



The Trusted Partner in Ethical Review

A Guide for Researchers

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Western Institutional Review Board®
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Revised in this version:

- *Update policy regarding protocol continuing review reports – WIRB will now only require them to be completed when WIRB is or may be the central IRB (see page 62)*

The purpose of this guide is to provide you with information about WIRB's processes. 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



Pioneering Together for More Than  Years.

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.

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 50 WIRB employees have since been certified.

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, 2009 and again in 2014, AAHRPP renewed WIRB's accreditation status. WIRB continues to be fully accredited.

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

In 2001, 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 a panel devoted to dedicated clinical pharmacology units (such as phase 1 units).

In 2012, Arsenal Capital Partners acquired WIRB and the Copernicus Group IRB and formed The WIRB Copernicus Group (WCG). Arsenal Capital Partners is a leading New York-based private equity firm that invests in middle market healthcare, specialty industrial, and financial services companies.

WIRB's position within The WIRB-Copernicus Group provides it access to nationally recognized experts and processes. WIRB continues to operate independently, but benefits from the support and resources of The WIRB-Copernicus Group, the world's largest provider of regulatory and ethical review services for human research. We also enjoy a strong relationship with our sister companies, and through those relationships, we will leverage every opportunity to bring added value to you.

The WIRB Copernicus Group (WCG) continues to expand its offerings via new acquisitions and service lines – go to www.wcgclinical.com to find out the latest.

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 or necessary. 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.

WIRB can help researchers and institutions comply with the NIH Single IRB policy – go to www.wirbsinglereview.com for more information.

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.

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 as stand-alone documents and are also integrated into the Initial Review Smart Form). 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.

4. Financial Conflicts of Interest

To meet the needs of its institutional clients, WIRB reviews financial interest of investigators, research staff and institutions consistent with the Department of Health and Human Services (HHS) guidance “Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection,”

The first step in managing financial conflicts of interest is disclosure of financial holdings, relationships, and other interests that might constitute a conflict of interest. During the application process investigators and research staff are required to disclose whether the Principal Investigator (PI), the PI's immediate family, or any other research personnel or their immediate families, have any of the following financial interests in an entity that is sponsoring the research, or an entity that is manufacturing the product or service being tested:

- Any remuneration from the entity in the previous twelve months that exceeds \$5,000, when aggregated for the individual and their immediate family. (Remuneration includes salary and any payment for services not otherwise identified as salary, such as consulting fees, honoraria, or paid authorship)
- Any equity interest in the entity. (Equity interest includes any stock, stock option, or other ownership interest)
- Any intellectual property rights and interests (e.g., patents, copyrights)
- Any governance or executive relationship with the entity (e.g., board of director, CEO)

If an individual has a financial interest in the research, the Board evaluates whether the financial interest is a Significant Financial Interest. Significant Financial Interest means a financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:

- With regard to any publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds \$5,000. For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;

- With regard to any non-publicly traded entity, a significant financial interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds \$5,000, or when the Investigator (or the Investigator's spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest);
- Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests; or Compensation of any amount that could be higher for a favorable outcome than for an unfavorable outcome, such as compensation that is explicitly greater for a favorable result or compensation to the investigator in the form of an equity interest in the sponsor of a covered study or in the form of compensation tied to sales of the product, such as a royalty interest.
- Board or executive relationship.

The term significant financial interest does not include the following types of financial interests: salary, royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed or otherwise appointed by the Institution, including intellectual property rights assigned to the Institution and agreements to share in royalties related to such rights; any ownership interest in the Institution held by the Investigator, if the Institution is a commercial or for profit organization; income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles; income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education; or income from service on advisory committees or review panels for a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an Institution of higher education.

If the Board determines that the financial interest is not a Significant Financial Interest, no further action is taken. If the interest is a Significant Financial Interest, the Board considers whether the interest affects the criteria for approval of research, and if so, does not approve the research unless the interest is eliminated or managed. The Board considers whether the individual with a Significant Financial Interest should have a role in the research, and if so, to what extent. If the individual can have a role in the research, the Board also considers whether the individual's role should be managed. At a minimum, the Board requires disclosure of the financial interest to subjects as part of the consent process. The Board may also require:

- Public disclosure of the financial interests
- Appointment of an independent research monitor
- Change of personnel or personnel responsibilities
- Disqualification of personnel from participation in all or a portion of the research
- Reduction of the financial interest

- Elimination of the financial interest
- Severance of relationships that create financial conflicts
- Modification of the research plan
- Involvement of external individuals in key portions of the research
- Transfer of IRB responsibilities
- Retrospective review
- Mitigation report
- Monitor the implementation of the management plan

5. The Informed Consent Process

A. Investigator responsibilities in regard to informed consent

- Give the person providing informed consent as much time as they need to make a decision.
- If the person providing informed consent needs more time than is allowed by the research design, not enroll the prospective subject.
- Evaluate whether the person providing informed consent is experiencing time pressure to make a decision, and if so, do not enroll the prospective subject, even if the person providing informed consent agrees to be in the research.
- Ensure there is no threat of harm or adverse consequences to the prospective subject for a decision to not take part in the research.
- Stop the informed consent process once the person providing consent indicates that he or she does not want to take part in the research.
- Evaluate whether the person providing informed consent is being coerced or unduly influenced by others to take part in the research, and if so, not enroll the prospective subject, even if the person providing informed consent agrees to be in the research.
- Communicate in the preferred language of the person providing informed consent.
- Adapt the presentation of the information to the subject's capacities in terms of intelligence, rationality, maturity and language.
- Invite and answer questions from the person providing informed consent.
- Evaluate whether the person providing informed consent understands the information provided, and not enroll a prospective subject who does not understand, even if that person providing informed consent agrees to be in the research.
- Ensure that no information is provided to the prospective subject or the person providing informed consent that is made to waive or appear to waive any of the prospective subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.
- Communicate to the person providing informed consent all the information in the consent document or script approved by the IRB.

- Invite and answer questions from the person providing informed consent. Not enroll a prospective subject when the person obtaining informed consent is unwilling to listen to or consider the information, even if the person providing informed consent agrees to be in the research.

B. Consent by Legally Authorized Representatives

Persons who can consent for adults who lack the capacity to personally provide informed consent are known as Legally Authorized Representatives (LAR's). See 45 CFR 46.102(i) and 21 CFR 50.3(l) -- These regulations define Legally Authorized Representative as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. We recommend you consult your state law and if necessary, obtain legal counsel to determine who represents a Legally Authorized Representative for your research.

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 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 _____." Sites should also be able to explain the process they use for verifying that an individual is qualified to serve as an LAR.

C. 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.

D. Waivers of Consent for non-FDA studies

If you are requesting a waiver of consent and the research is not an FDA regulated study, then criteria from 45 CFR 46.116(e), (f), or "45 CFR §46 Waiver of informed consent requirements in certain emergency research" must be met.

The most common waiver is revised Common Rule 45 CFR 46.116(f))

1. The research involves no more than minimal risk to the subjects;

2. The research could not practicably be carried out without the requested waiver or alteration;
3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
5. Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

If you are a covered entity under HIPAA, the necessary information is collected via our Initial Review Smart Form, or can be provided via the stand-alone WIRB form “Request for Full Waiver of Authorization Under HIPAA” available on the [Download Forms page](#) of www.wirb.com.

E. Waivers of Consent for FDA studies

In July 2017, the FDA issued new guidance titled “[IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects](#)”; the guidance states “FDA does not intend to object to an IRB waiving or altering informed consent requirements for certain minimal risk clinical investigations as described in Section IV of this guidance.” Prior to that guidance, waiver of consent for FDA regulated studies could be only allowed when the research met the requirements of either 21 CFR 50.23 (a) - (c) (waiver of consent for individual emergency use) or 21 CFR 50.24 (emergency research without consent), or FDA guidance issued 04-25-2006 for In Vitro Diagnostic Device Study Using Leftover Human Specimens That Are Not Individually Identifiable. Because the 2017 guidance covers all the situations covered in the 2006 guidance and is easier to implement, the IRB will use the 2017 guidance in lieu of the 2006 guidance.

For individual emergency waivers of consent, prospective IRB approval is not always necessary if a patient's life can be saved. See the Download Forms page of www.wirb.com, [Expanded Access tab](#) for more information or the section of this Guide titled “[About emergency and expanded access to investigational drugs, biologics, and devices](#)”.

F. Waiver of Documentation of Consent

A waiver of documentation of consent is a waiver of the requirement for a signature on a consent form. The regulations allow the Board to approve this type in the following situations:

For FDA or HHS regulated research (21 CFR §56.109(c)(1) and 45 CFR §46.117(c)(1)(ii)):

- The research presents no more than Minimal Risk to subjects; and

- The research involves no procedures for which written consent is normally required outside of the research context

For HHS regulated research (not applicable under FDA regulations) (45 CFR §6.117(c)(1)(i)):

- The only record linking the subject and the research will be the consent document;
- The principal risk is potential harm resulting from a breach of confidentiality;
- Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; and

For HHS regulated research (not applicable under FDA regulations) (45 CFR §6.117(c)(1)(iii))

- If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In general, the Board requires the investigator to provide subjects with a written statement regarding the research that embodies the elements of consent.

If you want to waive the requirement to obtain written documentation of consent, you need a subject information sheet. To create one use the template consent, change the title to "SUBJECT INFORMATION SHEET" and delete the signature blocks.

G. Waiver of Authorization for Use and Disclosure of Protected Health Information

If your organization must comply with the Federal Privacy Rule (HIPAA), and the research requires you to use or share identifiable health information, you must obtain an authorization for the use and disclosure of protected health information. If this is not practical, you need to request a waiver of authorization. If you are requesting a waiver of written documentation of consent, you also need to request a waiver of authorization.

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, when appropriate and possible WIRB requires that subjects who are not able to consent for themselves assent to participation. "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 indicate which subjects' assent must be obtained and whether and how assent is to be documented in writing.

In order to assent, a subject must have an understanding of what might be asked of them in the research and what might happen to a level consistent with the subjects capacity to understand.

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. Some state and local laws also further restrict enrollment of wards in research.

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 document must be accurate and complete
- The document must embody the required and appropriate additional elements of consent
- The document must be signed and dated by the subject or LAR
- The document must be signed and dated by the person obtaining consent
- A signed and dated copy must be given to the person signing the form
- The investigator must give the subject or LAR adequate opportunity to read it before it is signed and dated
- For clinical research: If the subject cannot read, an Impartial Witness must witness the consent process and sign and date the form

In order to obtain WIRB approval of a consent form, the sponsor may opt to do one, or a combination, of the following:

- Submit a *sponsor template* 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 *the WIRB Website for a sample Consent Template adopted by all WCG IRBs*. Consent templates provide a framework and structure upon which to build a consent form.

ii. Consent form elements

The following is a list of the required elements of a consent form:

Revised Common Rule new elements (45 CFR 46.116(a)(5)(i), (ii))

- (i) Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension. **(Note: the [WCG template consent form](http://www.wirb.com) available on the [Download Forms of www.wirb.com](http://www.wirb.com) has a section with prompts to assist you with this element.)**
- (ii) Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

- Study involves research
- Purposes of the research
- Expected duration of the subject's participation
- Procedures to be followed
- Identification of any procedures which are experimental
- Any reasonably foreseeable risks or discomforts
- Any benefits to the subject or to others which may reasonably be expected from the research
- Any appropriate alternative procedures or courses of treatment that might be advantageous
- The extent, if any, to which confidentiality of records identifying the subject will be maintained
- How to contact the investigator for questions, concerns, and complaints

- How to contact someone independent of the investigator for questions, concerns, complaints, and subject rights
- Whom to contact in the event of a research-related injury
- Participation is voluntary
- Refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled
- The subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
- Revised Common Rule (45 CFR 46.116(b)(9)(i):
 - One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
 - (i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or
 - (ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.
- Required for research involving more than Minimal Risk:
 - Whether any compensation is available if injury occurs and, if so, what they consist of, or where further information may be obtained
 - Whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained
- Required for FDA-regulated research
 - FDA may inspect the records
 - For controlled drug/device trials (except Phase I drug trials) and pediatric device surveillance trials: "A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."
 - The consent document does not give the subject the option of having data removed
- Required for research subject to ICH-GCP
 - A description of the IRB and its role
 - The probability for random assignment, if any
 - Any subject responsibilities
 - The reasonably foreseeable risks to an embryo, fetus, or nursing infant, if any
 - When there is no intended clinical benefit to the subject, a statement to that effect
 - The monitors, auditors, IRB, and regulatory authorities will be granted direct access to the subject's original medical records for verification of

clinical trial procedures and data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that,

- by signing a written informed consent document, the subject or the subject's legally acceptable representative is authorizing such access.
- If the results of the trial are published, the subject's identity will remain confidential
- Required when research involves a submission of genomic data to the NIH database of Genotypes and Phenotypes (dbGaP)
 - The identities of data subjects cannot be readily ascertained or otherwise associated with the data by the repository staff or secondary data
 - The 18 identifiers enumerated at section 45 C.F.R. 164.514(b)(2) (the HIPAA Privacy Rule) are removed
 - The submitting institution has no actual knowledge that the remaining information could be used alone or in combination with other information to identify subjects
- When appropriate
 - The research may involve risks to the subject which are currently unforeseeable
 - The research may involve risks to the embryo or fetus, if the subject is or may become pregnant, which are currently unforeseeable
 - Anticipated circumstances under which the subject's participation may be stopped without the subject's consent
 - Any additional costs to the subject that may result from participation in the research
 - The consequences of a subject's decision to withdraw from the research
 - Procedures for orderly termination of participation by the subject
 - New findings that may relate to the subject's willingness to continue participation will be provided to the subject
 - The approximate number of subjects involved in the study
 - Amount and timing of all payments
 - Revised Common Rule (45 CFR 46.116(c)(7-9))
 - (7) A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
 - (8) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
 - (9) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

In March 2016, WCG announced the creation of the WCG Gene Therapy Advisory Board. Through the Board, our clients have access to the best and most current

thinking in this new and emerging field. Go to www.wcgclinical.com for more information.

J. Review of “e-consent” (electronic consent) forms

Electronic consent (“e-consent”) via web applications and/or electronic tablets such as an iPad is growing in popularity. FDA has issued guidance titled “[Use of Electronic Informed Consent](#).”

WIRB reviews e-consent technologies during development and in their final form to ensure that they meet the regulatory requirements for the elements and documentation of consent. This section provides some simple best practices on how to prepare an informed consent IRB submission so that it is suitable for use in an electronic consent tool.

- i. e-consent submission timing
Sponsors and investigators considering eConsent may wish to obtain IRB approval of the consent document **text** prior to developing the electronic consent tool. Revisions based on IRB feedback are easier to implement before e-consent programming and animation has begun.
- ii. e-consent submission items
For a typical e-consent IRB submission, the Sponsor and e-consent vendor will jointly prepare the IRB submission of materials. Typical submissions include:
 - a. scripts for any video or audio files
 - b. storyboards for any planned video creation
 - c. content for any screens on the e-consent tool that will be viewed by the patient
- iii. Conditional and final approval
The IRB’s decision to conditionally approve versus defer will depend on the extent to which the draft version reflects the content of the final electronic version. If the bulk of the electronic process has been provided in draft text or in story boards, then the IRB can conditionally approve the consent form. However, if there is still substantial content to be developed, then the IRB must defer the consent form for future board review. Sponsors must determine how much time and resources they want to commit to developing an electronic consent before seeking an IRB decision.

The most optimal process is for the sponsor to provide in writing to the IRB a complete description of the electronic consent process, with story boards for videos if applicable. Then the IRB will likely be able to provide conditional approval and have a single individual review the final product.

If the final step is solely the transfer of the IRB approved consent form to the tablet, without any modification of the text wording, the IRB does not have to

conditionally approve the consent form and does not have to review the final version of the consent form on the tablet. The IRB can issue a final approval of the consent form. If there are photos or audio materials to add to the final version, then the IRB should review the final electronic version.

K. Description of WIRB's Preferred Vendor for e-Consent

In 2017, WCG acquired Patient Genesis' ConsentNow™ eConsent technology. ConsentNow improves the informed consent process by enabling healthcare companies to share important information with patients in a clear, easy-to-understand electronic format.

The technology employs custom video and animation segments to educate patients and online knowledge assessment questions to determine their level of understanding. This multimedia experience is delivered directly to the patient using a tablet device at the clinical site.

Knowledge empowers patients to make the best decisions for themselves and for their families - using a patient-friendly format that includes plain language, videos and animation, ConsentNow helps to ensure that patients truly understand the benefits and risks of their clinical trial participation.

In global clinical trials, communication can often pose significant challenges; ConsentNow enables providers to deliver important information in the patient's native language and capture their feedback via questionnaire. This helps to eliminate confusion for the patient, and increase efficiency for the trial's sponsor.

In addition to improving the quality of patient education and the consistency of trial communications, ConsentNow fosters regulatory compliance because it is always loaded with the latest version of the protocol and will not allow the consent process to be completed until all required signatures are in place. Another benefit of the ConsentNow solution is increased patient retention, as patients who are better informed at the start of the trial are less likely to drop out. And with a secure, web-based dashboard, it provides both the sponsor and clinical site team members with real-time access to valuable site statistics.

For clinical trial sites, the ConsentNow technology delivers an easier patient enrollment process, better informed patients, a significant reduction in paperwork, and real-time tracking of patient progress.

L. 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/regulations-and-policy/guidance/certificates-of-confidentiality/index.html>. Instructions for applying for a certificate are available here <https://humansubjects.nih.gov/coc/index>, but NIH is not the only source for one, as several federal agencies issue certificates.

The Department of Justice requires that researchers prepare a "Privacy Certificate" (PC), which is similar to a Certificate of Confidentiality (CoC) for all research it regulates. This requirement applies to the Department's research arm, the National Institute of Justice (NIJ) and its other parts, such as BJA, OJJDP, OJP, etc. More information is available here: <https://www.nij.gov/funding/humansubjects/pages/confidentiality.aspx>.

M. WCG Policy on Pregnant Partners

Effective January 22, 2018, WCG policy on collection of outcome data on partners of study subjects has changed. WCG policy is now as follows: the collection of outcome data on partners of study subjects who become pregnant does not meet the HHS definition of research, because it does not represent a systematic investigation designed to develop or contribute to generalizable knowledge. As a result, the IRB will no longer be making 45 CFR 46 Subpart B or D determinations for follow up of pregnant partners and their children.

If the protocol states that this procedure will occur, consent documents should continue to inform subjects of the plan to collect data if their partner becomes pregnant.

If you submit a consent document for pregnant partners, the IRB will review the document as a research consent form. However, if you do not submit a consent document for pregnant partners, the IRB will not require one.

This change does not affect the follow-up of subjects who become pregnant.

Those individuals are human subjects. Such data collection needs to be described in the consent document. Subpart B determinations are required to collect data about the pregnancy. Subpart D determinations are required to collect data about children resulting from the pregnancy.

6. Working With WIRB for IRB Review – An Overview

Western Institutional Review Board is composed of several individual review panels. Panels meet twice a week [except for WIRB's Canadian panel and the Executive Policy Committee]. Institutional IRBs formed under the Powered by WIRB program meet less frequently.

If not eligible for expedited review, 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 Action displays the panel assignment.

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 will be assigned to both a U.S. panel and the Canadian panel.

WIRB conducts expedited review of certain kinds of research involving no more than minimal risk to human subjects and one or more procedures listed in the categories published in the Federal Register. In minimal risk research, the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Users who create a [Connexus](#) account can access detailed tracking information and can download review documents from the site. Additionally, if you submit documents by email, mail, or facsimile, you may be charged additional administrative fees. Click on "LOGIN TO WCG CONNEXUS" link 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.

The protection of confidential business information and trade secrets is vital to the interests and the success of WIRB. All the employees and Board members are required to sign confidentiality agreements as a condition of employment, and WIRB follows industry standards on the protection of electronic data in our Part 11 compliant system.

Confidential Disclosure Agreements (CDAs) between sponsors and Western Institutional Review Board (WIRB) are not required by WIRB. However, we are happy to enter into a CDA if preferred by the sponsor. If you require a Confidentiality Agreement, your request will be directed to WIRB's General Counsel for preparation.

7. Submitting Documents for WIRB Review

A “smart” form is available for most WIRB submissions (such as initial review and changes in research). The “smart form” submission form dynamically omits questions that are not relevant, based on the answers you provide about the research.

Submit documents for review through the Connexus Web Portal or IRBNet. If you submit documents by email, mail, or facsimile, you may be charged additional administrative fees. Documents submitted via [Connexus](#) (and IRBNet) are also stored there for other users with access to your workspace to view (go to <https://connexus.wcgclinical.com/> to set up a Connexus account).

8. Materials required for initial review

The initial review submission form provides a listing at the end of standard documentation required for each submission (see first image below) and then a dynamic, customized list of required materials based on the answers provided in the form (see second image below)

Sample standard list of required attachments:

Required Submission Materials for Protocol and Site Submission

To avoid processing delays, remove security/password protection from all submitted documents.

Submit the following documentation:

- This form with all questions marked with a * answered
- Final protocol (or most recent version with any applicable amendments)
- Supporting documents
- All information intended to be seen or heard by subjects, including:
 - Consent documents (in Microsoft Word compatible format)
 - Information sheets (in Microsoft Word compatible format)
 - Advertisements and recruitment scripts (Advertisements and recruitment materials and changes to advertisements and recruitment materials must be IRB approved before their use)
- Curriculum vitae for the Principal Investigator (PI), if a current one is not already on file with the IRB

Sample dynamic, customized list of attachments needed based on your answers in the smart form:

Additional Submission Materials Based on Previous Answers

Based on previous answers, include the following additional documentation with this submission:

Reason



Submit a completed "Translation Request" form available on the IRB Web Site

Because you have indicated that you need translated documents:

- (Any commercially available validated instruments cited in the protocol that are used without modification are not listed individually on the Certificate of

Action; however, approval of the protocol does extend to the uses of such industry standard forms as described in the approved protocol.)

Physicians seeking approval to use a Humanitarian Use Device (HUD) on-label, may use the form titled [Clinical Use of a Humanitarian Use Device \(HUD\) \(HRP-284\)](#) designed for such review requests. [See the FDA guidance titled “Guidance for HDE Holders, Institutional Review Boards (IRBs), Clinical Investigators, and Food and Drug Administration Staff Humanitarian Device Exemption (HDE) Regulation: Questions and Answers” for more information about requirements for use of HUDs.]

A. 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 (such as, 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 (such as, 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 (such as, 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 (such as, 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. The definition of minimal risk for research involving prisoners is somewhat different: the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.
- **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 could be unduly influential or coercive.
- **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 trials; therapeutic benefit trials; and non-therapeutic trials where the objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally, the foreseeable risks to the subjects are low, the negative impact on the subject's well-being is minimized and low, the trial is not prohibited by law, and the approval of the IRB is expressly sought on the inclusion of such subjects, and the IRB written approval covers this aspect (ICH 4.8.14).

Note: Occasionally a site may have enrolled a subject in a trial where loss of capacity was not contemplated (such as an oncology trial), but would like to keep a subject who unexpectedly lost capacity enrolled and make arrangements for consent by a legally authorized represent; please request WIRB review of these situations as a change in research.

- **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 (such as, 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 (such as, 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. Payments should accrue as the study progresses and subjects do not have to complete the entire study to be eligible to receive a payment.

B. 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 on the ethics and regulations of human subject protections. For clinical research, the Principal Investigator (PI) must ensure that all investigators and research staff undergo training on Good Clinical Practice (GCP). *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.

When standard therapy is part of the research, WIRB only requires human research subject protection 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).

Examples of courses are listed below. You are not limited to these training resources. Additional opportunities are available through other sources. External links are provided for user convenience and do not represent an endorsement by WIRB.

Online:

- Courses available through [WCG Academy](http://wcgacademy.com). (The WIRB-Copernicus Group[®] (WCG) has partnered with UL EduNeering[®] (UL), the foremost provider of cloud computing learning solutions, to create WCG Academy[™], an FDA-adopted, Part 11-compliant training program for clinical research professionals. Designed by experts in clinical research and adult learning, the WCG Academy curriculum is interactive and role-based, helping adults to retain more information than any other learning solution. WCG Academy also provides robust dashboards and metrics to foster compliance and efficiency.) For more information, go to <http://wcgacademy.com/contactus.html>.
- WIRB is a participating organization in the Collaborative Institutional Training Initiative (CITI). Investigators submitting research to WIRB can meet the training requirement through CITI or CITI International. CITI training for U.S. research is available at: <https://www.citiprogram.org>. CITI International training for non-U.S. or international research is available at: www.citiprogram.org. (The international course is available in English, Spanish, and Chinese. Additional languages may be available in the future.)
- ACRP Certified Principal Investigator Training (CPI certification)
- DIA Clinical Research Certificate Program
- SOCRA Clinical Research Professional (CRP)
- Canadian researchers are required to complete training through the Tri-Council Policy Statement (TCPS) before their submission will be approved. The *TCPS 2 Tutorial Course on Research Ethics (CORE)* is available online in English <http://www.pre.ethics.gc.ca/eng/education/tutorial-didacticiel> and French <http://www.ger.ethique.gc.ca/fra/education/tutorial-didacticiel>.
- The NIH Office of Extramural Research provides an online tutorial called "Protecting Human Research Participants" (now updated with revised Common Rule requirements) <http://phrp.nihtraining.com/users/login.php> with basic information about human research protection, which WIRB accepts as training on the topic, but WIRB also encourages study teams to complete programs that provide a deeper, broader training on the topic.

Physicians and their teams who request approval of approval of Clinical Use of a Humanitarian Use Device (HUD) or compassionate use of a drug, biologic, or device are not required to complete training on the ethics and regulations of human subject protections.

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

WIRB's **initial review submission forms** ask for information about an IND. FDA 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 sponsor 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.

D. 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.

The submission form will prompt you to provide the appropriate, required documentation for review of research involving an SR device. The Board will automatically consider research with an IDE 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.

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.

If approved devices will be used as part of the research, each site may be asked to confirm that the device(s) they are using are being used within their approved labeling.

E. 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 completed initial review submission form, 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.

F. Special considerations for Federally Funded Research

i. FWAs

The submission form will prompt you to provide the appropriate, required documentation for review of research involving an FWA. 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.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-engagement-of-institutions/index.html>.

With 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/regulations-and-policy/guidance/guidance-on-engagement-of-institutions/index.html>. OHRP requires all FWA applications be submitted electronically using the electronic submission system available through the OHRP website at <http://ohrp.cit.nih.gov/efile/>, unless an institution lacks the ability to do so electronically. If an institution believes it lacks the ability to submit its FWA electronically, it must contact OHRP by telephone or e-mail (see <http://www.hhs.gov/ohrp/register-irbs-and-obtain-fwass/contact/index.html>) and explain why it was unable to submit its FWA electronically. The registration number for WIRB is IRB00000533. WIRB will request a copy of the DHHS-approved FWA application, but if it is not available, it is not required for review.
- 2) An IRB Authorization Agreement must be completed. A template [form](#) is available on the Download Forms page of www.wirb.com.

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.

G. Special considerations for multi-center studies

Each individual submission for a multi-center study must be accompanied by a completed initial review submission form.

Any site submission lacking a complete submission form and any required materials cited on the form may 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.

Contacts listed in the initial review submission form with the “Copy this person on IRB correspondence box marked will receive copies of the reviewed documents sent to investigators.

i. Consent forms for multi-center research

WIRB creates a “consent form template” which incorporates the IRB’s required changes into the sponsor template consent form. By using the consent form template you can be confident that you are starting with the most recent WIRB and sponsor-approved language, thereby ensuring accurate version control, while saving you time and effort.

If you do not require site specific customization, WIRB will create your site’s informed consent using the WIRB-approved template, as is. WIRB will add your site-specific information included in your submission form, such as investigator name, 24-hour telephone number, and subject payment language.

If you require customized language, request the WIRB-approved consent template from Client Services at clientservices@wirb.com. Track (redline) your changes on the WIRB-approved informed consent so WIRB can easily identify your site-specific customizations.

WIRB requires the use of IRB-approved informed consent(s) for initial review submissions of new principal investigators (PIs), effective July 3, 2018.

To expedite site review, WIRB recommends that sponsors/CROs provide sites with the WIRB-approved informed consent(s).

ii. 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.

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 submission 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.

iii. Pre-Review 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 consent form. The fee for initial review applies.

If the Board finds the research as reviewed acceptable, the submitter is issued an approval notice (listing any special Board determinations, if applicable), 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 the research cannot go forward until appropriate documentation for an investigator has been received and reviewed by the Board, and an unconditional approval has been issued for that investigator.

The submission form will prompt you to provide all the appropriate, required documentation for review.

Following Board review, individual investigators may be submitted.

- If you do not require site specific customization, WIRB will create the site's informed consent using the WIRB-approved template, as is. WIRB will add your site-specific information included in the submission form, such as investigator name, 24-hour telephone number, and subject payment language.
- If you require customized language, request the WIRB-approved consent template from Client Services at clientservices@wirb.com. Track (redline) your changes on the WIRB-approved informed consent so WIRB can easily identify your site-specific customizations.
- Sponsors of research involving multiple Canadian locations may benefit from requesting a pre-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 template 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).

iv. Single Review Solution™ (SRS)

WCG is the only ethical solutions provider –in the world– to offer a streamlined, unified [Single Review Solution™ \(SRS\)](#) for all sites involved in a clinical trial. Whether sites are private, central or institutionally based, each is reviewed under one Institutional Review Board (IRB) umbrella using WCG’s proprietary SRS process. SRS leverages the members of the WCG family of companies – Western Institutional Review Board® (WIRB), Midlands Independent Review Board (Midlands IRB), Aspire Independent Review Board (Aspire IRB), New England Independent Review Board (New England IRB) and Copernicus Group Independent Review Board® (Copernicus IRB) – to deliver increased efficiency in its review of clinical trials.

SRS connects WCG’s industry clients with over 1,000 academic medical centers, universities and hospitals for which WIRB is an IRB of record. SRS provides a single, seamless review of the protocol and its associated sites.

H. 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. The 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.

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 provide non-English speaking subjects with a

certified translation approved by WIRB of the approved consent form in the subject's language

If you will NOT be partnering with a local IRB who will oversee the translation(s), the translation must be approved by WIRB. If you produce your own translation, submit it for review along with a copy of the certificate from the translator attesting to the fact that the document(s) are true and accurate translations of the WIRB-approved consent form or other subject material.

I. Special considerations for investigators at institutions

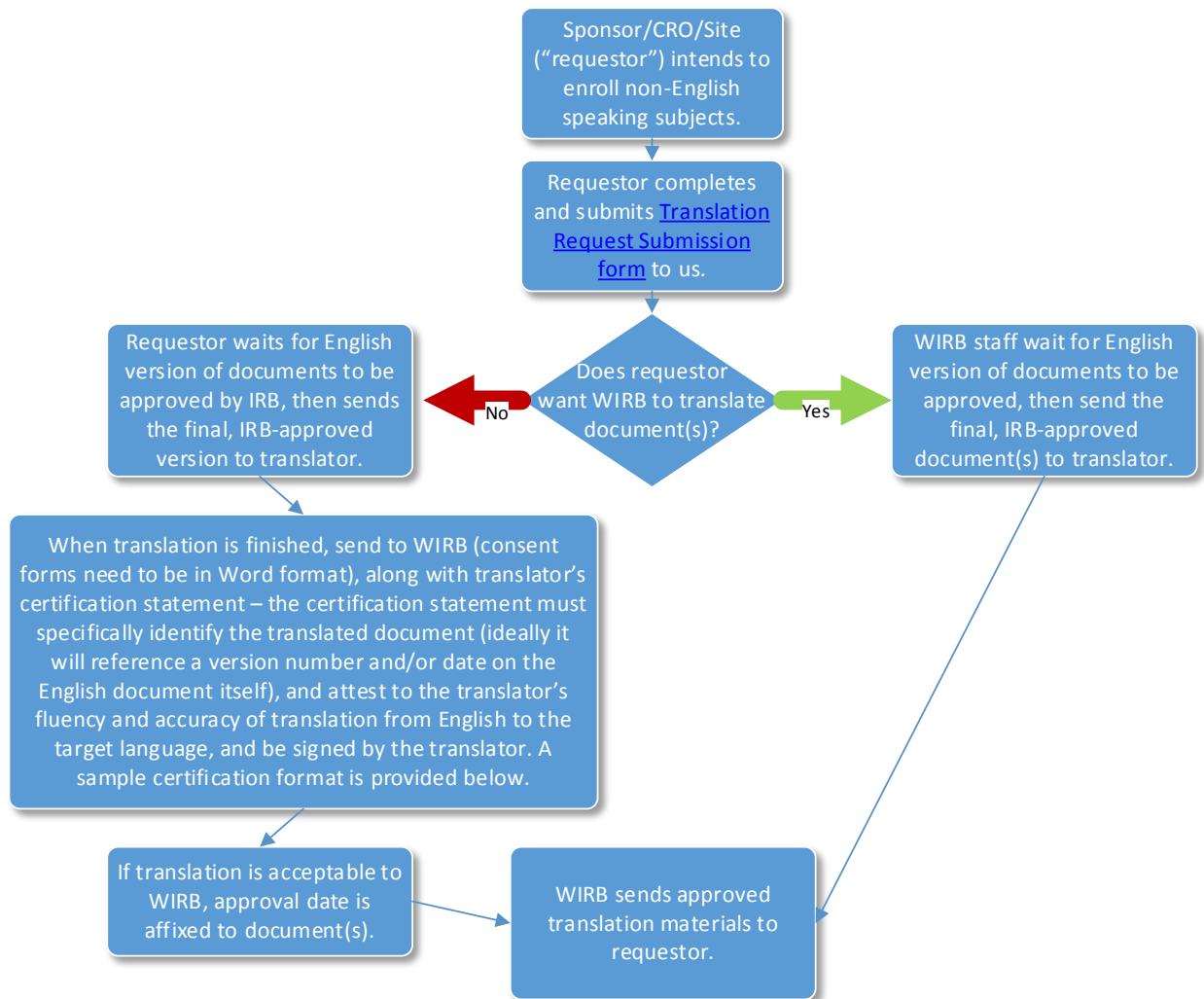
In addition to meeting the requirements of WIRB, an investigator at an institution may be subject to local institutional requirements. Institutional investigators should check with their local research office to determine what requirements, if any, must be fulfilled prior to submitting research to WIRB. 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.

J. 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. Our 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.

i. Translations Overview:



A [Translation Request Submission form](#) needs to accompany each initial request for translations (per site) -- this process applies whether you are using WIRB's Translations services or your preferred vendor. The form is available on the Download Forms page of www.wirb.com. If the initial request for Translations to be processed is provided without the Translations Request Submission form, the submission will not be processed until the form is received.

ii. WIRB-Arranged Translations:

Based on the instructions provided in the submitted [Translation Request Submission form](#), IRB translations staff send the document for translation 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, IRB approved 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 WIRB.

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 (see also "[Unexpected Translations Needs](#)" section below). 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).

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.

In January 2016, WIRB began issuing approvals for translated documents. This harmonizes our processes with that of our partner IRB, Copernicus Group IRB.

iii. 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 completed [Translation Request Submission form](#), 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 (such as subject diaries, subject instructions) need to be legible (faxed copies often are not legible) and accompanied by a translator certification statement as well.

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; such as, 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. _____

iv. Unexpected Translations Needs:

WIRB has the following policy regarding the use a short form consent process to enroll subjects who do not speak English. This policy is limited to the situation when **both** of the following are true:

- A full-length version of the consent form in a language understandable to the subject is not available, and
- It is in the subject's best medical interest to be enrolled in the research before a translated consent form can be obtained.

The short form will follow the [WCG template short form](#), and the subject will have to be reconsented with the current WIRB-approved consent form in a language understandable to the subject within 60 (business) days or at the first visit after receipt of the translated consent form (whichever is less). Some certified short form translations are posted and available for use on the www.wirb.com [Download Forms](#) page.

Each of the following steps must be followed:

1. The Principal Investigator is to insert study specific information, including title of study, principal investigator, appropriate signature lines (copy from the approved English version or keep the appropriate template ones provided in the translated short forms posted on www.wirb.com), and contact information into the OHRP template short form.

2. The subject must be given a copy of the short form in the language understandable to him/her to read;
3. A translator/interpreter must orally present the entire IRB-approved English ICF;
4. The consent process must be witnessed by an individual who is fluent in both English and the subject's language;
5. The English ICF must be signed by the person obtaining consent as authorized under the protocol and the witness;
6. The short form must be signed by the subject, person obtaining informed consent, and witness;
7. The subject must be given signed copies of the English ICF and short form;
8. The original signed English ICF and the original signed short form should be retained in the subject's research record and medical record, if appropriate;
AND
9. The PI will then obtain a fully translated version of the currently approved consent form at the earliest opportunity. The subject would then be re-consented using the translated consent form within 60 (business) days or at the first visit after receipt of the translated consent form (whichever is less).

V. Translations FAQs:

Q: I would like to get study documents translated from English to another language, what are my options?

A: WIRB can provide translations of WIRB-approved English study documents into many different languages. Use the WIRB [Translation Request Submission form](#) (available on the [Download Forms page](#) of www.wirb.com) to request translations.

If you prefer to use your own translation service, that is okay too! WIRB can also review and formally approve your translations of documents that WIRB has approved in English. See [the section above](#) for submission instructions.

Q: Does WIRB provide back-translations services?

A: Yes, upon request WIRB does provide back-translations services. However, the estimated completion date for the back translations is an additional 10 business days from the time that the initial translation is completed.

Q: How long does it take for WIRB to review/approve the translated documents I submit?

A: You can expect a turnaround time of ten business days.

Q: Does WIRB provide translations for non-WIRB sites?

A: As WIRB is not a translations service, we do not provide translations for non-WIRB sites.

Q. This sounds fantastic! How can I learn more?

A. *If you have more specific questions for us, you can call Client Services (1-800-562-4789).*

Q: What is the fee schedule for Translations?

A: *Please contact Client Services to obtain a copy of the Fee Schedule for Translations.*

Q.: Why do my translated documents have an approved date on it?

A. *In the continued effort to harmonize processes within the WIRB-Copernicus Group, beginning January 4, 2016, each Translated document receives a Board action.*

The Board action date is listed as the Translation Approval date in the footer of the approved translation. See example below:

TRANSLATIONS APPROVED
Dec 10, 2015
WIRB®

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The approval letter issued by WIRB also indicates the date of WIRB's approval of the translation.

K. Special considerations for enrollment of wards of the state

Our 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. Some state and local laws also further restrict enrollment of wards in research.

L. About emergency and expanded access to investigational drugs, biologics, and devices

FDA has set up several methods for patients and their physicians to access investigational drugs, biologics, and devices when patients with a life-threatening or serious disease have run out of options. There are four broad categories:

1. Emergency use of drugs and biologics: For situations where treatment cannot wait for IRB Chair concurrence.
2. Emergency use of devices: For situations where treatment cannot wait for IRB Chair concurrence.
3. Compassionate use of drugs and biologics: For situations where treatment can wait for IRB Chair concurrence.
4. Compassionate use of devices: For situations where treatment can wait for IRB Chair concurrence.

It usually takes no more than four days for IRB Chair concurrence.

Compassionate use is also called Expanded Access or Single Patient Expanded Access.

The WCG IRBs do not charge for review of single patient treatment use of a drug or device.

FDA maintains a 24-hour phone number for questions about emergency and compassionate use: Office of Crisis Management & Emergency Operations Center: (866) 300-4374.

i. Emergency use of drugs and biologics

You may use an unapproved drug or biologic without prior FDA authorization or IRB Chair concurrence if:

- The patient has a life-threatening or severely debilitating situation.

***Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do NOT require the condition to be immediately life-threatening or to immediately result in death. Rather, the patients must be in a life-threatening situation requiring intervention before a chair can concur with the use.*

***Severely debilitating** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.*

- NO standard acceptable treatment is available.
- There is insufficient time to obtain IRB approval
- FDA has authorized the use of the unapproved investigational drug or biologic

For authorization, contact FDA's Office of Crisis Management & Emergency Operations Center: (866) 300-4374. This phone number is staffed 24x7.

- The treating physician will obtain written informed consent of the patient or the patient's legally authorized representative (*See the [WIRB Web Site for the Template for Informed consent for Emergency and Compassionate Use](#)*) or certify in writing that:
 - The patient is confronted by a life-threatening situation necessitating the use of the drug or biologic.
 - Informed consent CANNOT be obtained from the patient because of an inability to communicate with, or obtain legally effective consent.
 - There is insufficient time to obtain consent from the patient's LAR.

- An alternative method of approved or generally recognized therapy that provides equal or greater likelihood of treating the patient is unavailable.
- Either:
 - In advance of the treatment, have a physician who is NOT otherwise participating in the treatment certify in writing that findings justifying an exception to informed consent are met.
 - After the treatment, certify that immediate use of the drug or biologic was required to preserve the life of the patient such that there was insufficient time to obtain a determination from an independent physician in advance of using the drug or biologic, and within 5 working days after the treatment, have an independent physician who is NOT otherwise participating in the treatment evaluate the treating physician's determinations justifying NOT obtaining informed consent

You must provide the IRB with a report of the conditions constituting the emergency and documentation of the above findings within 5 working days after the use.

Use ["FORM: Emergency Use of a Drug or Biologic \(HRP-280\)"](#) to submit a report. This form is on the IRB Web Site. Submit your completed report via e-mail (clientservices@wirb.com) or via [Connexus](#). The "Required Materials" section of this form lists the documents you must submit with your report.

ii. Emergency use of devices

You may use an unapproved drug or biologic without prior FDA or IRB Chair concurrence if:

- The patient has a life-threatening or serious disease or condition that needs immediate treatment, diagnosis, or monitoring.

Life-threatening disease or condition means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the patients must be in a life-threatening situation requiring intervention before obtaining FDA approval.

Serious disease or condition means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

Serious disease or condition includes sight-threatening and limb-threatening conditions as well as other situations involving risk of irreversible morbidity.

- NO generally acceptable alternative exists.
- Because of the immediate need to use the device, there is NO time to use existing procedures to obtain FDA approval for the use.
- The treating physician has assessed the potential for benefit from the use of the unapproved device, and has substantial reason to believe that benefits will exist.
- The treating physician will follow as many of the following patient protection procedures as possible:
 - Informed consent from the patient or a legal representative

See the IRB's Web Site for the [Template for Informed consent for Emergency and Compassionate Use](#) - for emergency use of a device, change all references in the template from "drug" to "device".

- Clearance from the institution as specified by their policies
- Concurrence of an IRB chair
- An independent assessment from an uninvolved physician
- Authorization from the device manufacturer

You must provide the IRB with a report of the conditions constituting the emergency, documentation of the above findings, and the patient protection measures that you followed within 5 working days after the use

Use "[FORM: Emergency Use of a Device \(HRP-281\)](#)" to submit a report. This form is on the IRB Web Site. Submit your completed report via e-mail (clientservices@wirb.com) or via [Connexus](#). The "Required Materials" section of this form lists the documents you must submit with your report.

If no IDE exists, you must submit a follow-up report on the use of the device (description of device used, details of the case, and the patient protection measures that you followed) to:

*Food and Drug Administration
Center for Devices and Radiological Health
10903 New Hampshire Ave
Document Control Center
WO66 Rm G-609
Silver Spring, MD 20993*

iii. Compassionate use of drugs and biologics

You may use an unapproved drug or biologic without prior FDA authorization if:

- The patient has a life-threatening or severely debilitating illness.

Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do NOT require the condition to be immediately life-threatening or to immediately result in death. Rather, the patients must be in a life-threatening situation requiring intervention before a chair can concur with the use.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

- NO generally acceptable alternative for the condition exists.
- The patient cannot obtain the drug under another IND or protocol.
- The probable risk to the patient from the drug is NOT greater than the probable risk from the disease.
- FDA has issued an Individual Patient Expanded Access IND authorizing the treating physician to treat this patient.

For authorization, contact FDA's Office of Crisis Management & Emergency Operations Center: (866) 300-4374. This phone number is staffed 24x7.

- An IRB Chair concurs with the use before the treatment begins. (See below for how to submit a request for IRB Chair concurrence.)
- The treating physician will obtain informed consent from the patient or legal representative.

See the WIRB Web Site for the [Template for Informed consent for Emergency and Compassionate Use](#).

To request IRB Chair concurrence for compassionate use of a drug or biologic, Completed "[FORM: Compassionate Use of a Drug or Biologic \(HRP-282\)](#)" and submit that form with all required attachments listed in the form to the IRB via e-mail (clientservices@wirb.com) or via [Connexus](#). The "Required Materials" section of this form lists the documents you must submit with your request.

iv. Compassionate use of devices

You may use an unapproved device without prior FDA authorization if:

- The patient has a life threatening or serious disease or condition.

Life-threatening disease or condition means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the

condition to be immediately life-threatening or to immediately result in death. Rather, the patients must be in a life-threatening situation requiring intervention before obtaining FDA approval.

Serious disease or condition means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. Serious disease or condition includes sight-threatening and limb-threatening conditions as well as other situations involving risk of irreversible morbidity.

- NO generally acceptable alternative treatment, diagnostic, or monitoring for the condition exists.
- The probable risk to the patient from the device is NOT greater than the probable risk from the disease.
- The treating physician has devised an appropriate schedule for monitoring the patient to detect any possible problems arising from the use of the device, taking into consideration the investigational nature of the device and the specific needs of the patient.
- If any problems occur as a result of device use, these will be reported to the IRB as soon as possible.
- The treating physician will obtain informed consent from the patient or legal representative.

If you do not have consent form, see the IRB's Web Site for the [Template for Informed consent for Emergency and Compassionate Use](#) - for compassionate use of a device, change all references in the template from "drug" to "device".

- The treating physician has obtained clearance from the institution, if any, as required by their policies.
- FDA has issued an IDE and will approve or has approved the use.

For authorization, contact FDA's Office of Crisis Management & Emergency Operations Center: (866) 300-4374 or (301) 796-8240. This phone number is staffed 24x7.

To request IRB Chair concurrence for compassionate use of a device, Completed "[FORM: Compassionate Use of a Device \(HRP-283\)](#)" and submit that form with all required attachments listed in the form to the IRB via e-mail (clientservices@wirb.com) or via [Connexus](#). The "Required Materials" section of this form lists the documents you must submit with your request.

V. Additional References

- [Emergency Use of an Investigational Drug or Biologic - Information Sheet](#)
- [Expanded Access to Investigational Drugs for Treatment Use — Questions and Answers](#)
- [Expanded Access: Information for Physicians](#)
- [FDA's Guidance on IDE Policies and Procedures, Expanded Access for Medical Devices](#)

M. Special considerations for Unregulated Research in Maryland, New York and Virginia

Due to the special state laws in New York, Virginia and Maryland in regard to research, WIRB has opted to apply the Revised Common Rule as an equivalent regulation to all unregulated (not federally funded or subject to FDA regulation) research in those states approved after January 21, 2019.

As a result, WIRB will require that the consent form has a concise summary and includes the required and appropriate additional elements of consent required under the Revised Common Rule.

9. IRB Transfer

An IRB transfer happens when a study that has been approved by another IRB is transferred to WIRB. Transfers happen for a variety of reasons -- if an investigator decides to change IRBs for some reason, if a local IRB is closing, or if the study is at an institution that has recently signed a contract with WIRB.

A. Required documentation for an IRB transfer review request:

- WCG Initial Review Submission Form (available on the Download Forms page of www.wirb.com) including all required attachments cited in the form
- Background information provided on the WIRB “[Cover Letter/Checklist for Transfer of IRB Oversight to WIRB](#)”
- A copy of the complete current protocol if not already on file at WIRB
- A copy of the currently approved consent form (the one approved by the previous IRB)
- Any documents that the submitter has been instructed to provide based on his/her answers to the questions on the [Cover Letter/Checklist for Transfer of IRB Oversight to WIRB](#) form (for example, the form instructs the submitter to provide any new risk or benefit information that was not submitted to the previous IRB).

B. Clinical trials undergoing IRB transfer fall into two categories:

1. “**Active**” – some or all subjects are on active* treatment and the site may recruit more subjects for the study.
2. “**Follow-up only**” – the site will not recruit any more subjects, but still has subjects in follow-up (subjects no longer on active* treatment).

*WIRB acknowledges that the definition of “active” may vary, depending on the type of research being transferred. For drug studies, generally if a subject is no longer receiving any study drugs (active drug, control, placebo, etc.), but the investigator is collecting follow-up data on them, then those subjects are in follow-up, not “active.”

C. Why the distinction between “active” sites and sites in “follow-up only?”

If a site is still enrolling and/or has active subjects, WIRB will provide the site with an updated consent form with instructions for how subjects can contact WIRB if they have questions about their rights as a research subject or with questions, concerns, input, or complaints about the research. Alternatively, if the site’s subjects are all in “follow-up only” status, WIRB will review the existing consent form for completeness, and if it is compliant with the regulations, will accept the existing consent form and provide a letter for the site to give to subjects notifying them of the change of IRB.

D. Recommended instructions for institutions deactivating their IRB or transferring multiple projects to WIRB:

1. Plan a conference call with WIRB to discuss preliminary steps toward transition of studies.
2. Begin to assess which studies have active subjects which will need to be transitioned first.
3. Begin to assess continuing review schedules which may necessitate immediate transfer to keep those studies open for active subjects. (Plan to keep the existing IRB functioning until all open studies have either closed or been approved by WIRB.)
4. Notify WIRB of the number of studies that are to be transitioned.
5. Communicate to the research community the plan to transfer active studies to WIRB.
6. Communicate to the research sponsors the plan to transfer active research to WIRB - notifying them of impending change with request for payment of transfer, and give the sponsor a deadline after which transfer will take place.
7. Establish a date for a startup meeting with a WIRB representative, if necessary or desirable, depending on staff familiarity with WIRB forms and systems, or volume of studies.

10. The review process

A. Board Actions

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

i. Approve

“Approve” means the IRB determines that the initial, continuing, or modification submission meets the criteria for approval.

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.

Approval is usually communicated to the investigator by a Certificate of Action (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 Action

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 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.

Explanatory notices relevant to the review.

ii. Conditionally Approve

Conditionally Approve means the IRB determines that the initial, continuing, or modification submission will meet the criteria for approval with minor or prescriptive changes or requirements that can be verified without considering the criteria for approval.

- 1) You will receive written notification of the conditions promptly after the review.
- 2) Once you submit the requested information, then your submission will be re-reviewed. Once that review is complete and all information is confirmed, you will receive your approval documents.
- 3) It is important to note that the study, change in research, or other submitted material **is not approved until we confirm that any/all of the condition(s) have been satisfied**. This process does not allow you to begin research-related activities until you receive your final approval documents.

iii. Defer

"Defer" means the IRB determines that the initial, continuing, or modification submission does not meet the criteria for approval and also does not meet the criteria for "Disapprove". When the IRB takes this action, it will summarize its reasons and recommendations, if any.

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

Reconsideration of a disapproval may be requested. 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.

iv. Disapprove

"Disapprove" means the initial, continuing, or modification submission does not meet the criteria for approval and the IRB considers the research to have extensive deficiencies.

When the IRB takes this action, it will summarize its reasons and recommendations, if any.

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.

Reconsideration of a disapproval may be requested. 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.

B. NURSING MAGNET DESIGNATION

WIRB has consistent membership and involvement by at least one nurse in the governing body responsible for the protection of human subjects. Each WIRB panel has either a nurse member or a nurse alternate member that is invited to attend and present at panel meetings, and a nurse Board member is always present and in voting status when a nursing protocol is reviewed. Our records indicate that the majority of our meetings have either a nurse member or nurse alternate member present and in voting status.

WIRB may also be asked to determine research to be exempt from IRB Review. Exempt determinations are made by a WIRB Board member. After discussion with Ms. Jan Moran, ANCC, she agreed that this is appropriate review under the IRB regulations, and that a nurse board member is not required to make an exempt review determination.

11. 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.

You may use the WIRB **Change in Research Submission Form** available on the Download Forms page of www.wirb.com 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**. In order to facilitate the submission of consent form changes, WIRB routinely provides sponsors and CROs with a clean copy of each WIRB-approved consent (without site specific information in it).

ii. How to submit a consent form modification

Requests for consent form modifications should consist of **Change in Research Submission Form**, and a copy of **the WIRB-approved consent form with proposed changes clearly-marked (or a document specifying the requested changes)**. Proposed changes to the consent form should be “redlined” into an electronic copy of the current WIRB-approved consent form. In order to facilitate the submission of consent form changes, WIRB now routinely provides sponsors and CROs with a clean copy of each WIRB-approved consent (without site specific information in it). Changes sent to WIRB on the *sponsor’s* template consent form will not be accepted.

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, and changes to study procedures that are described in the consent form must be supported in a revised protocol.

We recommend using the “smart” **Change in Research Submission Form** available on the Download Forms page of www.wirb.com. . Submit the form and all supporting documents through the Connexus Web Portal or IRBNet. If you submit documents by email, mail, or facsimile, you may be charged additional administrative fees.. Submissions should reference the sponsor protocol number, WIRB study number, and name(s) of applicable investigator(s).

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, your review will take place more quickly. You can contact WIRB Client Services to determine if pre-approved language exists for your change in research.

Because sponsor version dates or numbers listed in headers or footers of consent forms are not a WIRB requirement, but are voluntary information listed on consent forms, WIRB does not routinely update the information listed unless the submitted consent form indicates that information should be updated. WIRB uses its own methods and identifiers for its staff to track WIRB approved versions and content. We have observed that the consent form version identifiers used by sponsors, CROs, and institutions vary across the industry, so we don’t proactively make any changes to that information, but instead we follow the instructions provided by the submitter .

iii. How to Request a Reconsideration

Requests for a **reconsideration** of a Board action must 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

Submit the “Site being added to existing protocol, or **change of Principal Investigator (PI)**” branch of our **initial review submission form**, license, and CV for the new investigator (unless current versions are already on file with WIRB), a request to modify the existing consent form to reflect the new investigator’s name and contact information (when applicable), and any other materials the submission form prompts you to submit.

The Board requires written confirmation from the sponsor that the change is acceptable and has been approved. The Board expects departing PIs to arrange for an orderly transition of their research to the new investigator. The sponsor is required to select investigators under 21 CFR 312.53(a).

Once approved, the new PI is authorized by WIRB to carry out the study as previously approved for the prior investigator (unless the Board provides alternate instructions to the new PI). This includes continued use of the previously approved study materials (consent form, recruitment materials, subject materials, and so forth). WIRB considers the approval of the new PI a continuation of the original approval, so the identifying information about the study remains the same (study number, etc.)

v. How to Submit an Updated Drug Brochure

Updated drug brochures should be accompanied by a summary of changes, a cover letter identifying the name of the Principal Investigator, the drug, and the WIRB protocol and study numbers. Submit the documents through the Connexus Web Portal or IRBNet; if you submit documents by email, mail, or facsimile, you may be charged additional administrative fees.

B. Additional changes which require submission to WIRB

- Notify WIRB of changes of address or telephone for the investigator or the site(s) **before the move**. (If you are adding a site or moving to a new site, or download and complete a WIRB [Change in Research Submission Form](#) for each new or updated location and forward to us.
- Notify WIRB of changes of address, or telephone for study or sponsor contacts. We recommend using the [Contact Information Update form](#) available on the Download Forms page of www.wirb.com.

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.)

Complete our [Change in Research Submission Form](#) 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, approves it with modifications or as submitted. . The submitter receives a copy of the script displaying the Board’s required modifications, if any. The final recording must be submitted to WIRB for final approval before use with subjects and **MUST** match the WIRB approved script. Submit a copy of the corresponding script 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.

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, will be reviewed by the Board and, if acceptable, approved either as submitted or with modifications required by the Board.

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.

Doctor to Doctor Materials, Press Releases: 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 prior IRB review of doctor-to-doctor letters, press releases, or interviews with the media and there is no need to provide WIRB with copies of these materials. However, if you would like to have IRB review for such materials we will provide a review upon submission.

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

Criteria for approval of advertising:

- The advertisement does not state or imply a certainty of favorable outcome or other benefits beyond what is in the consent document and protocol
- The advertisement does not include exculpatory language

- The advertisement does not emphasize the payment or the amount to be paid, by such means as larger or bold type
- The advertisement does not promise “free treatment” when the intent is only to say subjects will not be charged for taking part in the research
- The advertisement is limited to the information prospective subjects need to determine their eligibility and interest
- Additional criteria for approval of an advertisement for clinical trial
 - The advertisement does not make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling
 - The advertisement does not use terms, such as “new treatment,” “new medication,” or “new drug,” without explaining that the test article is investigational
 - The advertisement does not include compensation for participation to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing

WIRB suggests the following elements be present in screening scripts:

Introductory Statement:

- 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 should 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 guidance is to prevent any possible misunderstanding that the answers will be held in complete confidence.
- When appropriate, the script should 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 is preferable 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

- Please submit for the IRB’s review the actual questions that will be asked, not just a general statement such as “inclusion/exclusion criteria addressed.”

Closing Statement

- The script should include a closing statement informing the subject of whether or not they have met the preliminary screening requirements.
- The script should 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, this should be described to the subject as well, and the subject must have an opportunity to decline.

Additional Issues

- The screening script should be in language understandable by lay people. If complicated medical terms must be included in the screening script, please provide the IRB with an explanation of how they will be explained to the subjects.
- The IRB realizes that the script may not be followed verbatim, as subjects may ask additional questions or stray from the topic. This is acceptable, but the IRB expects that the interviewer will keep as closely as possible to the spirit and letter of the script.
- It is useful to the IRB if the investigator informs it 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.

12. 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.

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.

13. WIRB reporting requirements

A. “Promptly Reportable Information” form

Use the WIRB [“Promptly Reportable Information” form](#)* to report the following information to us within 5 days:

- Audit, inspection or inquiry by a federal agency
- Written report from a federal agency (e.g., FDA Form 483)
- State medical board action or hospital medical staff action
- Allegation of noncompliance or finding of noncompliance
- Suspension or premature termination by the sponsor, investigator, or institution
- Incarceration of a subject in a research study not approved to involve prisoners
- New or increased risk
- Change in financial interest disclosure
- Protocol deviation that harmed a subject or placed subject at risk of harm
- Protocol deviation made without prior IRB approval to eliminate an immediate hazard to a subject
- Breach of confidentiality
- Subject complaint that cannot be resolved by the research team
- Unanticipated adverse device effect
- Adverse event or IND safety report that requires a change to the protocol or consent

Information not listed above does not require prompt reporting to WIRB (*We endeavor to keep this Guide aligned with the content of the Promptly Reportable Information form; however, in the event this Guide and form are not currently in sync, the information in the form supersedes the information in this Guide).

Please note, consistent with AAHRPP’s requirements in connection with its accreditation of IRBs, the individual and/or organization submitting research for review shall promptly communicate or provide, and where necessary cause each investigator to promptly communicate or provide, the following information relevant to the protection of human subjects to WIRB in a timely manner:

- a. Upon request of the IRB, a copy of the written plan between sponsor or CRO and site that addresses whether expenses for medical care incurred by human subject research subjects who experience research related injury will be reimbursed, and if so, who is responsible in order to determine consistency with the language in the consent document.
- b. Any site monitoring report that directly and materially affects subject safety or their willingness to continue participation. Such reports will be provided to the IRB within 5 days.
- c. Reports from any data monitoring committee, data and safety monitoring board, or data and safety monitoring committee in accordance with the time frame specified in the research protocol.

- d. Any findings from closed research when those findings materially affect the safety and medical care of past subjects. Findings will be reported for 2 years after the closure of the research.

B. Planned Deviations

Please note that planned deviations should be submitted to WIRB as a change in research for federally funded research and FDA drug and biologic studies. See the WIRB Certificate of Action for more info about WIRB's expectations for the conduct of approved research.

14. Overview of WIRB's continuing review activities and required 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)]. The Board may direct review be more frequent than annual review, as deemed appropriate.

i. Site Reporting:

Completed Site Continuing Review Report forms provide WIRB with the study-related data necessary to monitor the progress of the research at sites.

Forms are sent out approximately 86 days before the study expiration date, and are due approximately 56 days before the study expiration date. This time frame allows for IRB staff to review the completed form, follow up if they have questions, and send it to board with the study renewal review. If we have not yet received a completed report form, two "Reminder Notices" are sent out; one at about two weeks and another about four days prior to the due date of the form.

Report forms are sent to the person identified on the initial review submission form as the person to receive and complete continuing review forms:

Send continuing review forms to this person to be filled out and returned to the IRB

Identifying information including investigator name, sponsor name, protocol number and the "sequence" number of the form is listed at the top of each form.

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 does not conflict with any previous reports to WIRB.

The Board may take action to suspend or terminate approval of the research if a report is not accurately completed and returned promptly.

WCG

Site Continuing Review Report
HRP-251

Use Adobe version 11 or later (Reader or Acrobat)
Asterisked (*) fields are required.

Use this form to submit continuing review information for a site.
This is a smart form. Form elements will appear or disappear depending on answers to previous questions.
Blank & incomplete answers will result in delayed reviews.

Continuing Review Information

IRB	Due Date	IRB Tracking Number	Seq #	IRB Report ID
Western IRB (WIRB)				

Protocol title

Sponsor Protocol ID

Sponsor Name

Principal Investigator (PI)

Subject Accrual

ii. Sponsor Reporting:

Before each annual review, WIRB sends out a Protocol Continuing Review Report for each protocol for which WIRB is or may be the central IRB to the sponsor or CRO contact we have on file. (If you receive a protocol Continuing Review Report for a protocol for which WIRB is NOT the central IRB, please notify us and we will update our records.) The Protocol Continuing Review Report is designed to collect protocol-wide data as recommended in the FDA guidance document titled "IRB Continuing Review after Clinical Investigation Approval."

In this guidance, FDA recommends several times that both central and local IRBs should obtain and review protocol information. We are asking you to complete the

Protocol Continuing Review Report before the due date indicated on the form. The individual study sites will continue to receive separate site progress reports to complete and submit as well.

Identifying information including sponsor name, protocol number and the “sequence” number of the form is listed at the top of each form.

Forms are sent out approximately 100 days before the study expiration date, and are due approximately 56 days before the study expiration date. This time frame allows for IRB staff to review the completed form, follow up if they have questions, and send it to board with the study renewal review. If we have not yet received a completed report form, two “Reminder Notices” are sent out; one at about two weeks and another about four days prior to the due date of the form. The Board may take action to suspend or terminate approval of the research if a report is not accurately completed and returned promptly.

WCG

Protocol Continuing Review Report
HRP-250

Use Adobe version 11 or later (Reader or Acrobat)
Asterisked (*) fields are required.

Use this form to submit continuing review information for a study.
This is a smart form. Form elements will appear or disappear depending on answers to previous questions.
Blank & incomplete answers will result in delayed reviews.

Continuing Review Information

IRB	Due Date	IRB Tracking Number	Seq #	IRB Report ID
Western IRB (WIRB)				

Protocol title

Sponsor Protocol ID

Sponsor Name

Subject Accrual

We want to make the process as efficient as possible for all parties. Therefore, WIRB will accept receipt of the completed Protocol Continuing Review Report from any party. In addition, FDA notes in the guidance that existing sponsor reports containing the requested data could be re-purposed for the purposes of reporting protocol-wide information to the IRB, such as annual Progress Reports or the Development Safety Update Reports (DSUR) Executive Summary. WIRB is quite flexible as to the format in which we receive this information, and we will happily accept other reports that provide the same basic information.

iii. Delinquent Progress Reports (Site Continuing Review Reports and Protocol Continuing Review Reports)

If a completed form is not received by the due date, approximately 10 days after the due date a “past due” notification is sent; the email notice explains that if a satisfactory response is not received shortly, the delinquency will be reported to the Board and that the Board may take action to suspend the study.

- The site notification is sent to all contacts listed to receive approval documents for that site.
- The protocol notification is sent to all contacts on file for the protocol.

If the Board suspends the research, 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.

iv. Definition of Screen Failure

Report the number of screen failures on Continuing Review Reports according to the following definitions. WIRB acknowledges that the definitions for these terms vary across the industry, but please apply the following definitions when reporting to WIRB:

Screen failure: subject removed from the study during the screening process because they did 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 not be counted as a screen failure for reporting to WIRB, , even if the subject did not start the study treatment.

v. Study Renewal

Sites receive a WIRB Site Continuing Review Reports when the expiration date is approaching. The Board may conduct the study renewal review up to 30 days prior to the expiration date listed on the Certificate of Action. **Review fees apply for the renewal service** and review is carried out unless WIRB receives a study closure notice *prior to the Board’s renewal review*. If a closure notice is received by WIRB before the 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, no study activities may take place on June 15 or following.

If the Board approves renewal for an additional review period, a Certificate of Action is forwarded to the investigator and other study contacts as applicable. The Certificate of Action 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 renewal, the Board determines that a modification to the consent is necessary, the Certificate of Action 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. The protocol is permanently closed to enrollment
2. All subjects have completed all protocol related interventions and interactions
3. For research subject to federal oversight other than FDA:
 - a. No additional identifiable private information about the subjects is being obtained
 - b. Analysis of private identifiable information 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.

WIRB sends 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.

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)).

WIRB conducts the following types of site visits:

- 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, and the agenda for the visit. For the fees associated with a WIRB site visit, please consult the current fee schedule.

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.

15. 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, and the monitoring of research progress 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, if multiple consent forms are submitted, 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. **Research 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 report and

activities for the previous year, and if acceptable, grants approval for another period. The renewal review fee funds the costs of the Board's renewal review, as well as the costs of the ongoing review of promptly reportable information, 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 for services such as translations and acknowledgements. WIRB also may charge a fee for submissions **not** made via the Connexus or IRBNet portals

Items disapproved by the Board can be reconsidered upon written request. The request must include a rationale 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.

16. 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.

If you disagree with the Board's re-consent instructions directed for a change in research, you may **promptly** contact WIRB and ask for a reconsideration; however, we advise you not to delay complying with the Board's instructions.

17. Other WIRB services

A. Clinical Pharmacology Unit Services

In clinical pharmacology research reviews, timing is everything. The clock is always ticking for clinical pharmacology research. WIRB's Clinical Pharmacology Unit Services division is set up to respond quickly for a fast and thorough review. We have vast expertise with clinical pharmacology research, including Phase I, bioequivalence/bioavailability, diabetes, oncology, and renal research in healthy and diseased subjects.

With our clinical pharmacology review expertise, we have developed streamlined systems to meet almost any circumstance, while still placing the safety of our human subjects first.

Our Board is structured to be highly responsive, anticipating adaptive study design and addressing changes related to the safety and efficacy of the research.

During our pre-review site visits, we gather all critical information and ensure your site meets all safety standards, guaranteeing a faster review turnaround.

Our Board meets three times per week to provide accelerated turnaround times from completed submission to document delivery. From the time we receive your complete submission, our turnaround time is:

5–7 working days for initial reviews.

24–48 hours for deadline-driven material.

Your team will have a single point of contact who understands the unique needs of your organization, as well as time-saving online tools: All submissions and documentation are delivered electronically, and our secure portal, [Connexus](https://connexus.wcgclinical.com/default.aspx) (<https://connexus.wcgclinical.com/default.aspx>), lets you submit and track your research review at any time.

WIRB has a global network and decades of experience working around the world. In international reviews, our panel observes strict compliance with local and regional regulations, as well as cultural sensitivities, so you can be sure your study will pass the strictest scrutiny, anywhere in the world.

Nationally and internationally, you will have a local coordinator who will provide guidance and represent you to the Board. Our local coordinators are authorities in process submission, and specially trained as subject matter experts (SMEs) in their area.

WIRB's staff of experts and educators offers a wide array of education, consulting, and staffing services for investigators, local IRBs, and sponsors. WIRB can help you write your protocol or your consent form, and provide regulatory support for local IRBs.

To prepare your submission, please review the relevant industry regulations, view WIRB's submission resources, or contact us with questions. When you are ready to submit, log on to [Connexus](https://connexus.wcgclinical.com/default.aspx) (<https://connexus.wcgclinical.com/default.aspx>).

B. Human Gene Transfer and Institutional Biosafety Committee Review



According to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*, the majority of clinical trials involving deliberate transfer of genetically modified DNA or RNA into human subjects qualify as Human Gene Transfer (HGT). Depending on the sources of funding for investigational products, research sites, and sponsors, HGT research may be subject to the *NIH Guidelines* and require approval from an Institutional Biosafety Committee (IBC) for each dosing site. Management and administration of IBCs requires extensive specialized expertise and experience. WIRB IBC Services is the global leader in IBC oversight for clinical and preclinical research. Since the year 2000, we have registered IBCs with the NIH on behalf of over 600 research institutions, reviewed over 250 clinical trial protocols, and convened over 4000 individual IBC meetings.

In addition to clinical trials, the *NIH Guidelines* also require IBC oversight for preclinical and nonclinical research when associated with NIH funding. WIRB IBC Services partners with numerous institutions and funded entities who receive such funding and are looking for an expert partner for IBC review and *NIH Guidelines* compliance.

Getting started

To learn more and discuss your IBCS needs, contact us:

Institutional Biosafety Committee Services (IBCS)
Mail Stop: IBCS
1019 39th Avenue SE Suite 120
Puyallup, WA 98374-2115
Phone: (360) 252-2850 or (800) 562-4789 Ext. 2850
Fax: (360) 252-2820
E-mail: ibcs@wcgclinical.com

18. FAQs

Are we required to obtain the consent of subjects who were originally enrolled as children, but have now reached the age where they can consent for themselves?

Yes. Unless consent has been waived, WIRB generally requires you to obtain the consent of subjects who reach the age of majority during the research. You may use the current WIRB-approved consent form to obtain their consent, or, if the approved consent form is not appropriate for doing so, you may download the consent addendum and present it, along with the current WIRB-approved consent form, to the subject in order to obtain his/her consent.

If you use the [addendum available on our web site \(http://www.wirb.com/Documents/Minors_to_Adults_Addendum.doc\)](http://www.wirb.com/Documents/Minors_to_Adults_Addendum.doc), please remove the statement from it regarding authorization to use and disclose information if the consent form signed by the parent/guardian did not include an authorization section.

You do not have to seek WIRB approval of the generic addendum before using it if you use it without alteration (besides removal of the authorization statement if appropriate as outlined above).

Can I make changes to an advertisement without resubmitting to WIRB?

Changes made to an advertisement may alter the effect of the advertisement on potential subjects (changes to pictures, font sizes, font types, etc.) WIRB must review anything that could alter the impact of what was previously reviewed, as required in 21 CFR 56.108(a)(4).

Contact Client Services via e-mail at clientservices@wirb.com or call 1-800-562-4789 for more information about modifications to approved recruitment materials.

Can I submit a hand-written submission form?

Since the initial review smart form is a dynamic form that hides or reveals questions based on your answers, it cannot be printed out and completed by hand. Other hand-written documents can result in significant delays and miscommunications. You may contact Client Services at 1-800-562-4789 or ClientServices@wirb.com for help using the electronic copies of the submission form.

Can I submit paperwork before choosing a PI?

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

Does my study require a Certificate of Confidentiality, and if so, how do I obtain one?

WIRB's Board requires a Certificate of Confidentiality (CoC) for certain types of research in order to provide the subjects with extra protection of their confidential information as defined in 45 CFR 46.111(a)(7) and 21 CFR 56.111(a)(7). The determination to require a CoC is based on whether the research involves a subject

population that might be prone to face legal or social harm by another's discovery of private, confidential, or protected information, such as:

- illegal behavior (e.g., crime, quasi-crime, supervision violation, contempt, child abuse, domestic violence, etc.);
- illegal status (e.g., alien, child runaway, AWOL);
- stigmatized behavior and/or diseases (e.g., HIV, alcoholism, drug abuse, mental illness);
- embarrassing behavior (e.g., immoral behavior, sexual behavior);
- discriminatory condition (e.g., employability, reputation, financial standing).

Listed below are links to helpful pages on the Office for Human Research Protection (OHRP) website and the National Institutes of Health (NIH) website. The pages provide information about acquiring a Certificate of Confidentiality.

- <http://grants2.nih.gov/grants/policy/coc/>
- <http://grants.nih.gov/grants/policy/coc/contacts.htm>
- <http://www.hhs.gov/ohrp/regulations-and-policy/guidance/certificates-of-confidentiality/index.html>

Does WIRB provide services internationally?

Yes. With experience in more than 70 countries, we can help you meet all the logistical, cultural, and regulatory challenges of international research. We reference local laws, customs, and attitudes to ensure that research is culturally and legally acceptable.

How do I obtain consent for a cognitively impaired subject?

First check to be sure the protocol and WIRB allow enrollment of cognitively impaired subjects in the research – there are special criteria for enrollment of this vulnerable group in research. If enrollment of them is allowed by the protocol and no prohibition on their enrollment was provided by WIRB, WIRB expects that consent will be obtained from a legally authorized representative (LAR), and that the assent of the subject will be obtained to the extent compatible with their capacity.

FDA regulation 21 CFR § 50.20 states that: No investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.

If an adult subject is not medically capable and/or legally competent to consent to participate in a study, the federal regulations require that a legally authorized representative consent for the subject. The definition of "legally authorized representative," as described in FDA 21 CFR § 50.3 is:

An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

The applicable law is the law of the state, as well as any other local law. Thus, the definition of “legally authorized representative” will be determined by state law or other local law. If a subject is medically incapable and/or legally incompetent, then a legally authorized representative, as determined under state or local law, must consent on the subject’s behalf. The Office for Human Research Protections (OHRP) has determined that state laws addressing consent for treatment decisions concerning the same procedures involved in the research are an acceptable basis for determining who may serve as a “legally authorized representative.”

For questions regarding the legal status of an individual subject and the applicability of local law to an individual subject’s enrollment in research, contact a healthcare attorney admitted to the bar in that state. Sites should be aware that changes in statutes and regulations occur frequently, and that court decisions may determine or change the interpretation of such statutes and regulations. Legal counsel should always be consulted to determine the current state of applicable law.

The PI is unexpectedly no longer able to oversee the study. What do I do?

WIRB must be assured that the investigator can personally oversee the conduct of the research and the protection of human subjects [21 CFR 56.102 (h); for Canadian investigators: Part C Division 5 of the Food and Drug Regulations, Part 4 of the Natural Health Products Regulations (if applicable), Medical Devices Regulations (if applicable)].

As soon as possible, WIRB will need either a study closure request from the site, or a submission of a new PI for the Board’s review.

How does WIRB handle the requirement for [clinicaltrials.gov](http://www.ClinicalTrials.gov) text in consent forms?

As of March 7, 2012, consent forms for certain types of research must include the text outlined below. Federal regulation 21 CFR 50.25(c) states:

“When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act. The statement is: **“A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”**

How do I create a [Connexus](#) account?

Go to [Connexus](https://connexus.wcgclinical.com/default.aspx) (<https://connexus.wcgclinical.com/default.aspx>).

How do I obtain informed consent from someone who speaks and understands English, but cannot read English?

Sometimes potential subjects speak and understand English, but cannot read due to blindness, illiteracy, or some other reason. These individuals may still participate in a research study as long as the protocol has not excluded limited or non-readers and there is an impartial witness present for the consent process, in accordance with ICH 4.8.9, which states:

ICH 4.8.9 - If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative and that informed consent was freely given by the subject or the subject's legally acceptable representative.

The definition of impartial witness is provided at ICH 1.26, which states:

ICH 1.26 Impartial Witness - A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

Unless consent has been waived or the protocol excludes enrollment of limited readers or non-readers, involve an impartial witness in the consent process when enrolling limited or non-readers and document the participation of the impartial witness using the designated signature lines on the WIRB-approved consent form. In the absence of designated signature lines, download the WIRB standard impartial witness form from www.wirb.com.

The impartial witness block may not be used to enroll subjects who speak a language other than English. WIRB requires that non-English speaking subjects sign a translated consent form. See the frequently asked question "How is consent obtained from a non-English speaking subject?" for more information.

How does WIRB handle initial review of consent forms from affiliated institutions?

Multi-site protocols previously approved by WIRB:

If you do not require site specific customization, WIRB will create your site's informed consent using the WIRB-approved template, as is. WIRB will add your site-specific information included in your submission form, such as investigator name, 24-hour telephone number, and subject payment language, and institution-specific requirements.

If you require customized language, request the WIRB-approved consent template from Client Services at clientservices@wirb.com. Track (redline) your changes on the WIRB-approved informed consent so WIRB can easily identify your site-specific customizations.

If your institution has language that is chosen by a checklist or other documentation such as cover letters or grants and contracts forms, it must be included with the application to WIRB as usual. WIRB will incorporate this language into the consent form that will be approved for you.

Multi-site protocols NOT previously approved by WIRB:

Contact Client Services at clientservices@wirb.com to determine if WIRB has already [approved the research and obtain a copy of the approved consent form template](#). If WIRB has not previously approved the protocol, submit the sponsor's template as a Microsoft Word compatible file (please contact Client Services if you need assistance with submitting in this format). There is no need to incorporate any institution-required language because WIRB will do so as part of its review, including information from the submission form and any language from a checklist or other documentation such as cover letters or grants and contracts forms.

If your institution requires protocol-specific insertion of language to the text of the consent form, such as study visit durations or a listing of which procedures are standard care, clearly mark those changes on the sponsor's template in Microsoft Word compatible format.

Single-site protocols:

Submit a consent form as a Microsoft Word compatible file that will be reviewed as new. Please make sure you have reviewed the information on this website on consent forms. You may also request to have WCG write the consent form (extra fee applies); contact info@wgcclinical.com for more information. Please incorporate your institution-required language into the submitted consent form. Please contact your institutional department for the latest version of required language.

How is consent obtained from a non-English speaking subject?

WIRB requires that non-English speaking subjects sign a WIRB-approved translated consent form. WIRB's Translations staff can arrange to have a WIRB-approved consent form or subject material translated into any language, or the site/sponsor can submit to WIRB a translated document along with a signed translator certification statement for verification and approval. Specific submission requirements may be obtained from the WIRB Translations staff.

You must also explain your plans for 1) conducting the consent discussion in the language understandable to the subject, and for 2) ongoing communication with the subject throughout the research and in case of emergency. For example, your site might indicate "At least one member of the research team is fluent in the language that will be used for communication, and that research staff member(s) will be available during emergencies," "The research team has 24-hour access to a translation service with sufficient medical expertise to discuss the research in this study," or provide another appropriate plan.

Please provide these plans each time you request a translation into a new language for a particular study. Your translation requests may be delayed if you have not already provided an acceptable language-specific and research-specific plan.

If a site has an unexpected need for a translated consent form, see [the section of this guide that discusses use of the short form consent process](#).

How should consent forms be submitted?

Consent forms should be submitted in a Microsoft Word compatible format. This includes files with extensions .doc (Word 2003 and earlier), .docx (Word 2007 and later), and .rtf (Rich Text Format, available in most word processing programs). If you have received only a .pdf version from the sponsor, please attempt to get a Word version; WIRB maintains consent forms in Word format and conversion from pdf to Word can introduce errors. We encourage sites to check [Connexus](https://connexus.wcqclinical.com/default.aspx) (<https://connexus.wcqclinical.com/default.aspx>) or request the WIRB-approved consent template from Client Services at clientservices@wirb.com. The current protocol-level and site-specific consent form are posted and available for download. Contact Client Services if you need any assistance with submitting your documents in this format.

WIRB requires the use of IRB-approved informed consent(s) for initial review submissions of new principal investigators (PIs) effective July 3, 2018.

How will I be notified of my ad's approval?

Advertisements are approved in one of two ways: "As Submitted" (no changes) or "As Modified." Board-directed changes are indicated on the ad returned with the Certificate of Action (COA). Starting mid-2019, WIRB will discontinue adding the text " – as submitted" to items listed on the Certificate of Action that were approved without modification. This will be a phased approach; therefore, some previously reviewed items will continue to indicate " – as submitted" on the COA.

Ads submitted with the protocol and consent form at the time of initial review will be reviewed with the initial approval packet. Approved ad(s) will be listed on the certificate of approval, and show any changes required by WIRB.

WIRB does not routinely apply approval stamps to approved advertisements. The Certificate of Action listing approval of the ad is documentation of WIRB's review and approval of the advertisement.

How will I receive documents from WIRB?

Your approval documents will be posted on WIRB's secure online site ([Connexus](https://connexus.wcgclinical.com/default.aspx) -- <https://connexus.wcgclinical.com/default.aspx>), and you will receive an e-mail with a link to the documents when they have been posted. Contact WIRB Client Services to request a change to the delivery method.

If there is another IRB involved in my research, what are the options available for WIRB involvement in the oversight?

WIRB can engage in an agreement with another IRB to:

- Provide complete dual oversight of research with another IRB, in which both IRBs provide initial and continuing review of all aspects of the research;
- Provide split dual oversight of the research with another IRB, in which WIRB provides IRB oversight for specific physical locations, and an institutional IRB provides IRB oversight of the aspects of the study conducted at the institution; or
- Assume jurisdiction from an existing institutional IRB for the review of a study or studies.

The initial review submission form will prompt you to download and submit a Reliance Agreement suitable to your situation (available on the Download Forms page of www.wirb.com).

Is my protocol exempt from review?

Upon request, WIRB will provide a written opinion that a proposed project is exempt from the requirement for IRB review or that it does not require IRB review because the project does not involve research or does not involve human subjects. Complete the initial review submission form and answer the question "Yes" to the question "Do you want the IRB to issue an exempt or not human research determination instead of conducting IRB review?"

What are WIRB's requirements for consent form signatures?

1. Subject Signatures: The subject must sign and date the consent form [21 CFR 50.27(a); 45 CFR 46.117(a), ICH 4.8.8].

WIRB may waive this requirement, when appropriate, under 21 CFR 56.109(c) or 45 CFR 46.117(c)(1), or when consent is entirely waived under 21 CFR 50.23, 21 CFR 50.24, or 45 CFR 46.116(e), (f). Please see the WIRB FAQ on the Waiver of

Documentation of Consent and Waiver of Consent. For requests for waiver of consent, and if you are a covered entity under HIPAA, please complete Request for Full Waiver Authorization Under HIPAA.

2. Signature of Person Who Conducted the Informed Consent Discussion: The person who conducts the informed consent discussion must sign and date the consent form (ICH 4.8.8).

3. Witness Signature: WIRB does not require a witness signature on the consent form, except in rare cases or as required by state or local law. However, WIRB will include a witness signature block at the request of the investigator or the sponsor. Because WIRB does not require a witness signature, WIRB does not have written procedures identifying who may serve as a witness. The investigator or the sponsor should have written procedures describing who may be a witness and what the witness signature signifies. If a witness signature block is included on the consent form, it must be signed for each consent form, unless the investigator or sponsor written procedures allow otherwise.

4. Signature of Impartial Witness: If a subject or a legally authorized representative (LAR) is unable to read because of blindness, illiteracy, or some other reason, an impartial witness should be present during the entire consent process, and should sign and date the consent form in compliance with ICH E6 4.8.9. The definition of an impartial witness is provided at ICH E6 1.26. An impartial witness's signature may not be used to attest to ad hoc translation of the consent into a language different than the language in which the consent form is written.

Unless consent has been waived or the protocol excludes enrollment of limited readers or non-readers, involve an impartial witness in the consent process when enrolling limited or non-readers and document the participation of the impartial witness using the designated signature lines on the WIRB-approved consent form. In the absence of designated signature lines, download and use the WIRB standard impartial witness form available on www.wirb.com.

What if changes are desired in sponsor-approved language in a consent form?

Initial Review:

To request that WIRB consider at the time of initial review wording that differs from the sponsor's template consent form or the consent form already approved by WIRB (approved during WIRB's pre-review or approved for other sites), you have two options: 1) You may rewrite all or some of the consent form yourself and submit the changes clearly marked on the WIRB-approved copy of the consent form (or on the sponsor's template if no WIRB-approved version exists); or 2) You may send a cover letter communicating your concerns, and it will be used in the WIRB review and editing of the consent form.

After Initial Review:

To request changes to consent forms for approved research, WIRB requires either a copy of the current WIRB-approved consent form with proposed changes clearly marked, or a document specifying the requested changes.

Proposed new changes may be submitted either on a copy of the current WIRB-approved consent form with new changes tracked in redlined format or handwritten on the form, OR the changes can be detailed in a document that indicates each change and the section of the consent form where the change should be made.

For more information on submitting consent form changes, please contact Client Services via e-mail at ClientServices@wirb.com or by calling 1-800-562-4789.

Where do I find re-consent instructions?

WIRB's Certificate of Action (COA) provides re-consent instructions under the area titled **"Please note the following information"**.

What if I disagree with the Board's re-consent instructions?

If you disagree with the Board's re-consent instructions, you may PROMPTLY contact WIRB and ask for a reconsideration; however, we advise you not to delay complying with the Board's instructions.

What if I received two changes to the consent form recently and each accompanying Certificate of Action provided different re-consenting instructions?

The Board expects you to apply the more strict of the two sets of instructions. For example, if the first consent form change included updated risk information and was accompanied by instructions to re-consent all subjects, and the subsequent consent form change was the addition of a new site and the Board directed that the revised consent form only be presented to new subjects, the site is still expected to provide the updated risk information to all subjects using the most current version of the consent form.

What if the Board didn't require all subjects be re-consented, but the site would like to re-consent all subjects?

If the site is not required by the Board to re-consent all subjects, the site is still free to do so.

What information is required when submitting advertisements to WIRB for review?

The basic information required includes: investigator name, sponsor name, research protocol number, and the name of the person submitting. Ads must be submitted and approved by WIRB before they are used.

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 which items have been previously reviewed by WIRB. WIRB

support staff will provide the Board with information about the previous Board review, and the previous decision of the Board will be taken into account when the additional materials are reviewed.

If some recruitment will be done on a website, submit the recruitment portions of the website for WIRB review; do not submit the portions of the website that are not intended for subject recruitment.

Ads can be submitted via [Connexus](https://connexus.wcgclinical.com/default.aspx) (<https://connexus.wcgclinical.com/default.aspx>) or IRBNet. Review requests sent by email, mail, or facsimile may be charged additional administrative fees.

WIRB requires a copy of print ads as they will appear, to allow the Board to review the font size, font style, images, etc.

Advertisements that 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 ad materials for all participating sites.

Click here for additional guidelines regarding subject recruitment materials submitted to WIRB.

What information will WIRB need regarding the study staff, sub-investigators, and the sites?

WIRB must be assured that the investigator can personally oversee the conduct of the research and the protection of human subjects 21 CFR 50.3(d).

The initial review submission form solicits information about the number of staff on the research team. Once the study is approved, the PI must ensure the study continues to be adequately staffed, but WIRB does not require updates on staffing levels unless the staffing change represents a change in research (e.g., a staff person cited in the consent form is no longer associated with the research), or represents promptly reportable information (e.g., if a study staff person has left the study due to misconduct).

If the staffing change does not represent a change in research or promptly reportable information, WIRB does not need to be notified. If these type of staffing changes are submitted to WIRB, the items will (or could) be acknowledged, which could result in an additional fee.

The initial review submission form also solicits some basic information about each location where the research will take place. Approved locations are listed on the Certificate of Action.

What is a clinical trial?

The commonly used terms "research trial" and "clinical trial" generally refer to the overall research project at one or more investigator sites. WIRB does not use "trial" in consent forms because of possible misunderstanding by a lay reader.

What is a legally authorized representative (LAR)?

FDA regulation 21 CFR § 50.20 states that:

No investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.

If an adult subject is not medically capable and/or legally competent to consent to participate in a study, the federal regulations require that a legally authorized representative consent for the subject. The definition of "legally authorized representative," as described in FDA 21 CFR § 50.3 is:

An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

The definition of "legally authorized representative," as described in 45 CFR 46.102(i) is: *Legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

The applicable law is the law of the state, as well as any other local law. Thus, the definition of "legally authorized representative" will be determined by state law or other local law. If a subject is medically incapable and/or legally incompetent, then a legally authorized representative, as determined under state or local law, must consent on the subject's behalf. The Office for Human Research Protections (OHRP) has determined that state laws addressing consent for treatment decisions concerning the same procedures involved in the research are an acceptable basis for determining who may serve as a "legally authorized representative."

For questions regarding the legal status of an individual subject and the applicability of local law to an individual subject's enrollment in research, contact a healthcare attorney admitted to the bar in that state. Sites should be aware that changes in statutes and regulations occur frequently, and that court decisions may determine or change the interpretation of such statutes and regulations. Legal counsel should always be consulted to determine the current state of applicable law.

What is a Principal Investigator (PI)?

The PI is the named person who is responsible, under the regulations, for conduct of the research. WIRB prefers that only one investigator be named for this responsibility (Principal Investigator), but will allow a second person upon request (Co-Principal Investigator). Please note that federal regulations do not recognize Co-Principal Investigators; therefore, the Board approves the two investigators as if each is THE investigator and holds each individually responsible for the conduct of the entire study. Canadian regulations do not allow Co-Principal Investigators in this sense at all.

If there are multiple sub-investigators and/or sites, WIRB may require an explanation as to how the PI will personally conduct or oversee the research, as required under 21 CFR 50.3(d), 21 CFR 312.60, and Box 9 of the FDA Form 1572.

What is a Sub-Investigator?

In parallel with the FDA's definition of a sub-investigator (21 CFR 312.3(b)), WIRB considers a sub-investigator to be any team member, other than an investigator, who may help in the design and conduct of the investigation, but does not actually direct its conduct.

The FDA provides further detailed guidance on this topic in their guidance document titled "Frequently Asked Questions – Statement of Investigator (Form FDA 1572)" available here:

<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf>.

What is a protocol?

The "protocol" is the written, detailed description of the research project.

What is a research study?

The term "study" is used by WIRB to mean the combination of a particular research protocol and investigator.

What is a sponsor?

A sponsor is the company, person, agency, or other party that designs the research, typically funds the research, and bears the sponsor responsibilities under the regulations, but does not actually conduct the investigation ("sponsor-investigators" are an exception).

What is WIRB's policy regarding the Statement of Investigator, form FDA 1572?

Investigators are not required to submit a 1572 to WIRB, even when one is required by the FDA for the research being conducted. The FDA Information Sheet "Frequently Asked Questions - Statement of Investigator (Form FDA 1572)" defines the 1572 as: An agreement signed by the investigator to provide certain information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic.

The same information sheet goes on to explain that:

The 1572 has two purposes: 1) to provide the sponsor with information about the investigator's qualifications and the clinical site that will enable the sponsor to establish and document that the investigator is qualified and the site is an appropriate location at which to conduct the clinical investigation, and 2) to inform the investigator of his/her obligations and obtain the investigator's commitment to follow pertinent FDA regulations.

For questions regarding completion of and requirements for a 1572, sites may refer to the guidance issued by FDA here:

<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf>.

When submitting items to WIRB for review, is the use of the submission form required?

Yes, submission forms are required for initial review and for change of principal investigator requests. They are also recommended for submissions of changes in research, and subject recruitment review requests. Click "[Download Forms](#)" on www.wirb.com to download access your desired form.

If you need help with any of the WIRB submission forms, please contact Client Services via e-mail at ClientServices@wirb.com or by calling 1-800-562-4789.

If an affiliated institution requires protocol-specific insertion of language into the text of the consent form, such as study visit durations or a listing of which procedures are standard care, submit a copy of the WIRB-approved consent form with those changes clearly indicated. All other standard institution language will be incorporated by WIRB and does not need to be indicated on a submitted consent form – deviations must be approved by the institution.

Consent forms must be submitted as Microsoft Word compatible files.

Why did WIRB change the consent form?

WIRB makes changes to consent forms to meet regulatory requirements and to be consistent with information in the protocol. In the "redline" version, the superscript numbers and the accompanying explanatory legend cover sheet sent along with each redlined consent form provide information about why each change was made.

Why is there a signature block for the person who conducted the consent discussion?

WIRB will automatically include a signature block to be signed by "the person who conducted the informed consent discussion," in compliance with ICH 4.8.8. WIRB does not include a witness signature block unless requested by the site or sponsor.

What is the WCG/WIRB policy on the Pennsylvania Supreme Court ruling in regard to Pennsylvania Statutes Title 40 P.S. Insurance section 1303.504(a) for informed consent?

The Pennsylvania Supreme Court has interpreted a Pennsylvania statute to mean that a physician's duty to provide information to a patient sufficient to obtain informed consent is non-delegable.

Pennsylvania Statutes Title 40 P.S. Insurance section 1303.504(a) states:

Duty of physicians.--Except in emergencies, a physician owes a duty to a patient to obtain the informed consent of the patient or the patient's authorized representative prior to conducting the following procedures:

- (1) Performing surgery, including the related administration of anesthesia.
- (2) Administering radiation or chemotherapy.
- (3) Administering a blood transfusion.
- (4) Inserting a surgical device or appliance.
- (5) Administering an experimental medication, using an experimental device or using an approved medication or device in an experimental manner.

In the case *Shinal v. Toms* (Ref: *Shinal vs Toms*. # 31. Map 2016, 2017. Lexis 1385. June 20 of 2017), the Court found that "the duty to obtain a patient's informed consent is a non -delegable duty owed by the physician conducting the surgery or treatment." Therefore, the Court held that "a physician cannot rely upon a subordinate to disclose the information required to obtain informed consent."

The court further explains,

Under the plain language of this section, the duty to obtain a patient's informed consent for the several enumerated procedures, including surgery, belongs to the physician. Section 504 does not merely require that the patient's consent be informed; it specifically imposes the duty upon physicians to provide to the patient the requisite information and to obtain informed consent. Nothing in the plain language of the Act suggests that conversations between the patient and others can control the informed consent analysis or can satisfy the physician's legal burden.

If you have any questions about the interpretation or application of this Supreme Court decision to the conduct of this research, contact local counsel licensed in Pennsylvania. Nothing in this notice is intended to constitute legal advice.