subjects are being recruited for research based on a review of their non-public medical information, the contact should be initiated by a clinical provider who has had a provider relationship with the potential subject.
 - The process for recruitment of subjects is not described at all.
- **Inconsistency in documents.** If during review of the submitted documents (protocol, consent forms, advertisements), the Board finds inconsistency either within the documents or between documents, they may table the submission and request clarification of the inconsistencies.
- **Consent forms.** The Board can make changes to the consent form. However, some consent forms can not be fixed by Board when:
 - The consent form and protocol are not consistent (for example, the consent form cites additional procedures not included in the protocol, such as additional blood draws or collection of tissue samples for future research; or the consent form was developed from another protocol and there is language in the consent form that is left over from the other protocol).
 - The information in the consent form is internally inconsistent (for example, the compensation for injury text provided by the sponsor conflicts with the compensation for injury text required by the investigator’s institution).
 - The consent form is poorly written and requires extensive changes.

vi. Pull

The Board may “pull” an agenda item at the request of the submitter, WIRB staff, or the Board itself. An item generally is pulled before the Board begins consideration of the item in a meeting due to missing or incomplete review information.

Staff and/or Board members follow up as directed with the investigator or sponsor to address the reasons for pulling the item.

B. Diagram of WIRB Workflow



10. Changes to Research / Additional Document Submissions

A. Changes to Research

Whenever a **change to the protocol or consent form** is proposed, the change must be reviewed and approved by WIRB before being implemented, unless a serious safety concern requires immediate implementation by the investigator.

See [appendix 7](#) for a summary checklist of Change in Research submission requirements.

Use the **WIRB Change in Research and Subject Recruitment Submission Form** to submit requests for review of changes to protocols, consent forms or subject materials; review of new consent forms and subject materials; or review of new or modified recruitment materials.

i. How to submit a protocol change

Requests for review of protocol changes must include the exact text of the amendment, administrative change, or other revision to the protocol, a summary of changes, the rationale for the change and a copy of the WIRB-approved consent form with the proposed changes clearly marked (if applicable). Proposed changes to the consent form should be “redlined” into an electronic copy of **the current WIRB-approved consent form**. WIRB does not recommend marking changes with a highlighter alone, as the highlighting can be lost or obscure information when the document is scanned into WIRB’s electronic workflow system.

ii. How to submit a consent form modification

Requests for consent form modifications should consist of the WIRB Change in Research and Subject Recruitment (Ads) Submission Form, an updated 1572 (if applicable), and a copy of the WIRB-approved consent form with proposed changes clearly-marked (or a document specifying

the requested changes). Changes sent to WIRB on the sponsor's template consent form will not be accepted. Proposed changes to the consent form should be "redlined" into an electronic copy of the current WIRB-approved consent form. WIRB does not recommend marking changes with a highlighter alone, as the highlighting can be lost or can obscure information when the document is scanned into WIRB's electronic workflow system. In general, a statement justifying changes is very helpful and can reduce the need for WIRB to contact sites for explanations. Whenever revisions are requested to previously Board-approved language, the submission must include a rationale.

We recommend using the "smart" online form available via the WIRBNet Login button on wirb.com. The "smart form" submission is generally a shorter process because it dynamically omits questions that are not relevant, based on the answers you provide about the research. Requests for review can also be submitted to WIRB online from its web site, mailed, or e-mailed (clientservices@wirb.com). Submissions should reference the sponsor protocol number, WIRB study number, and name(s) of applicable investigator(s).

After January 1, 2009, whenever WIRB receives a request for a revised consent form in any format other than the two formats described above, the submission will be returned to the submitter with a request that the changes be sent to WIRB as described above.

If the changes are to be submitted for a multi-site study, the same changes might have already been approved by WIRB for another site. If you agree to accept the changes already approved, the review will take place more quickly. You can contact WIRB Client Services to determine if pre-approved language exists for your change in research.

iii. How to Request a Reconsideration

Requests for a *reconsideration* of a Board action should be accompanied by a rationale for the request. Additional information may allow the Board to favorably respond to the request. There is no additional fee for reconsiderations of disapproved items. Likewise, reconsiderations of board-directed modifications to consent forms and other subject materials or recruitment materials do not incur additional fees if the reconsideration is in regard to the language *originally reviewed* by the Board. If new or alternate language is submitted, the Change to Research fee applies.

iv. How to Submit a Change of Principal Investigator

The Board requires written confirmation from the sponsor that the change is acceptable and has been approved, a letter from the old investigator relinquishing responsibility for the study (when available), and a letter from the new investigator accepting responsibility for the study. The sponsor is required to select investigators under 21 CFR 312.53(a).

Also submit a WIRB **initial review submission form** (the shorter version titled "Investigator Submission Form for Multi-Center Protocols," may be submitted, as the protocol has already been approved), license and CV for the new investigator (unless current versions are already on file with WIRB), a modified 1572 (when applicable), and a request to modify the existing consent form to reflect the new investigator's name and contact information (when applicable).

v. How to Submit an Updated Drug Brochure

Updated drug brochures should be accompanied by a cover letter identifying the name of the Principal Investigator, the drug, and the WIRB protocol and study numbers. Since brochures provide factual background information for the research, WIRB does not “approve” drug brochures or revisions to them.

B. Additional changes which require notification to WIRB

- Notify WIRB of changes of address or telephone for the investigator or the site(s). (If you are adding a site or moving to a new site, complete a WIRB Additional Site form for each new or updated location and forward to us.)
- Notify WIRB of changes of address, or telephone for study or sponsor contacts.
- Notify WIRB of transfers of subjects (include information about why, to whom, and sponsor approval of transfer).
- Notify WIRB of increases in the number of subjects allowed at the specific investigator site (indicate if a consent form change is needed).

Minor administrative changes sent to the investigator from the sponsor generally should be submitted to WIRB for review as “Administrative Letters” or “Administrative Changes.” This type of change might consist of sponsor notifications of changes to the status of the protocol (such as completion of enrollment, completion of a cohort, ending development of a test article).

The above list is not an exhaustive listing of the changes in research that may need to be reported to WIRB. If you are in doubt about submitting a particular item, call Client Services at 1-800-562-4789 or e-mail clientservices@wirb.com.

C. Subject Recruitment Materials (Ads, etc.)

The WIRB “**Change in Research and Subject Recruitment Submission Form**” may be used to submit advertisements for review after initial review of the research. As much as possible, print ads should be submitted as they will appear in print, so that the Board can assess the impact of design details, such as photographs, other images, and font sizes and styles.

WIRB does not allow **referral fees** (offering or accepting payment for referring patients to research studies, sometimes referred to as “finder’s fees”) for medical professionals or research staff. Payments to subjects for referring others may be considered by the Board on a case-by-case basis. This is in accordance with the American Medical Association Code of Medical Ethics which states, “Offering or accepting payment for referring patients to research studies (finder’s fees) is also unethical.” Some states have laws that ban such practices.

Most changes to approved advertisements must be reviewed by WIRB prior to their use, particularly anything that could alter the impact of an advertisement previously reviewed by the Board. Changes to approved advertisements that do not need to be submitted for review include updates to phone numbers or contact names referenced in an advertisement and corrections to spelling.

For best results, when submitting subject recruitment materials or other subject materials (diaries, questionnaires, etc.) that have been previously reviewed by WIRB, state in the cover letter that the items have been previously reviewed by WIRB. WIRB support staff will provide the Board with information about the previous Board review, so that the previous decision of the Board will be taken into account when the materials are reviewed.

Information packets, patient brochures, sponsor brochures and informational videos are all considered recruitment materials if they are intended to be seen by a *potential* subject.

Audio and Video Recruitment Materials: All audio and video materials should be accompanied by the script.

To avoid unnecessary additional production costs due to re-work, it is strongly recommended that WIRB approval of scripts for planned audio or visual recruitment materials be obtained *before* producing the spots. Any Board-required modifications to the material must be reflected in the final version of the recording.

When audio or video scripts are sent to WIRB for review, WIRB pre-reviews the script and, if acceptable, finds the script “Approvable - As Modified” or “Approvable - As Submitted.” The submitter receives a letter documenting the Board’s determination, along with a copy of the script stamped with the WIRB “Approvable” stamp and displaying the Board’s modifications, if any. **Recruitment materials found “approvable” will not be considered “approved” until after the audio or video recording has been reviewed by the Board.** No additional fee is incurred for the review of recordings if the script was previously found “approvable.” The final recording **MUST** match the WIRB approvable script. Submit a copy of the corresponding script bearing the WIRB “approvable” stamp when you send the recording to WIRB for review.

Ads for all sites: Advertisements which will be used by some or all participating investigators should be identified as such in the cover letter or submission form. Identifying shared advertisements as such will help ensure consistent review of materials for all participating sites.

Press Releases: WIRB reviews submitted press releases as advertising.

Logos: If the Board considers elements of a logo in an advertisement to be coercive or overly reassuring, they will direct that the logo be removed from the ad or be modified to eliminate the objectionable element(s).

Public service announcements and phone system “on hold” messages: Public service announcements and audio scripts of messages that will be broadcast to callers who have been placed on hold are considered recruitment materials, and will be reviewed by the Board and, if acceptable, approved either “as submitted” or “as modified.”

Website Content: WIRB review requirements for web content are dependent on the type of content in question.

- ClinicalTrials.gov-type sites which provide a limited set of pre-formatted fields for inclusion of recruitment content do not need to be submitted for IRB review. If requested, WIRB will review submissions of such content. FDA Guidance regarding use of media advertising to recruit subjects can be found at <http://www.fda.gov/oc/ohrt/irbs/toc4.html#recruiting>.
- Subject recruitment content on sponsor websites requires IRB review. **Only the content relevant to research should be submitted for review.** It may be appropriate to request WIRB review of these materials as generic recruitment materials (for more information about generic reviews, see the section of this handbook titled “Review of “Generic” Materials”). The content should not be posted until WIRB has approved it.
- Subject recruitment content on investigator or SMO websites requires IRB review. **Only the content relevant to research should be submitted for review.** The content should not be posted until WIRB has approved it.

Only content pertaining to research needs to be reviewed by the IRB. Submit to WIRB only website content which provides information to potential subjects about research participation, as well as information about specific studies that WIRB oversees. General website information that does not relate to research participation, such as disease information or driving directions to the research office, does not require review.

WIRB does not review the content of the links to other websites that are present on submitted websites. The website owner should ensure the links are appropriate.

The web owner is responsible for making the Board-directed changes to reviewed website content before using that content for recruitment.

Changes made to approved website content should be submitted for Board review before the changes are posted to the web.

Website content can be reviewed either in relation to a specific protocol or as generic recruitment material. If the material is reviewed and approved as a “generic,” an expiration date is assigned (usually a year from the approval), and the Board conducts re-review of the content when the expiration date approaches, unless WIRB receives a request to close the file.

Recruitment materials that WIRB does not review

The FDA Information Sheets state:

Direct advertising includes, but is not necessarily limited to: newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects. **Not included** are: (1) communications intended to be seen or heard by health professionals, such as "dear doctor" letters and doctor-to-doctor letters (even when soliciting for study subjects), (2) news stories and (3) publicity intended for other audiences, such as financial page advertisements directed toward prospective investors.

Based on this guidance, WIRB does not require IRB review of doctor-to-doctor letters, or prior IRB review of interviews with the media (as noted previously, this does not apply to “press releases”).

D. “Do’s” and “Don’ts” for Recruitment Materials (Advertising)

Over time, WIRB has developed standards for ad review that are consistent with federal guidance on recruitment materials, and serve to maintain consistency in the Board review of these materials. The following points summarize these standards and serve as a guide to Board changes or disapprovals of recruitment materials.

Do:

- Comply with the guidance in the FDA Information Sheet, “Recruiting Study Subjects.”
- Include a clear statement that the information concerns a research study.
- Include general information about who is eligible to participate.
- Provide information about how to find out more.
- Be conservative with the use of pictures, graphics, fonts and symbols.

Don’t:

- Do **not** state or imply that the FDA or IRB has approved the research.
- Do **not** call investigational drugs, devices, or procedures “*new*,” “*safe*,” “*effective*,” “*a cure*,” “*treatment*” or “*therapy*.”
- Do **not** call the investigational medication simply “*medication*” or “*drug*;” qualify each use appropriately with “*investigational*” or “*study*” as in “*investigational medication*” or “*study medication*.”
- Do **not** emphasize payment to subjects or the word “free” (e.g., bold, large font, multiple dollar signs).
- Do **not** include payment amounts for studies involving underage subjects.
- Do **not** use the terms “*confidential*” or “*completely private*.”
- Do **not** include exaggerated statements about the potential benefits of participating in the research, receiving treatment from the investigator, or receiving treatment from the organization.
- Do **not** use the phrases “*Enrollment Limited*,” “*Study ends soon*,” or “*Call today!*”
- Do **not** include the statements “*You deserve to feel better*,” “*Join this study and take charge of your life*,” or similar phrases or logos.
- Do **not** include references to website recruitment content that has not been reviewed and approved by an IRB.
- Do **not** include statements of implied safety and/or efficacy.
- Do **not** include inappropriate promises of benefit.
- Do **not** include misleading content.
- Do **not** use potentially coercive or reassuring graphics, pictures, fonts or symbols.

E. WIRB Requirements for Screening Materials

Please complete the **WIRB Screening Procedures Information Form** (available on the Download Forms page of www.wirb.com or by contacting WIRB Client Services) and include it with requests for review of screening materials.

Submitted screening materials should conform to the following Board requirements. If you plan to screen Canadian citizens, please call Client Services for more information about Canadian screening requirements.

Introductory Statement:

- The screening script must include an introductory statement that informs the subject of the purpose of the questions and that they do not have to answer any questions they do not want to answer.
- The script must not describe the type of questions that will be asked as “confidential;” i.e., rather than saying “we would like to ask you some *confidential* questions,” say “we would like to ask you some questions.” It is acceptable to say “personal questions” or “sensitive questions.” The purpose of this policy is to prevent any possible misunderstanding that the answers will be held in complete confidence.
- When appropriate, the script must include an introductory statement warning the subjects of the sensitive nature of the questions that might make the subject uncomfortable, and preferably include an example (for instance, “We are going to ask you about drug or alcohol use.”) This will generally be limited to questions about mental illness, substance abuse, and sexual abuse. For these types of screening scripts, it may be appropriate to not collect any identifying information until after the questions are asked; i.e., collect the name and other identifying information at the end of the conversation and the form.

Here is a sample introductory statement:

[Thank you for calling] (or) [We are returning your call] about a research study we will be doing. The purpose of the study is [briefly describe study - e.g., “. . . to evaluate the safety and effectiveness of an investigational drug for arthritis”]. Participation in this study would last about [number of days, weeks, etc.] and (if applicable) would require up to [number] of visits to our office.

To see if you might qualify for this study, I need to ask you some questions about your health history and present condition. Some of these questions may be sensitive, such as questions about [give examples - e.g., drug use, birth control, mental health, sexual activity, etc.] You do not have to answer any questions you do not want to answer. You may stop this interview at any time. If you do not qualify for this study, the information you give me will be [e.g., “destroyed immediately” or “stored (where and for how long)”]. Do I have your permission to proceed? "

Body of Screening Form

- The Board expects to see the actual questions that will be asked, not just a general statement such as “inclusion/exclusion criteria addressed.”

Closing Statement

- The script must include a closing statement informing the subject of whether or not they have met the preliminary screening requirements.
- The script must address in a closing statement whether the information received from the subject will be destroyed immediately, or whether it will be stored, and if so for how long and where.
- If the site would like to keep information for future contact for new studies, the site should describe to the subject as well, and the subject must have an opportunity to decline.

Additional Issues

- The screening script must be in language understandable by lay people. If complicated medical terms must be included in the screening script, please provide WIRB with an explanation of how they will be explained to the subjects.
- WIRB realizes that the script may not be followed verbatim, as subjects may ask additional questions or stray from the topic. This is acceptable, but WIRB expects that the interviewer will keep as closely as possible to the spirit and letter of the script.
- It is useful to WIRB if the investigator informs WIRB of the use of the recruitment screen; e.g., if it is going to be used with subjects calling in from advertisements, for calling patients listed in a database, or for conducting cold calls.

11. Review of “Generic” Materials

“Generic” materials include items that an investigator would like to use outside of the context of a specific protocol, or materials that a sponsor/CRO/SMO would like to use that do not identify any one specific investigator and/or protocol. Common types of generic materials include:

- Generic Advertising, including Brochures, audio-visual materials, Web Content
- Generic Pre-Study Screening Consent Forms
- Generic Telephone Screening Scripts
- Generic Consent for Photography

A. Generic Consent Forms

Generic consent forms should contain all the usual consent form elements defined in federal regulations and guidance (see section titled Consent Form Elements). As much detail as possible should be included. Many times general research participation information will be included, with a listing of types of research the investigator is conducting.

WIRB imposes the following limitations on generic consent forms:

- Pre-study screening done outside of a specific research protocol should be limited to minimal risk procedures.

- Current treatment or medications should not be adjusted in order to do the screening.

Accordingly, prospective subjects should not undergo a washout or biopsy as a generic pre-screening activity; instead, the subject should be fully consented for the related protocol before beginning that protocol's screening activities.

B. Generic Advertisements

WIRB reviews “generic” advertisements linked to a company or an investigator and protocol-specific generics that do not contain any site-specific information. Approval documents for generic advertisements are transmitted to the submitter; courtesy copies of generic advertisements will not be distributed to multiple sites or investigators.

Unless subjects at all sites (and/or participating in all protocols) receive the same payment for every study visit, it is wise to omit dollar amounts from generic advertisements. A general statement such as “subjects will be paid for their participation” is recommended instead.

Changes to approved generic materials must be reviewed and approved before use.

C. Expiration and Renewal of Generic Materials

Approved generic items are generally valid for one year. When the anniversary date approaches, WIRB staff will contact the submitter and inquire if renewal is desired. WIRB will conduct an annual review of the item if a response is not received by the date cited in the correspondence to ensure continued use is valid and under IRB oversight. Study Renewal Review fees apply. Expired generic items cannot be used. To prevent unnecessary renewal reviews, notify WIRB when use of the generic material has ended.

Occasionally, the Board may modify an item during the renewal review, usually due to changes in regulatory guidance or Board policy. Board-directed modifications are indicated in the approval documentation provided to the submitter.

12. WIRB reporting requirements for unanticipated problems

Federal Regulation 21 CFR §56.108 (b) (1) and 45 CFR 46.103(b)(5) require the IRB to “follow written procedures for ensuring prompt reporting to the IRB...any unanticipated problems involving risk to human subjects or others.” WIRB’s expectations for reporting of unanticipated problems are described below.

An unanticipated problem is defined as any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document, or the Investigator Brochure; and (b) the characteristics of the subject population being studied;

- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the drugs, devices or procedures involved in the research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

All reports to the IRB of unanticipated problems should explain clearly why the event is "unanticipated" and clearly explain why the event represents a "problem involving risks to human subjects or others."

WIRB expects reports to the IRB of unanticipated problems to include a corrective action plan to address the issue, or written justification for why an action plan is not provided.

Please note that unnecessarily reporting problems that do not meet the criteria outlined above may impair the Board's ability to review and respond in a timely manner to actual situations where subject rights, welfare or safety are threatened.

A. Unanticipated Problems that are Adverse Events:

Adverse events are any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

FDA guidance documents recognize that:

1. "individual adverse event reports generally require an evaluation of their relevance and significance to the study, including an evaluation of other adverse events, before they can be considered to be an unanticipated problem," and
2. "All reports to the IRB of unanticipated problems should explain clearly why the event described represents a 'problem' for the study and why it is 'unanticipated.'"

FDA believes that reports that lack such evaluation should not be provided to the IRB.

The reporting requirements for WIRB may differ from the reporting requirements for the sponsor. Report to WIRB only adverse events that in the opinion of the investigator may **represent unanticipated problems involving risks to the other subjects in the research.**

i. Adverse events that are determined to be unanticipated problems occurring at your site:

Use the Report Form for Unanticipated Problems that are Adverse Events to report an unanticipated adverse event that occurred at your site.

Investigators are required to report adverse events that fit the following criteria *within 10 working days* of the time the investigator becomes aware of them:

- Event is **Unexpected** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document, or the Investigator Brochure; and (b) the characteristics of the subject population being studied,
- **Related or possibly related** to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research **places subjects or others at a greater risk of harm** (including physical, psychological, economic, or social harm) than was previously known or recognized.

If the adverse event is clearly not related to the study drug, device, procedures, or washout process, it would not represent a risk to other subjects in the research or a “problem” for the study and, therefore, does not have to be reported to WIRB.

ii. Adverse events that are determined to be unanticipated problems that did not occur at your site (non-site adverse reports such as IND safety reports, SUSAR reports, and so forth):

WIRB will accept non-site adverse event reports submitted by investigators and from sponsors on behalf of investigators, if, in accord with 21 CFR 312.32,

- the event described is both serious and unexpected,
- the report identifies all previous safety reports concerning similar adverse experiences,
- the report analyzes the significance of the current adverse experience in light of the previous reports, **and**
- the report outlines a corrective action plan (such as a consent form or protocol change).

WIRB will not accept non-site adverse events that do not identify all previous safety reports concerning similar adverse experiences, analyze the significance of the current adverse experience in light of the previous reports and outline a proposed correction action plan. These submitted reports will generally be returned to the submitter with a description of the WIRB reporting requirements and guidance encouraging the submitter to resubmit with the required analysis.

If you have arranged for the sponsor to report the unanticipated problem directly to WIRB, we do not expect you to provide us with a duplicate copy of the report received from the sponsor.

If the sponsor, CRO or SMO does not submit non-site adverse event that are determined to be unanticipated problems to WIRB on behalf of your site, you are required to submit them, **along with the required explanation outlined above**, within 10 days of the date you receive them.

WIRB recognizes that for multicenter studies, the sponsor is in a better position to process and analyze adverse event information for the entire study, and to assess whether an occurrence is both "unanticipated" and a "problem" for the study. Accordingly, you may rely on the sponsor's assessment and provide to WIRB a report of the unanticipated problem prepared by the sponsor.

B. Unanticipated Problems that are Not Adverse Events

Use the Report Form for Unanticipated Problems that are Not Adverse Events to report the following unanticipated problems:

- Unanticipated problems that do not fit the definition of an adverse event, but which may, in the opinion of the investigator, involve risk to the subject, affect others in the research study, or significantly impact the integrity of research data. For example, report occurrences of breaches of confidentiality, accidental destruction of study records, or unaccounted-for study drug.
- *Unplanned* protocol deviations/violations that have already occurred, that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data, AND for which you did not seek WIRB pre-approval.

Report occurrences within 10 days of becoming aware of them.

Note: Planned protocol deviations that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data should be submitted to WIRB for review and approval **prior to implementation** except where necessary to eliminate apparent immediate hazards to the human subjects [(DHHS 45 CFR § 46.103(b)(4); (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7)]. Use the **WIRB Change in Research and Subject Recruitment (Ads) Submission Form** to request approval of a *planned* protocol deviation prior to implementation. (Deviations necessary to eliminate apparent immediate hazards to the human subjects should be reported within 10 days on the attached **Protocol Deviations & Violations/Unanticipated Problems Reporting Form**.)

13. Overview of WIRB's continuing review activities and reports

A. Continuing Review

During the initial review of a protocol, the Board makes a determination on the required frequency for reporting information related to the research.

FDA regulations regarding continuing review require an IRB to conduct continuing review of the research at intervals appropriate to the degree of risk, but not less than once per year [21 CFR § 56.108 (a)(1) and § 56.109(f)]. Beginning in May 2009, for most types of research, the Board requires two reports per approval period, and conducts full board re-review annually. For a few types of research, however, full board review is conducted more frequently than once a year. The Board normally determines that a full review of phase I research, investigator-initiated

single-site interventional studies of investigational drugs and devices, emergency research conducted under 21 CFR 50.24, and child research conducted under 45 CFR 46.407 should be conducted every six months. The Board may also direct more frequent than annual review for other research as deemed appropriate. Sites approved for 6 months at a time should expect to receive and complete four reports per year (two for each six month approval period).

Completed Continuing Review Report Forms (CRRFs) provide WIRB with the study-related data necessary to monitor the progress of the research at sites. WIRB sends sites a CRRF three weeks prior to the due date, according to the frequency established by the Board. Identifying information including investigator name, sponsor name, protocol number and the “sequence” number of the form is listed at the top of each form. The due date is also listed at the top of the form. Over the course of a year, studies assigned to a two per period reporting cycle will receive one “Interim” CRRF and one “Study Renewal” CRRF. The Study Renewal CRRF is sent out approximately 50 days before the study’s expiration date, in order to ensure it is completed and sent back to WIRB before the Board conducts the study renewal review. The Board may take action to suspend or terminate approval of the research if reports are not accurately completed and returned promptly.

CRRFs must be filled out completely and returned to WIRB in a timely manner. Even if the site has not started enrolling subjects, the site must complete the CRRF and return it to WIRB before the due date printed on it, to inform the Board of the study’s status at the site.

Before sending a completed report form to WIRB, verify that the reported data (specifically, enrollment numbers) do not conflict with any previous reports to WIRB. WIRB will not accept data inconsistent with prior reports. If reported data conflicts with the previous report, WIRB will contact the site to obtain corrected information. This may delay or hinder study renewal.

i. Continuing Review Report Form (CRRF) Work Sheet:

The CRRF Work Sheet is a guide to completing the WIRB CRRF for study coordinators and PIs (see next page).

A guide to completing the WIRB Study Renewal CRRF for study coordinators and PIs

1. *AT YOUR SITE: Has the study begun?*

If no, skip to the next question indicated on your form.

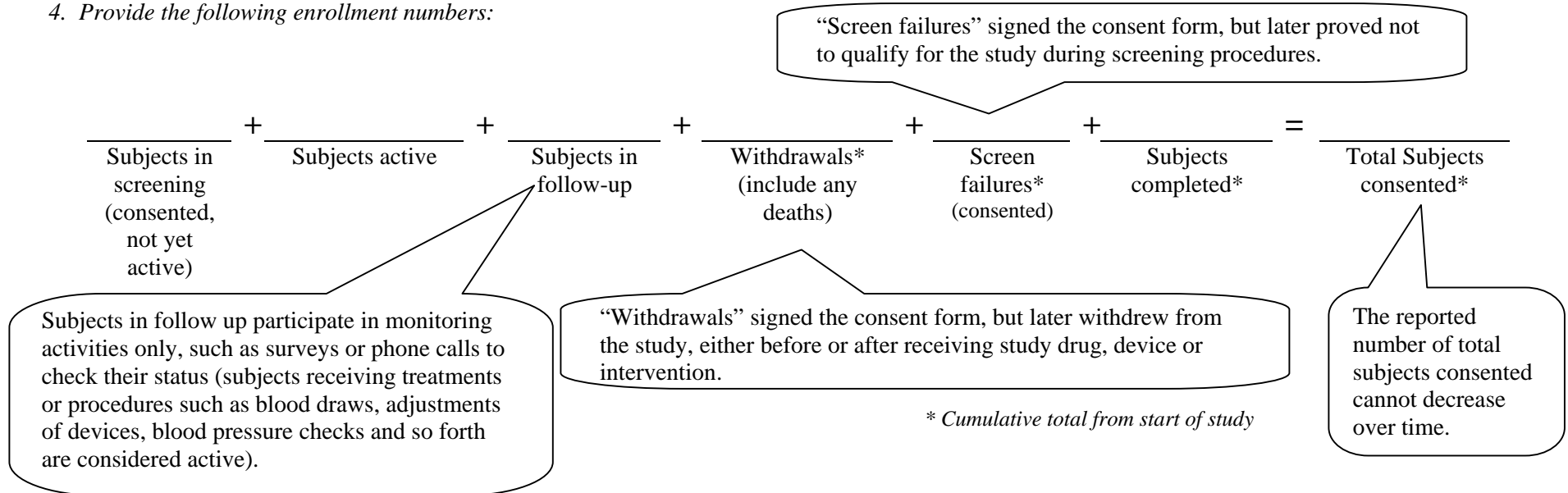
2. *If this is the first report submitted since a subject has consented to participate, attach a signed WIRB-approved consent document.*

You may mark “NA” if you have already submitted a signed consent form, or if WIRB approved a waiver of consent or waiver of documentation of consent for all subjects.

Subjects should be signing the clean version of the most current WIRB-approved consent form (redlined consent forms are provided for reference purposes only).

If the study at your site is under the oversight of another IRB in addition to WIRB, send only a signed copy of the WIRB-approved consent form.

4. *Provide the following enrollment numbers:*



5. *Number of females consented* _____

6. Number of racial minorities consented: _____

Federal regulations require IRBs to gather information about the racial make up of the subjects in the study.

7. Approximate racial makeup of consented subjects: (must add up to exactly 100%)

White: _____%

Black or African American: _____%

Asian: _____%

Native Hawaiian or other Pacific Islander: _____%

Other: (specify) _____%

American Indian or Alaska Native: _____%

8. **AT YOUR SITE:** Have there been any unanticipated study-related problems that involve risks to subjects or others which have not previously been reported to WIRB? If yes, complete and attach the appropriate WIRB reporting form.

Detailed instructions and forms for reporting are available at www.wirb.com.

9. **AT YOUR SITE:** Have there been any subject withdrawals which have not been previously reported to WIRB? If yes, indicate the reasons for the withdrawals.

“Withdrawals” signed the consent form, but later withdrew from the study, either before or after receiving study drug, device or intervention.

10. Does the scientific literature indicate changes in knowledge relevant to the conduct of the study? If yes, attach a brief summary of the information.

The summary should include a brief description of any changes in the currently accepted therapy or practices utilized in the protocol. Study coordinators should request a response from the Principal Investigator, who should be aware of relevant changes in the standard of care.

11. Is there new **risk** or **benefit** information **not previously** reported to WIRB? If yes, attach a copy.

These might be data safety monitoring reports or other updates to risk or benefit information related to the study.

12. Are there changes to the protocol or consent form or other material seen by subjects **not previously** reported to WIRB? If yes, attach a copy.

Attach an explanatory letter and the changes, or fill out and submit the WIRB Change in Research and Subject Recruitment Submission Form available at www.wirb.com.

13. Have you received any subject complaints since your last report?

If yes, summarize the complaint(s) (attach additional sheet if necessary).

14. Is the PI aware of any changes in state or local laws related to research? If yes, attach appropriate information.

A letter of explanation may be attached. The letter does not have to specify the exact change if the submitter is not entirely familiar with the change.

15. What is the PI's perception of the community's attitude toward research? If negative, please attach an explanation.

An explanatory letter may be attached, as well as applicable news clippings, etc., as applicable.

16. Is the PI aware of any recent events **in his/her community** (such as deaths or serious injuries) related to research? If yes, please attach any information you may have about the event.

An explanatory letter may be attached or just the applicable news clippings, etc.

17. Investigators must ensure each member of the research study team/staff has had training in the protection of human subjects. Have you added new study staff since your last report?

New team members must complete human subject protection training.

HIPAA training alone is not sufficient. WIRB's expectation is that training include topics such as ethical principles related to human subject protections, federal regulations for protection of human subjects, and Good Clinical Practice. A list of potential sources, including web-based tutorials and books, is available at www.wirb.com or by contacting WIRB's Client Services.

18. Have you been audited for **any study** by the FDA or OHRP since your last report? If yes, date of audit: _____. Please submit a copy of the FDA report as soon as available (or indicate if the report has been previously provided to WIRB).

If the FDA or OHRP has audited, but the information has already been reported to WIRB, mark "Yes" and the date of the audit, and note that the information has been previously forwarded to WIRB.

19. Has the research team conflict of interest information provided to the Board since the last review changed? If yes, please attach a summary of the changes (you may fill out and attach a copy of the WIRB Financial Disclosure Form available at www.wirb.com).

Studies approved since May 2003 have been required to provide information about possible conflicts of interest with the initial review submission. If the information provided to the board at initial review or since initial review has changed, provide the updated information. WIRB recommends using the form posted on its web site.

20. Are there any current investigations or charges involving the Principal or Sub-Investigator(s)?

If yes, please attach appropriate information.

21. Has the PI's medical license been renewed during this reporting period? If yes, please attach a copy.

22. *Have the hospital privileges of the PI or the subinvestigators at the hospital where subjects are treated or seen in case of emergency been reduced since your last report?
If yes, please explain how the change will affect the plan for treatment and/or emergency care of subjects: (attach additional sheet if necessary)*

WIRB must be assured that there is an appropriate system in place in the event that a subject is hospitalized. If neither the PI nor the sub-investigators have privileges at the designated emergency facility, please describe how subjects would be referred for hospitalization, what physician(s) would assume the role of the attending, and how communication between the attending physician and the investigator would be assured. It is not sufficient to state, "They will be referred to the emergency room."

23. *Is there any information you have not otherwise reported that summarizes study activity to date?
If yes, attach appropriate information.*

Such information might include a data safety monitoring committee report, the sponsor's Annual Report to the FDA, or communications from the sponsor addressing study-wide issues or progress.

24. *Signature of PI or designee.*

Unsigned forms will be deemed incomplete, and WIRB staff will follow up with a request for a signed form.

ii. Delinquent CRRFs

If a completed CRRF is not returned to WIRB, WIRB sends the site a second copy of the missing CRRF labeled "Reminder Notice." The Board may take action to suspend or terminate approval of research if reports are not accurately completed and returned promptly. If WIRB suspends or terminates the study, at a minimum, the investigator and sponsor will be notified of the Board's action, as well as any federal agencies with jurisdiction over the research, such as FDA and/or OHRP.

When a CRRF is not returned by the due date printed on it, WIRB takes the following action:

1. Seven days before the due date, a CRRF labeled "Reminder Notice" is mailed to the site.
2. If no response is received 7 days after the due date, WIRB staff prepare a "past due" letter which explains that if a satisfactory response is not received within 10 days, the delinquency will be reported to the Board and that the Board may take action to suspend the study at the site. The letter is sent to the investigator, sponsor contact, institution contact (if applicable) and other study contacts.
3. If no response is received 17 days after the due date on the CRRF, WIRB staff place a courtesy call to the sponsor notifying them of the continued delinquency and the likelihood that the Board will take action to suspend the study at the site if a response is not received.
4. If no response is received 24 days after the due date on the CRRF, the delinquency is reported to the Board. If the Board suspends the study, WIRB is required to report the suspension to the appropriate federal agency or agencies (FDA, OHRP, etc.) If the suspended investigator is at an institution which has notified WIRB that they will self-

report these actions to the appropriate agency or agencies, the institution will receive a notification of the Board's action and a cover letter reminding them of the reporting requirement. The institution has 30 days to then report to the agency and copy WIRB.

iii. Signed Consent Form Requirement:

The WIRB CRRF states "If this is the first report submitted after you have begun to enroll subjects, you must enclose a copy of a WIRB-approved consent document, signed by an enrolled subject." Sites are only required to send a signed consent form once; if the study involves multiple consent forms for this study, only a signed copy of the core consent form is required. Please note that if the site submits the correct version of the WIRB-approved consent form, but there are discrepancies in the signature lines (missing signatures, incorrectly completed signatures), WIRB staff will request an explanation from the site.

iv. Definition of Screen Failures and Withdrawals

Report the number of screen failures and withdrawals on the CRRF according to the following definitions.

Screen failure: subject removed from the study during the screening process because they do not meet all inclusion and exclusion criteria, or whatever other requirements must be met for research participation. Subjects who leave the study after randomization or assignment to study treatment should be counted as withdrawals rather than screen failures, even if the subject did not start the study treatment.

Withdrawal: Regardless of the reason for withdrawal, both subject-initiated decisions to withdraw and investigator- or sponsor- initiated withdrawals should be included in the reported number of withdrawals. Subjects who are withdrawn later in a study because they failed to meet study criteria for continued participation should be counted as withdrawals rather than screen failures. The majority of withdrawals take place after screening is completed.

v. Study Renewal

Sites receive a "Study Renewal" version of the WIRB CRRF when the study's expiration date is approaching. The Board may conduct the study renewal review up to 30 days prior to the study expiration date listed on the Certificate of Approval. **Review fees apply for the study renewal service** and review is carried out unless WIRB receives a study closure notice *prior to the Board's renewal review of the study*. If a closure notice is received by WIRB before the study expiration date, but after the Board's renewal review, the site is still billed for the renewal review. To avoid unnecessary reviews and fees, do not delay reporting a study closure to WIRB if the expiration date is approaching. Please note that if you plan to close a study that is approaching its expiration date, no study activities may take place on the expiration date or following; therefore, if the study's expiration date is, for example, June 15, all study activities must be completed by June 14.

If the Board approves renewal of the study for an additional review period, a Certificate of Approval is forwarded to the investigator and other study contacts as applicable. The Certificate of Approval states "Approval includes: Study and Investigator for an additional continuing

review period. This approval expires on the date noted above.” Approval of the study encompasses renewal of the protocol, all previously approved amendments or revisions, and the existing consent and study materials as previously approved.

If, at the time of study renewal, the Board determines that a modification to the consent is necessary, the Certificate of Approval will indicate approval of a consent form and will be accompanied by a revised consent form (and a redline illustrating the Board’s changes).

B. Study Closure

WIRB considers the study open at a site until a study closure report is received. A study closure report may be submitted when

1. all subjects have finished their final visits and follow-up **and**
2. the sponsor or the sponsor representative has indicated the study is closed at your site and,
3. if the study was conducted under a Federalwide Assurance, all data analysis at the site is completed.

WIRB will close the study upon receipt of the closure report. A **WIRB Study Closure Report Form** is available at www.wirb.com.

In May 2006, WIRB began sending closure confirmation notices to all study contacts upon receipt of a study closure form. Sites must have active on-going IRB approval in order to enroll subjects, perform any study interventions, collect/report new data, and/or, if under an FWA, analyze identified data at the site. If you receive a closure confirmation for a study you believe was closed in error, contact WIRB immediately to avoid a substantial gap in IRB oversight for the research.

Board may conduct renewal review of a site up to 30 days prior to the study expiration date listed on the Certificate of Approval. **Review fees apply for the study renewal service** and review is carried out if WIRB does not receive a study closure notice *prior to renewal of the study* (which, for logistical reasons, may be scheduled up to 30 days before the study expiration date). To avoid unnecessary reviews and fees, do not delay reporting a study closure to WIRB if the expiration date is approaching.

C. Site Visits

Federal Regulations grant IRBs the authority to observe the consent process and the research (21 CFR 56.109(f); 45 CFR 46.109(e)).

During site visits, the WIRB representative will focus on subject safety as well as regulatory compliance. The visits also offer an opportunity to the site to address research-related issues and ask questions of the WIRB visitor.

In preparation for the visit, WIRB asks the sites to set out the following review materials in a suitable work area, to allow for the visit to be conducted efficiently and with minimal disruption to the site's work:

- The site's informed consent policies, and the process by which consent is routinely obtained.

- The site's document files for WIRB-approved studies, including:
 - Protocol and amendments,
 - FDA form 1572 (if applicable),
 - IRB correspondence and approved consent form(s),
 - Participant charts or source documents and the consent form(s) for each study,
 - Investigator Brochure(s),
 - Curriculum Vitae (CV) for all research staff, and
 - The Principal investigator's CV and medical license.

WIRB may also ask to see the site's drug storage areas and emergency equipment.

WIRB conducts the following types of site visits:

- Routine (Site Assessment) – Routine site visits are generally brief and simple. However, some “routine” visits to sites at institutions with which WIRB has a contract are dictated by the terms the contract, and those visits’ length and depth will vary depending on the terms in the contract.
- For-Cause – WIRB staff initiate “for-cause” site visits in response to concerns raised about the site, investigator, etc. These visits are usually carried out by WIRB Regional Representatives, Board members or WIRB management.
- Board-Directed – The Board directs site visits in response to concerns raised about the site, investigator, etc. These visits are usually carried out by WIRB Regional Representatives, Board members or WIRB management.

Sites receive a site visit confirmation notice soon after the site visit has been scheduled. The notice provides the time of the visit, the basis for the visit, the name of the visitor and the agenda for the visit.

The Board reviews all site visit reports. If any follow-up is required, the investigator will be informed about the Board’s decision. WIRB does not release copies of site visit reports to sites or sponsors.

14. Fees

WIRB charges fees to cover the costs associated with the Board’s review and the related administrative responsibilities. Fees do not influence the decisions of the Board, and the same fee is charged regardless of the action taken by Board (fees are not billed until the Board review has occurred).

A copy of our current fee schedule is available upon request from Client Services at 1-800-562-4789 or clientservices@wirb.com.

Research Review fees at WIRB fall into four general categories:

1. **Initial Review of the research.** Initial review encompasses the review of the research protocol, qualifications of the investigator, associated consent forms, protocol-related

advertisements, questionnaires, screening scripts, and other submitted materials. The initial review fee funds the costs of the initial research review, as well as the costs of the ongoing review of unanticipated problems, site visits, and the monitoring of research progress via **WIRB Continuing Review Report Forms** for the first approval period.

In addition to the initial review fee, additional fees may be charged if teleconference or videoconference with the site is necessary to complete the initial review and if translation of consent forms and other subject materials is necessary.

Initial review of generic non-protocol related materials and exemption determinations are billed at a lesser rate than initial review of a protocol, consent form and investigator combination.

2. **Study Renewal Review fee.** In accordance with 45 CFR §46.109(e) and 21 CFR §56.109(f), IRBs must review ongoing research at least annually and that review must be substantive and at least comparable to the initial review. The protocol is reviewed on an annual basis, or more frequently as directed by the Board. The Board also examines each investigator's progress reports and activities for the previous year, and if acceptable, grants approval for another period. The study renewal review fee funds the costs of the Board's renewal review, as well as the costs of the ongoing review of unanticipated problems, site visits, and the monitoring of research progress via **WIRB Continuing Review Report Forms** for the additional year.
3. **Changes to Research.** Modifications to research which require board review, such as protocol amendments, revised protocols, updates to consent forms, and new recruitment or retention materials, incur a Change to Research fee, which covers the cost of reviewing the materials, and the related administrative responsibilities of preparing review documents and updating the investigator file at WIRB. The change in research fee applies each time board review and preparation of regulatory documentation is required for a research site.
4. **Miscellaneous.** WIRB bills additional fees if videoconferencing or teleconferencing with the site is necessary in the course of the review process and if translations are requested.

Items disapproved by the Board can be reconsidered upon written request. The request must include a justification for the reconsideration. There is no additional fee for the reconsideration. Reconsiderations of board-directed modifications do not incur additional fees if the requests concerns re-review of the **same language or item** originally reviewed by the Board. If new or alternate language is submitted, the Change to Research fee applies.

15. Reconsiderations

In accord with 21 CFR §56.109(e) and 45 CFR §46.109(d), WIRB notifies investigators in writing of the Board's decision to approve or disapprove proposed research activities, or of

modifications required to secure approval. Disapproval notifications include a statement of the reasons for the Board's decision and offers opportunity to address the Board in writing or in person.

Requests for reconsiderations are given the same priority in scheduling as new review requests. The reconsideration will be reviewed by the panel that originally reviewed the request. There is no fee for the review. Requests for reconsideration and supporting materials may be directed to the WIRB contact identified in the letter conveying the Board's action and rationale.

16. Other WIRB services

A. Phase 1

The mission of the Western Institutional Review Board is to protect the rights and welfare of the human research subject. In support of the mission, WIRB will review research from dedicated clinical/pharmacological units. Human subject safety is the primary focus with an emphasis on providing an impartial review to meet ethical requirements.

These ethical requirements include:

- Scientific or social value
- Scientific validity
- Fair subject selection
- Favorable risk-to-benefit ratio
- Independent Review
- Informed consent
- Respect for enrolled subjects

General Information

Phase 1 research units are dedicated inpatient facilities. The research has a specialized focus with standardized processes in recruitment, consenting and enrolling, specimen collection, and payment. WIRB's Phase 1 review division is designed to provide the special review expertise required for effective review of Phase 1 research.

The types of research reviewed by this division include all Phase 1 research; for example, bioequivalence, drug-drug and drug-food interaction, first in human trials, single and multiple dosing studies, pharmacokinetic and pharmacodynamic research, and may deal with special populations such as subjects with impaired liver or kidney function.

Prior to the first submission being received, a site assessment visit will be conducted and a template consent form will be established, which plays an integral part in the timeliness of the review process.

The WIRB Phase 1 Dedicated Panel meets on Monday, Wednesday, and Friday afternoons. The TAT for initial reviews 5 – 7 days. The TAT for changes in research is 24-48 hours. Documents will be transmitted within 24 hours of approval.

Anyone interested in receiving more information on the review of Phase 1 Research should contact:

Linda L. Morrison, CIP
Vice President,
Business Development/Institutions
Western Institutional Review Board
3535 Seventh Avenue, SW, Olympia, WA 98502
P: 360-252-2443 F: 360-252-2490
E-mail: lmorrison@wirb.com

B. Biosafety review

INSTITUTIONAL BIOSAFETY COMMITTEE SERVICES (IBCS)

A Division of Western Institutional Review Board (WIRB®)
PMB 2436 ♦ 2103 Harrison Avenue NW ♦ Olympia, WA 98502-2607
(360) 252-2850 ♦ Fax (360) 252-2820 ♦ ibcs@wirb.com

Institutional Biosafety Committee Services (IBC Services) administers IBCs for biomedical institutions engaged in research using recombinant DNA or related genetic material. Biological safety review by the IBC helps protect the safety of the research subjects and staff, the community, and the environment by promoting safe storage, handling, and disposal of gene-modified biohazardous materials. The IBC is also part of the Federal regulatory system for overseeing gene transfer research—the deliberate introduction of recombinant DNA (or RNA derived from recombinant DNA) into a human.

Each local institution registers its own IBC, because local membership is required—there is no such thing as a “central IBC” analogous to a “central IRB”. For information about whether IBC review is required please see below, “[Is IBC Review Required?](#)”

On behalf of the institution, IBC Services establishes a local IBC to comply with the requirements of the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines). The typical IBC will have 6-9 members. The IBC roster brings together prominent and experienced biosafety experts from around the country, with local members representing the institution and the surrounding community. Collectively, the membership is structured to provide scientifically sound review of the research that takes into account biosafety best practices as well as the current regulatory environment. The IBC provides periodic on-site visits to help promote and maintain a sound biosafety research setting.

Each site-specific IBC will provide prompt, expert reviews of recombinant DNA research to include:

- Evaluation of protocols, and any modifications to the research that may affect biosafety
- Assessments of the facility (physical capability, staff training, written procedures, biosafety practices, etc.)
- Assignment of biological safety containment levels
- Assessment of long-term follow-up plans

- Medical assessment of serious adverse events
- Biosafety assessment of research-related incidents (exposures, illnesses, loss of containment, etc.)

The staff of IBC Services of WIRB provides the following services for each site-specific IBC:

- Constitute and register IBC roster in compliance with NIH Guidelines
- Obtain confidentiality agreements and conflict of interest statements from members
- Train members on review and compliance functions, as well as scientific background of research
- Provide compensation (honoraria) to members unaffiliated with the institution
- Schedule all IBC meetings
- Distribute review materials to members
- Generate and distribute minutes to designated recipients
- Ensure IBC review of all modifications to the research that affect biosafety, in accord with NIH Guidelines

Is IBC review required?

Generally, NIH funding is what triggers the requirement for IBC review and compliance with the NIH Guidelines. Voluntary compliance is encouraged by the NIH Office of Biotechnology Activities.

If research is sponsored by or conducted by an institution that receives NIH funding for recombinant DNA research, the institution or clinical trial site must be reviewed and approved by an IBC before initiation of the research. Voluntary compliance by other institutions or sponsors is encouraged by NIH because it promotes safe conduct in recombinant DNA research and gives the public confidence that important safety matters are being addressed. Regardless of NIH funding, institutions or sponsors may be subject to local ordinances, federal or state regulations, or agency guidelines that require compliance with the NIH Guidelines. Vaccine trials exempt from Recombinant DNA Advisory Committee (RAC) review under Appendix M-I of the NIH Guidelines still require IBC review.

The NIH Office of Biotechnology Activities is the best source to determine what recombinant research requires IBC review. Contact OBA directly at: Phone: (301) 496-9838 or Email: oba@od.nih.gov

For more information about IBC Services, contact:

Institutional Biosafety Committee Services (IBCS)
 PMB 2436
 2103 Harrison Avenue NW
 Olympia, WA 98502-2607
 Phone: (360) 252-2850 or (800) 562-4789 Ext. 2850
 Fax: (360) 252-2820
 Email: ibcs@wirb.com

C. Consultations

Experienced staff members of WIRB are available to provide consultation to sponsors and investigators regarding many aspects of human subject research. Regulatory or ethical advice regarding protocols being developed for which IRB approval will be sought is a frequently-requested service. Although an opinion from WIRB staff does not represent an official action by the Board and is not meant to represent any actions the Board may take upon its review of the research, consultation may be helpful to identify issues likely to result in disapproval or in required modifications. Consultation fees are calculated on an hourly basis. To request this service, please contact

Vice President, Business Development
Phone: (360) 252-2443
Fax: (360) 252-2498

Additional consultation services include auditing, SOP review, consent form writing and specific training requests.

D. Exemption Determinations

Occasionally investigators need a formal IRB determination that research is exempt under 45 CFR 46.101(b) for the purpose of obtaining federal funding, or for meeting the submission requirements of medical journals. WIRB will provide formal exemption determinations for research under 45 CFR 46.101(b) for a fee. WIRB will also provide exemption determinations from the FDA regulations (21 CFR Parts 50, 56, 312 and 812) for those exemptions allowed under 21 CFR 56.104. However, WIRB generally does not provide determinations on whether a given research study meets the definition of a “clinical investigation” or a “marketing application,” because determination of these definitions involves the sponsor’s intent as to whether or not to submit data to FDA, which WIRB cannot independently determine.

Use the Request for Exemption Determination form available on the Download Forms page of www.wirb.com to request an exemption determination.

17. Appendices

A. Appendix 1: Template Consent Form

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE:

PROTOCOL NO.:

SPONSOR:

INVESTIGATOR:

SITE(S):

**STUDY-RELATED
PHONE NUMBER(S):**

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

[Add the following statement only if the study protocol expressly allows the enrollment of subjects not capable of consenting for themselves:] A person who takes part in a research study is called a research or study subject. In this consent form “you” always refers to the research subject. If you are a legally authorized representative, please remember that “you” means the research (study) subject.

SUMMARY

[The summary section should summarize for the subject what the informed consent process will tell them, including:

- *How research differs from regular health care.*
- *The rights and responsibilities of research subjects.*

- *Information subjects should have before joining a research study.]*

You are being asked to be in a research study. The purpose of this consent form is to help you decide if you want to be in the research study. Please read this form carefully. To be in a research study you must give your informed consent. “Informed consent” includes:

- Reading this consent form,
- Having the study doctor or staff explain the research study to you,
- Asking questions about anything that is not clear, and
- Taking home an unsigned copy of this consent form. This gives you time to think about it and to talk to family or friends before you make your decision.

You should not join this research study until all of your questions are answered.

Things to know before deciding to take part in a research study: *[remove any that do not apply]*

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- No one can promise that a research study will help you.
- Taking part in a research study is entirely voluntary. No one can make you take part.
- If you decide to take part, you can change your mind later on and withdraw from the research study.
- The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.
- Parts of this study may involve standard medical care. Standard care is the treatment normally given for a certain condition or illness.
- Other parts of this study may involve experimental (investigational) drugs or procedures, that are being tested for a certain condition or illness. An investigational *[drug, device, vaccine]* is one that has not been approved by the U.S. Food & Drug Administration (FDA).
- After reading the consent form and having a discussion with the research staff, you should know which parts of the study are experimental and which are standard medical care.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at and/or copied by the sponsor of this study and government agencies or other groups associated with the study.
- Your medical insurance may be billed for any standard medical care you receive during the research study. If your insurance company is billed then it may have access to the research records. Insurance companies may not pay for treatment that is part of a research study. Taking part in a research study could affect your current or future insurance coverage.

After reading and discussing the information in this consent form you should know:

- Why this research study is being done;

- What will happen during the research;
- What drug or device or procedures will be used;
- Any possible benefits to you;
- The possible risks to you;
- The other medical procedures, drugs or devices that could be used instead of being in this research study; and
- How problems will be treated during the study and after the study is over.

If you take part in this research study, you will be given a copy of this signed and dated consent form.

PURPOSE OF THE STUDY

[In simple language, explain the following:

- *Why the research is being done*
- *What the experimental components are]*

PROCEDURES

[In simple language and in a simple bullet format, explain the following:

- *The tests and procedures that will be done*
- *Which procedures/drugs are standard care and which are for research purposes only*
- *Whether a placebo or sham procedure will be involved*
- *The chances of being assigned to various study arms*
- *The method of assignment (random, etc.)]*

RISKS AND DISCOMFORTS

[In simple language and in a simple bullet format (whenever possible), explain the possible risks and discomforts:

Start with the side effects for the experimental drugs, devices or procedures. List, for example:

- *most common*
- *less common*
- *rare]*

[Follow with risks and side effects for all drugs, devices or procedures used in the study.]

There may be side effects that are not known at this time.

[Include any risks relative to pregnancy for both men and women. For example:]

Women who are pregnant or nursing a child may not take part in this study. Before entering the study, you and your study doctor must agree on the method of birth control you will use during the entire study. If you think that you have gotten pregnant during the study, you must tell your study doctor immediately. Pregnant women will be taken out of the study.

Men who are in this research study should not get a sexual partner pregnant while taking the study drug *[If applicable also add the following:]* and for *[specify amount of time]* after the last dose of study drug. The effect of the study drug on sperm is not known.

[Or other pregnancy language supplied by sponsor—rewrite, if necessary, to simplify]

Your condition may not get better or may get worse during this study.

[If study drug is taken home, insert this or similar language:]

Only you should take the study drug. It must be kept out of the reach of children or anyone else who may not be able to read or understand the label.

NEW INFORMATION

You will be told about anything new that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

BENEFITS

[In simple language indicate the possible benefit for both the subject and future patients.]

Your *[name of condition]* may improve while you are in this study; however, this cannot be promised. The results of this study may help people with *[insert name of condition]* in the future.

[or]

It cannot be promised that you will receive any medical benefits from being in this study.

COSTS

[In simple language state:

- *What will be billed to the subject or to their insurance*
- *Who pays if insurance does not (do not use exculpatory language).]*

[For example:]

[Sponsor Name] will provide the study *[drug/device]* free of charge during this study.

Procedures that are done only for the study, such as extra lab tests will not be billed to you or your insurance company.

You or your insurance company may be billed for:

- Any standard medical care given during this research study.
- *[list other costs as necessary]*

Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. This discussion should include the costs of treating side effects. Otherwise, you might have unexpected expenses from being in this study.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study. If your insurance company does not pay, you may be billed for those charges.

PAYMENT FOR PARTICIPATION

[Include this section only if subjects will be paid or if the sponsor requires subjects to be told that they will not be paid.]

You will be paid \$_____ for each completed study visit. If you do not finish the study, you will be paid only for the visits you have completed.

ALTERNATIVE TREATMENT

If you decide not to enter this study, there is other care available to you, such as *[List the major ones such as drugs / devices / procedures / supportive]*. The study doctor will discuss these with you. You do not have to be in this study to be treated for *[disease, condition, symptoms]*.
[Or]

This is not a treatment study. Your alternative is not to participate in this study.

[Use the following authorization format if the site is collecting health information, is a covered entity under HIPAA and is not using a separate HIPAA authorization form.

If the site is not collecting health information, is not a covered entity under HIPAA or is using a separate HIPAA authorization form, use the “Confidentiality” text that follows, rather than the authorization text below.

California sites: This entire HIPAA section plus authorization statement should be placed at the end of the consent form following a page break and must include its own set of signature lines.]

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

[Select additional from below, as appropriate.]

- Information gathered for this research about:
 - HIV / AIDS
 - Hepatitis infection
 - Sexually transmitted diseases
 - Other reportable infectious diseases
 - Physical exams
 - Laboratory, x-ray, and other test results
 - Diaries and questionnaires
 - The diagnosis and treatment of a mental health condition
- Records about any study drug you received
- Records about the study device.

Who may use and give out information about you?

The study doctor and the study staff. They may also share the research information with *[enter SMO name]*, an agent for the study doctor *[if no SMO, delete this sentence]*.

Who might get this information?

- The sponsor of this research. “Sponsor” means any persons or companies that are:
 - working for or with the sponsor, or
 - owned by the sponsor.

Your information may be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Western Institutional Review Board® (WIRB®)

[Add any institutional names above WIRB.]

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to see if the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

May I review or copy my information?

Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?

- Yes, but this permission will not stop automatically.
[or]
- This permission will be good until *[date]* *[required in CA, IN, WA, and WI].*

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission.

Confidentiality *[Use the following confidentiality text if the site is **not** collecting health information, is not a covered entity under HIPAA or is using a separate HIPAA authorization form.]*

Study information collected about you will be given to the sponsor. “Sponsor” means any persons or companies that are working for or with the sponsor, or owned by the sponsor.

It will also be given to the U.S. Food and Drug Administration (FDA). It may be given to governmental agencies in other countries where the study *[drug or device]* may be considered

for approval. Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by:

- the sponsor;
- *delete the following if no CRO or SMO*
- *[CRO name]*, an agent for the sponsor;
- *[SMO name]*, an agent for the study doctor;

[Add any institutional names above WIRB.]

and may be looked at and/or copied for research or regulatory purposes by:

- the FDA,
- Department of Health and Human Services (DHHS) agencies,
- governmental agencies in other countries, and
- Western Institutional Review Board® (WIRB®).

Total confidentiality cannot be guaranteed because of the need to give information to these parties. The results of this research study may be presented at meetings or in publications. Your identity will not be given out during those presentations.

COMPENSATION FOR INJURY

[Example:]

If you are injured or get sick as a result of being in this study, call the study doctor immediately. The study doctor will provide emergency medical treatment. Your insurance will be billed for this treatment. The sponsor will pay any charges that your insurance does not cover. No other payment is routinely available from the study doctor or sponsor.

[or other language supplied by sponsor, simplified.]

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any of the following reasons:

- it is in your best interest;
- you do not consent to continue in the study after being told of changes in the research that may affect you;
- *[if the protocol lists specific reasons, insert them here];*
- or for any other reason.

If you leave the study before the planned final visit, you may be asked by the study doctor to have some of the end of study procedures done.

SOURCE OF FUNDING FOR THE STUDY

The sponsor *[name]* will pay for this research study. *[Or other wording, as appropriate].*

QUESTIONS

Contact _____ [name] at _____ [number(s)] for any of the following reasons:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
3535 Seventh Avenue, SW
Olympia, Washington 98502
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com.

WIRB is a group of people who independently review research.

WIRB will not be able to answer some types of questions, such as questions about appointment times. You may contact WIRB if you cannot reach the research team or if you want to talk to someone else.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

CONSENT

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above *[remove if you used a Confidentiality section rather than an Authorization section above]*.

By signing this consent form, I have not given up any of my legal rights.

[Example signature block for research involving adults able to consent, minors, and adults who lack the capacity to consent:]

Consent and Assent Instructions:

Consent: Subjects 18 years and older must sign on the subject line below

Consent is provided by the Legally Authorized Representative for adult subjects unable to consent

For subjects under 18, consent is provided by the parent or guardian

Assent: Is not required for subjects 6 years and younger

Verbal assent is required for subjects ages 7 through [14] years using the Assent section below [and the Information Sheet for Children].

Verbal assent is required for subjects ages [15] through [17] years using the Assent section below [and the Information Sheet for Adolescents].

Subject Name (printed)

CONSENT SIGNATURE:

Signature of Subject (18 years and older)

Date

Signature of Legally Authorized Representative,
Parent or Guardian (when applicable)

Date

Authority of Subject's Legally Authorized Representative or Relationship to Subject

Signature of Person Conducting Informed
Consent Discussion

Date

ASSENT SECTION For Subjects Ages [7] - [17]:

Statement of person conducting assent discussion:

1. I have explained all aspects of the research to the subject to the best of his or her ability to understand.
2. I have answered all the questions of the subject relating to this research.
3. The subject agrees to be in the research.
4. I believe the subject's decision to enroll is voluntary.
5. The study doctor and study staff agree to respect the subject's physical or emotional dissent at any time during this research when that dissent pertains to anything being done solely for the purpose of this research.

Signature of Person Conducting
Assent Discussion

Date

Statement of Parent or Guardian:

My child appears to understand the research to the best of his or her ability and has agreed to participate.

Signature of Parent or Guardian

Date

ASSENT SIGNATURES, For Adult Subjects with a Legally Authorized Representative:

Assent:

For adult subjects who have a legally authorized representative, I confirm that:

I have explained the study to the extent compatible with the subject's understanding, and the subject has agreed to be in the study.

OR

The subject is not able to assent due to lack of mental capacity.

Signature of Person Conducting Assent Discussion Date

Ver. 12-23-2009

B. Appendix 2: Template Information Sheet for Children

RESEARCH SUBJECT INFORMATION SHEET FOR CHILDREN:

TITLE:

PROTOCOL NO.:

SPONSOR:

INVESTIGATOR:

SITE(S):

**STUDY-RELATED
PHONE NUMBER(S):**

You are being asked to participate in a research study because you have _____.
Most people with _____ have to take _____. If they do not take _____,
_____ may happen.

Our medicine is called _____. We do not know if it is better than other medicines,
so we are asking you to help us with this research study. We have used it in other people
with _____, but we are still checking to learn more about _____.
_____ might not make you feel better, or may make you feel worse.

This study will last _____ weeks. You will have to come to the study center ___ times.
You will be asked questions about _____ and be examined by one of the doctors
or nurses.

Blood will be taken from your arm with a needle at ___ different times during the study.
You will need to give a urine sample and will have _____ (other tests) _____.

You will need to take _____ every day.

If the medicine makes you feel different, or if you get ____ (side effects) ____ you must tell your parents or the study doctor.

Important things to know:

- You don't have to do this if you don't want to.
- We won't be mad at you if you decide you don't want to do this.
- Your doctor will still take care of you even if you don't want to do this.

If you are a girl and have started your periods, pregnancy testing will be done. You must use birth control or not have sex during the study. This is because _____ could cause bad birth defects in babies. You must not take part in this study if you become pregnant. If at any time you think you might be pregnant, you must tell your study doctor right away.

If later you have any questions about this study, please ask your parents or call the study doctor (Dr. _____) or his nurse at _____.

C. Appendix 3: Template Information Sheet for Adolescents

RESEARCH SUBJECT INFORMATION SHEET FOR ADOLESCENTS:

TITLE:

PROTOCOL NO.:

SPONSOR:

INVESTIGATOR:

SITE(S):

**STUDY-RELATED
PHONE NUMBER(S):**

You are being asked to participate in a clinical research study. Your decision to be in this study is voluntary. You do not have to participate in this study if you do not want to.

This information sheet will give you information about the risks and benefits of this study so that you can make a better decision about whether you want to take part or not.

PURPOSE OF THE STUDY

The purpose of this research study is _____. You are being asked to be in this study because you have _____.

_____ is approved for treating _____ in adults but is not approved in adolescents or children. In this study, you will receive _____ for at least ____ weeks. After the study, you will be treated with _____.

PROCEDURES

You will be in this study for approximately ____ weeks.

You will have _____ visits

Procedures done during this study include a history and examination, blood tests at most visits, and _____.

RISKS AND DISCOMFORTS

Side effects reported with _____ have included _____, _____, _____, _____, _____, _____, _____.

The risks of the blood draw include temporary discomfort from the needle in your arm, bruising, swelling at the needle site and, in rare instances, infection.

Side effects of other study procedures include: _____.

Additional side effects that are unknown at this time could occur during treatment.

The effects of _____ during pregnancy have not been adequately studied. Therefore, there might be unknown risks to the unborn child if you become pregnant during this study. Due to these potential risks you must not participate in this study if you become pregnant, plan to become pregnant during the research study period, or are breast-feeding a child. Pregnancy testing will be done during the study and an acceptable form of birth control (including no sexual intercourse) must be used during the study.

POSSIBLE BENEFITS OF THE STUDY

Your _____ may improve as a result of your participation in this study. However, this cannot be guaranteed. You may not experience any direct health benefits. Information from this study may lead to a better treatment in the future for adolescents and children with _____.

For further information about this study, please refer to the consent form discussed with you for this study.

D. Appendix 4: Pregnant Partner Consent Form Template
RESEARCH SUBJECT INFORMATION AND CONSENT FORM
Pregnant Partner

TITLE:

PROTOCOL NO.:

WIRB[®] Protocol #

SPONSOR:

INVESTIGATOR:

SITE(S):

**STUDY-RELATED
PHONE NUMBER(S):**

There may be words in this consent form that you do not understand. Please ask the study doctor or study staff to explain anything that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

SUMMARY

- *You are being asked to be in a research study.*
- Being in this study is voluntary.
- If you join the study, you can leave at any time.
- This is not a treatment study.
- If you are in this study, your medical records will become part of this research. They may be seen by a number of other people or groups associated with the study.

More detailed information about this study is in this consent form. In this consent form, the word “you” means both you and your child. Please read it carefully.

PURPOSE OF THE STUDY:

You are being asked to participate in this follow-up only research study because the biological father of your child was participating in a study called **[insert name of study]**. The purpose of this study is to gather medical information about your pregnancy and the birth and health of your child. We want to determine if the **[study treatment]** has any affect on your pregnancy and the health of your child.

PROCEDURES

We will ask you for your permission to review your and your child's medical records relating to your pregnancy, the delivery of your child and the health of your child up to **[insert length of time stated in protocol]** of age.

If you agree to take part in this study, your involvement will last until about **[insert length of time stated in protocol]** after the birth of your child.

RISKS AND DISCOMFORTS

The risk from this study is the loss of confidentiality of your or your child's medical record information.

NEW FINDINGS

You will be told about any new information that might change your decision to be in this study. You may be asked to sign a revised consent form if this occurs.

BENEFITS

This is not a treatment study. You are not expected to receive any direct medical benefits from the study.

The information from this research study may lead to a better treatment in the future for pregnant women and fetuses who are exposed to **[DRUG/DEVICE]**.

COSTS

You will not have any costs for being in this research study.

This study will not cover any costs related to your pregnancy, delivery or care of your child. You and/or your medical/hospital insurance carrier will still be billed for your regular medical care expenses.

PAYMENT FOR PARTICIPATION ONLY IF ARE PAYING, OR THE PROTOCOL SAYS MUST INFORM ARE NOT PAYING.

You will be paid \$_____ for each completed study visit. If you do not finish the study, you will still be paid for the visits you have completed.

ALTERNATIVE TREATMENT

This is not a treatment study. Your alternative is to not be in this study.

CA sites: This next HIPAA entire section plus authorization statement and signature must be in a separate (page break) section at the end of the form in 14 font. The revocation must have a specific date ... suggest December 31, 2050 or some other long term date.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information about you may be used and given to others?

The study doctor will get personal and medical information about your pregnancy and the health of your child.

Who may use and give out information about you?

The study doctor and the study staff.

Who else might get this information?

The sponsor of this research. "Sponsor" means any people or companies that are:

- working for the sponsor
- working with the sponsor, or
- owned by the sponsor.

Your information may also be seen by:

- The U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- Governmental agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- *[Add any other institutional names]*
- The Western Institutional Review Board® (WIRB®)

Why will my/my child's information be used and/or given to others?

Your/your child's information may be used by the study doctor or others:

- To do the research
- To look at the results
- To make sure the research was done right

- To publish the results to help others in future research

If the results of this study are made public, information that could identify you will not be used.

What if I decide not to give permission to use and give out my/my child’s health information?

Your information will not be included in the research.

May I review or copy my/my child’s information?

Yes.

May I withdraw or revoke (cancel) my permission?

- Yes, but this permission will not stop automatically.

OR

- This permission will be good until *[insert expiration date as required by local law]*.

You may withdraw your permission to use your health information at any time. You do this by sending written notice to the study doctor.

When you withdraw your permission, no new health information identifying you or your child will be gathered. Information already gathered for the research may still be used and given to others.

Is my/my child’s health information protected after it has been given to others?

There is a risk that your health information will be given to others without your permission.

COMPENSATION FOR INJURY

INCLUDE ANY REQUIRED SPONSOR OR INSTITUTIONAL REQUIRED LANGUAGE. OTHERWISE, THE BOARD MAY DETERMINE THAT THIS RESEARCH IS MINIMAL RISK AND THAT COMP FOR INJURY LANGUAGE IS NOT NECESSARY

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Your participation in this study is voluntary. You may decide not to join the study or allow your child to be in the study or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you or your child are entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason.

SOURCE OF FUNDING FOR THE STUDY

The study doctor [NAME] is being paid by [SPONSOR NAME] *[Or other wording, as appropriate]* to do this research.

QUESTIONS

Contact _____ at _____ for any of the following reasons:

- if you have any questions concerning your participation in this study,
- if at any time you feel you or your child have experienced a research-related problem, or
- if you have questions, concerns or complaints about the research

If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
3535 Seventh Avenue, SW
Olympia, Washington 98502
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com.

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in this study, you will receive a signed and dated copy of this consent form [*California sites add "and the Experimental Subject's Bill of Rights"*] for your records.

CONSENT

I have read the information in this consent form (or it has been read to me). All my questions about the study and my/my child's participation in it have been answered. I freely consent to be in this research study and consent to my child being in this research.

I authorize the use and disclosure of my and my child's health information to the parties listed in the authorization section of this consent for the purposes described above [*exclude if HIPAA authorization section has been excluded because subjects will sign a separate authorization form*].

By signing this consent form, I have not given up any of my or my child's legal rights.

Subject Name

CONSENT SIGNATURE:

Signature of Subject

Date

Signature of Person Conducting Informed
Consent Discussion

Date

----- **Use the following only if applicable** -----

If this consent form (addendum) is read to the subject because the subject (or legally authorized representative) is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form (addendum) and any other written information was accurately explained to, and apparently understood by, the subject (or the subject's legally authorized representative). The subject (or the subject's legally authorized representative) freely consented to be in the research study. *[adjust as needed]*

Signature of Impartial Witness

Date

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling subjects who do not speak English.

12/18/2009 version

E. Appendix 5: Authorization Agreement

Version Date: 12/20/2005

**Institutional Review Board (IRB)/Independent Ethics Committee (IEC)
Authorization Agreement**

Name of Institution or Organization Providing IRB Review (Institution/Organization A):
Western Institutional Review Board

IRB Registration #: IRB00000533 Federalwide Assurance (FWA) #, if any: N/A

Name of Institution Relying on the Designated IRB (Institution B):

FWA #: _____

The Officials signing below agree that _____ (name of Institution B) may rely on the designated IRB for review and continuing oversight of its human subjects research described below: (*check one*)

This agreement applies to all human subjects research covered by Institution B's FWA.

This agreement is limited to the following specific protocol(s):

Name of Research Project:

Name of Principal Investigator:

Sponsor or Funding Agency: _____ Award Number, if any: _____

Other (*describe*):

The review performed by the designated IRB will meet the human subjects protection requirements of Institution B's OHRP-approved FWA. The IRB at Institution/Organization A will follow written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the IRB's determinations and with the Terms of its OHRP-approved FWA. This document must be kept on file by both parties and provided to OHRP upon request.

Signature of Signatory Official (Institution/Organization A): _____ Date: _____

Print Full Name: _____ Institutional Title: _____

NOTE: The IRB of Institution A must be designated on the OHRP-approved FWA for Institution B.

Signature of Signatory Official (Institution B): _____ Date: _____

Print Full Name: _____ Institutional Title: _____

F. Appendix 6: List of forms available on the WIRB website Download Forms page

Have you tried WIRB's new online "smart form" submission process?
It can significantly reduce the number of questions you have to answer about your submission.

Smart forms are available for initial review submissions, change in research submissions, unanticipated problem submissions, study closure submissions, and requests for partial waivers of authorization for recruitment. Don't download your form, instead just click on the "WIRBNet LOGIN" button on www.wirb.com to establish an account and get started!

1. Initial Review Submission Forms:
 - a. Initial Review Submission Form (New Protocols)
 - b. "Additional Sites" page only
 - c. Annotated Initial Review Submission Form
 - d. Investigator Submission Form for Multi-Center Protocols
 - e. Initial Review Submission Form for Sponsors and CROs
 - f. Request for Exemption Determination
 - g. Request for Emergency Use
 - h. New Jersey Requirements for Inclusion of Decisionally Impaired Subjects
2. Request for a HIPAA Partial Waiver of Authorization for Recruitment
3. Request for a Waiver of Consent under the Common Rule And Waiver of Authorization under HIPAA (HIPAA Full Waiver of Authorization)
4. IRB Transfer Cover Letter Checklist & Summary Form
5. Waiver of Consent Request for In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable
6. Sample IRB Authorization Agreement (with WIRB filled in as institution A)
7. Change in Research and Subject Recruitment (Ads) Submission Form
 - a. Change in Research Additional Sites Page
8. Screening Procedures Information Form
9. Financial Interest Disclosure Form
10. Unanticipated Problem Reporting
 - a. Unanticipated Problems that ARE Adverse Events
 - b. Unanticipated Problems that ARE NOT Adverse Events
11. Study Closure Report Form
12. WIRB Investigator Handbook "A Guide for Researchers"
13. Legend Reasons for Change
14. WIRB Consent Form Template
15. Pregnant Partner Template Consent Form
16. Continuing Review Report Form (CRRF) Work Sheet
17. Continuing Review Report Form (CRRF) Instructions for sites using Humanitarian Use Devices (HUDs)
18. Template Information Sheet for Waiver of Documentation of Consent

G. Appendix 7: Checklist of requirements for submitting changes in research

Protocol Changes (Amendments, Administrative Changes, etc.):

Submit:

- A copy of the WIRB Change in Research and Subject Recruitment (Ads) Submission Form
- A rationale for the change(s)
- A **summary of changes** for the new amendment to the protocol (if WIRB has already received the protocol amendment, you may submit the protocol amendment title page and signature page only).

Planned Protocol Deviation:

Provide the details of the planned deviation. Planned protocol deviations that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data should be submitted to WIRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human subjects.

Consent Form Modifications:

Submit:

- A copy of the WIRB Change in Research and Subject Recruitment (Ads) Submission Form
- A **copy of the WIRB approved consent form with changes marked** and the **rationale for the changes**. Please note any **changes to addresses or phone numbers**. Address changes should be accompanied by an updated 1572 (if applicable). WIRB will also accept a document listing the requested changes to the consent form, but will not accept a sponsor template consent form with changes marked.

As of January 1, 2009, all requests for changes to previously approved consent forms must be submitted in one of two ways: The changes can be submitted using the currently approved WIRB consent form with only the new changes tracked in redline format or handwritten on the form, OR the changes can be detailed in a document specifying the requested changes.

Address and Phone Number Changes:

Submit:

- An updated 1572 (if applicable) and a completed copy of WIRB's Additional Site form for each new or updated location.

Recruitment Materials:

- A copy of the WIRB Change in Research and Subject Recruitment (Ads) Submission Form

- Indicate if any of the recruitment materials have been previously approved by WIRB and attach a copy of the previously-approved item(s), even if they are from a different protocol.
- Indicate if any submitted scripts will be used as Public Service Announcements, and whether they will be announcer-read (verbatim) or recorded.
- If you submit materials that **reference** a web site, attach a hard copy of the **recruitment sections** of the web site for WIRB review.
- If you submit any written or verbal screening materials for screening subjects prior to enrollment in the research (such as telephone call scripts, written or web-based questionnaires or pre-screening forms), **describe the screening plan on the Screening Procedures Information Form** found at www.wirb.com. WIRB reviews screening materials in the same manner as consent documents. WIRB's requirements for screening scripts are listed at the bottom of the Screening Procedures Information Form.
- A script for all audio and video materials.

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