

### **Overview:**

Legally effective consent must be obtained from every subject in accordance with IRB approval of the study in which subjects will participate unless the requirement for informed consent has been waived by the IRB.

### **Recruiting Human Subjects/Participants in Research**

The IRB will review proposed methods of recruitment and recruitment materials to ensure that the process will be conducted in a manner that is ethical. It is essential that subjects are recruited and if eligible, enrolled in research in a manner that does not introduce coercion and undue influence and provides subjects with all appropriate information to make an informed decision. Since the informed consent process is considered to start with the recruitment process and materials, the IRB also considers recruitment materials during its review of informed consent.

Only recruitment material that is presented directly to subjects needs review by the IRB. Materials or media coverage about the research that is intended for scientists, educators, health professionals or other individuals not targeted as subjects for the study do not need to be reviewed by the IRB.

### **Recruitment of Research Subjects**

The IRB will review all recruitment procedures, materials, and advertisements to ensure that they are consistent with the protocol, accurate, and non-coercive. If a Principal Investigator (PI) plans to pay subjects for participation in a study, the PI must contact the IRB office immediately for thorough discussion and determination of process to ensure all LLNL policies and procedures are followed.

### **Review of Advertisements**

All advertisements to recruit subjects must be reviewed by the IRB. The IRB will review the information contained in the advertisement and the mode of its communication.

Recruiting materials may include flyers, recruitment letters, advertisements, emails, and posting on social media, among other strategies. The IRB review of recruitment materials will ensure that benefits are not overstated or presented in a manner that may be coercive or pose undue influence over a subject's decision-making process. For these reasons, the information provided in recruitment materials should be limited to information that will explain and generate interest from the subject, determine their eligibility, and provide contact information for the research team. As relevant, the recruitment material may include following:

- An explanation of the purpose of the study.
- Eligibility information (e.g., a summary of the main inclusion/exclusion criteria).
- A summary or brief list of the benefits of the research.
- The name of the researcher and/or research institution or facility (if in addition to the LLNL site).
- Time or other commitments needed from the subjects.
- Contact information for the research team.
- A statement that the study has been reviewed and approved by the LLNL IRB.

### **Advertisements must not:**

- State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
- Include exculpatory language.
- Promise “free treatment” when the intent is only to say subjects will not be charged for taking part in the investigation.

Once the advertisements are finalized, the final copy of the printed, audio-taped, and/or video-taped advertisements must be submitted to, and given a stamp of approval by, the IRB before they may be utilized.

### **Informed Consent**

Legally effective informed consent must be obtained from every subject enrolled in human subjects research, unless the requirement for obtaining informed consent has been waived by the IRB.

#### **Legally effective consent**

No PI may involve a human being as a participant in research without obtaining the legally effective informed consent of the participant or the participant’s legally authorized representative. The only exception would be if a specific waiver of consent has been approved by the IRB. In general, the IRB considers individuals who are unable to consent for their own clinical care to be unable to consent for research participation. It is expected that the PIs will assess the comprehension and capacity of the subjects to understand the consent language.

- Consent must always be sought under circumstances that provide the prospective participant or the representative sufficient opportunity to consider whether or not to participate and minimize the possibility of coercion or undue influence.
- The IRB will consider where the consent process will take place and the individual(s) who will be obtaining consent (*e.g.*, the PI, collaborator, or qualified designee) in its determination regarding the appropriateness of the consent process. When the potential participant’s understanding of the research may be impaired due to the timing, location, or individuals participating in the proposed consent process, the IRB will require an alternative process
- The information that is given to the participant or the representative must be in language understandable to the participant or the representative. Any informed consent document that is translated into another language must be approved by the IRB prior to its use.
- No informed consent, whether oral or written, may include exculpatory language through which the participant or the representative is made to waive or appear to waive any of the participant’s legal rights, nor to release or appear to release the PI, sponsor, institution, or its agents from liability for negligence.
- A person knowledgeable about the consenting process and the research to be conducted (*i.e.*, a member of the project’s research team) must obtain the informed consent. If someone other than the PI conducts the interview and obtains consent, the PI needs to formally delegate this responsibility and the person so delegated must have received appropriate training to perform this activity.
- Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

The basic elements of informed consent are defined by federal regulations [[45 CFR 46.116](#), 21 CFR 50]. They include:

- a statement that the **study involves research**;
- an explanation of the **purpose** of the research and the expected **duration** of the participant's participation;
- a description of the research **procedures** to be followed and identification of any procedures which are experimental;
- a description of any reasonably **foreseeable risks** or discomforts to the participant;
- a description of any **benefits** to the participant or to others which may reasonably be expected from the research;
- a disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the participant;
- a statement describing the extent, if any, to which **confidentiality** of records identifying the participant must be maintained;
  - Statement(s) should be included to explain who has access to review the research records for inspectional purposes [e.g., LLNL, Food and Drug Administration (FDA) for FDA-regulated research and the Office for Human Research Protections (OHRP) for Department of Health and Human Services (HHS)-supported research].
  - Additionally, for National Institutes of Health (NIH)-supported grants or contracts, language should be included to explain the protections provided by the Certificate of Confidentiality, which are automatically provided for all NIH grants (as of October 1, 2017). For non-NIH-supported grants, an explanation of the protections provided by a Certificate of Confidentiality should be included whenever one has been obtained for the study.
- for **research involving more than minimal risk**, an explanation as to whether any compensation or **medical treatments** are available if injury occurs and, if so, what they consist of, or where further information may be obtained;
- an explanation of whom to **contact** for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the participant;
- a statement that participation is **voluntary**, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
- one of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
  - a statement that identifiers might be removed from identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another PI for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or
  - a statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

### **Additional Elements of informed consent**

When appropriate, one or more of the following elements of information should also be provided to each subject:

- for studies involving **clinical trials**, there must be added statements explaining that the clinical trial has been registered on the ClinicalTrials.gov website. The IRB shall ensure that the following statements are included in such consent forms: "A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time." These statements are usually placed toward the beginning of the consent document after the *Purpose* section.
- a statement that the particular treatment or procedure may involve risks to the participant (or to the embryo or fetus, if the participant is or may become pregnant) which are currently **unforeseeable**.
- anticipated circumstances under which the participant's **participation may be terminated by the PI** without regard to the participant's or legally authorized representative's consent.
- any additional **costs** to the participant that may result from participation in the research.
- the **consequences of a participant's decision to withdraw** from the research and procedures for orderly termination of participation by the participant.
- a statement that **significant new findings** developed during the research which may relate to the participant's willingness to continue participation will be provided to the participant.
- the approximate number of subjects involved in the study.
- a statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
- a statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.
- for research involving biospecimens, whether the research might include whole genome sequencing (*i.e.*, sequencing of a human germline or somatic specimen with the intent to generate the genome or exome of that specimen).

### **Waiver of Informed Consent**

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement for informed consent provided the IRB finds and documents in accordance with [45 CFR 46.116\(f\)\(3\)](#) that:

- the research involves no more than minimal risk to the subjects;
  - the research could not practicably be carried out without the requested waiver or alteration;
  - 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;
  - the waiver or alteration will not adversely affect the rights and welfare of the subjects; and
  - whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation;
- OR –
- in accordance with [45 CFR 46.116\(e\)\(3\)](#), the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

- public benefit or service programs;
- procedures for obtaining benefits or services under those programs;
- possible changes in or alternatives to those programs or procedures; or
- possible changes in methods or levels of payment for benefits or services under those programs; **and**
- the research could not practicably be carried out without the waiver or alteration.

The IRB must make a determination when granting a waiver of consent for identifiable data and specimens that it is impracticable to use de-identified data.

PIs may request a waiver of informed consent in their IRB protocol application. The request for waiver of consent should provide an explanation on why consent cannot be practicably obtained from subjects. Any waiver of informed consent must be approved by the IRB. The IRB will document the justification for waiver of informed consent either in the minutes of an IRB meeting or in the IRB records for studies reviewed by expedited review.

### **Documentation of Informed Consent (Signed Consent)**

Informed consent must be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117. Informed consent is documented using a written consent form approved by the IRB and signed and dated by the participant or the participant's legally authorized representative at the time of consent.

- a. A copy of the consent form must be given to the subject. For FDA-regulated research, the subject must be given a copy of the signed consent form.
- b. The consent form may be either:
  - i. **A written consent document** that embodies the elements of informed consent. The document may be read to the participant or the participant's legally authorized representative, but the participant or representative must be given adequate opportunity to read it before it is signed; or
  - ii. **A short form written consent document** stating that the elements of informed consent have been presented orally to the participant or the participant's legally authorized representative.
 

When this method is used:

    - there must be a witness to the oral presentation;
    - the IRB must approve a written summary of what is to be signed by the participant or representative;
    - for subjects who do not speak English, the witness must be conversant in both English and the language of the participant;
    - the participant or the participant's legally authorized representative must sign the consent document;
    - the witness must sign both the short form and a copy of the summary;
    - the person actually obtaining consent must sign a copy of the summary; and, a copy of the summary must be given to the participant or representative, in addition to a copy of the short form.

### **Waiver of Documentation of Informed Consent [[45 CFR 46.117\(c\)\(1-2\)](#)] (Verbal Consent)**

**The IRB may waive the requirement for the PI to obtain a signed consent form for some or all subjects if it finds that:**

- a. the only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality (**Note:** Subjects or legally authorized representative must be asked whether they want documentation linking them with the research, and their wishes must govern. For example, domestic violence research where the primary risk is discovery by the abuser that the participant is talking to researchers, **or**
- b. the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Procedures such as non-sensitive surveys, questionnaires, and interviews generally do not require written consent when conducted by non-researchers, **or**
- c. the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

PIs may request a waiver of documentation of informed consent on the general IRB protocol application. In cases in which the documentation requirement is waived, the IRB has to review a written script of the information to be provided to subjects to be sure that this includes all required and appropriate additional elements of consent disclosures. The IRB will consider whether to require the PI to provide subjects with a written statement regarding the research. The IRB will document the justification for waiver of informed consent either in the minutes of an IRB meeting or in the IRB records.

### **Review and Approval of the Informed Consent Form**

The IRB is responsible for the review and approval of the informed consent form prepared by the PI. The wording on the informed consent form must contain all the required elements and meet all other requirements as described in this section. If the wording of the informed consent has been initially prepared by an external entity (*e.g.*, a sponsor or cooperative study group) other than by an LLNL PI, the IRB needs to ensure that the wording of the consent meets all the requirements of the LLNL IRB, or has been reviewed by an IRB designated by LLNL. If the consent is amended during the protocol approval period, it must bear the approval date of the amendment rather than the date of the approved protocol.

### **Parental Permission and Assent**

See the section titled “Review of Research Involving Children” in the IRB SOP #15: *Vulnerable Populations* for procedures on parental permission and assent in research involving children.

### **Surrogate Consent**

This policy is designed to protect human subjects from exploitation and harm and, at the same time, make it possible to conduct essential research on problems that are unique to persons who are incompetent, or who have an impaired decision-making capacity. Regulations generally require that the PI obtain informed consent from subjects. Under appropriate conditions, PIs also may obtain informed consent from a *legally authorized representative* of a participant (surrogate consent).

A *legally authorized representative* means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participant's participation in the procedure(s) involved in the research [45 CFR 46.102(c) and 45 CFR 46.116]. For research conducted at LLNL, the IRB may consult with legal counsel and/or California state law to decide which individuals are "legally authorized representatives." When the research is conducted outside of California, the IRB may again consult with legal counsel to obtain information about a given state's law(s) for legally effective consent, particularly by a legally-authorized representative.

Such consent may be requested and accepted only when the prospective research participant is incompetent or has an impaired decision-making capacity. The PI must provide the IRB with the procedures that will help make this determination.

If feasible, the PI must explain the proposed research to the prospective research participant even when the surrogate gives consent. Under no circumstances may a participant be forced or coerced to participate in a research study.

### **Translation of Informed Consent for Non-English-Speaking Subjects**

Regulations require the researcher to submit translated consent forms for protocols that include non-English-speaking subjects. The IRB may require a "back-translation" into English or consult with language experts.

If the researcher meets a non-English-speaking person who expresses interest in the study, the researcher may not orally translate the approved English consent form or statement. The researcher must submit the appropriate translated consent documents via an amendment requesting approval to recruit non-English speaking subjects.

Sometimes a participant understands English but does not read or write English. The informed consent should be obtained in a language understandable to the subject or the authorized representative.

Whenever the PI anticipates that non-English speaking subjects may be enrolled in each study, plans should be included in the submission for a translated consent form(s) in that language.

If the IRB, during its review of the submission, determines that it is likely that non-English speaking subjects will be enrolled, the IRB will request a translated consent form(s). Once the IRB approves the study and the English version of the consent form(s), the IRB will request that a translated consent form is submitted to the IRB for each language that is anticipated.

The PI, IRB, and LLNL are all responsible for ensuring legally effective consent. Therefore, the translation of the IRB-approved English version of the consent must be translated in a manner that the PI and IRB have confidence that the translation effectively communicated the content and tone of the English version of the consent form. As a result, the IRB may require that the translation of the consent form is certified by any of the following:

- A company or organization that provides translations as a service to the public.
- An individual who is fluent in both English and the anticipated language of the non-English-speaking subject. For greater than minimal risk studies, the IRB may require a back-translation from another individual who is fluent in both languages to help ensure the accuracy of the translation.
- A sponsor, such as NIH or a medical device manufacturer.

In a situation where the PI did not anticipate a non-English speaking subject and time does permit for the review and approval of a translated (“*long-form*”) version of the consent because it would be in the subject’s clinical best interest to start the study as soon as possible, the PI may enroll the subject using the short form consent form and process as outlined below:

- i. the oral presentation and the short form written document should be in a language understandable to the subject. The IRB must approve a written summary of what is to be said to the subject (the approved full consent document may serve as this summary); and
- ii. there must be a witness to the oral presentation;
- iii. the short form document is signed by the subject; and
- iv. the witness must sign both the short form and a copy of the summary; and
- v. the person actually obtaining consent must sign a copy of the summary; and
- vi. a copy of the summary must be given to the subject or representative, in addition to a copy of the short form;
- vii. both the English version and the translated version of the informed consent will be placed in the study file.

Documentation of the consent process must include both versions of the consent form and translator information.

#### **Posting of a Clinical Trial Consent Form**

- a. For each clinical trial conducted or supported by a federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the federal department or agency component conducting the trial on a publicly available federal website that will be established as a repository for such informed consent forms.
- b. If the federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a federal website (*e.g.*, confidential commercial information), such federal department or agency may permit or require redactions to the information posted.
- c. The informed consent must be posted on the federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

The informed consent requirements in these policies and procedures are not intended to preempt any applicable federal, state, or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that require additional information to be disclosed in order for informed consent to be legally effective.

## Document Review History

Revision Number	Date	Author	Summary of Changes
01	September 2017	Ann-Marie Dake	Complete Revision
02	November 2018	Dawn Whalen	Document control process added
03	November 2019	IRB Office	Complete Revision
04	October 2020	Ann-Marie Dake	Revisions and updates