UCI University of California, Irvine

Office of Research
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September 2021

RE: General Information Often Requested by Study Sponsors

Dear UCI Investigators:

This letter is provided in response to requests from study sponsors.

Federalwide Assurance: UCI holds a current, approved Federalwide Assurance (FWA) of Compliance (**FWA 00004071**) with the Department of Health and Human Services (HHS). This assurance was approved on January 31, 2003 and remains in effect unless the University is otherwise notified. Renewal is required every five years. UCI agrees to uphold the ethical principles of the Belmont Report. UCI will apply DHHS regulations (45 CFR 46, including Subparts B, C, & D) to all federally funded research involving human participants. Commensurate protections are in place for all other human subject research conducted at or under the jurisdiction of UCI.

IRB Registration with the FDA: The Food and Drug Administration (FDA) require Institutional Review Boards (IRBs) to register through a system maintained by HHS. UCI is registered with HHS. **IORG0000236** represents the overall registration, with each IRB receiving a distinct identification number under the IORG. Renewal is required every three years. The following IRBs are currently registered with the Office for Human Research Protections (OHRP)

Identification #	Name	City	State
IRB00000393	UCI IRB #1 - Biomedical 'A'	Irvine	CALIFORNIA
IRB00000394	UCI IRB #2 - Biomedical 'B'	Irvine	CALIFORNIA
IRB00000395	UCI IRB #3 - Social Behavioral 'C'	Irvine	CALIFORNIA
IRB00008624	UCI IRB #4 – Compliance 'E'	Irvine	CALIFORNIA
IRB00011147	UCI IRB # 5 – Biomedical 'WB'	Irvine	CALIFORNIA
COMPONENTS IDENTIFIED FOR THIS ASSURANCE			
Name		**City**	**State**
The Regents of the University of California, as described in Article IX, Section 9 of the California Constitution (University of California, Irvine)		Irvine	CALIFORNIA

For additional information about UC Irvine's Federalwide Assurance or IRB Registration information visit the OHRP portal and type in FWA# 00004071 or IORG# 0000236.

IRB Membership: As noted above, UCI holds a current, approved FWA of compliance with HHS. In the document, UCI agrees to uphold the ethical principles of the Belmont Report. UCI will apply DHHS regulations (45 CFR 46, including Subparts B, C, & D) to all federally-funded research involving human participants. Commensurate protections are in place for all other human subject research conducted at or under the jurisdiction of UCI. UCI's IRB meets the FDA requirements for IRB membership as defined in Section 21 CFR 56.107, which is identical to Section 45 CFR 46.107. Please see the member rosters at on the UCI Human Research Protections web site.

In addition, any member of the IRB who is the Lead Researcher, Faculty Sponsor or Co-Investigator on a research protocol is prohibited from serving as a primary or secondary reviewer and must recuse him/herself from all IRB deliberations and voting relative to the protocol. IRB members are required to disclose such

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involvement in projects to be review by the IRB and must physically leave the room prior to the committee's review of the research.

Compliance with the Food and Drug Administration (FDA) Regulations and International Conference on Harmonization (ICH) Guidelines: All clinical investigations are reviewed in accordance with FDA regulations at 21 CFR Parts 50 and 56. All clinical investigations involving the investigational use of drugs and devices are reviewed in accordance with FDA regulations at 21 CFR Parts 312 (drugs) and 812 (devices). UCI IRBs follow ICH E6 to the extent it agrees with FDA Good Clinical Practice (GCP).

Compliance with HIPAA and CMIA: Due to the complexities of both HIPAA and CMIA, and the University of California's status as a hybrid covered entity, a separate, system-wide UC Research Authorization form is used to comply with all applicable laws concerning access, use and disclosure of medical health information for research and clinical trials. UCI IRBs require use of this form in situations where HIPAA regulations apply. The UCI IRBs do not review or approve the content of this form on a study by study basis, as it cannot be altered; therefore, the UCI IRB does not approve or stamp the form with a specific study/protocol number. When the IRB determines that subjects should sign a HIPAA Research Authorization in order to use or disclose Protected Health Information (PHI) for research, subjects are to sign the UC HIPAA Research Authorization as a part of the informed consent process for participation in the study. The IRB will document the requirement to obtain UC HIPAA Research Authorization on the IRB approval letter.

AAHRPP and Care-Q: UCI is not currently accredited with Association for Accreditation of Human Research Protection Programs (AAHRPP). UCI elected to not renew their Association for Accreditation of Human Research Protection Programs (AAHRPP) certification, which was maintained without lapse from September 2005 through September 2016. In 2018, UCI received certification from the Consortium for Applied Research Ethics Quality (Care-Q).

Exempt Research: Exempt confirmation may be made by various mechanisms at UCI. All undergraduate exempt research is submitted for exempt review and confirmation through the Undergraduate Research Opportunities Program (UROP). The Exempt Self-Determination Tool may be used for self- determining Exempt Research, including UROP. As part of the UROP and Exempt Self-Determination Tool process, IRB review is not required. Certain exceptions apply. Please refer to UCI HRPP Policy # 12 for current exceptions.

Expiration Date for HIPAA Authorization: Based on the Privacy rule, core elements of the HIPAA Authorization form includes an authorization expiration date or expiration event that relates to the individual or to the purpose of the use or disclosure. The current UCI HIPAA template provides this language (Section H): *Does my permission expire? This permission to release your Personal Health Information expires when the research ends and all required study monitoring is over*.

Compliance with 21 CFR 11: UCI will transition to Kuali Research Protocols (KRP) on September 7, 2021. KRP is a 21 CFR 11-ready system. Accordingly, the process of validation for 21 CFR 11 has begun. When the UCI version of KRP is validated, this letter will be updated, with a reference or link to supporting documentation.

Documents Approved and Stamped by the IRB: The UCI IRB approves the IRB application, all Informed consent documents, and all recruitment materials. The UCI IRB *approval stamp* is placed on all pages of the consent documents (i.e., informed consent form, study information sheet, assent form), and all pages of recruitment materials. Neither HHS nor the FDA regulations require an approval or expiration date stamp on IRB approved materials, however, per UCI Human research Protections (HRP Policy, the UCI IRB stamps the latest IRB approved documents with the date of approval in an effort to help ensure that the study team use IRB approved materials when enrolling subjects. For studies and transactions approved after September 7, 2021, these documents will be released by HRP Staff in KRP under the attachments section.

Please note: the UCI IRB approval stamp is placed on the most recently revised version protocol materials. At renewal, if protocol materials are unchanged, they *will not* be re-stamped. The most recent IRB approval dates, including the date of study expiration are stated on the UCI IRB approval letter.

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Attachments Submitted for IRB Review: The UCI IRB approval letter does not approve the sponsor master protocol and investigator's brochure. This is because the IRB only reviews these documents. These documents are not developed by UCI personnel. Moreover, they do not contain all of the information needed for UCI IRB, such as local context details. Additionally, these sponsor documents may contain information not under purview of the IRB such as the method of transmitting data and the shipping of specimens.

IRB Approval Letters: Neither HHS nor the FDA regulations require a signature for the IRB approval letter. In accordance with federal regulations, and in an effort to facilitate the expediency of approval processing, it is not UCI IRB policy to require a signature on IRB approval letters.

Re-Consent Process: Per HHS 45 CFR 46.116(b)(5) and FDA 21 CFR 50.25(b)(5) significant new findings that develop during the course of the research which may relate to the research subject's willingness to continue participation must be provided to subjects. When significant new findings occur, researchers must submit an amendment request, revising study related materials, including the consent document, as applicable. In addition, UCI IRB recommends that researchers submit a re-consent cover letter. The re-consent cover letter is designed to facilitate the re-consent process by emphasizing the revisions made to the study. The IRB approved re-consent memo should be attached to the front of the revised consent form and used as a supplement to facilitate the re-consent process. If the subject agrees to continue participation, appropriate signatures must be obtained on the revised consent form. Subject initials and a date may also be obtained on the re-consent cover memo as requested by the investigator or required by the IRB. The IRB will document the requirement to obtain re-consent on the IRB approval letter. Should the IRB determine that re-consenting subjects is not necessary, the IRB approval letter will be "silent" on re-consent requirements.

Witness to the Consent Process: A witness is required to observe the informed consent process and attest that consent is voluntary and freely given by the subject, parent/guardian, or surrogate decision maker without any element of coercion or undue influence under the following circumstances:

1. Consent is obtained from the subject using the Short Form Consent process, as approved by the IRB.
2. The subject has the decision-making capacity to consent, but cannot read, write, talk or is blind.
3. The subject's parent/legal guardian, or surrogate decision maker cannot read, write, talk or is blind.
4. The IRB specifically mandates a witness signature for the study (e.g., Phase 1 clinical trials, high risk research procedures, etc.). This requirement would be reflected on the IRB approval letter.

When a witness is required to be present, the witness must be impartial (i.e. not a member of the subject's family, not a member of the study team). There may be exceptions made. See HRPP Policy.

Signature Line on the California Bill of Rights: Per Health and Safety Code Section 24170-24179.5 – the Protection of Human Subjects in Medical Experimentation Act, holding an HHS Federalwide Assurance exempts UCI researchers from the requirement to obtain a signature on the California Bill of Rights (BoR). The requirement is to provide the BoR to all research subjects in medical experiments. This BoR is attached as necessary to the IRB approved Consent Form.

Reporting Unanticipated Problems: Investigators are required to report promptly "to the IRB… all *unanticipated problems* involving risks to human subjects or others," including adverse events that are considered unanticipated problems. Unanticipated Problems involving Risk to Subjects or Others are defined as any incidents, experiences, or outcomes that meet ***all*** of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

2. Related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Unanticipated Problems occurring at UCI IRB-approved sites: Unanticipated problems involving risk to subjects or others occurring at UCI IRB-approved sites are reportable to the UCI IRB via the submission of an UP report. Once submitted, the IRB will review the UP report in a timely manner to verify whether that the reported event constitutes an unanticipated problem. Federal regulations require that UCI promptly report unanticipated problems involving risk to subjects or others to appropriate institutional officials, the funding agency or study sponsors, and federal department or agency heads including the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), when applicable.[1]

Unanticipated Problems occurring at external multi-center sites: FDA guidance on Adverse Event Reporting to IRBs — Improving Human Subject Protection[2] states that it is neither useful nor necessary for reports of individual adverse events occurring at other multi-center sites to be distributed routinely to investigators or IRBs at all institutions conducting the research. As such, UCI IRB accepts reports of external adverse events if in the judgment of the UCI Researcher the event constitutes an unanticipated problem. UCI Researchers should submit external unanticipated problems to the IRB through an amendment request that includes appropriately updated IRB-approved documentation.

We hope that the above statements aid in addressing your study sponsor's questions. If there are additional questions not addressed in this document, please contact a member of the HRP staff.

[1] UCI complies with Office for Human Research Protections regulations at 45 CFR 46.103(b)(5) which mandates reporting of unanticipated problems involving risks to human subjects or others. For clinical investigations of drug and biological products conducted under an investigational new drug (IND) application, the FDA also requires that investigators promptly report to the reviewing IRB all events considered unanticipated problems (21 CFR 56.108(b)(1), § 312.53(c)(1)(vii), and § 312.66). Unanticipated adverse device effect (UADEs) must be reported by the investigator to the sponsor and the reviewing IRB as soon as possible, but no later than 10 working days after the investigator first learns of the event (§ 812.150(a)(1)).

[2] http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079753.pdf