APPENDIX A: Informed Consent

Most of the questions about Informed Consent can be answered by:

UC Davis IRB SOP HRP-090 Informed Consent Process for Research.
UC Davis IRB SOP HRP-091 Written Documentation of Consent.

What is Informed Consent?

Informed Consent is the **process** of communication between a patient and physician that results in the patient’s authorization or agreement to undergo a specific medical intervention (from American Medical Association, 1998). …*It’s more than a signature on a piece of paper!*

The informed consent process is just one part of a larger system in place to safeguard participants who voluntarily participate in research projects to study new practices that may improve treatment, supportive care, screening, and disease prevention. The informed consent process provides the participant with ongoing explanations that will help them make educated decisions about whether to begin or continue participating in a trial. Rather than an endpoint, the consent document should be the basis for a meaningful exchange between the investigator and the subject.

- Obtaining informed consent is the provider’s legal responsibility. Failure to obtain informed consent renders any U.S. physician liable for negligence or battery and constitutes medical malpractice.
- Granting informed consent is the patient’s exclusive right.

Steps of the Informed Consent Process include:

- A clear discussion of the information in the Informed Consent Form;
- A signed and dated Informed Consent Form;
- Source document containing a progress note/chart note.
Special considerations and procedures are required to be employed when obtaining consent from a legally authorized representative. Prior to engaging in any research that may involve obtaining surrogate consent, please refer to UC Davis (UCD) SOP HRP-013 (http://research.ucdavis.edu/wp-content/uploads/HRP-013-SOP-Legally-Authorized-Representatives-Children-and-Guardians-2.pdf) to determine which individuals may serve as legally authorized representatives.

- Research conducted in California the following individuals are legally authorized representatives:
  1. Individual authorized to make the surrogate health care decisions
  2. Spouse
  3. Domestic Partner
  4. Adult Child
  5. Other individuals defined in California Health and Safety Code Section 24170-24179.5

- Research outside California, contact legal counsel for determination who is a legally authorized representative

Note:

- When there are two or more available persons who may give surrogate consent and are in the same order of priority, if any person expresses dissent to participation, consent shall not be considered as having been given.

- When there are two or more available persons who may give surrogate consent and are in different order of priority, refusal to consent by a person who is a higher priority surrogate shall not be superseded by the consent of a person who is a lower priority surrogate.
Informed Consent may be required if the study involves:

- living individuals about whom an investigator conducting the research obtains (1) data through intervention or interaction with the individual, or (2) information is both private information and identifiable information
- a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge
- use of human organs, tissue, or biological fluids
- clinical data or other sensitive personal information
- investigational drugs and devices
- surveys/questionnaires
- research meets the State of California’s definition of a “medical experiment”
- Effective March 16, 2015 research with newborn screening blood spots

Informed Consent may not be required if the study involves:

- Observation of legal public behavior
  - unless interaction with the subjects occur
- Study of existing publicly available data/records
  - unless interaction with the subjects occur
- Normal educational practices
  - unless interaction with the subjects occur
- Where the researcher does not manipulate the subjects’ behavior and the study does not involve more than minimal risk
- Surveys and questionnaires involving perception, cognition, or game theory and do NOT involve gathering personal information, invasion of privacy or potential for emotional distress

Waiver or Alteration of Informed Consent may be given if:

- The research is not FDA regulated
  - FDA allows for waiver of the consent process for FDA regulated research involving anonymous tissue specimens and planned emergency research. See HRP-410 Waiver or Alteration of the Consent Process for criteria
- The research does not involved non-viable neonates
- The research does not meet the State of California’s definition of a “medical experiment”
- The research involves no procedures for which written consent is normally required outside of the research context.
- The research involves no more than minimal risk to the subjects
- The waiver or alteration will not adversely affect the rights and welfare of the subjects
- The research could not practicably be carried out without the waiver or alteration
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation

Note: For a list of all criteria for an alteration or waiver of informed consent to be given at UCD see HRP-410 Waiver or Alteration of the Consent Process

Subjects should be consented prior to:

- Screening procedures performed solely for eligibility determination
- Altering the subject’s care for the purpose of research
Consent Document Content

For studies that are subject to the requirements of the FDA regulations, the informed consent documents should meet the requirements of 21 CFR 50.20 and contain the information required by each of the eight basic elements of 21 CFR 50.25(a), each of the six elements of 21 CFR 50.25(b) that is appropriate to the study, and the element in 50.25(c) for clinical trials posted on clinicaltrials.gov. IRBs have the final authority for ensuring the adequacy of the information in the informed consent document.

21 CFR 50.20 points out that except as provided in 21 CFR 50.23 and 21 CFR 50.24, an investigator may not involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative.

Importantly 21 CFR 50.20 also states:

- An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence;
- The information that is given to the subject or the representative shall be in language understandable to the subject or the representative;
- No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject’s rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

Elements of Informed Consent (FDA Regulations 21 CFR 50.25)

(a) Basic elements of informed consent.

(1) 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 identification of any procedures which are experimental.

The statement that the study involves research is important because the relationship between patient-physician is different than that between subject-investigator. Any procedures relating solely to research (e.g., randomization, placebo control, additional tests) should be explained to the subjects. The procedures subjects will encounter should be outlined in the consent document, or an explanation of the procedures, such as a treatment chart, may be attached to and referenced in the consent document.

Consent documents for studies of investigational articles should include a statement that a purpose of the study includes an evaluation of the safety of the test article. Statements that test articles are safe or
statements that the safety has been established in other studies are not appropriate when the purpose of the study includes determination of safety. In studies that also evaluate the effectiveness of the test article, consent documents should include that purpose, but should not contain claims of effectiveness.

(2) A description of any reasonably foreseeable risks or discomforts to the subject.

The risks of procedures relating solely to research should be explained in the consent document. The risks of the tests required in the study protocol should be explained, especially for tests that carry significant risk of morbidity/mortality themselves. The explanation of risks should be reasonable and should not minimize reported adverse effects.

The explanation of risks of the test article should be based upon information presented in documents such as the protocol and/or investigator’s brochure, package labeling, and previous research study reports. For IND studies, the IRB should assure that the clinical investigator submits the investigator’s brochure (when one exists) with the other study materials for review.

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research.

The description of benefits to the subject should be clear and not overstated. If no direct benefit is anticipated, that should be stated. The IRB should be aware that this element includes a description not only of the benefits to the subject, but to “others” as well. This may be an issue when benefits accruing to the investigator, the sponsor, or others are different than that normally expected to result from conducting research. Thus, if these benefits may be materially relevant to the subject’s decision to participate, they should be disclosed in the informed consent document.

If a conflict of interest has been determined by the Research Compliance and Integrity (RCI) unit, then this conflict must be disclosed within the consent form to the participants. University of California Office of the President (UCOP) has approved the following language for UCD, “This research is being funded by [Insert name of sponsor. If any personal or institutional conflicts have been identified, add additional language consistent with RPAC Op. Guid. 11-04: http://www.ucop.edu/raohome/cgmemos/11-04.pdf].

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

To enable a rational choice about participating in the research study, subjects should be aware of the full range of options available to them. Consent documents should briefly explain any pertinent alternatives to entering the study including, when appropriate, the alternative of supportive care with no additional disease-directed therapy. While this should be more than just a list of alternatives, a description of the important risks/benefits of the alternatives should be included in the written document. The person(s) obtaining the subjects’ consent, however, should be able to discuss available alternatives and answer questions that the subject may raise about them. As with other required elements, the consent document should contain sufficient information to ensure an informed decision.
(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.

Study subjects should be informed of the extent to which the institution intends to maintain confidentiality of records identifying the subjects. In addition, they should be informed that FDA might inspect study records. If any other entity, such as the sponsor of the study, may gain access to the study records, the subjects should be so informed. The consent document may, at the option of the IRB, state that subjects’ names are not routinely required to be divulged to FDA. When FDA requires subject names, FDA will treat such information as confidential, but on rare occasions, disclosure to third parties may be required. Therefore, absolute protection of confidentiality by FDA should not be promised or implied. Also, consent documents should not state or imply that FDA needs clearance or permission from the subject for access. When clinical investigators conduct a study for submission to FDA, they agree to allow FDA access to the study records. Informed consent documents should make it clear that, by participating in research, the subject’s records automatically become part of the research database. Subjects do not have the option to keep their records from being audited/reviewed by FDA.

UCOP has approved the following language for UCD, “Efforts will be made to limit use or disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the IRB and other University of California representatives responsible for the management or oversight of this study.

(6) For research involving more than minimal risk, an explanation as to whether any compensation 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.

Informed consent documents should describe any compensation or medical treatments that will be provided if injury occurs. If specific statements cannot be made (e.g., each case is likely to require a different response), the subjects should be informed where further information may be obtained. The consent should also indicate whether subjects will be billed for the cost of such medical treatments.
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No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or 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., see 21 CFR 50.20.

(7) 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.

This requirement contains three components, each of which should be specifically addressed. The consent document should provide the name of a specific research personnel and the telephone number to contact for answers to questions about: 1) the research subjects’ rights; 2) a research-related injury; and 3) the research study itself. It is as important for the subject to know why an individual should be contacted as it is for the subject to know whom to contact. In addition, a 24-hour emergency number should also be included within the consent form for emergency situations outside of regular business hours. The IRB also requires that the IRB contact information be provided within the consent form to answer any research related questions.

(8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

This element requires that subjects be informed that they may decline to participate or to discontinue participation at any time without penalty or loss of benefits.

UCD IRB provides the following UCOP approved wording “It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by University or the study sponsor or may be billed to your insurance company just like other medical costs.”

The consent document must explain whether there is compensation available in case of injury but must not waive or appear to waive the rights of the subject or release or appear to release those conducting the study from liability for negligence. Preferred UCOP approved wording is: “The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, you may call the IRB Administration at (916) 703-9151 or email at IRBAdmin@ucdmc.ucdavis.edu.” Wording such as: “will be your responsibility or that of your third-party payor” has been erroneously interpreted by some subjects to mean the insurance company is required to pay.

No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or 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., see 21 CFR 50.20.

Preferred UCOP approved wording, “You may decide not to take part in the research and it will not be held against you.”
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Language limiting the subject’s right to withdraw from the study should not be permitted in consent documents. If the subjects who withdraw will be asked to permit follow-up of their condition by the researchers, the process and option should be outlined in the consent document.

(b) Additional elements of informed consent (provided when appropriate)

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.

A statement that there may be unforeseen risks to the embryo or fetus may not be sufficient if animal data are not available to help predict the risk to a human fetus. Informed consent documents should explain that mutagenicity (the capability to induce genetic mutations) and teratogenicity (the capability to induce fetal malformations) studies have not yet been conducted/completed in animals. [Note: The lack of animal data does not constitute a valid reason for restricting entry of women of childbearing potential into a clinical trial.] Subjects, both women and men, need to understand the danger of taking a drug whose effects on the fetus are unknown. If relevant animal data are available, however, the significance should be explained to potential subjects. Investigators should ensure that the potential risks that the study poses are adequately explained to subjects who are asked to enter a study. If measures to prevent pregnancy should be taken while in the study, that should be explained.

Preferred UCOP approved wording, “The procedures in this research are known to hurt a pregnancy or fetus in the following ways: [Omit the previous sentence if there are no known risks.] The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death. [Omit the previous two sentences for research whose risk profile in pregnancy is well known.] You should not be or become pregnant [include as applicable “or father a baby”] while on this research study.”

FDA guidance on the inclusion of women in clinical trials [58 FR 39406] now gives IRBs broader discretion to encourage the entry of a wide range of individuals into the early phases of clinical trials. FDA urges IRBs to question any study that appears to limit enrollment based on gender and/or minority status. Statements such as, “you may not participate in this research study if you are a woman who could become pregnant” should not routinely be included in informed consent documents.

2. Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent.

When applicable, subjects should be informed of circumstances under which their participation may be terminated by the investigator without the subject’s consent. An unexplained statement that the investigator and/or sponsor may withdraw subjects at any time does not adequately inform the subjects of anticipated circumstances for such withdrawal.

A statement that the investigator may withdraw subjects if they do not “follow study procedures” is not appropriate. Subjects are not in a position to know all the study procedures. Subjects may be informed, however, that they may be withdrawn if they do not follow the instructions given to them by the investigator.
(3) Any additional costs to the subject that may result from participation in the research.

If the subjects may incur an additional expense because they are participating in the research, the costs should be explained. IRBs should consider that some insurance and/or other reimbursement mechanisms may not fund care that is delivered in a research context.

(4) The consequences of a subjects’ decision to withdraw from the research and procedures for orderly termination of participation by the subject.

When withdrawal from a research study may have deleterious effects on the subject’s health or welfare, the informed consent should explain any withdrawal procedures that are necessary for the subject’s safety and specifically state why they are important to the subject’s welfare. An unexplained statement that the subject will be asked to submit to tests prior to withdrawal, does not adequately inform the subjects why the tests are necessary for the subject’s welfare.

For FDA regulated research, subjects that wish to withdraw from the study must be informed that already collected data from research cannot be removed from the research database.

(5) 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.

When it is anticipated that significant new findings that would be pertinent to the subject’s continued participation are likely to occur during the subject’s participation in the study, the IRB should determine that a system, or a reasonable plan, exists to make such notification to subjects.

(6) The approximate number of subjects involved in the study.

If the IRB determines that the numbers of subjects in a study is material to the subjects’ decision to participate, the informed consent document should state the approximate number of subjects involved in the study.

Appropriate Use of Language

The IRB should ensure that technical and scientific terms are adequately explained, and that complex scientific concepts are properly converted into simple concepts that the typical subject can read and comprehend. Although not prohibited by the FDA regulations, use of the wording, “I understand…” in informed consent documents may be inappropriate as many prospective subjects may not fully understand the scientific and medical significance of all the statements. Consent documents are more understandable if they are written just as the clinical investigator would give an oral explanation to the subject, that is, the subject is addressed as “you” and the clinical investigator as “I/we.” This writing style also helps to communicate that there is a choice to be made by the prospective subject. Use of first person may be interpreted as presumption of subject consent, i.e., the subject has no choice. Also, the tone of the first person “I understand” seems to misplace emphasis on legal statements rather than on explanatory wording enhancing the subject's comprehension.

Subjects are not in a position to judge whether the information provided is complete. Subjects may certify that they understand the statements in the consent document and are satisfied with the explanation provided by the consent process (e.g., “I understand the statements in this informed
consent document). “They should not be required to certify completeness of disclosure (e.g., “This study has been fully explained to me,” or, “I fully understand the study.”)

The FDA discourages use of phrases such as, “FDA has given permission...” or “FDA has approved...” in consent documents. Technically, the FDA does not “approve” drug studies under an IND (Investigational New Drug) Application. FDA does approve device studies under IDE (Investigational Device Exemption).

Consent documents should not contain unproven claims of effectiveness or certainty of benefit, either explicit or implicit, that may unduly influence potential subjects. Overly optimistic representations are misleading and violate FDA regulations concerning the promotion of investigational drugs [21 CFR 312.7] or investigational devices [21 CFR 812.7(d)] as well as the requirement to minimize the possibility of coercion or undue influence [21 CFR 50.20].

The FDA believes that an explicit statement that an IRB has approved solicitation of subjects to participate in research could mislead or unduly induce subjects. Subjects might think that, because the IRB had approved the research, there is no need to evaluate the study for themselves to determine whether or not they should participate.

The informed consent documents may not contain any exculpatory language through which the participant is made to waive or appear to waive any of the participant’s legal rights, or releases or appears to release the investigator, the sponsor, the University, or its agents from liability for negligence.

**Consent Documents for FDA Submissions**

Investigational New Drug Application (IND) is not required to contain a copy of the consent document. If the sponsor submits a copy, or if FDA requests a copy, the Agency will review the document and may comment on the document’s adequacy.

For significant risk medical devices, the consent document is considered to be a part of the investigational plan in the Application for an Investigational Device Exemption (IDE). FDA always reviews these consent documents. The Agency’s review is generally limited to ensuring the presence of the required elements of informed consent and the absence of exculpatory language. Any substantive changes to the document made by an IRB must be submitted to FDA for review and approval.

**Revision of Consent Documents during a study**

Under certain circumstances subjects have to be re-consented.

- Study participation is ongoing and
  - Subject reaches age 18
  - Subject regains competency
- New study information
  - Substantial Amendments to Protocol
  - Changes in study procedures
  - Changes in risk
  - Changes in subject payment
- New treatment became available
When these changes require revision of the informed consent document, the IRB has to approve the changes to the informed consent document prior to utilization by research personnel. In addition, the IRB should have a system that identifies the revised consent document, in order to preclude continued use of the older version. Recommendation from most IRB’s is that the investigator places version dates within the informed consent document. Documentation of re-consent should be provided.

Readability of Informed Consent

**Basic Principles of Readability:**

- Write at 8th grade level or below (use MS Word to check readability levels)
- Use common, everyday words
- Define complex words using “Alternative word suggestions” or Glossary of Human Subject Terminology: [http://research.ucdavis.edu/gt/g](http://research.ucdavis.edu/gt/g)
- Use short sentences < 15 words
- Use active form
- Use formatting (Bullets, white spaces, shaded boxes) to improve the visual understanding. Use visual aids, examples, analogs

**Non-English Speaking Subjects**

In the case of a non-English speaking subject, the FDA fully expects that a translated version of the ICF will be provided to the study subject. IRB approves the translated ICF prior to utilization.

A person who reads and speaks this language should administer the consent; alternatively, a translator could be called in, however, while a translator may be helpful in facilitating conversation with a non-English speaking subject, routine ad hoc translation of the consent document should not be substituted for a written translation.

If a non-English speaking subject is unexpectedly encountered, and investigators do not have a written translation of the consent document and the IRB has approved the research for inclusion of non-English speaking subjects, the investigators must rely on oral translation. Investigators should carefully consider the ethical/legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented, the subject’s consent will not truly be informed and may not be legally effective.

If investigators enroll subjects without an IRB approved written translation, a “short form” written consent document, in a language the subject understands, should be used to document that the elements of informed consent required by 21 CFR 50.25 were presented orally. The UC Davis IRB has a list of pre-approved short forms available for this use. Documentation of a short form is described in 21 CFR 50.27(b)(2). Briefly, when a short form consent document is to be used the IRB should review and approve the written summary of the full information to be presented orally to the subjects. An impartial witness is required to attest to the adequacy of the consent process and to the subject’s voluntary consent. Therefore, the witness must be present during the entire consent interview, not just for signing the documents. The subject or the subject’s legally authorized representative must sign and date the short form and a copy of the summary. The witness must sign and date both the
short form and a copy of the summary, and the person actually obtaining the consent must sign and date the short form and a copy of the summary. The subject or the representative must be given a copy of the signed and dated summary as well as a copy of the signed and dated short form.

The translator should be fluent both in English and the language understood by the subject/representative. The translator may be a family member or friend of the subject/representative. The translator can also act as the impartial witness.

Impartial witness is a person not involved in the design, conduct, or reporting of the research study. The impartial witness may be a family member or friend.

For specific guidance on using “short forms” at UC Davis see HRP-090 Informed Consent Process for Research.

**Illiterate English-Speaking Subjects**

A person who speaks and understands English, but does not read and write, can be enrolled in a study by “making their mark” on the consent document, when consistent with applicable state law. In addition, if a subject is unable to read or if a legally authorized representative is unable to read, an impartial witness must be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject’s legally authorized representative, and after the subject or the subject’s legally authorized representative has orally consented to the subject’s participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject’s legally authorized representative, and that informed consent was freely given by the subject or the subject’s legally authorized representative.

Impartial witness is a person not involved in the design, conduct, or reporting of the research study. The impartial witness may be a family member or friend.

For specific guidance on using “short forms” at UC Davis see HRP-090 Informed Consent Process for Research and HRP-091 Written Documentation of Consent.

**Physical disabilities preventing reading or writing**

A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be entered into a study if they are competent and able to indicate approval or disapproval by other means. The subjects may be entered into the study if:

1. the person retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally (still competent), and
2. is able to indicate approval or disapproval to study entry.

The consent form should document the method used for communication with such subject and the specific means by which the subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document. A video tape recording of the consent interview is recommended.
**Vulnerable Populations**

The federal regulations require that IRBs give special consideration to protecting the welfare of particularly vulnerable subjects, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. For research to which the HHS regulations are applicable, the HHS regulations set forth specific provisions on research involving fetuses, pregnant women, and human in vitro fertilization [45 CFR 46 Subpart B], prisoners [45 CFR 46 Subpart C]; and children [45 CFR 46 Subpart D]. In general, these special regulations allow IRBs to approve research that is of minimal risk or that will benefit the subjects directly. Investigations involving these subjects that present significantly greater than minimal risk without direct benefit to them must be reviewed and approved by the Secretary of Health and Human Services, in consultation with appropriate experts.

**Consent and Assent of children**

Where the research subject is a minor, special attention should be given to the informed consent process, because, as a general rule, minors lack the legal capacity to consent to the treatments or procedures involved in the research. The HHS regulations for conduct of studies in children may be used as guidance [45 CFR 46, Subpart D].

Unless the IRB has waived the requirement to obtain consent, when research involves children consent may only be obtained from biologic or adoptive parents or an individual legally authorized to consent on behalf of the child to general medical care. Before obtaining permission from an individual who is not a parent, contact legal counsel (HRP-013 Legally Authorized Representatives, Children, and Guardians)

**Financial responsibilities of subjects**

Financial responsibilities of the subjects should be clearly explained in the consent documents. Generally, there are three options.

1. the study is fully paid for by the sponsor, and no billing to the patient insurance occurs;
2. the study is fully paid for by insurance and no billing to the study occurs;
3. some study costs are billed to the insurance and some are covered by the study sponsor. This delineation should be reflected in the consent documents.

The consent should also clearly explain, if applicable, that subjects are still responsible for co-pays and deductibles based on their insurance coverage. Self-pay patients will be responsible for the costs of all services and procedures, unless the sponsor pays for all services/procedures for all participants on the study. The sponsor cannot be billed for the costs already billed to the third party, unless the patient qualifies for assistance under UCDHS’ charity care policy (UCDHS P&P 1891).

**Subject Compensation for Participation**

It is not uncommon for subjects to be paid for their participation in research, especially in the early phases of investigational drug, biologic or device development. Payment to research subjects for participation in studies is not considered a benefit; it is compensation for their time and effort for participation. Financial incentives are often used when health benefits to subjects are remote or non-existent, such as in cases when healthy subjects are recruited. The amount and schedule of all payments should be presented to the IRB at the time of initial review. The IRB should review both the amount of payment and the proposed method and timing of disbursement to assure that neither is
coercive or presents undue influence [21 CFR 50.20]. It is not advisable to pay a financial incentive to a subject when the patient is seen for research related services and insurance is going to be billed.

Any credit for payment should accrue as the study progresses and not be contingent upon the subject completing the entire study. Unless it creates undue inconvenience or a coercive practice, payment to subjects who withdraw from the study may be made at the time they would have completed the study (or completed a phase of the study) had they not withdrawn. For example, in a study lasting only a few days, an IRB may find it permissible to allow a single payment date at the end of the study, even to subjects who had withdrawn before that date.

While the entire payment should not be contingent upon completion of the entire study, payment of a small proportion as an incentive for completion of the study is acceptable to FDA, providing that such incentive is not coercive. The IRB should determine that the amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn. All information concerning payment, including the amount and schedule of payment(s), should be set forth in the informed consent document.

Subject injury
Since 1978, both HHS and FDA have required an additional element of consent regarding treatment and compensation for injury resulting from participation from research.

The current regulations for consent forms for research involving more than minimal risk indicate that the following must be included:

- An explanation as to whether any compensation and whether any medical treatments are available if injury occurs and,
- If so, what they consist of, or where further information may be obtained

Documentation of Informed Consent
A signed and dated consent form is not sufficient in documenting the informed consent process for clinical trials. A written note (i.e. progress report, clinic note, etc.) should be created at each encounter documenting the communication between investigator and subject about the research. This note should include what was discussed; the fact that the subject’s questions were answered, if the subject received a copy of the consent form to take home, or if the subject signed the consent form. The accumulation of these notes over a period of time will document the consenting process (see SOP HRP-091 Written Documentation of Consent).

In limited circumstances, the IRB can waive the requirement for the investigator to obtain a written documented (signed) consent form for some or all research participants (HRP-411).
A. Risk of Breach of Confidentiality

The IRB can waive the requirement for written documentation of informed consent for non-exempt research if all of the following criteria are met:

- The only record linking the participant and the research would be the consent document;
- The principal risk would be potential harm resulting from a 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;
- The research is not FDA-regulated.
- The research does not meet the State of California’s definition of a medical experiment.

B. Minimal Risk Research

The IRB can waive the requirement for written documentation of informed consent for non-exempt research if all the following criteria are met:

- The research presents no more than minimal risk of harm to participants;
- The research involves no procedures for which written consent is normally required outside of the research context.
- The research does not meet the State of California’s definition of a medical experiment.
- Written information describing the research is to be provided to the subject or the subject’s legally authorized representative,

-OR-

- Written information describing the research does not need to be provided to the subject or the subject’s legally authorized representative

C. Additional Requirements

1. When the requirement for written documentation of consent is waived, the IRB must review a written description of the information (i.e., a “script”) that will be provided to participants (e.g., when consent is obtained by telephone, online, or presented orally). This information must include the elements of informed consent and any applicable additional elements as described above unless an alteration of consent has also been approved by the IRB.

2. When the requirement for written documentation of consent is waived, the IRB may also require that an investigator provide participants with a document regarding the research. Examples include approved consent forms (without signature lines), cards containing researcher and/or third party contact information, and information sheets outlining study procedures.
Waiver or Alteration of the Consent Process (HRP-410).

If the study falls under the State of California Definition of a medical experiment, the waiver cannot be granted.

A “medical experiment” is defined in the California Health and Safety Code Section 24174, as:

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.

If it does not fall under this definition then other criteria must be met in order to justify the Waver of Informed Consent process (see HRP-410 for options).

Separate provisions are given for FDA-regulated research involving anonymous tissue specimens (in vitro diagnostic studies with leftover human specimens that are not individually identifiable) and Planned Emergency Research.

Use of Facsimile, Mail, Secure email or Secure Internet access to Document Informed Consent

The IRB may approve a process that allows the informed consent document to be delivered by facsimile, mail, secure e-mail account or secured internet address to the potential participant or the potential participant’s legally authorized representative and to conduct the consent interview by telephone when the participant or the legally authorized representative can read the consent document as it is discussed with the person obtaining consent. Alternatively, the subject may bring the signed and dated consent form to their next visit with the researcher. All other applicable conditions for documentation of informed consent must also be met when using this procedure.

Deception Studies

As a general rule, deception is not acceptable when doing research with humans. Deception is the intentional misleading of subjects or the withholding of full information about the nature of the experiment. Misleading or omitted information might include the purpose of the research, the role of the researcher, or what procedures in the study are actually experimental. Deception increases ethical concerns, because it interferes with the ability of the subject to give informed consent. However, deception is arguably necessary for certain types of behavioral research. Because humans act differently depending on circumstances, full knowledge by the subject might bias the results. For example, in order to learn about decision-making practices of physicians without influencing their practice-style, they may be told that the research study involves “communication behaviors” in a broad sense. Federal regulations permit but establish limitations on the use of deception. The IRB will review any proposal that suggests using deception or misrepresentation very carefully. The IRB will require an in-depth justification of why the deception is necessary for the study and the steps the investigator will take to safeguard the participants. This is considered to be an alteration of the informed consent process and must meet specific Federal and State regulations for approval.
Consenting Patients for Data Use in Advertising and Social Media

The consent form (Consent for Media, Public Communication, Fund raising or Marketing Purposes) is referenced in P&P 1426 (“Authorization and Consent to Photograph or Interview”).


The actual consent form can be found on the Patient Care Services website under the heading PCS Templates:


California Subject Bill or Rights

California Assembly Bill 1752 and the Health and Safety Code’s definition of medical experimentation encompasses almost all studies involving biomedical procedures, placebo controls, innovative therapy, and/or normal volunteer subjects. Thus, for these types of studies, the Experimental Subject’s Bill of Rights must be given to subjects along with a copy of the consent form or information sheet for the study. There should be a reference at the end of the consent form indicating that the subject has received or will receive the Experimental Subject’s Bill of Rights.

Experimental Subject’s Bill of Rights

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any drug or device to be used.
  - Any common or important discomforts and risks.
  - Any benefits you might expect.
  - Other procedures, drugs, or devices that might be helpful, and their risks and benefits compared to this study.
  - Medical treatment, if any, that is available for complications.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document.
  If you agree to take part, you will be given a copy of this document.