

Policy Number: 32

Title: Waiver or Alteration of Informed Consent for Human Subjects Research

Date of Last Revision: 01/21/07; 11/20/10, 09/14/18, 04/07/22, 07/29/22

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to grant a waiver or alteration of informed consent for research in accordance with the Federal regulations and IRB policies and procedures.

Generally, the IRB must assure that provisions are made to obtain legally effective informed consent prospectively from each research participant or the participant's legally authorized representative.

If the research involves accessing Student Records the research must comply with Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99): The federal regulation that protects the privacy of student education records. This regulation applies to all schools that receive funds under an applicable program of the U.S. Department of Education. Generally, a waiver of the consent process is prohibited. The parent or eligible student must provide permission or consent to obtain any information from a student's education record for research purposes.

When research involves a [test article](#) and is subject to Food and Drug Administration (FDA), except as provided in 21 CFR 50.23 and 21 CFR 50.24 and described below in sections V, VI and VII, no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.

In order for an IRB to waive or alter consent, the IRB must find and document one of the following options:

- I. **Requirements for Waiver or Alteration of Consent – Screening, Recruiting or Determining Eligibility (Common Rule 2018)**
 - A. An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:
 1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
 2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

- II. **Broad Consent Preclusion for Waiver of Consent (Common Rule 2018)**
 - A. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements of Broad consent at 45 CFR 46.116(d) and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.
 - B. **UCI has elected to not implement Broad Consent.**

- III. **Requirements for Waiver or Alteration of Consent (Items in blue are shared with the FDA per the July 2017 Information Sheet Guidance)**
 - A. The research or clinical investigation involves no more than minimal risk (per 21 CFR 50.3(k) or 21 CFR 56.102(i)) to the participant; and
 - B. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format; and
 - C. The waiver or alteration will not adversely affect the rights and welfare of the participants; and
 - D. The research or clinical investigation could not practicably be carried out without the waiver or alteration; and
 - E. Whenever appropriate, the participants will be provided with additional pertinent information after participation

- IV. **Requirements for Alteration of Consent (45 CFR 46.117(c)(1)) (also known as a waiver to obtain a signed informed consent form)**
 - A. That 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. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; and
 - B. That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
 - C. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.
 - D. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.

- V. **FDA Enforcement Discretion for In Vitro Diagnostics**

Under FDA's regulations governing the conduct of in vitro diagnostic (IVD) device studies, the definition of "subject" includes individuals on whose specimens an investigational device is used [see 21 CFR 812.3(p)]. This means that this research is subject to FDA regulations and thus a waiver of consent cannot be granted. The FDA believes that it is possible in certain circumstances for IVD device investigations to be conducted using leftover specimens obtained without

informed consent while protecting the human subjects who are the source of such specimens.

The FDA intends to exercise enforcement discretion as to the informed consent requirements for clinical investigators, sponsors, and IRBs if an in vitro diagnostic device investigation is performed and all of the following are true:

1. The investigation meets the IDE exemption criteria at 21 CFR 812.2(c) (3): A diagnostic device, if the testing:
 - (i) Is noninvasive,
 - (ii) Does not require an invasive sampling procedure that presents significant risk,
 - (iii) Does not by design or intention introduce energy into a subject, and
 - (iv) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
2. The study uses leftover specimens, that is, remnants of specimens collected for routine clinical care or analysis that would have been discarded. The study may also use specimens obtained from specimen repositories or leftover specimens that were previously collected for other research purposes.
3. The specimens **are not individually identifiable**, i.e., the identity of the subject is **not known to and may not readily be ascertained by the investigator or any other individuals associated with the investigation**, including the sponsor. If the specimen is coded, it will be considered to be not individually identifiable if neither the investigator(s) nor any other individuals associated with the investigation or the sponsor can link the specimen to the subject from whom the specimen was collected, either directly or indirectly through coding systems.
4. The specimens may be accompanied by clinical information as long as this information does **not make the specimen source identifiable** to the investigator or any other individual associated with the investigation, including the sponsor.
5. The individuals **caring for the patients are different from and do not share information about the patient** with those conducting the investigation.
6. The **specimens are provided to the investigator(s) without identifiers** and the supplier of the specimens has established policies and procedures to prevent the release of personal information.
7. The **study has been reviewed by an IRB**.

VI. **Emergency use of a Drug or Device Exception to the Requirement for Consent at 21 CFR 50.23(a)-(c)**

Emergency Use means the use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. FDA regulations exempt research from prior IRB review for the use of a test article in a life-threatening situation in which no standard treatment is available. Exception

The use of informed consent is required unless the physician imposing an emergency use situation and another physician not otherwise participating in the clinical investigation certify in writing that all of 21 CFR 50.23(a) have been met:

- A. The human subject is confronted by a life-threatening situation necessitating the use of the test article.
- B. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
- C. Time is not sufficient to obtain consent from the subject's legal representative.
- D. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

(See Policy # 45.)

VII. **Exception from Informed Consent Requirements for Planned Emergency Research (21 CFR 50.24 or 45 CFR 46.101(i))**

The IRB may approve planned research in an emergency setting without the informed consent of the participants or their legally authorized representatives in a limited class of emergency situations when the following criteria are met and documented:

- A. The target population for the research is in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
- B. Obtaining informed consent is not feasible because:
 1. The subjects will not be able to give their informed consent as a result of their medical condition;
 2. The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
 3. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
- C. Participation in the research holds out the prospect of direct benefit to the subjects because:
 1. The subjects are facing a life-threatening situation that necessitates intervention;
 2. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
 3. The risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of the proposed intervention or activity.
- D. The clinical investigation could not practicably be carried out without the waiver.
- E. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the Investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The Investigator must agree to summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing

- review.
- F. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Federal regulations and IRB policies and procedures. The informed consent procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.
 - G. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
 1. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
 2. Prior to the initiation of the clinical investigation, public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn of plans for the investigation and its risks and expected benefits;
 3. At the completion of the clinical investigation there are plans for public disclosure of sufficient information to apprise the community and researchers of the study. The information must include the demographic characteristics of the research population and results of the clinical investigation.
 4. Establishment of an independent data and safety monitoring committee to exercise oversight of the clinical investigation; and
 5. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the Investigator must commit to attempting to contact within the therapeutic window, the subject's family member who is not a legally authorized representative and asking whether he/she objects to the subject's participation in the clinical investigation. The Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
 - H. Procedures must be in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document, specifically that the he/she may discontinue the subject's participation at any time without penalty or loss of benefits of which the subject is otherwise entitled.
 - I. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible.
 - J. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.
 - K. All clinical investigation records, including regulatory files, must be maintained for at least 3 years after the completion of the clinical investigation and will be accessible for inspection and copying by the regulatory authorities, as applicable.
 - L. Clinical investigations that are granted an exception to the informed

consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies that the clinical investigation may include subjects who are unable to consent. The submission of these clinical investigations to the FDA for a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for this IND/IDE may not be submitted as an amendment to the existing IND/IDE.

- M. If the IRB determines it cannot approve a request for exception from informed consent requirements in planned emergency research because the clinical investigation does not meet the criteria according to Federal regulations, IRB policies and procedures, or other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the Lead Researcher who will forward to the sponsor of the clinical investigation.

VIII. **Planned Emergency Research Not Subject to FDA Regulations (Informed Consent Requirements in Emergency Research (OPRR Letter, 1996))**

The IRB Committee determines:

- A. The research does not meet FDA regulations in 21 CFR 50; and Items A-J as stated above are met. The term “clinical investigation” may be replaced by “research.”
- C. For the purposes of this waiver “family member” means any of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the participant was the equivalent of a family relationship.

IX. **Planned Emergency Research funded by a Department of Defense entity:** If the research subject meets the definition of “experimental subject,” a waiver of the consent process is prohibited unless a waiver is obtained from the Secretary of Defense.

- A. If the research participant does not meet the definition of “experimental subject”, policies and procedures allow the IRB to waive the consent process.

X. **Waiver for Research Activities Designed to Study Certain Aspects of Public Benefit or Service Programs**

- A. The research or demonstration project is to be conducted by or subject to the approval of State or local government officials and is designed to study, evaluate, or otherwise examine:
 1. Public benefit or service programs;
 2. Procedures for obtaining benefits or services under those programs;
 3. Possible changes in or alternatives to those programs or procedures;or
 4. Possible changes in methods or levels of payment for benefits or services under those programs; *and*
 2. The research could not practicably be carried out without the waiver or alteration.

References:

45 CFR 46
45 CFR 46.116

21 CFR 50 and 56

21 CFR 50.24

DoD: 10 USC 908(b)

ED: 34 CFR 99

Informed Consent Requirements in Emergency Research (OPRR Letter, 1996):

<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/emergency-research-informed-consent-requirements/index.html>

FDA Information Sheets- Exception from Informed Consent for Studies Conducted in Emergency Settings: <https://www.fda.gov/media/80554/download>

FDA Guidance Waiver of Consent/ Minimal Risk:

<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM566948.pdf>

FDA Guidance / In Vitro Devices:

<https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm071265.pdf>

FDA Guidance/ Children:

<https://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/ucm119111.htm>

Procedure Number: 32.A**Title: Procedure for Waiver or Exception of Informed Consent****Purpose:**

This procedure provides guidance on obtaining a waiver of informed consent; and requesting approval for exception from informed consent in planned emergency research from the UCI Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. Waiver or alteration of informed consent.
 - 1. The LR will assess the proposed research to determine if it meets regulatory requirements for a waiver or alteration of informed consent.
 - 2. The LR will complete and submit the applicable documentation to support the request for a waiver or alteration of informed consent, in accordance with the current and any related IRB policies.
- B. Exception from informed consent requirements for planned emergency research.
 - 1. The LR is responsible for providing all study documents and any additional materials requested by the IRB to prepare and conduct community consultation and public disclosure of the proposed research.
 - 2. The LR will prepare and submit to the IRB materials in preparation for public disclosure following completion of the research.
 - 3. The LR will establish an independent data and safety monitoring committee to exercise oversight of the clinical investigation.
 - 4. When the LR is unable to locate a legally authorized representative, the LR will attempt to contact, within the therapeutic window, the participant's family member who is not a legally authorized representative, to ask whether he or she objects to the individual's participation. A summary of efforts to contact the legally authorized representative and family members is made available to the IRB at the time of continuing review.

II. IRB Committee Responsibilities

- A. The IRB Reviewers will consider the request for a waiver of informed consent and the LR's justification verifying and documenting those regulatory conditions are applicable to the proposed research activity.
- B. If the IRB differs in their determination from the LR's request, this will be documented in the electronic IRB submission and management system.
- C. IRB determinations will be noted on the final, IRB approved IRB Application, along with the IRB approval letter.
- D. When amendments are made to a currently approved research study, the waiver of informed consent is reassessed by the IRB Committee, Chairperson or their designee, and a determination made as to whether the conditions for the waiver have been altered, necessitating the rescinding of the waiver. If this occurs, the IRB also determines whether currently enrolled participants must be re-consented by the LR.
- E. Exception from informed consent requirements for planned emergency research requires additional protections for the rights and welfare of the participants including, but not limited to the following:
 - 1. Consultation with representatives of the communities in which the investigation is conducted and from which the participants are drawn;

2. Public disclosure of plans for the investigation and its risks and expected benefits to the communities in which the research is conducted and from which the participants are drawn;
3. Public disclosure at the completion of the research to apprise the community and researchers of the study. This may include the demographic characteristics of the research population and study results.

III. IRB Analyst or Higher Responsibilities

- A. As applicable to the level of review, and considering the IRB review timeframe, the Analyst conducts a pre-review of the informed consent process and documents submitted with an IRB application to determine that the correct forms have been utilized for the targeted population; assesses the readability of the document and assures that all the necessary elements as required by the Federal regulations are present for adequate informed consent, including if any additional elements are appropriate.
- B. If additional information regarding the informed consent process or documentation is needed, the Analyst contacts the LR and requests the additional information.