Chapter 10:

Informed Consent Requirements

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Chapter 10
Informed Consent Requirements

Investigators are required to obtain informed consent as a legal and ethical obligation. This chapter discusses the process of consent, the elements of consent, and legal requirements involved when obtaining informed consent from subjects.

No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or to appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the Institution or its agents from liability for negligence.

10.1 The Process of Consent

Informed consent is more than a form; it is a process. Information must be presented to participants so that they can voluntarily decide whether or not to participate in research. Thus, the informed consent form must be written in "lay language" to ensure participants can understand its content. The amount of information contained in the consent and the manner of presentation is related to the complexity and risk involved in the study. The consent form serves to document the basis for consent and also serves as future reference for study subjects.

While the informed consent process is prospective and takes place prior to any research activity, consent should also be an ongoing interaction between the investigator and the research subject for the duration of the study. Subjects must be informed about significant new information or findings that develop during the course of the study that may affect their willingness to continue participation. Refer to Section 10.14 – Providing Significant New Information/Findings (SNIF) to Participants for more information.

The informed consent form must be signed before any study procedures begin. The investigator or research staff verbally explains the purpose and procedures involved in the study. The research staff answers questions and provides information to allow the subject to make an informed decision with ample time to consider participation. Thus, investigators should consider whether obtaining consent on the same day that study procedures begin provides participants enough time to consider participation.

The consent process must be free of coercion or undue influence. If an investigator has a relationship with potential subjects (physician-patient, instructor-student, employer-employee), care should be taken to avoid recruitment methods that may be seen as coercive due to the special relationship between the parties.

The consent document should be revised when new information becomes available or when changes will improve the consent process. Any proposed changes to an IRB-approved informed consent form must be reviewed and approved by the IRB before changes are implemented (unless the change is necessary to avoid immediate harm to subjects or others). Refer to Section 9.1 – Amendments – Changes to Research after Approval for additional information.

Consent and Assent

Only competent adults can give legally effective informed consent to participate in research.

Minors and those individuals who are not competent to give consent should be asked for their agreement to take part in the research. Assent is a knowledgeable agreement to participate in a research project.

Adequate provisions should be made for soliciting the independent, non-coerced assent from minors/children or cognitively-impaired persons who are capable of knowledgeable agreement. In general, the IRB recommends that children ages seven and older and most cognitively-impaired adults be given the opportunity to assent. In cases where assent is obtained from a minor or cognitively-impaired subject, permission must also be obtained from a legally authorized representative. The legally authorized representative may be a parent, a court-appointed guardian, or the court.

Special attention must be given to state law regarding attaining the age of majority (18 years of age) and situations involving emancipated minor subjects. Refer to Section 10.13 – Child Assent Special Requirements for more information.

For additional information about the consent process, refer to "Tips on Informed Consent" from the Office for Human Research Protections (OHRP).

10.2 Required Elements of Informed Consent

Campus-specific informed consent Templates provide sample language, instructions, and guidance. The templates include the HSIRB Informed Consent Template which is to be used when there is no model template provided by an industry sponsor or cooperative group. Also available is a template to be used when a model consent form is provided by an industry sponsor, cooperative group or external IRB. The use of the latter template should require less editing and allow for a more expedient processing for industry sponsored studies.

These templates can be found at: http://oprs.usc.edu/review/forms/.By following the consent templates, investigators ensure that the basic and additional elements of consent are included as required by federal regulations.

Federal regulations (45 CFR 46.116 and 21 CFR 50.25) specify eight basic elements and six additional elements of informed consent described below.

Purpose and Procedures of the Study

The informed consent form must include "a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed and the identification of any procedures which are experimental." This section should clearly identify the procedures that will be followed during the course of the research. The procedures should be presented to the subject in the order of their occurrence and include expected duration of participation. Studies that involve experimental procedures or agents must clearly distinguish procedures or agents that are clinically indicated (standard of care) from experimental interventions.

Potential Risks and Discomforts

The informed consent form must include "a description of any reasonably foreseeable risks or discomforts to the subject."

The informed consent form must provide subjects with a clear understanding of any risks or discomforts which are reasonably anticipated during their participation in the research.

Risks should not be understated or overstated. If enough data are available, it may be appropriate to state the frequency of potential risks, risk prevention measures, and reversibility and treatment of discomforts and risks.

Anticipated Benefits

The informed consent form must include "a description of any benefits to the subject or to others which may reasonably be expected from the research."

Direct Benefits

The informed consent form should state whether there are any direct benefits to the subject that may reasonably be expected as a result of participation in the research. Examples of direct benefits to the subject may include treatment of an illness or acquiring knowledge of value to the subject (such as results of a cardiac stress test or an educational test). The potential benefits to the subject should not be overstated or guaranteed. Payment for participation in the study cannot be listed as a benefit. If there are no benefits to the subject, this should be clearly stated.

Benefits to Society

All research should have some underlying potential benefit to society (such as advancement of knowledge or new treatments for people in the future).

NOTE: This section should not include payment as a benefit. Payment is addressed in the Compensation section of the consent form (Refer to Section 10.3 – Additional Elements of Informed Consent).

Alternatives to Participation

The informed consent form must include "a disclosure of appropriate alternative procedures or courses of treatment, if any, which might be advantageous to the subject."

Therapeutic Alternatives

In clinical research, all informed consent forms are required to state any therapeutic alternatives available to the subject. Alternatives may include approved treatments, other clinical trials, continuing with current care, or supportive care only. For medical

protocols that are not therapeutic in nature, the alternative would be to not participate in the study.

Non-Therapeutic Alternatives

In non-medical research, the informed consent form should state any alternatives that may be advantageous to the subjects. For instance, if the subjects are students who will receive academic credit, the informed consent form should describe the available alternatives to earn equivalent academic credit.

Confidentiality Statement:

The informed consent form must include "a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained."

The amount of information provided to subjects about confidentiality will vary greatly depending on the nature of the study. Specific language may be required in certain situations, such as when the research involves an FDA-regulated product, when the research has a Certificate of Confidentiality, or when researchers must report potential abuse, harm, or communicable diseases as mandated reporters.

FDA Regulated Research:

Consent forms used to enroll subjects in FDA-regulated research must contain a statement informing the subjects that the FDA may inspect the research records. Researchers will maintain confidentiality of records identifying the subject, to the extent possible.

ClinicalTrials.gov Registration:

Consent forms for "*applicable clinical trials*" (see end of this section for definition) must contain the following statement:

''A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US 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.''

For additional information regarding ClinicalTrials.gov Registration, refer to Section 18.11 – Registration of Clinical Trials and Other Types of Research.

"*Applicable clinical trials*" generally include interventional studies (with one or more arms) of drugs, biological products, or devices that are subject to FDA regulation, meaning that the trial has one or more sites in the U.S, involves a drug, biologic, or device that is manufactured in the US (or its territories), or is conducted under an investigational new drug application (IND) or investigational device exemption (IDE). For more information on definitions of terms, refer to FDA's draft guidance document "Elaboration of Definitions of Responsible Party and Applicable Clinical Trial"

Limits to Confidentiality

Depending on the subject matter of the research, there may be limits to the investigator's promise of confidentiality to the subject. An example would be if a subject reveals information about possible child or elder abuse or if the investigator and/or the research staff discover the possibility of abuse. See Section 13.13 – Mandatory Reporting for more information.

Certificates of Confidentiality

If a Certificate of Confidentiality is requested for a study, the consent must include specific language. See the IRB Informed Consent Template and Instructions. For more information about Certificates of Confidentiality, refer to: https://humansubjects.nih.gov/coc/index

Mandatory Reporting

Study subjects must be informed if the investigator is a mandated reporter (as defined by state and federal law) required to report any sexual or physical abuse to the appropriate authorities.

Injury Statement

The informed consent form must include "for research involving more than minimal risk, an explanation as to whether any compensation for study-related injury and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained".

The informed consent form should explain whether medical treatment is available for a research-related injury and who will pay for the treatment. USC may provide treatment at its health care facilities, but the cost of medical treatment is typically paid by the study sponsor or billed to the subject's health insurance. Specific language is required for studies conducted at the USC Clinical Trials Unit (CTU). For most biomedical studies,

the USC Clinical Trials Office (CTO) will provide injury language that must appear in the consent form.

Compensation is not offered by USC or by study sponsors if a subject is injured.

No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or to appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the Institution or its agents from liability for negligence.

Contact Information

The informed consent form must include "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 subject."

The informed consent form must provide phone numbers for subjects to call if they have questions about the research or if they have a research-related injury. For greater than minimal risk studies, the consent form must provide a phone number where the study doctor can be reached **24 hours a day, 7 days a week**.

The informed consent form must also include a statement that subjects may contact the IRB if they would like to speak to someone independent of the research team, obtain answers to questions about the research, learn about their rights as participants, or if they cannot reach the research staff.

Voluntary Participation and Withdrawal

The informed consent form must include "a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled". The form should also state that gradual withdrawal may be necessary for safety reasons, as applicable.

10.3 Additional Elements of Informed Consent

Six additional elements of informed consent may apply, depending on the nature of the study [45 CFR 46.116(b)]. When appropriate, informed consent forms must also include one or more of the following elements:

Risks Involving Pregnancy

For research studies intending to enroll females of child bearing potential, the consent form must include "a statement that the particular treatment or procedure may involve risks to the subject or embryo or fetus if the subject is or may become pregnant, which are currently unforeseeable."

Termination of Participation by Investigator

The informed consent must include "anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent." These circumstances include when the subject fails to follow the investigator's instructions, if the subject's disease gets worse, if the subject's side effects are too severe, or if the sponsor or FDA closes the study.

Subject's Withdrawal from Research

The consent form must include "the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject."

For FDA-regulated research, specific data retention requirements must be adhered to and disclosures to the subject must be included in the informed consent form when a subject withdraws from research. Refer to Section 18.10 – Data Retention Requirements Related to Subject Withdrawal from FDA-Regulated Research.

Additional or Incurred Costs

The informed consent must note "any additional costs to the subject that may result from participation in the research." For most biomedical studies, the USC Clinical Trials Office (CTO) will provide language describing the costs of participation.

Disclosure of New Findings

The informed consent form must include "a statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject." Guidelines for telling subjects about significant new information are provided in Section 10.14 – Providing Significant New Information / Findings (SNIF) to Participants.

Number of Subjects

The informed consent should include "the approximate number of subjects involved in the study." This additional element is required for research projects submitted to the Health Sciences IRB.

Other Information to be Included in Consent

Compensation

The informed consent form should describe any compensation available to subjects. This may include payment for participation and reimbursement for expenses such as parking fees, travel expenses, and childcare incurred during the study. The consent form should explain how and when subjects will receive payment. In alignment with Food and Drug Administration (FDA) recommendation, USC encourages the adoption of a pro-rated payment system whenever possible. The nature, amount, and method of payment must not constitute undue inducement to participate. The payment alone should not serve as sufficient inducement for the subject to volunteer.

If subjects will receive more than $600 per year for taking part in one or more research studies, the consent form should explain that subjects may receive an Internal Revenue Service (IRS) Form 1099. The $600 per year amount does not include reimbursements for expenses.

Academic Credit

If payment will be in the form of academic credit that will be awarded for research participation, the amount and type of credit should be clearly stated as well as any required conditions for credit.

Commercial Products

Investigators are required to inform subjects in the informed consent form if their biological human materials (such as tumor tissue, bone marrow, or blood) may be used to establish a commercially useful product (such as a cell line). Subjects should also be informed that they will not receive payment for any commercial product developed from their specimens.

Sponsor or Funding Agency Identification

If applicable, subjects should be told what entity is funding the research (such as the drug company, device manufacturer, federal agency, or foundation). This information should appear in the introductory section of the consent form.

Conflict of Interest

The research team must disclose all financial or other personal considerations that compromise, or have the appearance of compromising, professional judgment in proposing, conducting, supervising, or reporting research. Conflicts include financial, non-financial and institutional interests.

Disclosure of Incidental Findings

The consent form must clarify whether or not subjects will be informed about information obtained but not sought as part of the research project.

Consent of Pregnant Partner

Sponsors of drug studies may provide a sample informed consent for pregnant partners. This consent form is used if a female partner of a male participant becomes pregnant during the study and there are potential risks to the woman or fetus from exposure to the drug. The purpose is to obtain medical information about the partner's pregnancy and birth outcomes to learn more about the risks of the study drug.

Investigators should not prepare and submit pregnant partner consent forms to the IRB for review. The IRB will not review and approve a pregnant partner consent form unless a pregnancy occurs. If a pregnancy occurs in a partner of a USC participant, the investigator should prepare the pregnant partner consent form and submit it as an amendment at that time.

10.4 Who May Conduct the Informed Consent Process

The federal regulations 45 CFR 46.116 state: "No investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under the circumstances that provide the prospective subject or representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence." Further, a basic element to be included in a consent document is "an explanation of whom to contact for answers to pertinent questions about the research…" Therefore, the following is the USC policy on who can conduct the informed consent process for human research studies:

- Individuals who are knowledgeable about the protocol must obtain consent from subjects for participation in a study. Specifically, they must be able to describe the purpose, procedures, benefits, risks, and alternatives to participation in the study. They must be able to answer subjects' questions about the protocol and about risks of the research procedures and alternatives.

- For studies involving medical procedures, the person obtaining consent should be licensed and privileged to conduct those procedures. Sometimes more than one person on the research team participates in the consent process. For example, study coordinators may describe the study procedures and a physician investigator may discuss specific issues related to the medical interventions and potential alternative treatments.

- All individuals who participate in the informed consent process must first successfully complete the online USC Human Subjects Education Program through the Collaborative IRB Training Initiative (CITI). More information on CITI is available at the following website http://oprs.usc.edu/education/citi/.

- The PI must identify all individuals who will obtain consent and attest that they fit the above criteria. The PI is ultimately responsible for ensuring that ethically and legally valid consent is obtained from all research subjects.

- The investigator or other person obtaining informed consent must sign the study consent document(s) on the signature line labeled “Person Obtaining Informed Consent”.

10.5 Legally Authorized Representative

Informed consent may be obtained from a subject’s family member or authorized agent in certain situations. California law specifies who can be the Legally Authorized Representative and provide consent when a subject is not able to provide informed consent.

For studies involving cognitively-impaired adults, consent guidelines and the use of legally authorized representatives are governed by California Health and Safety Code Section 24175. For more information, refer Section 14.4 – Cognitively-Impaired Persons. If studies relate to the subject’s cognitive impairment, lack of capacity, or serious or life-threatening diseases and conditions, consent must be sought from the surrogate decision makers based on the order defined in California Law CA Health and Safety Code 24178.

If the person from whom assent is sought refuses, the person should not be enrolled, even if the parent or authorized representative gives permission. Alternatively, if the person from whom assent is sought agrees to participate, the person may not be enrolled if the parent or authorized representative does not give permission. In rare circumstances, depending on the nature of the study and the age and circumstances of the minor, the IRB may waive the requirement for parental or authorized representative’s permission.

10.6 Documentation of Informed Consent

The purpose of an informed consent form is to provide subjects with a written source of information for future reference and to document the fact that the process of informed consent occurred prior to the subject's participation. The form generally serves as a basis for the initial presentation of the study to the potential subject. Typically, informed consent is documented by using the IRB-approved, written informed consent form which is signed and dated by the subject, or the subject's legally authorized representative, at the time of consent. A copy of the informed consent form must be given to the subject. Unless the investigator has requested a waiver of documentation of consent, the

subject's signature on an informed consent form is required prior to beginning any study procedures.

Information given to the subject or the representative must be in a language understandable to the subject or representative.

When deception is used as a technique in research, there should be a prompt and complete debriefing of the subjects. Debriefing may include explaining the research, and if possible, providing the opportunity for withdrawal of personal responses or withdrawal from participation in the study. A debriefing statement for IRB review should be submitted along with the informed consent form.

The informed consent form signed by a study subject, or the subject's legally authorized representative, must be the version currently approved by the IRB that bears the date stamp of the IRB. One copy must be given to the subject and the original consent with the original signature must be maintained by the investigator. Another copy of the informed consent form must be maintained in the subject's research chart, medical record, or equivalent file in medical research studies.

If informed consent is obtained using the Short Form method (oral translation of the consent form in a language understood by the participant supplemented with the written Short Form in the participant's language), the subject, or the subject's legally authorized representative, and a witness must sign and date the informed consent. If applicable, the subject or (legally authorized representative) must also sign the California Bill of Rights translated into a language understood by the subject. Refer to Section 10.7 – Obtaining Consent from Non-English Speaking Subjects for additional information regarding use of the Short Form.

10.7 Obtaining Consent from Non-English Speaking Subjects

If a study includes non-English-speaking subjects, the investigator must provide methods for assuring the subject or legally authorized representative (LAR) understands the research. When an investigator anticipates enrollment of non-English speaking subjects, the IRB-approved informed consent form must be translated into each anticipated language. If a consent form is not available in a language understood by the subject or LAR, the Short Form process can be used to obtain and document consent for the study.

Guidelines for the Use of the Short Form

If there is occasional and unexpected need to enroll subjects who are not fluent in English, a written *short form* informed consent must be used in conjunction with the written IRB-approved English version of the consent. The *short form* consent includes the basic and possible additional elements of disclosure. The short form is available in English and many languages on the HSIRB and UPIRB websites. Investigators can download the short form and fill in the blanks as appropriate. The language has already been approved by the IRB.

The process for enrolling subjects with the short form is outlined below. Substitute "Legally Authorized Representative (LAR)" for "subject" when an LAR is involved in the process. All of the following requirements must be completed:

- A translator must orally translate the entire IRB-approved English version of the consent form to the subject in a language understandable to him/her, and the subject must be given a copy of the translated "short form" consent document to read
- The entire consent process must include a witness to the oral presentation
- The IRB-approved English version of the consent form must be signed by the individual authorized by the IRB to obtain consent, and signed by the witness to the consent process. The translated short form must be signed by the subject and the witness to the consent process
- The California Bill of Rights must be provided to the subject for studies that involve a "medical experiment" as defined by California law. The Bill of Rights is available in the same languages as the short form. The subject must sign and date the form, AND
- The subject must be given copies of the IRB-approved English version of the consent form and the translated versions of the short form consent document and California Bill of Rights. The original signed English version with the original signed short form attached should be placed in the subject's research record, medical record, or equivalent file as appropriate.

For additional information, refer to "Consent and Short Forms: Who Must Sign?": http://oprs.usc.edu/files/2013/01/Consent_and_Short_Forms_Final.pdf.

Translation of Consent Forms into Languages Other than English

When the study subject population includes people who do not understand English, and the investigator or the IRB anticipates that consent interviews are likely to be conducted in a language other than English, the IRB will require translation of the IRB-approved consent documents into those languages.

Translation Options

If the study population is likely to include subjects whose primary language is Spanish, the consent documents must be translated into Spanish. The HSIRB office will provide Spanish translation of the IRB-approved consent form at no cost to investigators. The HSIRB does not provide translation services in languages other than Spanish, nor does the HSIRB translate study documents other than consent forms. Investigators must request Spanish translation by checking the appropriate box in the iStar application. Once consent forms have been translated, they are uploaded into the iStar application and stamped by the IRB. Investigators will receive email notification that the translated consent form is ready for use.

For languages other than Spanish, it is the responsibility of the investigator or study sponsor to provide translation using a translation service. The investigator must obtain IRB approval of the English version of the forms before providing them to the translator. A consent form translated by a translation service must be submitted to the IRB along with a certificate of translation. The translated consent form will be uploaded into the iStar application and stamped by the IRB. Investigators will receive email notification that the translated consent form is ready for use.

The investigator or study sponsor is also responsible for sending revised consent forms to the translation service. After changes to the English consent form are approved by the IRB, the changes must be made to the translated consent forms as soon as possible and submitted to the IRB for stamping.

For OHRP and FDA guidelines on obtaining consent from subjects who do not speak English, refer to the links below.

Helpful Links:

- OHRP "Obtaining and Documenting Informed Consent of Subjects Who Do Not Speak English": http://www.hhs.gov/ohrp/policy/ic-non-e.html

- FDA "A Guide to Informed Consent – Information Sheet" http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm#nonenglish

10.8 Consent Documentation when Subjects Cannot Read, Hear, or Sign Consent Forms

Additional protections are needed for subjects who cannot see, hear, or speak or who cannot read or sign consent forms. The consent process must be conducted in a language or manner understandable to the subject and must allow the subject to communicate his or her willingness to participate. The study team must ensure that the subject is adequately informed and properly document the consent process.

English-speaking subjects who cannot see or are unable to read and write may have the informed consent form read to them. A witness must be present during the consent process and must sign the consent form. Subjects who are unable to sign the consent form can consent to participate in the research by "making their mark" (providing an alternative form of signature) on the signature line. The name of the subject, date, and time (if applicable) can be completed for the subject by either the witness or the person obtaining consent. A note must be included in the research record stating the method used for communicating with the subject and the means by which the subject communicated agreement.

For non-English speaking subjects who cannot see, read, or write, the process described above should be used. The study team must use a consent form or short form translated into a language the subject understands.

People who can read but cannot physically write can give verbal consent. A witness must be present during the consent process and must sign the consent form. The name of the subject, date, and time (if applicable) can be completed for the subject by either the witness or the person obtaining consent. A note must be included in the research record

stating the method used for communicating with the subject and the means by which the subject communicated agreement.

For people who can read and write but cannot hear or speak, sign language or specialized oral interpreters should be used to enhance communication with the study team. A witness must be present during the consent process and must sign the consent form. A note must be included in the research record stating the method used for communicating with the subject and the means by which the subject communicated agreement.

When consent is obtained from a Legally Authorized Representative (LAR), follow the procedures above substituting LAR for subject as applicable.

10.9 Electronic Consent and / or Signatures

The USC IRB will allow use of electronic consents for minimal risk research and full board review clinical research studies. Electronic consents or electronic signatures may be used if the procedures for obtaining them are approved by the IRB and the risk of breech is minimized. The IRB will consider vendor security and issues such as how a copy of the consent document may be provided for review if requested by the subject. As noted by the Office of Human Research Protections (OHRP), "If properly obtained, an electronic signature can be considered 'original' for the purposes of recordkeeping."

OHRP also notes that it "would allow electronic signature of the document if such signatures are legally valid within the jurisdiction where the research is conducted." The Federal Electronic Signatures in Global and National Commerce Act (eSIGN) and California's Uniform Electronic Transactions Act (UETA) require that subjects agree to use the electronic format and that subjects be informed about their rights to obtain the electronic consent in non-electronic form and a description of any procedures that must be followed to withdraw their agreement to use an electronic record.

Vendors producing electronic consents will also need to comply with established FDA regulations. "Electronic" documents would be subject to a specialized set of requirements found at 21 CFR Part 11. Compliance with these standards is used to assure that electronic records are "trustworthy, reliable, and generally the equivalent to paper records and handwritten signatures executed on paper." Investigators are responsible for ensuring compliance with 21 CFR Part 11 requirements.

For studies that involve social media websites, investigators must ensure informed consent language does not conflict with terms of service agreements from those websites (such as Facebook, Twitter).

10.10 Waivers of Informed Consent

Waiver of Documentation of Consent

In some situations, the IRB may waive the requirement for obtaining a signed informed consent 45 CFR 46.117(c). Investigators may request the IRB waive the requirement for a signed, written, informed consent. The IRB may waive the requirement for a signed consent if it finds:

- The only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality (for example, the subjects would be placed at risk by documents linking them with an illegal or stigmatizing characteristic or behavior), and the research is not subject to FDA regulations. Each subject will be asked whether they want documentation linking them with the research, and the subject's wishes will govern; or
- The research presents no more than minimal risk of harm to the subjects and involves no procedures for which written consent is normally required outside of the research context (such as surveys without identifying information about compliance with a smoking cessation program).

In some cases, when a waiver of documentation of consent is granted, no written document is provided to the subject. For example, with a random-dial telephone survey study, the telephone interview would begin with a script that includes all of the required elements of consent but the study subjects would receive no written information about the study either before or after the interview. The telephone script containing the elements of consent must be included in the research application and reviewed and approved by the IRB.

In other cases, the waiver of documentation of consent can mean the subject is given a consent document but no signatures are needed. IRB regulations stipulate that the IRB may still require the investigator to provide the subject with a written statement about the

research even when a waiver of documentation is granted. For example, for an Internet-based survey, the IRB may determine that it is reasonable for the investigator to provide the subjects with an information sheet containing all of the basic elements of consent. The information sheet would state that completing the survey constitutes the subject's consent/agreement to participate in the research study.

OHRP Human Subject Regulations Decision Chart 10 provides more information.

Waiver of Elements of Consent or Consent Itself

Some research projects would not be possible if obtaining consent from subjects was required. The IRB may consider waiving the requirement for some or all of the elements of informed consent 45 CFR 46.116(d). The regulations state that informed consent may be waived in full or in part if the IRB determines that all 4 conditions below are met:

- The research involves no more than minimal risk to the subjects and
- The waiver or alteration will not adversely affect the rights and welfare of the subjects and
- The research could not ***practicably**** be carried out without the waiver or alteration and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation and
- The research is not subject to FDA regulation

*For the purposes of this policy, ***practicably*** means *reasonably capable of being accomplished; feasible*. The investigator must provide justification as to why the research cannot "practicably" be carried out without a waiver or alteration of consent. The investigator must document either that it is not possible to obtain consent from most subjects or their legally authorized representatives, or that limiting enrollment to subjects from or for whom consent can be obtained may bias the study results significantly. It is **not** sufficient to state there is not enough time or resources to obtain consent. Meeting the criteria for "not feasible" will be decided on a case-by-case basis. IRB considerations include: the number of subjects involved, the difficulty involved in obtaining informed consent, the nature of the research, and provisions for protecting the confidentiality of the data (chart reviews, specimen research).

Obtaining informed consent would not be practicable if the investigator will have no direct contact with subjects, will not know their identities or addresses, or subjects are lost to follow-up.

Alternatively, Public Demonstration Projects may obtain waiver of consent if the IRB finds that all criteria below are satisfied:

- The research is to be conducted by or subject to the approval of state or local government officials, and
- The research is designed to study, evaluate or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) 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, and
- The research is not FDA-regulated.

Examples of Waiver of Consent:

- Retrospective chart reviews. Example: review of medical records of patients who have undergone abdominal surgery in the past two years to correlate the data with blood chemistry values kept by pathology. Researchers collect limited data that will be assigned a random code number and the link between the subjects' names and code numbers is known only to the researchers. Results of the research will not affect clinical care of the individuals, because they have already left the hospital and may be lost to follow-up.

- Large population studies such as testing new biometric scanners at busy airports.

- Research on existing pathology specimens (in which all specimens to be studied have already been collected and are "on the shelf" at the time of the IRB application)

Examples of Waiver of Some Elements of Consent:

- Certain ethnographic research. For example: when obtaining *signed* consent is not appropriate or feasible according to the cultural standards of the population being studied and there is minimal risk involved in the study.

- Studies utilizing deception. For example: in a study that involves playing a computer game to test subjects' responses to differential payoffs or reinforcements, the investigator indicates in the consent form that the purpose of the study is to test reaction time. This deception may be necessary because the study would be compromised if subjects were told the true purpose. In this scenario, one of the basic elements of consent – the purpose of the study – could be waived by the IRB, and not be included in the consent form. Note: studies involving deception require a debriefing statement that is provided to the subjects (written and oral) at the conclusion of the study procedures.

- When there is a possible legal, social or economic risk to the subject by *signing* the consent form. For example, undocumented immigrants, HIV-positive individuals, and victims of domestic violence might be identified as such by *signing* the consent form.

In emergency situations, an exception to the informed consent process may be justified. Refer to Section 18.7 – Planned Emergency Research with Exception from Informed Consent.

*OHRP Human Subject Regulations Decision Chart 11 provides more information.

10.11 California Experimental Subject's Bill of Rights

The California Experimental Subject's Bill of Rights is legally required for all studies involving a medical experiment. A medical experiment is defined under section 24174 of the California Health and Safety Code as follows: "(a) The severance or penetration or damaging of tissues of a human subject or the use of a drug or device, as defined in Section 109920 or 109925, electromagnetic radiation, heat or cold, or a biological substance or organism, in or upon a human subject in the practice or research of medicine in a manner not reasonably related to maintaining or improving the health of the subject or otherwise directly benefiting the subject; (b) The investigational use of a drug or device as provided in Sections 111590 and 111595; (c) Withholding medical treatment from a human subject for any purpose other than maintenance or improvement of the health of the subject."

California law requires that the Experimental Subject's Bill of Rights should remain a separate document from the informed consent form. It must be attached to the front of the informed consent form as illustrated in the Informed Consent Template and Instructions available on the HSIRB and UPIRB websites. In addition, the copy is to be dated and signed by the subject or the subject's legally authorized representative. The subject or subject's legally authorized representative is given a copy of the Experimental Subject's Bill of Rights before giving consent to participate in any medical experiment.

The California Experimental Subject's Bill of Rights must be provided to the subject or subject's legally authorized representative in his or her language during the consent process. This also applies when a Short Form is used in the consent process. The Bill of Rights is available in various languages on the HSIRB and UPIRB websites.

10.12 HIPAA Research Authorization Form

For research involving protected health information (PHI), a current **Health Insurance Portability and Accountability Act** (HIPAA) research authorization form must be signed. The subject or legally authorized representative must sign and date the authorization form. If the subject is a minor (under 18 years old), a parent will sign the HIPAA authorization form. HIPAA authorization templates can be downloaded from the following website: http://oprs.usc.edu/rules/hipaa/.

Investigators should refer to "Instructions for Completing HIPAA Research Authorization Forms" provided by the USC Office of Compliance. This instruction sheet explains what sections can and cannot be changed. If additional changes to language in the HIPAA Authorization are required, these changes must be submitted to the Office of Compliance for approval before they are used. For additional information regarding HIPAA Privacy Regulations, refer to the Office of Compliance at http://ooc.usc.edu/hipaa-privacy-regulations.

California Law requires the HIPAA Authorization to remain as a separate document from the informed consent form.

10.13 Child Assent Special Requirements

Special informed consent procedures and forms are required when children participate in research. Children have not attained the legal age to consent to research treatments or procedures. Assent is a child's affirmative agreement to participate in research. Investigators must obtain permission from parents and agreement (assent) from children. Additional information about research involving children is found in Section 14.1 – Protection of Children Involved as Subjects in Research.

Assent Form Requirements for Permission by Parents

Subpart D of the federal regulations (45 CFR 46 Subpart D) addresses permissible research with children and consent requirements. Some situations require permission from one parent, while other situations require permission from both parents. In other cases, waiving the requirement to obtain consent may be necessary (See Section 14.1 – Protection of Children Involved as Subjects in Research for more about Subpart D).

Requirements for Parental Signature and Waiving Consent:

Permission of One Parent

The IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 (research not involving greater than minimal risk) or §46.405 (research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects).

Permission of Both Parents

Where research is covered by §46.406 and §46.407, permission is to be obtained from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

Waiver of Consent Requirements

If the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in 45 CFR 46 Subpart A and 45 CFR 46.408(b), provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state or local law.

Additionally, Public Demonstration Projects may obtain a waiver of parental permission if the IRB finds that all criteria below are satisfied:

- The research is to be conducted by or subject to the approval of state or local government officials, and
- The research is designed to study, evaluate or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) 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, and
- The research is not FDA-regulated.

10.14 Providing Significant New Information / Findings (SNIF) to Participants

Regulations require that participants be provided with significant new information/findings (SNIF) developed during the course of the research that may affect their willingness to continue participating [45 CFR 46.116(b)(5) and 21CFR50.25(b)(5)].

Examples of situations that may require the investigator to provide new information to the participants:

- Changes to the procedures that may affect a participant's willingness to continue in the research

- Identification of new risks or that risks previously described are known to occur with greater frequency or severity than previously reported
- Significant changes in potential costs to participants
- New conflict of interest for an investigator
- Notification of significant findings from this study or related studies

Methods for Providing Significant New Information/Findings to Participants

The regulations do not specify how significant new findings should be provided to participants. The IRB must review the new findings and approve the proposed method of informing participants. It is important that such changes in approved research not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to participants [21 CFR 56.108(a)(4)]. See the Appendix L - Informing Participants about Significant New Information and Findings for more information.

Method for SNIF Involving an Apparent Immediate Hazard

If an apparent, immediate hazard to participants is identified, participants must be notified and corrective actions implemented as soon as possible. This is a rare exception to ensure participant safety. However, the IRB must be informed about these occurrences and the investigator must submit a reportable event (Protocol Change Initiated to Eliminate Immediate Hazard) to the IRB promptly (within 30 days). Subsequently, an amendment with revised study documents (such as an updated consent form, a SNIF form, and updated protocol) must be submitted to the IRB. The Principal Investigator must notify the sponsor as required by the sponsor or FDA.

When investigators must contact participants immediately, notification can be made in writing or verbally. However, study files must document when participants were notified, how they were notified (in person, by phone, or by email or letter), what information was provided to them, and who contacted them.

Methods for SNIF that Do Not Involve an Apparent Immediate Hazard

If significant new information/findings do not warrant immediate notification of participants, the investigator must inform participants of the new information/findings using one or more of the following methods. Each method requires prior IRB review and approval.

- **Signed SNIF Form**
  The most common method is to prepare a brief SNIF form. The purposes of the SNIF form are to: (1) provide information to current and former participants who are affected by the new information and (2) to document that the new information was shared with participants. Use of the SNIF form is not considered "re-consenting." Only information that is both new and significant enough for subjects to reconsider their participation should be described in the SNIF form. When appropriate, the form must state that the information in the previously signed consent form is still current and valid. Participants are required to sign a copy of the form, and a copy must be kept in the research records. SNIF form templates are available for each campus:

  - For the HSC SNIF template, click: Health Sciences Forms and Templates
  - For the UPC SNIF template, click: University Park Forms and Templates

- **Verbal, Script, or Information Sheet**
  In certain situations, the IRB may approve alternative methods for telling participants about significant new information. The study staff can tell participants in person or over the phone, using scripts, or send participants an information sheet that provides the same information as the SNIF form but does not request the participant's signature.

- **Revised Consent Form, New Consent Form, or Consent Form Addendum**
  When the new information affects several elements of informed consent and/or involves extensive changes not easily described in a few pages, the participant may be asked to sign a revised informed consent form, a new informed consent form, or an addendum to the current informed consent form. The chart below compares when a SNIF can be used and when a full informed consent form may be needed. A full consent form or addendum may be necessary to provide

sufficient context regarding the new information and to document the participant's decision to remain in the study ("re-consent"). Occasionally, a study sponsor may insist that participants sign a revised consent form, even if the new information can be shared using a SNIF form. The IRB may require that participants also sign a SNIF form to ensure that changes and new information are clearly identified for participants.

Translation of SNIF forms

The HSIRB will provide Spanish translation of SNIF forms. For participants whose language is neither English nor Spanish, an interpreter must be used to read the SNIF form to the participant in the participant's language. Use of the translator must be documented in the research records.

Use a SNIF Form For:	Use a Full Informed Consent Form or an Informed Consent Addendum For:
New side effects or risks	Study extensions
Meaningful changes in frequency or severity of side effects or risks	Major changes in study design
Addition of a test or procedure	Addition of substantial research procedures
Notification of findings from this study or related studies	Changes affecting multiple sections of the consent
New conflict of interest for an investigator	

SNIF Form versus a Revised Informed Consent Form

Reminder: If the study is still open to enrollment, the informed consent form must be updated to include the new information. The updated consent form is then used to enroll new participants.

10.15 Obtaining Consent for Screening Procedures

Screening procedures to determine eligibility are considered part of the subject selection and recruitment process, and therefore, require IRB oversight. Examples include collecting data directly from subjects through written screening tools, oral responses to questionnaires, accessing private information, and medical testing. Interactions or interventions performed as part of the practice of medicine and which would be done whether or not study entry was contemplated, such as for diagnosis or treatment of a disease or medical condition, may be performed and the results subsequently used for determining study eligibility without first obtaining consent. However, a partial waiver of HIPAA authorization for screening and recruitment is required to access medical records.

Depending on the nature of the research, consent may be required before any screening procedures are performed. There are several potential options for obtaining consent for screening procedures.

Examples of screening procedures that can be performed without consent:

- When no data is kept and no medical or psychological intervention occurs
- When screening activities generally pertain to non-medical minimal risk research
- When screening involves a procedure for which written consent is normally NOT required outside the research context

Screening procedures that require a separate consent form for screening:

- When requested by sponsor / IRB
- When screening involves a medical/psychological interaction or intervention that is greater that minimal risk or involves a procedure for which written consent is normally required
- When screening data are kept
- When impractical or not feasible to enroll a subject immediately after screening