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# WCG IRB Guide for Researchers

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Association for the Accreditation of Human Research Protection Programs, Inc. Full Accreditation

*Revised in this version:*

- *Add additional guidance about including HIPAA waiver language in ICFs.*
- *Add additional guidance for sponsors and CROs about identifying site-specific information sections in template consent forms.*
- *Add guidance about reviewing non-English medical records using a translator*
- *Add guidance about sponsor/CRO/site coordinated translations using AI*
- *Add guidance about PI's who are not regular, full time employees of the institution or site.*
- *Add rationale for WCG policy to not include signatures on US Certificates of Action*
- *Add guidance about sending DSUR reports to WCG IRB for review*
- *In this version, references to the Connexus portal have been universally replaced with references to the ClinSphere® eReview Manager portal – but please note that migration of records from Connexus to eReview Manager is ongoing and users will continue to access their records and make submissions for existing research via Connexus until they receive notification that their records have been migrated to eReview Manager.*

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# Introduction

WCG IRB is pleased to provide this handbook as a resource for organizations and investigators partnering with us. It offers practical guidance on submission requirements, IRB review processes, ongoing oversight, and other topics relevant to your work. We encourage you to use this information to support your research efforts as we work together to protect the rights, safety, and well-being of human research participants.

Visit the Insights page on wcgclinical.com to access our latest thought leadership and perspectives on accelerating clinical research.

# Working with WCG IRB for IRB Review - An Overview

New protocols submitted to WCG IRB for review (that are not eligible for expedited review) are assigned for review based on the next available panel meeting. U.S. panels meet daily. Reviews for investigators at Canadian locations are assigned to the Canadian panel; therefore, a protocol taking place in both the United States and Canada will be assigned to both U.S. and Canadian panels.

WCG IRB conducts expedited review of certain kinds of research involving no more than minimal risk to human research participants according to federal regulations. 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.

To learn more about accessing research review details, WCG IRB's panel structure, or to determine the panel assignment of a protocol, call Client Care at 855-818-2289 or email clientcare@wcgclinical.com.

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

Confidential Disclosure Agreements (CDAs) between sponsors and WCG IRB are not required by WCG IRB. However, we are happy to enter into a CDA if preferred by the sponsor. If you require a CDA, your request will be directed to WCG's legal department for preparation.

If you are registering research overseen by WCG IRB on Clinicaltrials.gov, use the following information:

**IRB Approval Number:** [initial protocol approval date mm/dd/yyyy]

**Board name:** WCG IRB

**Board affiliation:** WCG Clinical, Inc.

**Board address:**

5000 Centregreen Way
Suite 200
Cary, NC 27513

**Board phone and/or email:** 855-818-2289 / clientcare@wcgclinical.com

Note: WCG Clinical refers to people who participate in research as "subjects" or "participants." The term "subject" is more traditional, but "participant" has become more common in recent years. This Guide uses the term "subject" when quoting regulations and federal guidance that use that term or

when citing other published materials that use the term “subject,” but otherwise this Guide uses the term "participant" when possible.

# Exemptions

In addition to IRB review, WCG IRB offers a service to determine if research is exempt from, or does not require, IRB review.

Research that is not a clinical investigation of an FDA-regulated product (drugs, devices, biologics, food including supplements, cosmetics, etc.) may not require IRB review. Projects that do not require IRB review include where all research activities:

1. Do not involve a human subject [45 CFR 46.102(e)(1)].
2. Do not meet the definition of research [45 CFR 46.102(l)].
3. Fit in the categories of research that are exempt from IRB review (45 CFR 46.104).

OHRP has decision charts here to help you determine if research requires IRB review. Please note, these charts do not replace consideration of the full regulation and other institutional, sponsor, or local requirements.

OHRP also notes here that the regulations do not specify who at an institution may determine that research is exempt under 45 CFR 46.101(b). However, OHRP recommends that, because of the potential for conflict of interest, investigators not be the ones who make a determination that human subjects research is exempt. In addition, many publications require some form of IRB determination for research results to be published.

If you would like WCG IRB to determine if research is exempt from, or does not require IRB review, please submit through the “new study” pathway on ClinSphere® eReview Manager or WCG IRBNet. Please note that submission of an investigator is not required for exempt research to be reviewed/approved or conducted.

If research is determined to be exempt or not human subject research, that determination will be communicated in IRB outcome documents in the same manner as IRB review, through an approval on the Certificate of Action

WCG will review and make exemption determinations only for prospectively conducted studies and will not review a study which is already completed or started.

Single patient case report publication/presentation in a de-identified manner can be reviewed for non-human subject research Exemption (NHSR). Also see section on **Single Patient Case Reports - Dissemination of Clinical Study Data by Investigators for Education and Research Purposes** in this Guide.

For WCG-determined IRB exempt studies, sponsors and investigators may use their own independent translation services to translate WCG-reviewed materials, and submission of the translated materials to WCG is optional.

# Submitting Documents for IRB Review

Set up an account or log in to ClinSphere® eReview Manager to submit a new study. (Clients who use IRBNet to submit should submit new studies through there.) Please note we do not accept submissions via fax or postal mail. If you need assistance submitting, contact clientcare@wcgclinical.com.

If a submission is made and we are subsequently instructed to withdraw that submission, a fee will be charged to cover the costs of the work done on the submission prior to withdrawal.

All studies require a Principal Investigator (PI) to assume responsibility for the conduct of research either for the study as a whole or for an individual site. This includes studies where there is no direct participant interaction, such as online surveys, retrospective chart reviews, and studies using biospecimen samples sourced from a third party vendor. If no PI or site information is provided with the initial review submission, it will need to be submitted in the future to WCG or another IRB before beginning research activities.

Please note that for research conducted outside North America, WCG IRB is happy to provide U.S. review **in conjunction with a local IRB** when required for funding or regulatory reasons. Other cases can be considered on an individual basis. We do not provide IRB review of research in other countries where there is not a local IRB. This includes research for which it is unclear if local regulations require IRB review, such as stem cell research, device research, tissue collection studies, and questionnaires and surveys.

# Materials Required for Initial Review

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

**Items Required for All Initial Review Requests**

- **Initial Review Submission Form:** Use ClinSphere® eReview Manager or IRBNet for study submissions.
- **Protocol:** If you're unsure of what requirements are needed for a Protocol document, please see the WCG whitepaper here. For protocol templates, there are multiple online options, including the WCG Protocol Assistant, Word template documents and Protocol writing tool from NIH.
- **Current Professional License** for PI, showing the expiration date.
  (Federal regulations do not recognize coprincipal investigators; therefore, if two PIs plan to share oversight of a single study, the Board requires a completed submission form for each investigator and holds each individually responsible for the conduct of the entire study.)
- **Curriculum Vitae (CV)** for principal investigator.

**Consent Form** (If WCG IRB has not already approved one). Please submit consent forms as Microsoft Word compatible files (.doc, .docx, .rtf).

**Other Materials to be Provided to the Participants** which are not included in the protocol, such as advertisements, questionnaires, participant diaries, etc. (Any commercially available validated instruments cited in the protocol that are used without modification are not listed individually on the approval letter. However, approval of the protocol does extend to the uses of such industry standard forms as described in the approved protocol.)

Submitters will benefit from submitting advertising and other recruitment materials with the initial review submission, as later submissions incur a fee for review. **Please review the guidance in the section of this Guide outlining best practices for submitting ads and other subject facing materials**.

**For Drugs, Biologics, and Food Supplements**

- Investigator's drug brochure (in most cases).
- Background information for food supplements.

- Documentation from sponsor or FDA verifying the IND (Investigational New Drug) number, if one is required for the research. If an IND is not required, provide the reason why in writing.

**For Device Studies:**

- **Device manual** is required for device studies (also called "Instructions for Use") and ONE of the following:
    - **Unredacted FDA letter** granting the Investigational Device Exemption (IDE); OR
    - **Letter from sponsor** stating that the study is a non-significant risk device study and the basis for that determination; (**unredacted**) OR
    - **Documentation of why the investigation is exempt** from the IDE requirements under 21 CFR § 812.2(c) (such as the PMA approval letter/number or 510(k) clearance letter/number) or otherwise exempt.
- Physicians seeking approval to use a Humanitarian Use Device (HUD) for treatment, not part of a research study, may use the form titled Clinical Use of a Humanitarian Use Device (HUD) (HRP-284) designed for such review requests.

# Regulations Affecting Clinical Research, Including HIPAA: The Regulatory Framework Within Which WCG IRB Functions

WCG IRB Compliance Statement:

WCG IRB is duly constituted and has written procedures in compliance with requirements defined in 21 CFR Parts 50 and 56, 312, 812, 45 CFR 46 and ICH Guidelines relating to Good Clinical Practice. WCG IRB's mission is to ensure that research is conducted ethically according to the principles of the Belmont Report and in compliance with all federal and international (ICH) regulations, state laws and that the rights and welfare of human participants are protected.

WCG IRB is registered with FDA/OHRP.

WCG IRB registration number is IRB00000533 (IRB00002354 for our Canadian panel), and WCG IRB's parent organization number is IORG0000432.

WCG IRB reviews many types of human participant research, including clinical research, behavioral research, and epidemiological research, in the United States and Canada. WCG IRB 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) "E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry."

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 participants. Usually, the type of

assurance will be a Federal-wide 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 WCG IRB Client Care at 855-818-2289 or 1-617-243-3924 or clientcare@wcgclinical.com.

WCG IRB can help researchers and institutions comply with the NIH Single IRB policy – contact us 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.

WCG IRB has established written procedures that ensure that research approved by WCG IRB meets these three primary standards. However, WCG IRB 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 participant 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 participant.

In addition, WCG IRB reviews research funded by the Department of Defense, the Department of Education, and other federal agencies.

### Research Conducted Globally

For research conducted outside North America, WCG IRB is happy to provide U.S. review in conjunction with a local IRB when required for funding or regulatory reasons. Other cases can be considered on an individual basis.

We do not provide IRB review of research in other countries where there is not a local IRB. This includes research for which it is unclear if local regulations require IRB review, such as stem cell research, device research, tissue collection studies, and questionnaires and surveys.

### HIPAA

WCG IRB also provides services under the Privacy Rule (45 CFR Parts 160 and 164 of the Health Insurance Portability and Accountability Act of 1996). WCG IRB will review requests for waivers of authorization and partial waivers of authorization for covered entities upon request (requests for review of partial and full waivers of authorization can be made through ClinSphere® eReview Manager or IRBNet). WCG IRB 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. WCG IRB will review separate authorization documents upon request.

## Conflicts of Interest

To meet the needs of its clients and comply with the Department of Health and Human Services (HHS) guidance entitled "Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection," WCG IRB has established a policy for reviewing financial conflicts of interest of investigators, research staff and institutions (WCG IRB defines research staff as

people who are involved in the actual study conduct and the assessment of eligibility and outcomes, obtaining consent, and recruitment, or as otherwise defined by applicable institutional policy.) Please complete the designated Financial Interest Disclosure Form available on the Forms page of wcgclinical.com.

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

The investigator or study staff will be considered to have a financial conflict of interest if the investigator, investigator's immediate family (spouse and dependent children), the study staff, or the study staff's family:

- Has a financial interest in the research with value that cannot be readily determined (for example, stock that is not publicly traded);
- Has a financial interest in the research with value that exceeds $5,000 other than payments for conducting the trial as outlined in the clinical trials agreement;
- Has a financial interest in the research with value that exceeds 5% ownership;
- Has received or will receive compensation with value that may be affected by the outcome of the study;
- Has a proprietary interest in the research, such as a patent, trademark, copyright, or licensing agreement;
- Has received or will receive payments other than payment for the conduct of clinical research from the sponsor that exceed $5,000 in the last 365 days;
- Any governance or executive relationship with the sponsor (e.g., board of director, CEO);
- Has a financial interest that requires disclosure to the sponsor or funding source;
- Has any other financial interest that the investigator believes may interfere with his or her ability to protect participants; or
- Is affiliated with an institution that has a lower conflict of interest threshold than the amounts referenced above.

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

With respect to rules issued by NIH (NOT-OD-11-109) effective Aug. 24, 2012, our reporting threshold for study teams was changed to $5,000. [U.S. Department of Health and Human Services (HHS) issued a final rule] (https://grants.nih.gov/grants/policy/coi/index.htm) in the Federal Register that amends the Public Health Service (PHS) regulations on Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought (42 C.F.R. Part 50, Subpart F) and Responsible Prospective Contractors (45 C.F.R. Part 94).]

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

- First, the Board considers whether the financial conflict of interest could challenge the integrity of a reasonable individual.

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

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

## Amount of Risk

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

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

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

## Amount of Interaction Between the Conflicted Party and the Participants

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

## Other Parties Involved in Overseeing the Conflict of Interest

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

- For FDA-regulated studies, the FDA will provide a scientific review of the research results.
- NIH does detailed reviews of research proposals in advance, and inquiries about conflicts of interest at certain procedural steps.
- Some institutions have assigned participant advocates who sit in on the consent process.

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

## Training in Conflict of Interest

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

**Nature of the Interest, and Relationship to the Research:** The interest may be one in which large change is possible based on the outcomes of the study under review. An equity interest in a start-up company could be drastically affected by the research results, whereas stock in a large pharmaceutical

company is not as likely to be affected. Is it a single site study or a multi-center study? The ability of the investigator or other conflicted party to affect the financial interest varies greatly in these different situations.

## Unique Qualifications

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

## Possible Board Actions

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

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

## Compensation to Investigators and Study Teams for the Conduct of Research

Financial compensation to investigators and to other members of the study team should be at fair market value for the time, procedures, and services provided.

**Recruitment Bonuses:** WCG IRB defines a recruitment bonus as an additional payment or incentive provided to the investigator, study staff, or site dependent solely on a number of participants being enrolled, dependent on the speed at which participants are enrolled, or payment or incentive that is offered only after a certain number of participants have been enrolled. Recruitment bonuses create a conflict of interests concern because the study team members stand to directly and financially benefit from enrolling more participants, or from enrolling participants faster, which may (intentionally or even unintentionally) encourage study team members to recruit less appropriate participants, or to pressure or persuade patients to enroll in research studies. **WCG IRB does not allow recruitment bonuses (extra payments tied to the rate or timing of recruitment or enrollment).** WCG IRB does allow payment for time spent screening for recruitment purposes on a fair market value basis to be built into the study budget.

The term "payment or incentive" includes any items of value, such as direct payment, gift certificates, travel vouchers, physical items such as watches, and so forth. Any recruitment plans that include recruitment incentives, whether planned at study start or added later during the study, must be reported to and approved by the IRB. The IRB will assess these proposals on a case-by-case basis, with the intention of preventing apparent or potential conflicts of interest that may impact the rights and welfare of research participants. These should be submitted in the form of administrative letters for consideration.

Referral fees/finder's fees, which are payments made to people who are not members of the study team in return for referring potential participants to the study, are discussed in the section on Participant Recruitment Practices and Materials.

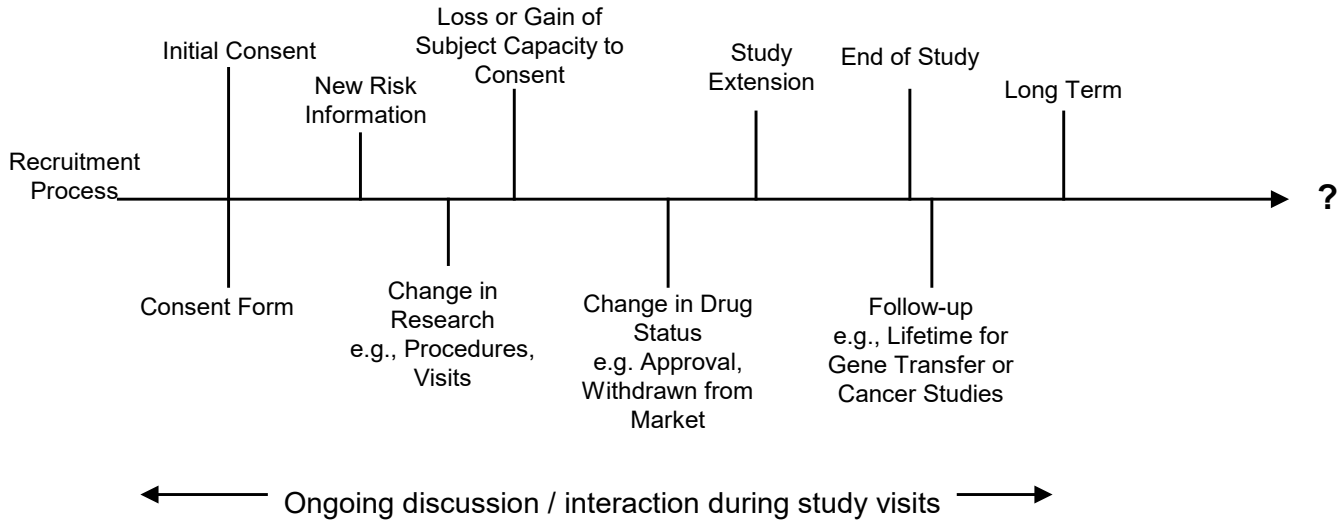
# The Informed Consent Process

The informed consent process is central to the ethical conduct of research. It is an ongoing conversation between the human research participant and the researchers that begins before consent is given and continues until the end of the participant's involvement in the research (see consent process diagram, below). There are various tools for the investigator to use to optimize this conversation, but the most important feature of informed consent is the investigator's commitment to the process. More information about informed consent is available in the FDA guidance document titled "Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors."

## Goals for the Informed Consent Process

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

## Consent Process Diagram



## Issues to Consider During the Consent Process

- Was the participant alert and, in your opinion, able to read and understand the language in the consent form?
- If the participant was unable to read the consent form, and limited or non-readers were allowed to participate, did you have an impartial witness present for the entire process? (An impartial witness is someone with adequate reading ability who is independent of the trial, who cannot be unfairly influenced by people involved in the trial, who attends the informed consent process while the consent form is being read to the participant, who reads the informed consent form and any other written information supplied to the participant, and who is willing to attest to this by signing the consent form.)
- If the participant is not fluent in English, was an approved translation of the consent form provided in the primary language of the participant? Was there also a bilingual translator present to assist with the informed consent process? Note: a translator alone is not considered adequate.
- Was the participant under any pressure (for example, family pressure, lack of medical insurance) to participate in the research? Was this discussed?
- Did the participant take time to carefully read the consent form, or read it along with you?
- Were the risks, as set forth in the consent form, carefully explained to the participant?
- Are there any other risks or concerns not stated in the consent form and were these explained to the participant?
- Was the participant asked if they had any questions about the study?
- Did the participant have any questions or concerns?
- Were the participant's questions answered?
- Was the participant satisfied with the answer(s) they were provided?
- Did the person conducting the consent discussion check for participant understanding by asking some basic questions about the research? Did the responses reflect adequate understanding?
- Did the participant express a clear decision to proceed with the study?
- Was the consent form signed by the person who conducted the informed consent discussion?
- Was the consent form signed by a witness (if required)?
- Was the consent form signed by the principal investigator (if required)?
- If a Legally Authorized Representative is allowed to sign for the participant, were additional concerns about the participant's understanding and assent considered and addressed?

## Investigator Responsibilities Regarding Informed Consent

- Obtain consent before initiating study-specific procedures, using the current IRB approved consent form (bearing the WCG IRB approval stamp wherever feasible).
- Give the person providing informed consent as much time as they need to make a decision.
- Provide a quiet, comfortable, and private setting for the informed consent process whenever possible.
- Explain the consent process to the participant.
- Make sure the participant has time to consider all options; allow participant to take the form home before signing (whenever possible). If the person providing informed consent needs more time than is allowed by the research design, do not enroll the prospective participant.
- Evaluate whether the person providing informed consent is experiencing pressure to make a decision, and if so, do not enroll the prospective participant, 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 participant for a decision to not take part in the research.
- Stop the informed consent process once the person providing consent indicates that they do 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, do not enroll the prospective participant, 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 participant'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 do not enroll a prospective participant 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 participant or the person providing informed consent that is made to waive or appear to waive any of the prospective participant'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.
- Do not enroll a prospective participant 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.
- Consider the participant's reading abilities. Check to make sure the protocol does not exclude participants unable to read. If enrollment of limited or non-readers is allowed, involve an impartial witness in the informed consent process.
- Answer all questions.
- To the extent possible, make sure the participant understands enough information about the research study to give informed consent.
- To the extent possible, make sure the participant can consent free from coercion or other undue influence.
- Since the informed consent process continues throughout participation in the study, consent should be informally verified on a continuing basis.
- Significant new information must be given to the participant, and continuing consent documented in some way; for example, new risk information presented to the participant in an addendum to be signed by participants who agree to continue to participate.

### Tools an Investigator Might Use to Assist the Informed Consent Process

- Consent Form - also called Informed Consent Form (ICF), Informed Consent Document (ICD) or Patient Consent Form (PCF)*
- Pamphlets or Other Reading Materials*
- Internet Information*
- Instruction Sheets*
- Audio-Visual Presentations*
- Charts or Diagrams*
- Discussions

- Consultation with Others

  **These items require IRB review before use.*

## Ensuring Consistency of Risk Information Across Multiple Sites in a Study

When the IRB reviews and approves the template consent form in a study, it will identify the risk language that will be held consistent. This is to promote consistent disclosure of risk information across WCG sites. All site consent forms should follow the template study product risk language throughout the life of the study, including formatting when submitted. For example, if a site submits changes to the risk language and confirmation to apply the change to all sites is not received from the sponsor, additional actions may be required prior to unconditional approval.

## Consent by Legally Authorized Representatives

The laws regulating who can consent for *adults* who lack the capacity to consent for themselves are defined at the state level and vary from state to state. Persons who can consent for adults who lack the capacity to personally provide informed consent are known as Legally Authorized Representatives (LARs). See 21 CFR 50.3(l) and 45 CFR 46.102(i). These regulations define LAR as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the 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 LAR for your research.

WCG IRB makes determinations about whether participants requiring consent by LAR are allowed in a study at the protocol level. Sites will, by default, have LAR signature lines and any associated Assent instructions/signatures on informed consent forms if this was approved for the protocol. If sites wish to enroll participants requiring consent by LAR, they will need to comply with all local laws and institutional guidelines when considering whether to enroll participants requiring consent by LAR. If a site does not want these signature lines/instructions on their consent form because they will not be enrolling them, a redlined consent form needs to be submitted for review with these lines/instructions removed.

## Summary of WCG IRB's requirements for consent form signatures when consent is required

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

**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).

**Witness Signature**: WCG IRB does not require a witness signature on the consent form, except in rare cases or as required by state or local law. However, WCG IRB will include a witness signature block at the request of the investigator or the sponsor. Because WCG IRB does not require a witness signature, WCG IRB 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's or sponsor's written procedures allow otherwise.

**Signature of Impartial Witness:** If a participant 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. In the absence of designated signature lines, download the WCG IRB standard impartial witness form from the Download Forms page.

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.”

An impartial witness’ 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.

The impartial witness signature block should be left unsigned unless there is an impartial witness present for the consent process. Please see the Frequently Asked Question, “How do I obtain informed consent from someone who speaks and understands English, but cannot read English?” for further discussion of the impartial witness requirements.

**Signature of Legally Authorized Representatives (LARs):** In research that allows the enrollment of adult participants who are not legally competent, the consent form will include a signature block for an LAR. If an adult participant is not legally competent, a LAR must participate in the consent process, agree to the enrollment of the participant in the research, and sign the consent form. If the research allows the enrollment of adult participants who are legally competent and participants who are not legally competent, then the LAR signature block will be labeled, “when necessary.” In this case, the LAR signature block should not be signed if the participant is legally competent. The LAR signature block will only be signed when the participant is not legally competent.

**Signature of Person Conducting Assent Discussion:** If the participant is unable to consent due to incapacity, or because they are a minor, the person conducting the assent should also sign the consent form.

**Signature of Principal Investigator:** WCG IRB does not require an investigator’s signature on the consent form, only the person conducting consent; however, if a consent form is submitted with an investigator signature line, WCG IRB will not remove it, but may add a designation for the person conducting assent if not already included. If an investigator signature line is on the consent form, the investigator or an “equally qualified” sub-investigator must sign the consent form. WCG IRB does not require that the investigator’s signature date coincide with the participant’s signature date.

## Consent by Participants Who Cannot Physically Sign the Consent Form

WCG IRB does not require a Legally Authorized Representative to provide consent for participants who are *cognitively capable* of consenting, but *physically* unable (for example, due to paralysis). In those cases, obtain consent from the participant with the assistance of a witness.

## Consent of Cognitively Impaired Participants

You cannot enroll participants who do not have the capacity to consent unless inclusion of such adults is noted on your Certificate of Action.

If an adult participant is not capable to consent to participate in a study, WCG IRB requires that a legally authorized representative consent for the participant and in some cases also requires participants to assent to taking part in the research as well. 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. For questions regarding state and local law, contact a healthcare attorney admitted to the bar in that state. Changes in state and local law may occur frequently. Therefore, legal counsel should always be consulted to determine the current state of applicable law.

### Obtaining Informed Consent from Someone Who Speaks and Understands English, but Cannot R*ead* English

Sometimes potential participants speak and understand English, but cannot read due to blindness, illiteracy, or some other reason. If consent is needed for a participant in this situation, please see the section of this guide regarding possible use of a short form consenting process.

### Obtaining Informed Consent from Deaf Participants

Investigators should first assess overall literacy and communicative modalities available to the participant, such as the participant's ability to read, capability to communicate by writing, and use of American Sign Language (ASL). If the participant has literacy issues, then use of ASL is the preferred option. Investigators may utilize a translator with ASL expertise. If an impartial witness is not available, the translator can also serve as a witness; please refer to WCG's policy on Short Forms in this guide.

### Navigating Multilingual Research Intended to be Conducted Solely in a Non-English Language

WCG recognizes that there is a need to conduct studies in languages other than English, in pursuit of inclusion, and that some studies are developed never to include English speaking participants. WCG also recognizes that this presents unique challenges in the ethical review process, particularly when it comes to ensuring the accuracy and cultural relevance of translated materials. For example, if a study will be solely conducted in Spanish, ethical review is still required. Unless an Institutional Review Board (IRB) is equipped to offer ethical review services in Spanish, the documents will need to initially be submitted in English for review. Which means that materials would have to be back translated from Spanish to English for review.

Unfortunately, back translation often results in grammatical errors or changes to the original content, and additional changes made during the review process may ultimately harm the original messaging. This can result in the loss of more nuanced concepts or terminology, potentially resulting in misunderstandings or misrepresentations of the original content. In addition, direct translations may not always convey the same implications or relevance in the target language, which can compromise the cultural sensitivity and validity of the research.

### Current Recommendations for Multilingual Research Review Through WCG

WCG recognizes the importance of accommodating multilingual research, and we are working to develop solutions to support our clients' needs. While we do not currently have a mechanism for conducting ethical review of non-English materials without first reviewing the English version and thereafter approving a translation, our current recommendation for studies intended to be conducted only in a non-English language is to:

1. **Develop materials in the target language**: Create participant-facing materials in the language that will be presented to participants.
2. **Translate materials into English**: Translate the developed materials into English for ethical review.
3. **Submit with an administrative letter**: Submit the translated materials with an administrative letter that requests the IRB make minimal changes to grammar and readability of the document. This letter should note that the document may not read well in English since it is intended for a non-English audience and clarify any special terms or phrases that may not have direct English equivalents.

This approach will support the development and implementation of culturally responsive and accurate participant-facing materials, acknowledging the complexities of multilingual research, while also supporting the ethical review process.

### 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) must be met:

1. The research involves no more than minimal risk to the participants.
2. The research could not practicably be carried out without the 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 participants.
5. Whenever appropriate, the participants will be provided with additional pertinent information after participation.

WCG IRB applies this standard to all requests for waiver of consent for non-FDA regulated research.

### Waivers of Consent for FDA Studies

On Dec. 21, 2023, A final rule was published in the Federal Register regarding waivers of consent for FDA studies https://www.govinfo.gov/content/pkg/FR-2023-12-21/pdf/2023-27935.pdf. The final rule is effective January 22, 2024, If you are requesting a waiver of consent and the research is an FDA regulated study, then criteria from 21 CFR 50.22 must be met:

1. The clinical investigation involves no more than minimal risk to the subjects;
2. The clinical investigation could not practicably be carried out without the requested waiver or alteration;
3. If the clinical investigation involves using identifiable private information or identifiable biospecimens, the clinical investigation 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.

For individual emergency waivers of consent, prospective IRB approval is not always necessary if a patient's life can be saved. For more information refer to 21 CFR 50.23 (a)-(c).

### 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 Board will need to review the information that is provided to participants to obtain consent to ensure that the required elements of consent are included in the consent discussion. If you are requesting a waiver of documentation of consent, please submit a written statement or script of this information for the Board's review, a "participant information sheet." To create one, use the template consent, change the title to "PARTICIPANT INFORMATION SHEET" and delete the signature blocks.

The regulations that allow the Board to approve this type of waiver:

**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; and

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

**For HHS Regulated Research (not applicable under FDA regulations) (45 CFR §46.117(c)(1)(i)):**

The only record linking the participant and the research would be the consent document, and the principal risk of the research is the risk of breach of confidentiality.

Each participant will be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern; and

Participants enrolling in a study under this type of waiver must be provided with the elements of consent required by the regulations and participants must consent to participate.

**For HHS Regulated Research (not applicable under FDA regulations) (45 CFR §46.117(c)(1)(iii)**

If the participants 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 participants and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

### California Experimental Subject's Bill of Rights (BOR)

Submission of the California Bill of Rights (BOR) by research sites with the consent form is optional. Sites may use their own version if it contains all the information outlined in the California Health and Safety Code §24172. In addition, for sites in California, WCG automatically provides an approved BOR version along with approval documents after review. However, WCG can review and approve a BOR if submitted in the submission package and a specific request for review is made. Otherwise, these are typically just filed without review.

Additionally, according to California Health and Safety code Section 24173, a signed and dated BOR does not apply to the University of California system of institutions.

# HIPAA Authorization

HIPAA stands for the Health Insurance Portability and Accountability Act. The privacy rule within this regulation outlines the standards for privacy for individuals and confidentiality of individually identifiable health information. The specific regulations for HIPAA are in Title 45 CFR 160 and 164.

Clinical investigators need to assess if they are a covered entity as defined by the Office for Civil Rights. All PIs who are covered entities must have HIPAA Authorization language for potential

participants for study-related medical records to be available for review by the sponsor, CRO, IRB, and regulatory bodies. For your studies under the approval of WCG IRB, your HIPAA authorization language must be submitted to and approved prior to its use.

WCG IRB will review research materials to determine how the privacy and confidentiality of participants' personal health information is protected in accordance with applicable laws and regulations. The burden of HIPAA compliance rests with the covered entity.

Researchers who are covered entities and do not wish to request a waiver, may satisfy the HIPAA requirement for authorization by choosing one of the following alternative methods:

- Obtain a HIPAA compliant signed authorization from the research participant using a stand-alone document that the covered entity has created; or
- Incorporate the HIPAA language into the ICF and submit to WCG IRB for review in accordance with applicable laws and/or institutional policy. Submission of a combined document (ICF + HIPAA authorization) is optional because some institutions and sponsors/CROs prefer to use their own separate HIPAA authorization form (stated above) for research without incorporating HIPAA language into the ICF. However, if submitted, the Board will review the incorporated information. (Note: For research that may include California sites, WCG routinely appends a complete State of California HIPAA authorization form to the **template** ICF); or
- Provide a separate ICF addendum that contains the HIPAA language and submit to WCG IRB for review in accordance with applicable laws and/or institutional policy.

WCG IRB will 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. WCG IRB will review separate authorization documents upon request.

### Waiver of Authorization for Use and Disclosure of Protected Health Information

If you are a covered entity or your organization must otherwise comply with the 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 consent or written documentation of consent, you also need to request a waiver of authorization. The necessary information is collected via our Initial Review Submission Form, or can be provided after initial review through ClinSphere® eReview Manager or IRBNet.

# Assent

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

Assent is usually required for research involving *underage participants* and research involving *adults with diminished capacity*. Assessing an adult's capacity to consent may be somewhat difficult, depending on the participant's medical/mental condition and the requirements of the protocol. If the

investigator anticipates that some participants 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 participant is best protected by involving a LAR who knows the participant and is willing and able to participate in the informed consent process with the potential participant.

In order to assent, a participant must have at least a basic understanding of what might be asked of them in the research and what might happen to a level consistent with the participant's capacity to understand.

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

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

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

If the parent(s) of a minor child pass away after providing consent, the child can remain in the study without additional re-consent if guardianship is transferred to the state or a relative and the child's caretaker(s) agree to the child's continued participation in the research study.

# 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 required elements (as defined by the regulations) must be appropriately included.
- The content of the consent form must be understandable to a non-scientist.
- No waiver of rights or other exculpatory wording may be present or appear to be present in the consent form.
- The investigator must give the participant or LAR adequate opportunity to read it before it is signed and dated.
- The document must be signed and dated by the participant or LAR.
- The document must be signed and dated by the person obtaining consent.
- For clinical research: If the participant cannot read, an Impartial Witness must witness the consent process and sign and date the form.
- A signed and dated copy must be given to the person signing the form

# WCG IRB Policy on Consent Forms

The IRB will require consent forms approved with new protocols **starting March 1, 2024,** to start with a concise summary/key information section at the beginning of the consent form, along with requiring any other applicable additional elements of consent under the common rule. If a consent form is submitted without these elements, the Board will add this language to the consent form.

This will not apply to consent forms reviewed under protocols that were approved prior to March 1, 2024. Thus, if you are submitting a new investigator or a change in research for a protocol approved prior to this date, these additional consent form elements will not be added unless the research was already required to be reviewed under the current common rule (i.e. was federally funded, or had other state or institutional requirements to apply the common rule).

WCG IRB makes changes to consent forms to ensure the content complies with our SOPs (which includes a review to ensure compliance with the regulations), is factually correct and conforms to the requirements of institutions and sponsors. In the "redline" version, the superscript numbers and Legend Reasons for Change provide information about why a change was made.

# Assent Forms

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

Assent requires that participants have at least a basic understanding of what might be asked of them, and what might happen.

# 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.

Electronic consent is a broad term and can describe the exact representation of the IRB-approved document on an electronic device as well as refer to a consent process using electronic devices and audio-visual aids.

WCG reviews the electronic (e-consent) platform at the study level, where approved consent forms are uploaded as participant material templates. Sites that intend to use the platform are not required to submit the platform with their site-specific consent forms. The platform is reviewed once at the study level, with the expectation that each site will upload its own IRB-approved consent form. Exact representation of the IRB-approved document on an electronic device does not require IRB review of screen shots of the consent form on the device. The IRB need only approve the static version. (This is also true of other participant-facing forms that require IRB review, such as participant diaries and eCOAs.)

For all FDA-regulated electronic consents, including exact representation of an IRB-approved document on an electronic device, the IRB requires the signatures be confirmed to be 21 CFR part 11 compliant and requires a certificate of authenticity.

Electronic consent processes that are not just exact electronic representations require further details to be submitted. WCG IRB 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.

### e-Consent Submission Timing

Sponsors and investigators considering e-consent 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.

### 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 participant.

## Bring-Your-Own-Device (BYOD) for data collection

WCG permits participants to utilize their own device, such as a smartphone or tablet, for completion of electronic patient-reported outcomes (ePRO) data. Sponsors are required to provide only name(s) of the validated patient-reported outcomes (PRO) surveys/questionnaires utilized in their proposed study. A copy of unvalidated or customized PRO surveys/questionnaires must be only provided for review.

## Certificates of Confidentiality (CoC)

A CoC 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.

Research studies that are funded by NIH are automatically issued a certificate under the NIH Policy on Certificates of Confidentiality. Non-NIH funded research that collects identifiable, sensitive information can request a certificate from NIH for health-related studies that are not funded by NIH, but the granting of a CoC in these cases will be at the discretion of the NIH.

Investigators might consider applying for a certificate for research involving participant 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 participants involved in illegal, stigmatized, or embarrassing behavior; participants with illegal status (alien, child runaway, AWOL, etc.); and participants with a stigmatized disease (HIV, alcoholism, mental illness, etc.) might have additional protection if a CoC has been obtained.

If the study for which the CoC is granted involves informed consent, the investigator must inform research participants of the protections and limits on protection provided by the CoC. If language is not included in the consent form, WCG IRB will insert the following language (or similar):

"Information about a Certificate of Confidentiality for this research:

[Name of research site and investigator] has received a Certificate of Confidentiality from the government which will help protect the privacy of research participants. The certificate protects against the involuntary release of information about participants collected during the course of this research. The researchers involved in this study cannot be forced to disclose any information collected in this study in any legal proceedings.

However, the participant may choose to voluntarily disclose the protected information and this certificate does not prohibit such voluntary disclosure. Furthermore, the parties listed in the Confidentiality / Authorization section of this consent form may review our records under limited circumstances and this certificate does not prohibit such disclosure."

For some types of research, the Board may direct an investigator to obtain a certificate of confidentiality.

- Frequently asked questions about CoCs are available on the NIH web site here: https://humansubjects.nih.gov/coc/faqs.
- OHRP has posted guidance here: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/certificates-ofconfidentiality/index.html.
- Instructions for applying for a Certificate are available here https://grants.nih.gov/grants/policy/coc/appl_intramural.htm. NIH is not the only source for certificates, as several federal agencies issue certificates.

The Department of Justice requires that researchers prepare a "Privacy Certificate" (PC), which is similar to a 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.

# WCG IRB Policy on Pregnant Partners

Effective Aug. 1, 2022, WCG policy on collection of outcome data on partners of study participants has changed. WCG policy is now as follows: the collection of outcome data on partners of study participants who become pregnant does meet the HHS definition of research, as it is a systematic investigation designed to develop or contribute to generalizable knowledge. As a result, the IRB will make 45 CFR 46 Subpart B and D determinations for follow up of pregnant partners and their children.

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

If you submit a consent document or HIPAA authorization 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 unless/until one is needed to consent a pregnant partner.

This change does not affect the follow-up of participants who become pregnant. Those individuals are human participants. 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.

# Requirements for Human Research Protection Training

WCG IRB requires investigators to verify on the initial review submission form and each Continuing Review Report form that each member of the research team has successfully completed training in human research protection. Your institution may have additional training requirements, please check with your institutional official. Please note that HIPAA training or prior research experience alone does not satisfy this requirement for training in human research protection. 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 research protections.

WCG IRB's expectation is that training include topics such as ethical principles related to human research protections, federal regulations for protection of research participants, and Good Clinical Practice. If your team has not completed training, please be sure an equivalent training has been completed and is listed in the submission.

When standard therapy is part of the research, WCG IRB only requires human research 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.

WCG IRB 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 WCG IRB.

Online:

- Investigators can meet the training requirement through the Collaborative Institutional Training Initiative (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: https://about.citiprogram.org/.
- ACRP Certified Principal Investigator Training (CPI certification)
- DIA Clinical Research Certificate Program
- OCRA Clinical Research Professional (CRP)
- Canadian researchers and study staff are required to complete Tri-Council Policy Statement (TCPS 2) training before their submission will be approved. The new TCPS 2: CORE-2022 Course on Research Ethics (CORE) is based on the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans – TCPS 2 (2022)*. The online tutorial takes about 4 hours to complete and is available in English TCPS 2: CORE-2022 and French EPTC 2 : FER-2022.
- The NIH Office of Extramural Research provides an online tutorial called "Protecting Human Research Participants" .

# Special Considerations for Drug Research: Do You Need an IND

WCG IRB's Initial Review Submission Form asks for information about an IND. As a general rule, WCG IRB 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 WCG IRB 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 WCG IRB.

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

# Special Considerations for Device Research: IDE, NSR (Nonsignificant risk) and IDE Exempt

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 WCG IRB.

The submission form will prompt you to provide the appropriate, required documentation for review of research involving an SR device. In most cases, submitters should ensure WCG IRB 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 research is SR, The IRB requires proof of the IDE number at the time of submission. The Board will automatically consider the research to be SR.

If the participant must undergo a medical procedure as a part of the study, and that medical procedure is not one which the participant would otherwise undergo as part of their care regardless of the research, the Board must consider the risks associated with the procedure as well as the use of the device. If potential harm to participants 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.

# Special Considerations for Behavioral Research

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

# Special Considerations for Federally Funded Research

## 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 Federal-wide 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 Federal-wide 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/policy/engage08.html.

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

- As described in the OHRP guidance entitled "Engagement of Institutions in Research," a Federal-wide Assurance (FWA) must be filed for all sites engaged in federally-funded research. The guidance is available at: http://www.hhs.gov/ohrp/policy/engage08.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 email (see http://www.hhs.gov/ohrp/assurances/contact/index.html) and explain why it was unable to

submit its FWA electronically. The registration number for WCG IRB is IRB00000533 (Canadian sites use IRB00002354). WCG IRB will request a copy of the DHHS-approved FWA application, but if it is not available, it is not required for review.

- An IRB Authorization Agreement must be completed. The form (Reliance Agreement) is available on the Forms page of https://www.wcgclinical.com/irb-resources/.

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 WCG IRB's Client Care for clarification or assistance regarding these requirements.

# IND Exemptions and Compounded Drug Research

For a clinical investigation to be exempt from IND requirements, the drug product must be lawfully marketed in the United States and meet all conditions outlined in 21 CFR 312.2(b).

Research involving modifications to the lawfully marketed drug may also be IND-exempt, provided they do not introduce risks exceeding those associated with the product's standard, labeled use. This exemption would typically apply to low-risk modifications to the lawfully marketed dosage form, such as minor variations to solid oral dosage forms. For example, changes to the color, scoring, or capsule size of the marketed dosage form for blinding purposes would generally be considered low risk, if they do not involve significant manufacturing or formulation changes.

While sponsors are primarily responsible for determining the need for an IND (21 CFR 312.2(a)), Institutional Review Boards (IRBs) play a critical role in ensuring study compliance with regulations, protecting the rights and welfare of human subjects, and assessing that the research does not introduce new risks (21 CFR 56.101). IRBs rely on sponsors/investigators to provide the documentation to support IND exemption claims.

Compounded drugs present unique challenges. They lack FDA approval, possess an unknown safety and efficacy profile, and may have incomplete labeling. In addition, poor compounding practices can lead to serious drug quality issues, potentially resulting in patient harm or death. Consequently, compounded drugs in research studies are not in compliance with FDA regulations for IND exemption and IRBs cannot determine whether the research will not significantly increase risks associated with the use of the product (21 CFR 312.2(b)(1)(iii)).

Ultimately, the FDA has the final authority to determine what are the requirements to investigate the compounded drug in the research. Sponsors and investigators should proactively consult the FDA when studying compounded versions of lawfully marketed drugs to determine IND requirements.

# Utilization of Third-Party Resources Such as Person Locating Services for Collection of Long-Term Follow-Up (LTFU) Data

At times, a sponsor or other entity will establish a Long-Term Follow-Up (LTFU) plan in order to assist in obtaining data about the research participants in a protocol. The LTFU plan is usually described in the protocol and may be limited to one country or conducted across multiple countries. The plan is normally executed by the site, sponsor or CRO research staff, but on occasion they are also executed by third party person/patient locating firms. WCG IRB will review protocols and consent forms that describe LTFU strategies. The plans should describe the person or entity that will be utilized, the

confidentiality/privacy protections in place, and how the research staff or locator service will locate participants.

A third-party locator service cannot be used unless the participants have been notified in the consent form(s). If participants have consented to the use of a third-party locator service, then the data that they consent to being collected can be obtained using such a service, in addition to the service of locating participants who have been lost to follow up.

Alternatively, if participants have not or cannot provide consent, the sponsor/investigator can review publicly available records as per their state or local guidelines to collect LTFU data without IRB review.

In addition to utilizing a third-party service, the Investigator may use a third person contact (parent, legal guardian, legally authorized representative, caretaker) to collect LTFU data if a participant provides demographic information for such a person as well as consent to contact them as part of the consent process.

# Single Patient Case Reports - Dissemination of Clinical Study Data by Investigators for Education and Research Purposes

Investigators may present data from an individual patient from their clinical practice as a case study analysis/report in the format of a presentation or a journal article. The investigator must protect the participant's privacy and confidentiality by taking appropriate measures during dissemination. The case study analysis/report does not meet the regulatory definition of research (45 CFR 46.102 (e)(7)(l)) because an individual participant case study does not contribute to generalizable knowledge. Given this, it does not require IRB review. However, if required, WCG IRB can also review the case study analysis/report and provide an official letter that it is "Not Research" to satisfy any applicable requirements of the entity to which the analysis/report will be presented.

# Special Considerations for Multi-Center Studies

Each individual submission for a multi-center study must be accompanied by a completed initial review submission (through ClinSphere® eReview Manager or IRBNet).

Any site submission lacking a complete submission form, current CV and license, or proof of a current medical license (when applicable) 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 WCG IRB for information about submission requirements for specific types of research.

For new research, the IRB reviews the protocol and related participant materials for each investigator. Each investigator's initial approval Certificate of Action cites all the protocol-level items that the IRB has approved for that research (unless we have received instructions otherwise, see below).

Each time a new item is submitted for review for a multi-center protocol, advise us if any documents should be excluded from automatic review for all sites — identify any documents that should be **excluded from default, all-site approval** (e.g., payment-vendor documents or site-specific consent forms). In the absence of such notation, WCG IRB will assume the document applies to all sites. Please refer to the "Documents for Select Sites" section of this document for additional information on this process.

If some or all sites will rely on the same billing instructions, it is acceptable to put “see attached” in one of the submission form billing fields and provide them with a completed copy of our “Billing Information Stand-Alone Form” (available on the web site here) to send to us with the submission in lieu of filling out the billing section of the form each time. Initial review submissions lacking either a completed billing information section or the stand-alone form will be placed on hold and missing information requested.

# Consent Forms for Multi-Center Research

When first submitting a consent form for a multi-center protocol, sponsors and CROs should clearly identify all placeholders for site-specific information within the template consent form. Placeholders should be formatted using **red font** and enclosed in **brackets** (e.g., [Insert Site Name]).

Providing clearly formatted placeholders supports accurate and efficient incorporation of site-specific details. Please note that if required site-specific information is not provided at the time of the Investigator’s initial submission, delays in processing of the site-level consent form and initial review may occur.

Once the Board has reviewed and approved a consent form for a multi-center protocol, the IRB will provide an approved version of that form, unless the submitter provided alternate instructions. **Reliance on the previously approved version can significantly reduce the processing time and result in more rapid receipt of approval documents**. By using the consent form template, you can be confident that you are starting with the most recent IRB and sponsor-approved language, thereby ensuring accurate version control, while saving you time and effort. WCG IRB will generate a consent form for the PI by incorporating any institutionally required language that has been provided to the IRB and the site-specific information such as payment information, etc. into the previously approved consent form template.

**Site-specific information** which must be provided on the WCG IRB submission form includes:

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

To determine if a previously approved consent form is available for a particular protocol or request to preview it, contact Client Care at 1-855-818-2289 or check the ClinSphere® eReview Manager page for that protocol (your sponsor or CRO contact can grant you access). If you require customized language, track (redline) your changes on the approved informed consent so we can easily identify your site-specific customizations. Please manually track your changes and do not use Word’s “compare” feature to create your redlined consent form, as this may result in more holds and a longer processing time (the compare feature often introduces extraneous formatting changes, duplicative changes, or other changes that are not meaningful, and potentially reverses Board-directed changes).

We require the use of IRB-approved informed consent(s) for initial review submissions of new principal investigators (PIs).

**WCG IRB Template Consent Form Maintenance:**

In order to ensure WCG IRB's approved consent template always contains all the current and correct information about the research, any time we receive updated protocol information, risk profile changes, or consent form changes that impact the template, the Board will make the necessary changes to the template and provide the sponsor/CRO with the updated consent form. Please note that if we receive information that affects the template from a site, we do not routinely place that change on hold and request sponsor or CRO approval to proceed with the template update. This ensures that we are able to make the necessary changes to the template without delay. If you have questions or concerns about this policy, contact WCG IRB Client Care at 855-818-2289, or e-mail clientcare@wcgclinical.com.

# 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. Please review the guidance in the section of this Guide outlining best practices for submitting ads and other subject facing materials.

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 participant recruitment materials or other participant materials (diaries, questionnaires, etc.) that have been previously reviewed by WCG IRB, state in the submission that the items have been previously reviewed by WCG IRB. Board support staff will provide the Board with information about the previous Board review, so that the previous decision of the Board can be considered when the additional materials are reviewed.

# Special Considerations for Participants Who Do Not Speak English: Translations

All consent forms and other participant materials must be in a language easily understood by the participant, and all translations must be approved by WCG IRB. If you are enrolling non-English speaking participants, you must have plans for conducting the consent discussion in the language understandable to the participant, and for ongoing communication with the participant throughout the research and in case of emergency. 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. Sites and study teams are asked on the translations request form to acknowledge "*The research team will involve individuals fluent in both English and the language spoken by the person providing consent to ensure that information provided will be understandable, and that the research team will conduct ongoing communication in the language spoken by the person providing consent throughout the research and in case of emergency.*"

Additionally, **WCG expects the plans to obtain translations to remain consistent throughout the progress of the study; for example, if WCG-facilitated translations are requested at initial review, WCG expects to facilitate all translations for the remainder of the study.**

**Translations Considerations for Initial Screening of Medical Records**

Sites may review medical records in a non-English language. Sites can use a certified third-party translator vendor service and may request redaction of items which are not necessary for the screening process. This activity does not require submission to the IRB (note that investigators should ensure they have appropriate HIPAA authorizations or other appropriate authorization to review the records).

## Translations Considerations

WCG will process translations requests as received, unless otherwise noted by the sponsor/CRO. WCG recommends sites confirm with their sponsor/CRO if translation arrangements have already been made and which translations they should proceed with. WCG IRB will not be held financially responsible for translation service bills that the sponsor will not pay on behalf of sites. WCG IRB requires written confirmation that an invoice will be accepted should it need to be redirected to another party for payment. Sponsors/CROs can request WCG place site translation requests on hold for ponsor/CRO authorization. WCG will not provide translations for non-WCG IRB sites. WCG does not require back-translations for approval of translated documents. If there is an urgent need for translations, please refer to WCG's policy on Short Forms in this guide.

1. **Translations Facilitated by WCG IRB**

WCG IRB can facilitate and provide translated study materials upon request. The chart below outlines the translations process when WCG facilitates the translation. **Please note, once approved English documents are sent to the translator, the translations process cannot be stopped.**

| | For Documents That Have Not Been Previously Translated | For Documents That Have Been Previously Translated and are Modified |
|---|---|---|
| **How and When to Submit** | Each request for translation must be requested by selecting the appropriate translations request option in ClinSphere® eReview Manager and answering all questions (IRBNet clients should use the WCG IRB Translation request form available in their IRBNet library). | WCG IRB staff will automatically initiate translations after changes are made to the English version via a change in research submission and are approved by the IRB. If translations are not needed for a submitted change in research, indicate "no" to the Change in Research Submission form question "**Will you need translated documents or approval of translated documents?**" when the change to the English document is initially submitted for review. |
| **IRB Process** | 1. English documents are reviewed and cannot be translated until approved.<br>2. Approved English documents are sent to a qualified translator to be translated. **Once sent to the translator, the translations process cannot be stopped**.<br>3. Translated documents and their corresponding Certificate of | 1. Updates to English documents are reviewed and approved first.<br>2. WCG IRB staff check to see if the corresponding change in research submission form indicates "no" for "Will you need translated documents or approval of translated documents?" If "no" is selected, WCG will not proceed with translations.<br>3. If the CIR form does not indicate a translation is not needed, the approved |

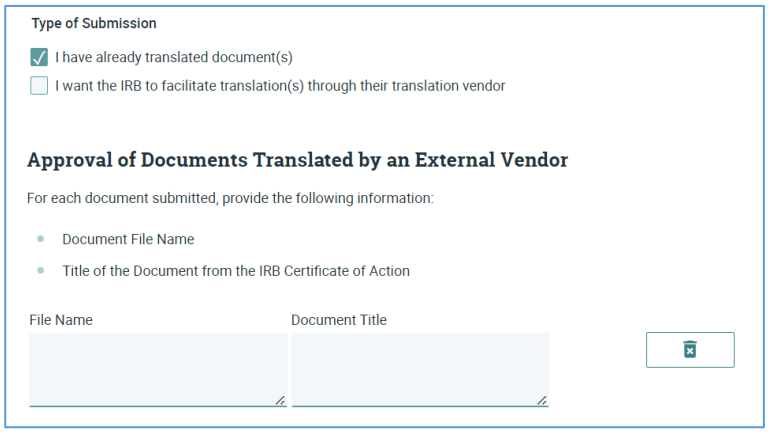
| | For Documents That Have Not Been Previously Translated | For Documents That Have Been Previously Translated and are Modified |
|---|---|---|
| | Translations are received from a translator.<br>4. The translated document(s) and their corresponding translations certifications are sent to an IRB member for approval. | English documents are sent to be translated. **Once sent to the translator, the translations process cannot be stopped**.<br>4. Translated documents and their corresponding Certificate of Translations are received from translator.<br>5. Translated documents are sent to an IRB member for approval. |
| **Turn Around** | 7-10 business days to translate documents.<br>3-5 business days to review and approve translated documents. | |
| **Billing** | WCG IRB bills an administrative fee for translation services in addition to the translator's fee. Translation costs vary depending on the volume and complexity of the translation request. WCG does not provide quotes. | |

### 2. Translations Facilitated by Sponsors, CROs, and/or Sites (including AI-facilitated translations)

Sponsors, CROs, and sites can facilitate their own translations of WCG IRB English approved documents. The translations must correspond to the WCG IRB approved English versions; therefore, a translation of the sponsor template consent form, for example, or any materials not yet approved by WCG IRB are not acceptable. If the sponsor/CRO/site is facilitating translations, it is their responsibility to arrange translations for updated materials with their vendor, and then submit the updates to WCG IRB for review. The chart below outlines the translation process when translations are facilitated by the sponsor, CRO, or site.

| | For Documents That Have Not Been Previously Translated and Reviewed | For Documents That Have Been Previously Translated and Reviewed |
|---|---|---|
| **How and When to Submit** | **Sponsor/CRO/site translations cannot be submitted at the time of the initial review of the English documents** (via initial review submission or change in research submission of new documents). **WCG IRB must approve the English version of the materials before the sponsor/CRO/site translates them.** Translated documents can be submitted to WCG IRB by selecting the appropriate Translations request option in ClinSphere® eReview Manager and answering all questions (IRBNet clients | Updated translated documents should be submitted to WCG IRB by selecting the appropriate Translations request option in ClinSphere® eReview Manager and answering all questions (IRBNet clients should use the WCG IRB Translation request form available in their IRBNet library) **after English approvals are granted**.<br>It is expected that you submit updated translated materials within 30 days of the English document approvals. |

| | | |
|---|---|---|
| | should use the WCG IRB Translation request form available in their IRBNet library) **after English approvals are granted**.<br>*Note: AI algorithms can be used to generate automated translations. However, the translation thereafter requires review by certified translator as an accurate representation of the approved English version.* | |
| **Submission Requirements** | 1. Submit via the translations request option in ClinSphere® eReview Manager (IRBNet clients should use the WCG IRB Translation request form available in their IRBNet library).<br>2. Provide the translated materials. Consent forms must be submitted in Word-compatible format (PDF not accepted). The format of the translated material must match its English counterpart exactly.<br>3. Provide a Certificate of Translation that includes the following:<br>a. Document title of the English approved document as it appears on the IRB Certificate of Action.<br>b. IRB approval date of the English approved document; or version number and date; or consent form codes (i.e. S0-1; IN0-0, etc.).<br>c. IRB tracking number and/or sponsor protocol number.<br>d. Sponsor<br>e. PI Name<br>f. Source and Target languages<br>g. A statement confirming that the translator is fluent in English and the target language, or otherwise able to translate.<br>h. A statement confirming that the document is an accurate representation of English.<br>i. For first-time review of a translated document, a certificate of translation attesting to tracked changes-only will not be accepted. The translator must attest to the accuracy of the entire document(s).<br>4. Ensure one of the following methods are used for WCG staff to be able to accurately match each translated document with its corresponding WCG English IRB approved version.<br>a. Complete this section on the Translation Request Submission Form completely and accurately. The Document Title should be referenced from the Certificate of Action of the approval of the corresponding English document. | |

| | |
|---|---|
| |  <br>b. Include the WCG IRB English Document title or the IRB document identifiers directly on the translated document. |
| **WCG IRB Process** | 1. WCG IRB staff review the translated documents provided to ensure the formatting matches the English versions exactly (mirror copies), the content appears to align, and the corresponding Certificate of Translations appropriately identifies the translated documents (reference above).<br>2. WCG IRB staff send the translated documents package to an IRB member for approval. |
| **Turn Around** | 3-5 business days to review and approve translated documents. |
| **Billing** | WCG IRB bills a review fee per language and per submission and a distribution processing fee per language per PI. |

### Short Forms

WCG IRB has the following policy regarding the use of a short form consent process to enroll participants. WCG's policy may be more restrictive than federal requirements, and can only be applied in situations **when both of the following are true**:

1. A full-length version of the consent form in language understandable to the participant is not available, or is not appropriate for the participant. This may include unexpected translations, low literacy, or visual impairment.
2. It is in the participant's best medical interest to be enrolled in the research, and for unexpected translations, before a translated consent form can be obtained.

**Below are the steps required for WCG's short form policy:**

1. Access the appropriate WCG Short Form Template here. For unexpected translations, use form HRP-503 in the appropriate language. For English speakers with low-literacy, visual impairment or similar situations, use form HRP-511.
2. Insert study-specific information, including title of study, principal investigator, appropriate signature lines (copy from the IRB approved consent form or keep the appropriate template ones provided in the translated short forms, and contact information into the OHRP template short form.)
3. Verbally review the information in the IRB approved long version of the consent form to the participant with an impartial witness. For unexpected translations, a translator who is fluent in

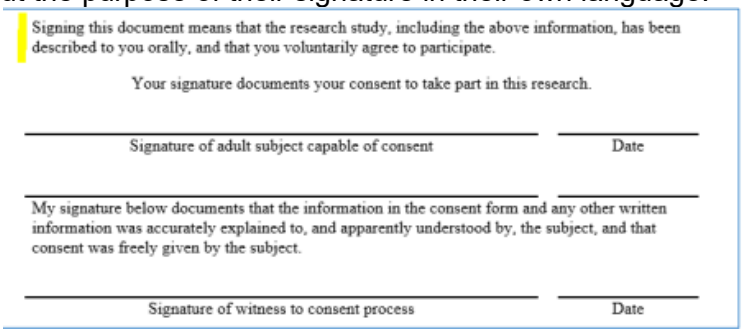
both English and the participant's language is required and the translator may serve as the witness.

4. Obtain the following signatures:

a.

| | Required to Sign |
|---|---|
| **Person obtaining consent** | Long Form (e.g., English ICF) |
| **Witness** | Short Form and Long Form |
| **Participant**<br>*If the participant is incapable of consent and either a legally authorized representative (as allowed by protocol) or parent(s) signature is required, replace the participant signature block below with the signature block from the IRB approved main ICF* | Short Form |

b. Note: WCG IRB has made available a limited number of translated short forms on its website. The signature lines in that collection are in English so that site staff can read and follow the instructions for obtaining signatures. The line immediately above the English statement "Your signature documents your consent to take part in this research" says in the translated language "Signing this document means that the research study, including the above information, has been described to you orally, and that you voluntarily agree to participate." Therefore non-English speakers receive the important information about the purpose of their signature in their own language.


Signing this document means that the research study, including the above information, has been described to you orally, and that you voluntarily agree to participate.

Your signature documents your consent to take part in this research.

Signature of adult subject capable of consent — Date

My signature below documents that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process — Date

5. Provide the participant signed copies of the IRB approved long form consent form and the short form in the language understandable to the participant.
6. File the original signed IRB approved long form consent form and the original signed short form in the participant's research record and medical record, if appropriate.
7. For unexpected translations, the site must obtain a fully translated version of the IRB approved long form consent form at the earliest opportunity. The participant should be re-consented using the fully translated consent form within 60 (business) days or at the first visit after receipt of the translated consent form (whichever is less).

If the participant doesn't meet the criteria above for the use of WCG's Short form policy, but may need to be enrolled in emergent situations such as those listed below, researchers can plan to not enroll the participant, or refer to the appropriate regulations (for FDA, 21 CFR 50.24; for Non-FDA, 45 CFR 46.101(i)) to utilize the pathways for a waiver of a consent.

1. Subjects are unable to give their informed consent as a result of their medical condition.
2. The intervention under investigation must be administered before consent from the subject's LAR is feasible.

3. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

# Special Considerations for Site Investigator's (PI) Employment Status

The employment relationship of the PI with the institution/site will be evaluated on a case-by-case basis, if the PI is not a full-time employee of the institution. The PI may hold an independent contractor role and may still provide oversight of the study. The Board will evaluate this in the context of the proposed study.

# 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 participant. Some state and local laws also further restrict enrollment of wards in research. Additional guidance is also available in the FDA guidance document titled "Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors".

# Special Considerations for Canadian Research

The WCG 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 (REB). For more information about the Canadian Panel, please call Client Care at 855-818-2289.

Submitting the No Objection Letter from Health Canada: The sponsor must submit clinical trials of drugs and devices to Health Canada before the study can begin. If there are no objections or issues, Health Canada will issue a No Objection Letter (NOL), typically within 30 days. Review by Health Canada and the Research Ethics Board may occur in parallel so the NOL may not have been issued prior to Board review. If the sponsor has received the NOL prior to submitting to the REB, they should include it as part of the submission. If the sponsor has not received the NOL prior to submitting to the REB, they should submit it as soon as they receive it.

While the Tri-Council Policy Statement (TCPS) does not generally apply to the research reviewed by WCG IRB, the Board will apply it to all Canadian Research. TCPS has additional consent requirements for consent, storage of biospecimens, and research that involves genetic analyses.

If the protocol requires collecting biospecimens, the Board requires information on where and for how long the samples are stored. The Board prefers to know the exact location of where the samples will be stored, but at a minimum the Board will need to know the country they will be stored.

For more information about the TCPS requirements please see: https://ethics.gc.ca/eng/policy-politique_tcps2-eptc2_2022.html.

**The TCPS has additional elements of consent not included under the U.S. regulations including:**

1. Information about biological samples and genetic research. To avoid conditional approvals or deferrals, the Board asks for the necessary information on the required Canadian Supplement HRP-213. For more information please see TCPS Chapter 12 and 13.
2. A statement that if a subject withdraws consent, the subject can also request withdrawal of their data or human biological materials; and any circumstances that do not allow withdrawal of data or human biological materials once collected.
3. Confidentiality of personal information is protected under the Personal Information Protection and Electronic Documents Act (PIPEDA). While there is a lot of overlap between PIPEDA and HIPAA, there are some key differences. Specifically PIPEDA is broader than HIPAA and applies to Personal Information used in a commercial context.
4. A statement that, by consenting, subjects have not waived any rights to legal recourse in the event of research-related harm.
5. Information concerning the possibility of commercialization of research findings.
6. To avoid therapeutic misconception, TCPS indicates that the preferred term is participant as opposed to patient; the Board will change patient to participant when appropriate.
7. Units of measure should be in both Metric and Imperial units; for example, 10 mL (2 teaspoons).

**Other considerations for Canadian research:**

- **Research Ethics Training:** Prior to approval, Principal Investigators and those study team members who interact with participants (and their personal information) complete the online tutorial TCPS 2: CORE-2022 (Course on Research Ethics), https://www.tcps2core.ca/welcome
- **Province of Québec:** In respect of Article 21 of the Québec Civil Code, WCG IRB Canada will not review research involving minors and incapacitated adults from the province of Québec.
- **Review of studies involving adults lacking capacity to consent in British Columbia** -- WCG is not a designated Research Ethics Board (REB) under the British Columbia Representation Act, and as such the Board cannot review research studies involving adults lacking capacity to consent unless the individual has entered into a representational agreement that allows the legally authorized representative to enroll the individual or continue the individual's participation in medical research.
- **Review in Various Provinces:** WCG is not able to review research is several provinces without local review. For a complete list of the Provinces that WCG can and cannot review in please contact Client Relations.

# Special Consideration: Nursing Magnet Designation

WCG IRB has consistent membership and involvement by at least one nurse in the governing body responsible for the protection of human participants. 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.

WCG IRB may also be asked to determine research to be exempt from IRB Review. Exempt determinations are made by a WCG IRB 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.

# Special Considerations for Single Patient Expanded Access/Compassionate Use

When appropriate — and with approval from FDA, the manufacturer and an IRB — patients with no other options can gain access to experimental drugs and medical devices. Because insurance typically does not cover expenses associated with approval process, many patients can't afford what they consider a last chance for hope. WCG IRB provides single patient expanded access reviews at no charge.

# For Review of Single-Patient Expanded Access

WCG IRB does 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.

**The Process for Single-Patient Expanded Access Requests (Drugs/Biologics)**

Single-patient expanded access requests are processed differently, using the following process:

- Please submit FDA Form 3926, the same form that is submitted to the FDA to request the single-patient IND, as well as other appropriate submission forms (HRP-280 for emergency use, HRP-282 for other single-patient expanded access).
- In accordance with FDA guidance, the request can be reviewed by an IRB Chair and does not need to go to the full IRB. Responses to complete single-patient expanded access review requests are usually returned within 24 to 48 hours of receipt.
- Because there is no protocol sponsor, WCG IRB does not charge a review fee for single-patient expanded access review — there is no additional burden on the patient.
- For questions about submitting single-patient expanded access requests, please contact clientcare@wcgclinical.com.

WCG IRB does not provide review for pre-approval access to investigational products that do not follow the FDA's Expanded Access process.

**Additional Resources**

In 2019, the FDA created Project Facilitate, a pilot project to assist physicians and patients with understanding and negotiating the process of expanded access for oncology products.

The FDA has created a Q&A document with information about treatment use for investigational products.

**Expanded Access for Medical Devices**

The process for obtaining approval to use an investigational medical device outside a clinical trial is very similar to that for obtaining an investigational drug or biologic. For devices, single or small

treatment group access is called Compassionate Use, whereas the process for a large treatment group is referred to as a Treatment IDE (Investigational Device Exemption).

The IRB review process for single patient compassionate use requests is the same as for single patient expanded access for drugs. The following WCG IRB forms should be used for submission of these requests:

- EMERGENCY USE OF AN INVESTIGATIONAL DEVICE (HRP-281)
- COMPASSIONATE USE OF AN INVESTIGATIONAL DEVICE (HRP-283)

For questions about submitting investigational medical device requests, please contact clientcare@wcgclinical.com.

**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*

# IRB Transfers

An IRB transfer happens when a study that has been approved by another IRB is transferred to WCG IRB. 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 WCG IRB.

## Required Documentation for an IRB Transfer Review Request

- Initial Review Submission Form (accessed via ClinSphere® eReview Manager or IRBNet) .
- Background information provided on the WCG IRB Form IRB Transfer Cover Letter Checklist & Summary.
- Any documents that the submitter has been instructed to provide based on his/her answers to the questions on the IRB Transfer Cover Letter Checklist & Summary. https://www.wcgclinical.com/irb-resources/irb-forms/ (for example, the form instructs the submitter to provide any new risk or benefit information that was not submitted to the previous IRB).
- A copy of the complete current protocol if not already on file at WCG IRB.
- 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 IRB Transfer Cover Letter Checklist & Summary form (for example, the form instructs the submitter to provide any new risk or benefit information that was not submitted to the previous IRB).

## IRB Transfers Fall Into Two Categories

**"Active"** - some or all participants are on active* treatment and the site may recruit more participants for the study.

**"Follow-up only" -** the site will not recruit any more participants, but still has participants in follow-up (participants no longer on active* treatment).

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

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

If a site is still enrolling and/or has active participants, WCG IRB will provide the site with an updated consent form with instructions for how participants can contact WCG IRB if they have questions about their rights as a research participant or with questions, concerns, input, or complaints about the research. Alternatively, if the site’s participants are all in “follow-up only” status, WCG IRB 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 participants notifying them of the change of IRB.

### Recommended Instructions for Institutions Deactivating Their IRB or Transferring Multiple Projects to WCG IRB:

1. Plan a conference call with WCG IRB to discuss preliminary steps toward transition of studies.
2. Begin to assess which studies have active participants that 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 participants. (Plan to keep the existing IRB functioning until all open studies have either closed or been approved by WCG IRB.)
4. Notify WCG IRB of the number of studies that are to be transitioned.
5. Communicate to the research community the plan to transfer active studies to WCG IRB.
6. Communicate to the research sponsors the plan to transfer active research to WCG IRB - 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 WCG IRB representative, if necessary or desirable, depending on staff familiarity with WCG IRB forms and systems, or volume of studies.

# The Review Process: Board Actions

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

#### Approve

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

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

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

**Outcome Documentation:**

Once your study has been reviewed, we will prepare and send the outcome documents to you and all designated contacts (via ClinSphere® eReview Manager or WCG IRBNet), including:

- Certificate of Action (this will convey the Board's action as well as any special Board determinations, requirements, or other necessary information). (Initial review COAs for sites list all materials approved to date for the protocol.) Note: Canadian panel Certificates of Action are signed (they serve as the REBA form for the review); however US regulatory guidelines in 45 CFR 46.109(d) require written notification of the IRB's actions but do not require signatures on IRB action notification letters and therefore US Certificates of Action are not signed.
- Copies of all approved participant materials (such as diaries, ID cards, etc.) and advertisements (these documents are labelled with the date the IRB originally approved them; they are not labelled with the date each individual site received approval of them). Note: When the Board approves participant materials and/or advertisements, any redlined changes that were provided by the submitter or required by the Board for approval will remain visible in the outcome document(s); however, recipients are expected to accept the tracked changes in the document before using it. Do not make any additional modifications (including font size and other visual effects) to the approved materials.
- Copy of the Board-approved consent form (when applicable), ready for use.
- Description of the changes to the consent form (depending on the type and extent of the Board's changes).

Bracketed placeholders (<< xx >>) will appear in protocol-level approved consent forms; the brackets may appear in red text for enhanced visibility. These are text fields that will be populated by IRB staff with customized language for each PI/site using information provided by the site. The following table outlines the description of commonly bracketed sections you can expect to see:

| Placeholder title and text field | Information that will populate per PI |
|---|---|
| ***Investigator information***<br><<CF-Main Investigator Full Name-Title>> | **INVESTIGATOR:** Full Name<br>Address |
| ***Study Related Phone Numbers***<br><<CF-Main User Defined #1>> | XXX-XXX-XXXX<br>XXX-XXX-XXXX (24 hours)<br>OR<br>XXX-XXX-XXXX (24 hours) |
| ***California research subjects Bill of Rights language***<br><<CF-Main User Defined #2>><br><<CF-Main California Bill of Rights>> | , as well as a signed and dated copy of the Experimental Subject's Bill of Rights |
| ***Conflict of Interest Disclosure***<br><<CF-Main Financial Disclosure>> | Site submitted or Board directed conflict of interest statement |
| ***SMO name to be included in the Confidentiality section***<br><<CF-Main User Defined #3>><br><<CF-Main SMO Company 1>><br><<CF-Main SMO Company 2>> | , [SMO Company Name], an agent for the study doctor, |

| Placeholder title and text field | Information that will populate per PI |
|---|---|
| ***Institution name to be included in the Confidentiality section***<br><<CF-Main User Defined #4>><br><<CF-Main Affiliated IN Language 1>><br><<CF-Main Affiliated IN Language 2>> | , the institution where the research is being done, |
| ***Site Payment***<br><<CF-Main Payment for Part. Paragraph>> | Site specific compensation language or template compensation language with site specific payment amounts incorporated |
| ***SMO name in the HIPAA section***<br><<CF-Main User Defined #5>><br><<CF-Main SMO Company 1>><br><<CF-Main SMO Company 2>> | , [SMO Company Name], an agent for the study doctor, |
| ***Institution name in the HIPAA section***<br><<CF-Main User Defined #6>><br><<CF-Main Affiliated IN Language 1>><br><<CF-Main Affiliated IN Language 2>> | , the institution where the research is being done, |

Please note that the table above explains the most common situations where these text fields will be used. Additional text fields may be included based on individual consent form and/or state requirements.

When advertisements or participant materials are approved, WCG IRB will provide a copy of the approved participant material(s) and/or advertisement(s) bearing an IRB approval stamp and a unique IRB identifier number (which corresponds to the identifier for that item on the Certificate of Action). The stamped copy is for your records and is not intended as the copy to be disseminated to participants (it may also include annotations indicating changes the IRB requires as a condition of approval). WCG requires that the approved material be used with all required changes made and without any other alteration from what was approved; WCG does not have an expectation that a copy displaying the IRB stamp and/or unique identifier will be used. (Changes to phone numbers or contact names referenced in approved advertisements and participant materials, and corrections to spelling do not need to be submitted for IRB review.)

Since WCG does not require the submitter to use the version with the IRB approval stamp/identifier, requests for WCG to re-issue a document with the approval stamp or identifier moved to a different area in the document will not be fulfilled.

Please note that if your organization is using the (legacy) WCG IRB Connexus Teams feature, the Team manager(s) is/are responsible for updating members of the Team in WCG IRB Connexus, but WCG IRB staff must be notified via the Contact Information Update Form when the Team name or designated Team email changes (if WCG IRB staff are not notified of changes to the team name or email, Team members may not receive notifications when documents require pre-review authorization). The Team name appears on the distribution list on the Certificate of Action when applicable.

## Approval with Conditions

“Approval with conditions” means the Board has reviewed a submission and determined it meets the requirements for approval but requires specific changes to the study and/or study documents as outlined by the Board before final approval can be provided.

You will receive written notification of the conditions promptly after the review.

Once you submit the requested information, your submission will be re-reviewed. Once that review is complete and all information is confirmed, you will receive your approval documents.

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.

## Disapprove

"Disapprove" means the submission does not meet the criteria for approval and the IRB considers the research to have extensive deficiencies. Disapproval may occur for a variety of reasons, most of which involve participant safety and/or scientific validity. Disapproval is communicated to the investigator by letter, in which the reasons for disapproval are explained.

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

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

Reconsideration of a disapproval decision 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.

## Defer

"Defer" means the IRB determines that the submission does not meet the criteria for approval and also does not meet the criteria for "Disapprove." The Board takes a 'deferred' action to remove an item from board consideration at a scheduled meeting and obtain additional information or clarification. 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.

Staff and/or board members follow up as directed with the investigator or sponsor to address the reasons for deferring the item. Reconsideration of a deferral 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.

Staff prepare the item and reschedule it for the Board to complete its review.

**Incomplete submissions and inaccurate information.** If answers on the WCG IRB submission form are left blank, the answers don't make sense, or they conflict with the protocol, the Board is unable to make an appropriate decision and may defer the item to request further information.

## Pull

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

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

# Changes to Research/ Additional Document Submissions

Whenever a change to the protocol or consent form is proposed, the change must be reviewed and approved by WCG IRB before being implemented, unless a serious safety concern requires immediate implementation by the investigator, or if the change is a non-substantive formatting change to an already IRB-approved consent form as described in the section below titled “Non-Substantive Consent Form Format Updates.”

Submit a change in research review request via the ClinSphere® eReview Manager or IRBNet.

## Non-Substantive Consent Form Format Updates

While the content of consent forms is key, sometimes minor formatting characteristics of the document can impair the ability of participants to understand the content, or study staff to convey the content, so the following types of limited formatting changes can be made when necessary or appropriate to enhance participant understanding:

- Add page breaks before headings to ensure that the heading is connected to the related paragraph.
- Add page breaks to prevent signature lines and signature instructions from being spread out over two or more pages.
- Remove extra carriage returns within a document to shorten it from, for example, 5 ¼ pages to 5 pages.

WCG IRB does not consider these changes substantive or to require IRB review and approval, but because changes like this can change the number of pages in the document, we encourage you to verify any minor changes like the ones above are acceptable under your local policies and to the sponsor/CRO and/or SMO involved in the research.

Font changes can be impactful, so we do not allow changes meant to emphasize text, such as size, color, bolding, italicization, underlining, or other changes with similar intent. However, if study staff would like all text in a paragraph to be uniformly the same font, such as all Arial or all Times New Roman, this change can be made without IRB approval,

We encourage submitters to use Word tools like styles, “keep lines together,” or “keep with next” to automate formatting and eliminate the need for the manual fixes outlined above.

## Changes to Research to Eliminate Apparent Immediate Hazards to Research Participants

WCG IRB has received questions from research sponsors about the appropriate process for making changes to clinical studies in response to emergencies such as the COVID-19 epidemic, hurricanes, earthquakes, and other natural disasters. These changes may include things like:

- Decreasing the number of protocol-mandated in-person study visits to healthcare facilities.
- Replacing protocol-mandated visits to healthcare facilities with home visits or telemedicine, allowing blood draws at remote or commercial laboratories
- Shipping investigational products directly to research participants.

We want to provide information on the requirement for IRB review of changes in research made in response to this situation.

The FDA regulations require that:

Each IRB shall … (a) Follow written procedures for ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human participants. 21 CFR 56.108(a)(4).

If a sponsor or investigator needs to make a change to research plans in order to eliminate apparent immediate hazards to research participants, these changes can be made and then reported to the IRB within five (5) days, as per WCG policy. Eliminating immediate hazards may include actions to reduce potential exposure to a pandemic, or to continue to provide medically necessary study care (including study drug) to participants unable to physically visit a healthcare facility. WCG encourages sponsors and investigators to take such steps as necessary to eliminate apparent, immediate, or additional risks to participants.

The notification to the IRB may be a full protocol amendment, but it does not have to be. The notification of the change in research (CIR) plans may also be a memo, letter, or other document that explains the changes being made, and provides enough information for the IRB to assess the relative risks resulting from the changes. The amendment or CIR document will proceed through IRB review as per the usual process.

If you have questions, please contact your WCG IRB representative, or Client Care, and they will connect you with a member of our regulatory, medical, or compliance teams as needed.

## Changes to Research: 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 WCG IRB-approved consent form with the proposed changes clearly marked (if applicable).

When submitting a change to the protocol with corresponding consent form changes, use the Change in Research submission pathway and indicate you have *both* a consent form change and a protocol revision. Incomplete and inaccurate information may result in delayed reviews.

Please note: if you are a sponsor or CRO representative who is submitting a change in research and new PI(s) are currently pending initial approval, you should provide instructions in your submission regarding how to proceed with the PI's currently pending initial review:

- **Provide instructions to IRB staff as to whether IRB staff should "hold the review of the new PI(s) until the change in research is complete so that the PI(s) pending initial approval can receive the new change in research as part of their initial review approval package," or indicate if the "review of the new PI(s) should proceed without waiting for the review of the new change in research to be completed."**
- **If you instruct us to continue processing the PI(s) that are pending review and NOT hold them, WCG IRB will need to receive a separate change in research request to issue approval of the change to any PI's who need it and have not yet received it.**

### A Consent Form Modification

Requests for consent form modifications should be submitted via a change in research request via erm or IRBNet. You'll be prompted to submit a copy of the current WCG IRB-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 WCG IRB approved consent form. In order to facilitate the submission of consent form changes, WCG IRB now routinely provides sponsors and CROs with a clean copy of each WCG IRB-approved consent (without site specific information in it). Changes sent to WCG IRB on the *sponsor’s* template consent form will not be accepted.

WCG IRB does not recommend marking changes with a highlighter alone, as the highlighting can be lost or can obscure information when the document is scanned into WCG IRB’s electronic workflow system.

In general, a statement justifying changes is very helpful and can reduce the need for WCG IRB 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.

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

Investigators who provide instructions for use of a consent form other than the one already approved by WCG IRB, or who request significant changes to that version, will experience delays in the review process while their unique consent forms are prepared for Board review. Additional delays may occur if the Board has questions about the consent form or if the investigator does not accept Board-required changes to the submitted consent form.

Because sponsor version dates or numbers listed in headers or footers of consent forms are not an IRB requirement, but are voluntary information listed on consent forms, WCG IRB does not routinely update the information listed unless the submitted consent form indicates that information should be updated. WCG IRB uses IRB approval date stamps to track the IRB-approved versions and content. We have observed that the consent form version identifiers used by sponsors, CROs, and institutions vary across the industry. As a general rule, the IRB will not proactively make any changes to sponsor/CRO or institution versioning, but instead we follow the instructions provided by the submitter.

WCG IRB does not routinely list site addresses on consent forms, other than the investigator's main address, as the inclusion of site locations on a consent form causes unnecessary revisions to these documents, is not required by regulation, and provides no additional safety protection for participants. This results in shorter, simpler consent forms that require fewer administrative updates. If a site address must be included on an investigator’s consent form, rationale should be provided to the Board for the inclusion of the additional locations.

The Board will provide instructions on the Certificate of Action indicating what participants should be re-consented with the updated consent form. If you have a preference for which participants should be re-consented with the updated consent form, you may provide that information via the submission form when the consent form changes are submitted, and the Board will accommodate the request if possible, but may require you to re-consent more participants than you indicated in your preference. The Certificate of Action indicates the **minimum** expectation for re-consent, but you are welcome to re-consent more participants than required (there is no need to ask the Board for permission to do so). If you would like the Board to require re-consent of **fewer** participants, you may PROMPTLY contact WCG IRB and ask for a reconsideration (citing your rationale); however, we advise you not to delay complying with the Board’s instructions. More information about application of the Board’s re-consent instructions is provided in the section below.

### Applying the Board's Requirements for Re-consenting Subjects

After the Board reviews new information in the consent form(s) and determines the appropriate participants that should be provided with the new information, the Board's requirements are communicated on the Certificate of Action (COA). Three commonly used re-consent requirements are outlined below and referenced in the tables below.

> **Study Visit** = "WCG IRB reviewed new information in the above Consent Form(s). Please inform all participants for which there is an in-person or remote interaction and new participants (if enrolling) of the changes. Document the communication in the research records (e.g., Note to File or participants signing the consent form). This is the Board's minimum expectation. Sites can choose to inform or re-consent additional participants."
>
> **All =** "Please have current participants, including those who are in follow-up and no longer completing study visits, and all future participants sign the Consent Form(s) specified in this approval."
>
> **Future =** "Please have all future participants sign the Consent Form(s) specified in this approval. This is the Board's minimum expectation. Sites can choose to inform or re-consent additional participants."

The two tables below provide the Board's expectations regarding who to obtain consent from and which consenting method(s) can be used based on the issued phrase.

| **Board's Consent Determination from COA**: *(see notes above for details of each determination)* | **Status of Participants**: | | | |
|---|---|---|---|---|
| | **Screening (New)** | **Receiving Treatment** | **Safety FUP* after EOT** (clinic visit or remote)** | **LTFU*** or survival FUP*** |
| **Study Visit** | Yes | Yes | Yes | No |
| **All** | Yes | Yes | Yes | Yes |
| **Future** | Yes | No | No | No |

*FUP = Follow-up
**EOT = End-of-Treatment
***LTFU = Long term follow-up

| **Board's Consent Determination from COA**: | **Consenting Method**: | | | |
|---|---|---|---|---|
| | **Clinic Visit** | **Mail** | **E-Consent*** | **Telephone/Telehealth** |
| **Study Visit** | Yes | Yes | Yes* | Yes |
| **All** | Yes | Yes | Yes* | No |

*If the Board has approved use of e-consent for some or all subjects in the research.

### How to Request a Reconsideration:

Items disapproved by the Board can be reconsidered upon written request. The request must include a rationale for the reconsideration. Additional information may allow the Board to favorably respond to the request. There is no additional fee for the reconsideration of disapproved items. Reconsiderations of Board-directed modifications do not incur additional fees if the requests concern 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.

# Delegation of Principal Investigator (PI) responsibilities during a Leave-of-Absence (LOA)

During any period of unavailability, the principal investigator (PI) should delegate responsibility for study oversight to an appropriately qualified research staff person, typically a sub-investigator (SI).

Planned leave of less than one month does not require a management plan to be submitted to the IRB.

Planned leave of one to three months is generally acceptable with submission of a management plan detailing how study oversight will continue uninterrupted.

The management plan should include the following information:

- Anticipated dates of absence.
- Name(s) of the SI/research staff person who will provide oversight during the LOA. [And, if not previously submitted, Curriculum Vitae, any Financial Conflict-of-Interest disclosure, and acknowledgement of Human Subjects Research training].
- A list of the impacted studies under WCG oversight.
- Whether the PI will be available for consultation purposes during the LOA period to help the designated SI with the study conduct.
- Any concurrence from the sponsor/CRO regarding nomination of the SI providing coverage, if available.

Planned leave of more than three months requires a change in PI (see “A Change of Principal Investigator”).

For unplanned PI leave of absences of any length, the site should inform the IRB as soon as possible so that either a management plan can be developed or a change in investigator initiated.

# A Change of Principal Investigator

Please note that if the current investigator has not been overseeing the study, WCG IRB will also need to know how long the PI has been gone, why the PI left, who has been overseeing the study in the PI’s absence, and if there have been any participant safety concerns during this time. The Board expects departing PIs to arrange for an orderly transition of their research to the new investigator. The Board requires written approval from the sponsor directed to WCG that the change is acceptable and has been approved per 21 CFR 312.53(a).

If you submit via ClinSphere® eReview Manager, select Modification to Research (under “Start Something New” on the home page) and then “Change in Investigator” on the following screen; submitters using IRBNet to submit, should use the offline initial review form available to you.

In most cases, WCG IRB will provide an updated consent form with the new PI’s name and contact information included. Once approved, the new PI is also authorized by WCG IRB to carry out the study as previously approved for the prior investigator (except where the Board provides alternate instructions to the new PI). This includes continued use of the previously approved study materials (recruitment materials, participant materials, and so forth). For more information about when an updated consent form is not needed, please contact us.

When changes to translated documents that were provided to WCG IRB for approval are necessary, the client (site, sponsor, CRO) is responsible for arranging those updates with their vendor and then submitting the updates to WCG IRB, including the signed translator certification statement, for processing.

If changes to a translated consent form do not require a translator (for example, name, phone numbers, etc.), then the staff at the site (or the sponsor/CRO) can make those changes, and a new translation certification statement is not required. Only changes that require translation need to be done by a translator and confirmed with a new translation certification statement.

# Updated Drug Brochures, DSUR, DSMB reports, and other Reports

When WCG IRB receives an updated Drug Brochure, prescribing information, DSMB report, or annual/final report, the IRB will review the submission and apply any resulting action automatically to all investigator sites associated with the affected protocol(s).

IRB approval indicates that the document has been reviewed and is on file for the research.

### How WCG IRB Reviews Drug Brochures

Updated Drug Brochures should be submitted with a summary of changes. WCG IRB reviews the **most complete version of the Drug Brochure on file** at the time of submission. For example, if "Drug Brochure Version 17" is submitted but WCG IRB already has "Drug Brochure Version 17 with Addendum 1" on file, the IRB will document its review of the combined, most complete version. If an older version is submitted, the COA will not reflect approval of that older version, but will instead reference the newest version on file that the IRB relied upon in its review of the research. Drug Brochure addenda, indexes, annexes, errata, or similar documents are **not reviewed as stand-alone submissions --** These materials are reviewed in combination with the associated Drug Brochure version on file, and the COA will reflect review of the combined document.

Submission of a DSUR (Development Safety Update Report) to WCG is optional unless it requires protocol or ICF updates related to risks in the DSUR. However, if mandated by the protocol, DSUR's can be submitted as a full report or as a summary.

# Additional Changes Which Require Submission to WCG IRB

### Contact Updates

When research is submitted to us for review via one of our portals (ClinSphere® eReview Manager or WCG IRBNet) the submitter defines who on their team will have access to the outcome documents in the portal - adding and removing access over the life of the research as appropriate.

The Contact Information Update form is primarily used for updating contacts in the IRB's internal system. ClinSphere® eReview Manager workspace permissions are usually granted by sponsor or site contacts who are workspace managers so please remember to periodically review Connexus study and site workspaces to ensure proper permissions are granted and former team members/employees are removed when appropriate.

WCG IRB can also list a limited number of research team contacts in our internal system, and those distribution contacts are listed on the last page of each Certificate of Action; when a distribution contact listed on the Certificate of Action or a Continuing Review Report Form recipient changes, submit those requests for changes via our Contact Information Update form available on wcgclinical.com. Submitting

the Contact Information Update form ensures the IRB has the correct contacts in the IRB's internal system for notifications or questions.

**Administrative Changes**

Request review of increases in the number of participants allowed at the specific investigator site if a consent form change is needed.

Minor administrative changes sent to the investigator from the sponsor should generally be submitted to WCG IRB 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 WCG IRB. If you are in doubt about submitting a particular item, call Client Care at 855-818-2289 or e-mail clientcare@wcgclinical.com.

# Participant Recruitment Materials and Practices

## Participant Recruitment Practices

Recruitment plans sometimes include the use of Referral Fees or Finder's Fees. These are payments to someone who is not a member of the study team (for example, a physician with a practice near the study site) paid in return for assistance in finding potential study participants.

In general, fees that are based on actual referrals  that is, paying $X per referred patient - are not considered to be appropriate, because this payment structure creates a financial incentive for referring someone to a study and perhaps encouraging them to be in a study, when the study may not be in their best interests. While this potential conflict of interest applies to all health care providers, the American Medical Association Code of Ethics specifically prohibits the payment of "finder's fees" for either specialist care referrals or clinical trial referrals and considers this a form of fee-splitting (AMA Code of Medical Ethics Opinion 11.3.4).

It is possible to compensate referral sources if that compensation is based on the time and effort put into identifying or contacting potential study participants. Compensation for time and effort should be clearly based on that factor- that is, structured as $X/ hour of time spent, or $X for X number of medical records reviewed, regardless of whether that time results in actual referrals. In particular, payment should not be contingent on whether a referred potential participant is eligible for the study (vs. a "screen failure") or whether they agree to participate in the study. A referral source cannot control whether a potential participant is medically eligible for study participation or whether they decide to participate, and both eligibility assessment and participation decisions of potential study participants should be private.

Referral programs in which fees or other incentives are paid to either current study participants or to other persons who are not health care providers for referring potential participants to a study must also be reviewed by the IRB. The conflict of interest for referral fees is not the same here, since the referring parties are not health care providers, and "per referral" payments are possible in this setting.  Again, payment should not be contingent either on whether a referred potential participant is eligible for the study (vs. a "screen failure") or whether they agree to participate in the study. A referral source cannot control whether a potential participant is medically eligible for study participation or whether they decide to participate, and payment based on eligibility or consent may encourage the referring party to pressure the referred person to give inaccurate information or to agree to participate when they would

prefer not to. Both eligibility assessment (which may reveal personal medical history) and participation decisions of potential study participants should be private.

## Participant Recruitment Materials (including advertisements)

Request for review of new or revised participant materials or advertisements can be made through ClinSphere® eReview Manager or IRBNet. Print ads should be submitted as closely as possible to how they will appear in print, so that the Board can assess the impact of design details, such as photographs, other images, font sizes, and styles.

Most changes to approved advertisements must be reviewed by WCG IRB 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.

Please ensure that each of the following materials are submitted as separate, stand-alone documents for individual review (do not combine multiple materials into a single file/document):

- Scripts/Storyboards (TV, Radio, Screening)
- Print ads
- Brochures
- Flyers
- Dr. to Dr. Letters/Press Releases

The following items are recommended to be submitted as a single review item (a single document for each):

- Website (must be submitted together as screenshots of each web page)
- Text messages (unless you want each message reviewed separately)
- Email blasts (will be grouped and reviewed by type, such as reminder emails vs. new emails)
- FAQs (unless you want each reviewed separately)
- Social media
- Ad-words Search (unless you want each reviewed separately)
- Pictures (Images)
- Banner ads (unless submitted separately)
- Retention items (unless you want each reviewed separately)
- Screenshots of applications (unless you want each reviewed separately)

For best results, when submitting participant recruitment materials or other participant materials (diaries, questionnaires, etc.) that have been previously reviewed by WCG IRB, state in the cover letter that the items have been previously reviewed. Our 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.

When submitting revisions to previously IRB-approved materials, you may submit a redlined (tracked changes) version of the previously approved material or a clean version incorporating the requested changes for review. If you submit a redlined version, the Board will review the material and may approve as submitted or require additional modifications. The IRB-approved material showing the submitted redlined changes and any additional changes required by the Board will be included in the review outcome documentation. Beyond accepting the tracked changes, do not make any additional modifications (including font size and visual effects) to the approved materials.

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

**Documents for Select Sites:** WCG automatically approves all study-level documents for new sites during initial review. If any documents are not intended for all sites, provide a list specifying which sites they apply to, in advance. This process applies to, for example, documents specific to particular arms of the research, cohorts, sub-studies, or payment vendors. Supplying this information upfront helps us ensure accurate approval for all submitting sites and can prevent unnecessary holds or delays in the review process. Documents limited to select sites will be labeled "SELECT SITES" at the start of their titles.

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

To avoid unnecessary additional production costs due to re-work, it is strongly recommended that WCG IRB 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 us for review, we pre-review the script and, if acceptable, approve 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 for final approval before use with participants and MUST match the approved script. Submit a copy of the corresponding script when you send the recording to us 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 unduly influential, incorrect, or out of compliance, 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 "as modified."

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

ClinicalTrials.gov and similar 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, WCG IRB will review submissions of such content. FDA Guidance regarding use of media advertising to recruit participants can be found at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recruiting-study-subjects.

Website content can be reviewed either in relation to a specific protocol or as generic recruitment material. (See Generics.) 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 WCG IRB receives a request to close the file.

Content on websites and changes made to approved website content should be submitted for Board review **before they are posted to the web**. The website owner is responsible for receiving approval before using that content for recruitment. Websites should be submitted as screenshots of individual web pages combined into one PDF of the whole website (only pages relevant to the research must be submitted).

Participant recruitment content on sponsor, investigator, or Site Management Organization websites requires IRB review. Only the content relevant to research should be submitted for review. Submit to us only website content which provides information to potential participants about research participation, as well as information about specific studies that WCG IRB 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.

It may be appropriate to request WCG IRB review of these materials as “generic” recruitment materials (See section below titled Review of “Generic” Materials). The content should not be posted until WCG IRB has approved it.

WCG IRB 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.

**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, WCG IRB 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 WCG IRB with copies of these materials. However, if you would like to have IRB review for such materials, we will provide a review upon submission. **Please note WCG IRB Policy on submitted press releases:** WCG IRB reviews submitted press releases as advertising.

When multiple advertisements or participant materials are submitted as one document, WCG IRB staff separate the file into individual documents for review. Each document is considered a unique material due to differences in text/content and communication method (video, social media, etc.). As even minor changes in text can alter the meaning or impact for participants, any differences in the documents would require a separate review and are listed individually on the IRB Certificate of Action. Your invoice will reflect this.

When separating multiple items into individual documents for review, staff try to keep similar materials together for cost savings and efficiency in the review. For example, “social media” ads are routinely processed as one document, as opposed to being reviewed individually into separate Facebook, Instagram ads, etc.

## Recruitment Material: Criteria for Approval of Advertising

- No statement or implication of a certainty of favorable outcome or other benefits beyond what is in the consent document and protocol.
- No exculpatory language.
- No emphasis on payment or the amount to be paid, by such means as larger or bold type.
- No promise of “free treatment” when the intent is only to say participants will not be charged for taking part in the research.
- Limit the information to what the prospective participants need to determine their eligibility and interest.

Additional criteria for clinical trials:

- No claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.
- No use of terms, such as “new treatment,” “new medication,” or “new drug,” without explaining that the test article is investigational.
- No inclusion of 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.

## Recruitment of Participants From International Locations

WCG does not restrict research sites in the U.S. from enrolling eligible participants in clinical research studies that require them to cross the international border by land or by air.

## Special Considerations for Use of Artificial Intelligence (AI) Tools in The Recruitment Process in Research Studies

WCG will review the Investigator or site’s use of third-party AI tools as part of their recruitment plan. WCG recommends the investigators use only validated AI tools and perform test runs on their datasets to ensure it meets their expectations. The recruitment plan should include a description of the third-party AI tool, source of data interrogated, and privacy and confidentiality measures implemented to protect the participants.

WCG envisions several scenarios where third-party AI tools can be utilized in a recruitment plan.

1. An AI tool with chatbot functionality that analyzes user generated interrogated EMR datasets to confirm eligibility criteria and contacts the eligible participants via SMS text messages or e-mail to gauge their interest in the proposed study before directing them to research staff at the site.
2. An AI chatbot that engages with potential participants who respond to WCG approved advertisements posted on social media platforms. The AI tool may perform initial screening before directing them to research staff at the site.
3. An AI tool to facilitate searching for eligible participants in accessible, publicly available datasets, and patient registries with permission to build a cohort for further screening.

# Requirements for Screening Materials

The Board recommends that submitted screening materials should conform to the following:

### Introductory Statement:

- The screening script should include an introductory statement that informs the participant 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;” (e.g., rather than saying “we would like to ask you some *confidential* questions,” say “we would like to ask you some questions.”) It is acceptable to say, “personal questions” or “sensitive questions.” The purpose of this policy is to prevent any possible misunderstanding that the answers will be held in complete confidence.
- When appropriate, the script should include an introductory statement warning the participants of the sensitive nature of the questions that might make the participant uncomfortable, and

preferably include an example (for instance, “We are going to ask you about drug or alcohol use.”) This will generally be limited to questions about mental illness, substance abuse, and sexual abuse. For these types of screening scripts, it may be appropriate to not collect any identifying information until after the questions are asked; that is, collect the name and other identifying information at the end of the conversation and the form.

**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 - such as, “. . . 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 - such as, 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 [such as, “destroyed immediately” or “stored (where and for how long)”]. Do I have your permission to proceed?"

## Body of Screening Form

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

## Closing Statement

- The script should include a closing statement informing the participant of whether they have met the preliminary screening requirements.
- The script should address in a closing statement whether the information received from the participant will be destroyed immediately, or whether it will be stored, and if so for how long and where.
- If the site would like to keep information for future contact for new studies, the site should describe that to the participant as well, and the participant 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 an explanation of how they will be explained to the participants.
- We realize that the script may not be followed verbatim, as participants may ask additional questions or stray from the topic. This is acceptable, but we expect that the interviewer will keep as closely as possible to the spirit and letter of the script.
- It is useful to us if the investigator informs us of the use of the recruitment screen; such as, if it is going to be used with participants calling in from advertisements, for calling patients listed in a database, or for conducting cold calls.

# Terms of Use Documents

As noted above under "Materials Required for Initial Review," materials to be provided to participants require IRB review. When research studies involve the use of digital technology, there may be Terms of Use or similar, otherwise named articles to which participants are required to agree if they are to be in the research. Often, these Terms of Use include exculpatory language that would not meet regulatory criteria for IRB approval. Sometimes the sponsor of the research has control of these Terms of Use and can modify them at the IRB's request, but often, third parties own these documents. In 2020, The Secretary's Advisory Committee on Human Research Protections (SACHRP) published recommendations on review of these titled Attachment B – Clarifying Requirements in Digital Health Technologies Research (Attachment B-Clarifying Req. Digital Health Technologies Research | HHS.gov), and WCG uses this recommendation document as the basis for our policy on reviewing Terms of Use for digital technologies used in research studies. This policy addresses the four scenarios in which the technology and associated Terms of Use are encountered and the resulting requirements.

1. The technology is acquired by the participant outside of the research context and is being used in the research for the same purpose for which it was acquired:
    a. The risks involved in the use of the technology are not research risks.
    b. The Terms of Use **does not** need to be reviewed by the IRB.
    c. Exculpatory language in the Terms of Use document is not part of the research and does not need to be edited.
2. The technology is acquired by the participant outside of the research context and is being used in the research for a significantly different purpose than for which it was acquired:
    a. The risks involved in the use of the technology may alter the risks of the research.
    b. The Terms of Use document **does not** need to be reviewed by the IRB.
    c. The existence of the Terms of Use document should be disclosed to the participants and any risks of the use of the technology in the research should be considered as research risks and be disclosed in the consent form/process.
3. The technology is required as part of the research, but the technology is not designed or controlled by the sponsor of the research.
    a. The risks involved in the use of the technology are research risks and should be disclosed in the consent form/process.
    b. The Terms of Use document **does** need to be reviewed by the IRB.
    c. The IRB should ensure that any differences in confidentiality protections or other provisions between the Terms of Use document and the rest of the research are disclosed to participants.
4. The technology is required as part of the research, and the technology is designed or controlled by the sponsor of the research.
    a. The risks involved in the use of the technology are research risks and should be disclosed in the consent form/process.
    b. The Terms of Use document **does** need to be reviewed by the IRB.
    c. The Terms of Use document should be edited as needed to meet regulatory requirements (non-exculpatory).
    d. In the rare case where it is not possible or practicable for the document to be altered, the IRB may still decide that the study may proceed, and the IRB should ensure that any differences in confidentiality protections or other provisions between the Terms of Use document and the rest of the research are disclosed to participants.

# Review of “Generic” Materials

“Generic” materials include items that an investigator wishes 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, and do not include research procedures. Common types of generic materials include:

- Generic Advertising, including Brochures, audio-visual materials, Web Content
- Generic Telephone Screening Scripts
- Generic Photography releases

Changes to approved generic materials must be reviewed and approved before use. Please note that generic document approvals are not linked to specific research protocols by the IRB, so board reviewers may have questions about documents referenced in submissions that were previously approved as generic documents. Please consider noting any previously approved generic documents related to new submissions in a cover letter.

## Consent Forms for Pre-screening and Similar Activities

As consent forms for IRB review are to obtain agreement for research procedures, they are only reviewable in the context of a description of those procedures. Therefore, pre-screening programs and similar kinds of activities should be submitted with a protocol that describes the activities to which participants are consenting through the new research submission process.

Accordingly, prospective participants should not have current treatment or medications adjusted, undergo a washout, or have a biopsy as a pre-screening activity. In those cases, the participant should be fully consented for the related protocol before beginning that protocol’s screening activities.

## Generic Advertisements

WCG IRB 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 participants 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 “participants will be paid for their participation” is recommended instead.

# Expiration and Renewal of Generic Materials

Approved generic items are generally valid for one year. When the anniversary date approaches, WCG IRB staff will contact the submitter and inquire if renewal is desired. WCG IRB 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 WCG IRB 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.

# IRB Reporting Requirements

Submit promptly reportable information via ClinSphere® eReview Manager or IRBNet. Promptly reportable information should be submitted within five days of becoming aware of the event (calendar days). If there is a delay, please include an explanation for the delayed reporting.

The following are reported by a submission of a promptly reportable information submission:

1. New or increased risk.
2. Protocol deviation that harmed a participant or placed a participant at risk of harm. This includes any site monitoring report that directly and materially affects subject safety or their willingness to continue participation.
3. Protocol deviation made without prior IRB approval to eliminate an immediate hazard to a participant.
4. Audit, inspection, or inquiry by a federal agency.
5. Written reports of federal agencies (e.g., FDA Form 483).
6. Allegation of Noncompliance or Finding of Noncompliance.
7. Breach of confidentiality.
8. Unresolved participant complaint.
9. Suspension or premature termination by the sponsor, investigator, or institution.
10. Incarceration of a participant in a research study not approved to involve prisoners.
11. All IND safety reports. Any adverse events or SUSARs that require a change to the protocol or consent.
12. State medical Board actions.
13. Unanticipated adverse device effect.
14. Information where the sponsor requires prompt reporting to the IRB.

The following are reported by submission of a change in research:

1. Change in financial interest disclosure.
2. Any findings from closed research when those findings materially affect the safety and medical care of past subjects. Findings will be reported for two years after the closure of the research.

**Sponsors no longer planning or able to provide financial support for conduct of the study:** When a site learns that sponsor is no longer able to fulfill their financial support for conduct of the study due to financial concerns, bankruptcy, or a general business decision, the site should promptly submit a PRI report (category 9 above) or administrative letter as a change in research with this information. This submission would include information regarding the status of the study overall and at the site, including any enrolled participants, and their plan for those participants.

Information not listed above does not require prompt reporting to WCG IRB.

Please note, only adverse events or SUSARs that prompt a change to the protocol or consent document are required to be reported to the IRB. We have based our guidance on the most current FDA recommendations, and it is our goal to try and encourage the submission only of the items required and to avoid submission of non-reportable events, which causes delays in review and detracts from our mission of human participant protection.

When new information is submitted to WCG, if additional action/information is required, you will be contacted within 30 days. Otherwise, please consider this information filed only with no additional formal acknowledgment or confirmation.

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 participants to WCG IRB in a timely manner:

- Upon request, a copy of the written plan between Client and Site that addresses whether expenses for medical care incurred by Human Research participants 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.
- Any site monitoring report that directly and materially affects participant safety or their willingness to continue participation. Such reports will be provided to the Review Board within five days.
- Reports from any data monitoring committee, data and safety monitoring Board, or data and safety monitoring committee in accordance with the timeframe specified in the study protocol.
- Any findings from a closed study when those findings materially affect the safety and medical care of past participants. Findings will be reported for two years after the closure of the study.

To safeguard participant privacy, wherever possible provide records relating to participants in **de-identified form.**

# Planned Deviations

Please note that planned deviations should be submitted to WCG IRB as a change in research for federally funded research and FDA drug and biologic studies. If the research is federally funded, conducted under an FWA, or is a clinical investigation of a drug or biologic, then all planned protocol deviations must be submitted to WCG IRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human research participants [(DHHS (FDA 21 CFR § 56.108(a)(4); ICH 3.3.7].

However, if the research is a clinical investigation of a device and the research is not federally funded and not conducted under an FWA, then only planned protocol deviations that may adversely affect the rights, safety or welfare of participants or the integrity of the research data should be submitted to WCG IRB for review and approval prior to implementation except where necessary to eliminate apparent immediate hazards to the human research participants [DHHS 45 CFR § 46.108(a)(3)(iii); FDA 21 CFR § 56.108(a)(4); ICH 3.3.7].

These different requirements regarding planned protocol deviations are necessary because the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) drug and biologic divisions have adopted the regulatory interpretation that every planned protocol deviation is a change in research that needs prior IRB review and approval before implementation; however, the FDA device division operates under a distinct regulation (See 21 CFR 812.150(a)(4)).

### Investigator Noncompliance

WCG IRB expects PIs to conduct research activities in accordance with the IRB's requirements, as set forth in this Guide and in compliance with all federal, state, and local regulations. We define investigator noncompliance as the failure to follow the applicable regulations and/or the requirements and determinations of the IRB.

### Examples of Noncompliance

The following are examples of investigator noncompliance. This list is not meant to be all-inclusive. Please reference the Promptly Reportable Information form. The actions of anyone in the Human Research Protection Program may result in noncompliance if one of the following occurs:

- Performing human participant research without first obtaining IRB approval or an IRB declaration of exemption.
- Deviating from or violating the provisions of an IRB-approved protocol when the deviation harms a participant or placed participant at risk of harm.
- Failing to secure IRB approval of a protocol due for periodic continuing review prior to its expiration date.
- Permitting a protocol's IRB approval to lapse without stopping all research-related activities and submitting a Principal Investigator Closure Report to the IRB or, in the event of an overriding safety concern or ethical issue such that it would be in the individual participant's best interest to continue study participation, arranging with the IRB to continue those activities.
- Failure to report complaints or results of audits to the IRB.
- Failure to follow the regulations or the requirements and determinations of the IRB.

If evidence is received by the IRB to indicate potential noncompliance, the Board reviews this information and determines appropriate actions, including, but not limited to:

- Temporary suspension or termination of all or some previously approved research activities (suspensions and terminations of previously approved research are reported to applicable regulatory authorities in accordance with federal regulations.)
- Determination of serious or continuing noncompliance (in accordance with federal regulations, serious and/or continuing noncompliance is reported by the IRB to the applicable regulatory authorities.)
- Request for the conduct of an investigator site visit.
- Communication with the PI to document the issues and to provide the opportunity to respond.
- Request for additional information from the PI, submitting body, or other source.
- Other actions as determined by the Board.

WCG IRB reserves the right to visit your site and/or interview your sponsor or others as needed to assess possible noncompliance issues.

## Suspensions and Terminations

Federal regulations require that an IRB have the authority to suspend or terminate approval of research or investigators. WCG IRB may suspend or terminate approval of previously approved research or investigators under the following circumstances:

- When research is not conducted in compliance with federal, state, and local requirements and in accordance with our requirements, or
- When the risk-to-benefit ratio no longer justifies continuing the study (based on information received by the IRB related to safety or other unanticipated risks to research participants or others).

When suspensions or terminations occur, the PI is required to send the Board a written course of action that will be undertaken to ensure the protection of the rights and welfare of each enrolled research participant. Additionally, if the suspension or termination is for investigator noncompliance, we reserve the right to initiate immediate review of all the PI's active studies.

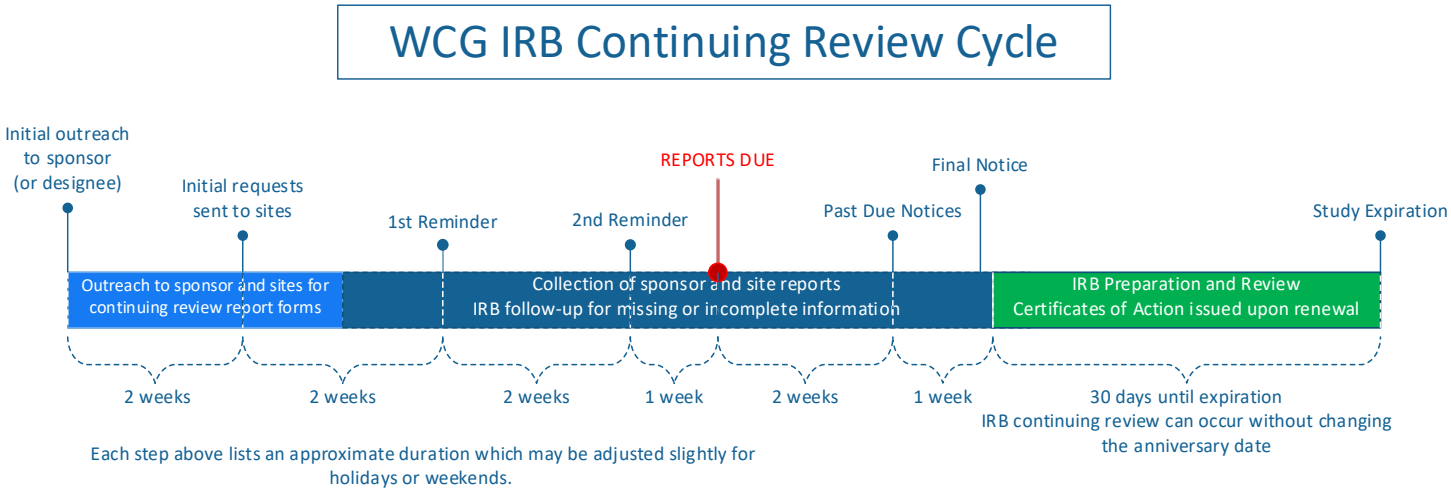
The IRB reserves the right to suspend or terminate activity for all other approved studies until a convened Board has made a determination. If the IRB terminates or suspends approval of the clinical trial, the Investigator must promptly notify the sponsor.

In accordance with federal requirements, suspensions or terminations of previously approved research or investigators are reported by the IRB to the sponsor and to the appropriate regulatory authorities

# Overview of Continuing Review Activities and Required Reports

During the initial review of a protocol, the Board makes a determination regarding 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)]. For a few types of research, however, full Board review is conducted more frequently than once a year. The Board may also direct review more frequently than annually for other research as deemed appropriate.




# Contacts for Continuing Review Form Notifications

For new initial review site submissions, all site level contacts receive notification when the site level continuing review report form is due.

For new initial review protocol submissions, all sponsor and CRO contacts receive notification when the protocol level continuing review report form is due, if one is required.

Although notifications regarding the continuing review reports will be sent to multiple contacts, please only submit one completed copy. Multiple copies can result in unnecessary follow-ups by our staff for clarification.

# Site Reporting

Completed Site Continuing Review Report Forms (CRRFs) provide the IRB with the study-related data necessary to monitor the progress of the research at sites. Identifying information including investigator name, sponsor name, protocol number and the “sequence” number of the form is listed at the top of each form. The CRRF is sent out approximately 86 days before the study’s expiration date, in order to ensure it is completed and sent back to us before the Board conducts the study renewal review. The Board may take action to suspend or terminate approval of the research if a report is not accurately completed and returned promptly.

CRRFs must be filled out completely and returned to us 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.

Even if the site has not started enrolling participants, the site must complete the CRRF and return it to WCG IRB before the due date printed on it, to inform the Board of the study’s status at the site.

Please ensure reports are complete and consistent with previous reporting. Incomplete and inconsistent information may result in delayed reviews.

As a reminder, it is the Principal Investigator's responsibility to ensure a current medical license, if applicable, is on file with the IRB.

# Sponsor Reporting

Before each annual review, WCG IRB sends out a Protocol Continuing Review Report (PCRR) to the sponsor or CRO contact that we have on file. The PCRR 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 ask that you complete and return the PCRR 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.

WCG IRB aims to make the PCRR process as efficient as possible for all parties. Therefore, WCG IRB will accept receipt of the completed PCRR form 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. WCG IRB is flexible as to the format in which this information is received and will accept other reports that provide the same basic information.

The PCRR is sent out approximately 100 days before the protocol’s expiration date and are due approximately 56 days before the expiration date in order to ensure it is completed and sent back to WCG IRB before the Board conducts the continuing review of the study. 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.

Please ensure reports are complete and consistent with previous reporting. Incomplete and inconsistent information may result in delayed reviews.

# Delinquent Progress Reports

WCG IRB will continue to follow-up with the investigators, sponsors and CRO contacts to facilitate timely receipt of a 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 Board may take action to suspend or terminate approval of research if reports are not accurately completed and returned promptly. If WCG IRB suspends or terminates the study, at a minimum, the investigator and sponsor will be notified of the Board’s action.

If the Board suspends the research, WCG IRB is required to report the suspension to the appropriate federal agency or agencies (for example, FDA and/or OHRP) If the suspended investigator is at an institution which has notified WCG IRB 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 WCG IRB.

# Supporting Documentation Submitting with Continuing Review Reports

Documents submitted with continuing review reports may be processed separately and incur additional charges.

For example, such documents could include, but are not limited to, press releases (see additional section related to press release in this guide), DSMB reports, updates, protocol revised consent, modified recruitment materials.

If the research includes a data monitoring committee/data safety monitoring board, please note that the reports of all meetings of this committee should be submitted to the IRB even if the outcome of the meeting results in no changes to the study.

# Definition of Screen Failures and Withdrawals

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

- Screen failure: Participant(s) removed from the study during the screening process because they did not meet all inclusion and exclusion criteria, or other requirements that must be met for research participation. Participant(s) who leave the study after randomization or assignment to study treatment should be counted as withdrawals rather than screen failures, even if the participant did not start the study treatment.
- Withdrawal: Participant(s) are considered to have been withdrawn/discontinued from the research when the participant(s) either stopped participation or the research team stopped the participant's participation early for reasons other than reaching a study endpoint. Do not count screen failures when reporting withdrawals.
- Participant deaths: Because some protocols anticipate that a participant may pass away during the research / during long term follow-up, and include death as a possible endpoint, a participant who passes away may be counted among the completed participants on the report. If the protocol does not have death as a study endpoint, a participant who passes away would be

considered a withdrawal (enter in the field for “How many subjects decided on their own to stop taking part in the research?”)
Therefore, there are two possible fields on the form where deceased participants may be part of the participant count:

- “How many participants decided on their own to stop taking part in the research?” and
- “How many participants did you remove from the research before reaching a study endpoint?”

As long as the numbers are reported consistently from one form to the next, either category is acceptable to WCG IRB. (Note that the CRRF prompts the submitter to enter a reason whenever a number is entered for participants who stopped taking part in the research.)

# Study Renewal vs. Closure

Sites receive a WCG IRB Site Continuing Review Reports when the expiration date is approaching. Federal regulations allow the IRB to perform continuing review of the research within 30 days before the IRB approval period expires and retain the anniversary of the expiration date of the initial IRB approval as the expiration date of each subsequent one-year approval period. The Board generally conducts the study renewal review 20-30 days prior to the expiration date listed on the Approval letter. **Review fees apply for the continuing review service** and review is carried out unless WCG IRB receives a study closure notice *prior to the Board’s renewal review.* If a closure notice is received by WCG IRB before the expiration date, but after the Board’s continuing review, the site will still be billed for the renewal review. To avoid unnecessary reviews and fees, do not delay reporting a study closure to WCG IRB 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 or after the expiration date. For example, if the study’s expiration date is June 15, no study activities may take place on June 15 or following.

If the Board approves the continuing review for an additional review period, an Approval letter is forwarded to the investigator and other study contacts as applicable. The Approval letter 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 form is necessary, the Approval letter will indicate approval of a consent form and will be accompanied by a revised consent form.

# Study Closure

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

1. All participants have finished all protocol related interventions, interactions, final visits, and follow-up; and
2. The sponsor representative reports the study is closed at your site or permanently closed to enrollment.
3. If the study was conducted under a Federalwide Assurance for research participant to federal oversight other than FDA: No additional identifiable private information about the participants is being obtained and all data analysis at the site is completed.

WCG IRB will close the study upon receipt of the closure report. Submit closures via ClinSphere® eReview Manager (IRBNet clients can access a closure form from their IRBNet forms library.)

To avoid unnecessary reviews and fees, do not delay reporting a study closure to WCG IRB if the expiration date is approaching – renewal review is generally conducted 20-30 days before the expiration date; therefore, closure forms should be received before that window to ensure continuing review for the closing study is not carried out and billed.

WCG IRB 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 participants, 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 WCG IRB immediately to avoid a substantial gap in IRB oversight for the research.

# Study closure

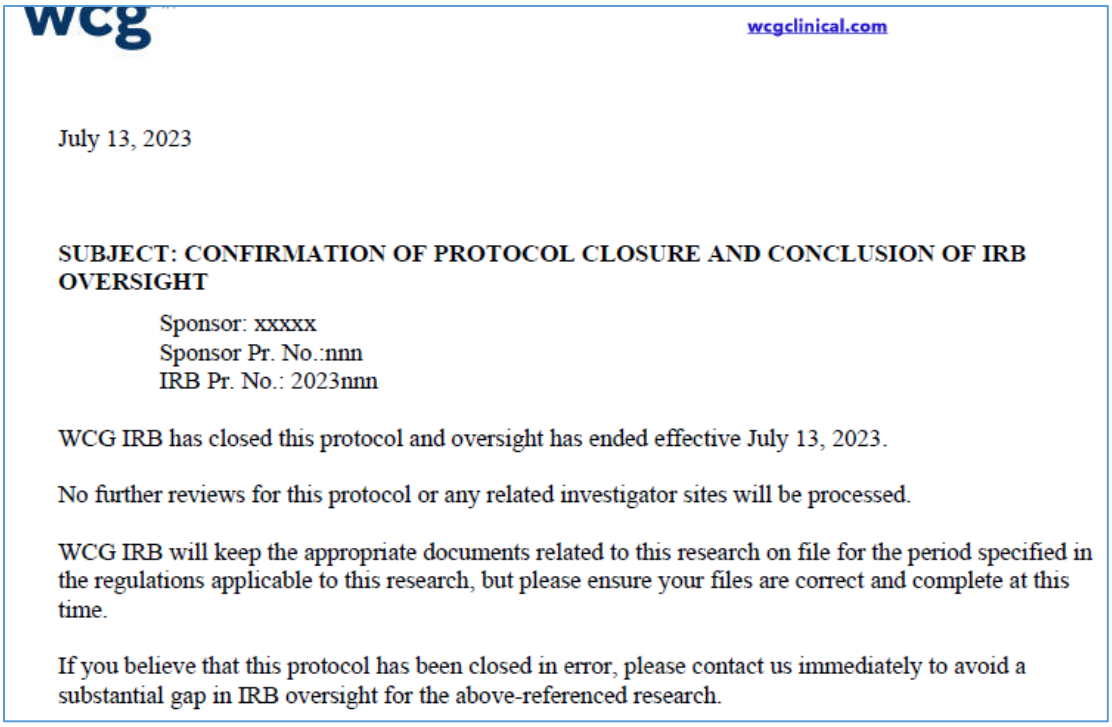
WCG IRB closes studies and provides a confirmation of closure as outlined below:

- When we receive closure notices for all remaining open sites and a directive to close the study.

and

- For the scenarios listed below, WCG IRB will automatically close the study when the last site/only site under WCG IRB oversight is closed:
    - Involves only one Investigator or site globally
    - Single patient expanded access
    - Exempt/NHS
    - Study termination or intent to close letter or memo reviewed by Board
    - Intent to close correspondence received from the sponsor or CRO
    - Completed Study Closure Form submitted via ClinSphere® eReview Manager or IRBNet.
    - There are no current contacts designated to receive study notifications on file
- For any situations not covered by the above bullet points, when the last open site under WCG IRB oversight closes and there is no directive from a sponsor or CRO representative, WCG IRB staff will proactively reach out to the sponsor or CRO to confirm whether the study should be closed as well. WCG IRB will hold the closure of the study for a maximum of 30 days while awaiting a directive to close the study. If no response is received after 30 days, WCG IRB will proceed with closure.

A notification like the one pictured below will be posted to ClinSphere® eReview Manager or IRBNet when WCG IRB has closed the study (a.k.a. protocol) in our system:



wcg wcgclinical.com

July 13, 2023

**SUBJECT: CONFIRMATION OF PROTOCOL CLOSURE AND CONCLUSION OF IRB OVERSIGHT**

Sponsor: xxxxx
Sponsor Pr. No.:nnn
IRB Pr. No.: 2023nnn

WCG IRB has closed this protocol and oversight has ended effective July 13, 2023.

No further reviews for this protocol or any related investigator sites will be processed.

WCG IRB will keep the appropriate documents related to this research on file for the period specified in the regulations applicable to this research, but please ensure your files are correct and complete at this time.

If you believe that this protocol has been closed in error, please contact us immediately to avoid a substantial gap in IRB oversight for the above-referenced research.

Please note that each Certificate of Action (COA) states "*…the individual and/or organization shall promptly communicate or provide, the following information relevant to the protection of human subjects to the IRB in a timely manner: …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*." More guidance about required reporting of post-study activities can be found on the WCG Clinical Website here.

The approval period expires at 11:59 p.m. on the expiration date cited in the current Certificate of Action.

# Requesting Re-opening of Studies and/or Sites:

To request that your closed, previously approved study and/or site be re-opened, email your request and any related documentation to clientcare@wcgclinical.com for processing.

If you have questions about fees associated with re-opening your study and/or site, contact Client Care at 855-818-2289 or clientcare@wcgclinical.com.

# Site Visits

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

WCG IRB conducts the following types of site visits:

- For-Cause - WCG IRB staff initiate “for-cause” site visits in response to concerns raised about the site, investigator, etc. These visits are usually carried out by WCG IRB Regional Representatives, Board members or WCG IRB 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 WCG IRB Regional Representatives, Board members, or WCG IRB 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 WCG IRB site visit, please consult the current fee schedule.

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

# Fees

WCG IRB 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 the Board (fees are not billed until the Board review has occurred).

A copy of our current fee schedule is available upon request from Client Care at 855-818-2289 or clientcare@wcgclinical.com.

## Research Review fees at WCG IRB fall into four general categories:

### Initial Review of the Research

Initial review encompasses the review of the research protocol, one associated consent form, 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.

Additional fees are required for the review of an investigative site 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 participant materials are necessary.

### Research Continuing Review Fee

In accordance with 45 CFR §46.109(e) and 21 CFR §56.109(f), IRBs must review ongoing research at least annually. 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.

### Changes to Research

Modifications to research that require 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. The change in research fee applies each time review and preparation of regulatory documentation is required for a research site.

### Miscellaneous

WCG IRB bills additional fees for services such as translations and acknowledgements. We may charge a fee for submissions not made via ClinSphere® eReview Manager or IRBNet portals.

# Reconsiderations

In accordance with 21 CFR §56.109(e) and 45 CFR §46.109(d), WCG IRB 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 an opportunity to address the Board in writing or in person.

Requests for reconsiderations are given the same priority in scheduling as new review requests. There is no fee for the review. Requests for reconsideration and supporting materials may be directed to the WCG IRB 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 WCG IRB and ask for reconsideration; however, we advise you not to delay complying with the Board's instructions.

# WCG IBC Services

Human gene transfer (HGT) is a growing, promising area of medical research studying drug products that incorporate engineered or artificial DNA or RNA. Clinical trials involving HGT products must meet the specific oversight requirements found in the NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules (NIH Guidelines).

Before clinical research subject to the NIH Guidelines can begin, it must be approved by an NIH-registered Institutional Biosafety Committee (IBC). IBCs ensure that research with potentially biohazardous agents is conducted according to the NIH Guidelines and current best biosafety practices.

## Why Choose WCG for IBC Review?

WCG IBC Services provides the experience, personalized service, and streamlined process you need for efficient, safe, and compliant oversight of gene transfer research. With a dedicated WCG IRB team partnering on your review and remote IBC meetings scheduled on demand, we're committed to providing an efficient and thorough turnaround for each review.

Our experts have extensive experience in all aspects of site start-up for human gene transfer research and are ready to answer your questions, including:

- Is my research subject to the *NIH Guidelines*?
- How can I prepare for a multicenter trial involving human gene transfer research?
- Which sites are best prepared to start enrolling subjects as soon as possible?
- How does WCG IRB register an IBC on behalf of a new site?
- What are the requirements for IBC approval?

- What are best practices for transportation, storage, administration, and disposal of genetically modified products?
- What are the timelines associated with IBC review for different types of studies?
- How does WCG IBC Services work in tandem with IRB review, site selection, contracting, and billing?

## For Clinical Trial Sponsors and CROs

Most drug products that incorporate engineered DNA or RNA qualify as human gene transfer products. Our experts can help you determine whether your clinical trial requires IBC review and review prospective site lists to advise on the best start-up approach for each site requiring IBC review.

We recommend that sponsors and CROs contact WCG IBC Services during the project planning phase to discuss:

- Timelines and enrollment dates
- Applicability of NIH Guidelines and IBC review requirements
- Document preparation (protocol, investigators' brochure, pharmacy manual) for IBC review
- Qualification of prospective site list (identification of sites that are in-network or that require registration)
- Distribution of study documentation to sites

## For Research Institutions

Our IBC network includes nearly 450 active sites, ranging from small clinics to community hospitals and major academic medical centers. Our review teams work closely with clinical coordinators and investigators at each site to learn about your needs and concerns and advise on best practices for safety and compliance.

For each new study at your site, we provide a customized biosafety standard operating procedure (SOP) and walk you through the steps required to get to IBC approval. IBC operations are transparent and interactive and allow sites to fully understand and direct compliance activities related to gene transfer research.

## Coordinating IRB and IBC Reviews

Clients that utilize both WCG IRB and WCG IBC Services reap greater synergies as smoother communications between our IRB and IBC teams accelerate both review processes.

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 the IBC administration and review page on the WCG website for more information.

# Disclaimer

The purpose of this guide is to provide you with information about WCG's processes. We will from time to time amend or update the guide. We 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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