

<b>California Pacific Medical Center (CPMC)</b>	<b>Standard Operating Procedure</b>	
<b>Institutional Review Board (IRB)</b>	<b>Initial IRB Review of Proposed Research</b>	<b>July 23, 2010</b>

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## Purpose

This Standard Operating Procedure (SOP) complies with U.S. Department of Health and Human Services (DHHS) regulations 45 CFR 46 (Common Rule), Food and Drug Administration (FDA) 21 CFR 50 and 56, DHHS 45 CFR 160 and 164 (Privacy Rule), as it relates to research participant authorization, including waiver and alteration of HIPAA authorization requirements, as well as California Pacific Medical Center's (CPMC) Federalwide Assurance (FWA).

## Policies and Procedures

### 1. Submission to the IRB

- 1.1 Go to the IRB's Web site and pull down the current research application and the current application checklist. The CPMC IRB Web site can be found at: [www.cpmc.org/research/irb/](http://www.cpmc.org/research/irb/)
- 1.2 For all research proposed to be conducted in whole or in part at CPMC, an application to conduct the research must be submitted to the IRB for review and approval before the study is begun.
- 1.3 The IRB will require the CPMC Principal Investigator (PI) to provide information to the IRB in sufficient detail for the IRB to determine whether the study complies with federal regulations and CPMC policy.
- 1.4 The submission should include, as appropriate to the specific study, the information needed to protect the safety, welfare, and rights of research subjects:
  - a. Research application (which includes: a protocol summary, a HIPAA compliance form)
  - b. Conflict of Interest (COI) Form from the CPMC Principal Investigator and all CPMC co-, sub- and unaffiliated investigators

**Note:** An unaffiliated investigator is a researcher who is not associated with an institution covered by an OHRP FWA. An unaffiliated researcher will need to sign an unaffiliated

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investigator agreement (call the IRB Administrator for more information)

- c. Biosketch or 3-page CV for each investigator (PI, co- and sub-investigators; both CPMC and non-CPMC affiliated)
- d. Proof of Human Subjects' Training for each CPMC investigator
- e. Study protocol (i.e.; Pharma studies, NIH studies)
- f. Investigator's Brochure, package insert, and/or other safety information
- g. Draft consent and/or assent form(s) and privacy authorization form(s)
- h. NIH Grant: If the PI is the *primary awardee* of the NIH grant, the following parts of the research grant must be reviewed by the IRB:
  - 1. Face Page
  - 2. Specific Aims
  - 3. Background and Significance
  - 4. Research Design & Methods
  - 5. Inclusion enrollment report
  - 6. Bibliography & References
  - 7. Protection of Human Subjects
  - 8. Inclusion of women & minorities
  - 9. Targeted or planned enrollment
  - 10. Inclusion of children

**Note:** If the PI is *not* the primary awardee on the NIH grant, do not submit the grant.
- i. Questionnaire(s), surveys and/or other instrument(s)
- j. Draft participant contact letter(s) (if applicable)
- k. Draft physician/provider contact letter(s) (if applicable)
- l. Draft recruitment telephone script(s) (if applicable)
- m. Draft recruitment materials (flyers, ads, etc) (if applicable) and

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n. Other miscellaneous study documents and/or study information for research subjects requested by the IRB.

1.5 The CPMC IRB will establish written procedures, including guidelines, forms, instructions, and timelines relating to the submission of application materials and make this information available to CPMC investigators.

1.6 The CPMC IRB will provide investigators with instructions on implementing the Privacy Rule as it pertains to obtaining and documenting participant authorization, such as the requirement to provide a signed copy of the authorization to the subject.

## **2. Membership, Authority, and Responsibilities of the CPMC IRB**

2.1 Initial review of research must be conducted by a quorum of the IRB at a convened meeting except where expedited review is conducted as allowed under DHHS regulations.

2.1.1 A quorum is defined as a majority (at least 51%) of the voting members of the IRB, including at least one member whose primary concern is in a non-scientific area.

2.1.2 When a new study includes the review of investigational drugs, devices, or biologics, a quorum will include at least one physician.

2.2 IRB members may not participate in the initial review of a project in which they have a conflict of interest except to provide information requested by the IRB. IRB members must leave the meeting room when the IRB deliberates and votes on studies in which they have a conflicting interest. They cannot be counted toward the quorum for that vote, and meeting minutes must document that the member(s) did not vote on the study.

2.3 The IRB may request a review by an individual(s) who is not a member of the IRB with a specific expertise, experience, or awareness (e.g., awareness of the special needs of a vulnerable population) to enhance the IRB's review.

2.3.1 This non-IRB member may not vote with the IRB.

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- 2.4 Generally, the IRB requires the study PI (or designate) to attend the IRB meeting in person (or, in some cases, by telephone) to present a summary of the study and to answer questions posed by the IRB. First-time investigators must attend the meeting in person.
- 2.5 The CPMC IRB has the authority to approve or disapprove proposed studies based on the information submitted to assure human participant protection. The IRB also has the authority to place restrictions or conditions on studies in order to protect the safety, rights and welfare of human subjects and confidential information relating to them.
- 2.6 The CPMC IRB has the responsibility to assess whether the anticipated benefit, either of new knowledge to be gained or of improved health for research subjects or others, justifies asking any person to undertake the risks of the study.
- 2.7 The CPMC IRB has the responsibility to disapprove research in which the risks of conducting the research are judged unreasonable in relation to the anticipated benefits for study subjects.
- 2.8 The CPMC IRB may request modification(s) to the study as a condition of IRB approval or defer action pending further review or receipt and review of additional study-related documents or information.
- 2.9 The CPMC IRB may cede authority to review and monitor a study being carried out at CPMC to another IRB operating under a current Assurance with the Office for Human Research Protections (OHRP).
  - 2.9.1 The IRB to which the CPMC IRB wishes to cede review authority must agree to accept authority.
  - 2.9.2 When CPMC IRB cedes review authority to another IRB, it will complete an IRB Authorization Agreement and have the Institutional Official (aka FWA Official) sign the form.

### **3. Conducting Initial IRB Review**

- 3.1 The CPMC IRB will consider and apply all applicable provisions of the Privacy Rule as part of their initial review of research.

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3.2 The following documents, as appropriate to the initial review of the specific study, will be sent to IRB members or the primary reviewer at least five full days prior to the IRB meeting:

- a. Research application (includes a protocol summary);
- b. Full study protocol (generally the IRB Chair, the scientific merit reviewer and the primary reviewer will receive this document);
- c. Investigator's brochure, package insert, and/or other safety information (generally the IRB Chair and the primary reviewer will receive this document);
- d. Investigational New Drug/Investigational Device Exemption letter from the FDA/NIH (as applicable);
- e. Draft consent and/or assent form(s) and privacy authorization form(s);
- f. Questionnaire(s) and/or survey instrument(s);
- g. Draft participant contact letter(s);
- h. Draft physician/provider contact letter(s);
- i. Draft recruitment telephone script(s);
- j. Draft recruitment material(s);
- k. Biosketch for each investigator (PI, co-, sub-investigator)
- l. NIH grant (designated sections only if PI is a primary awardee); and
- m. Other documents, as appropriate and/or requested by the IRB (e.g., Medical Record Review form, Stored or Discarded Biological Specimens form, and the Waiver of Consent/HIPAA Privacy Authorization form).

Federal regulations require that all IRB members receive a study summary and a copy of any proposed new or modified consent form(s) in adequate time for review.
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- 3.3 The IRB will consider the qualifications of the PI and all co- and sub-investigators to conduct the proposed research.
- 3.4 The IRB will conduct a risk assessment of each proposed study, which takes into account at least the following factors:
  - a. Are there reasonably anticipated potentially serious risks to the safety or welfare of study subjects such as a prolonged in-patient hospitalization, a life threatening event, long-term disability or functional impairment, congenital anomaly or birth defect, or death?
  - b. Are there reasonably anticipated potentially serious breaches of privacy or confidentiality of participant medical information that could lead to loss of employment, health insurance, relationships, or reputation for study subjects?
  - c. Is it reasonably possible that the study could lead to an unintended termination of a pregnancy or loss of fertility?
  - d. Is it reasonably possible that a study-related revelation of a genetic predisposition or diagnosis could have significant consequences for research subjects or their families?
  - e. Is it reasonably possible that the anticipated knowledge can be gained by means other than this study as currently designed?
- 3.5 If any of the above risks are identified, the IRB will not approve the study unless adequate offsetting benefits to study subjects or society can be reasonably anticipated.
- 3.6 The IRB will consider the potential risks and benefits of the procedures involved in the research and will differentiate those procedures that are performed for research purposes from those that are performed for routine care or evaluation.
- 3.7 The IRB will determine whether adequate procedures are in place to:
  - a. Monitor the subjects' experiences throughout the research;
  - b. Monitor the data collected and maintain its confidentiality;

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- c. Protect the privacy of subjects; and
  - d. Ensure that potential research subjects will be provided with an accurate and complete description of the possible risks or discomforts and the anticipated benefits of participation in the study.
- 3.8 The IRB will approve new studies based on its determination that the following requirements are satisfied:
- a. Risks to participants are minimized by using procedures that are consistent with sound research design and do not unnecessarily expose subjects to risk and, whenever appropriate, by using approved procedures already being performed for diagnostic or treatment purposes;
  - b. Risks are reasonable in relation to anticipated benefits (if any) to participants and the importance of knowledge that may reasonably be expected to result;
  - c. Selection of research subjects is equitable;
  - d. Informed consent will be required from each subject or his/her legally authorized representative unless this requirement is waived by the IRB and the reasons for this waiver are appropriately documented, as required by federal regulations;
  - e. A signed consent form (including an assent form if applicable) will be obtained from each prospective subject unless the requirement is waived by the IRB and the reasons for this waiver are appropriately documented;
  - f. Appropriate additional safeguards will be provided to protect the rights, safety and welfare of research subjects who are members of a vulnerable population.
  - g. Methods are in place to adequately monitor the safety and welfare of research subjects.

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- 3.9 When approving studies, the IRB will consider the appropriate duration of approval, not to exceed one year. The following criteria and others as determined to be appropriate by the IRB, will be considered in the determination of which studies require review more frequently than annually:
- a. The type and nature of the study;
  - b. The degree of potential risk to research subjects;
  - c. The degree of vulnerability of research subjects;
  - d. The research experience of the principal investigator; and
  - e. Others, as determined by the IRB.
- 3.10 The IRB may require that the principal investigator, and others as determined by the IRB, apply for a Certificate of Confidentiality from the federal government to further protect subjects from the disclosure of confidential information of a sensitive nature.
- 3.11 When researchers not on CPMC's workforce will have access to confidential or proprietary information, the IRB should request that such individuals sign confidentiality agreements with CPMC.
- 3.12 Outside (non-CPMC) investigators who are not affiliated with an institution with a current Assurance (FWA) with OHRP must sign an "Unaffiliated Investigator Agreement" with CPMC, agreeing to comply with CPMC IRB policies and procedures and the terms of CPMC's FWA.
- 3.12.1 An unaffiliated investigator may not be a PI of a study at CPMC. He/she will need to have a qualified CPMC employee or physician agree to serve as the study's PI.
- 3.13 When the convened IRB stipulates specific revisions requiring concurrence by the investigator, the IRB may approve the research subject to subsequent confirmation by the IRB chair or delegate via expedited review.
- 3.14 If the IRB has substantive unanswered questions or requests substantive clarifications or modifications of the protocol or consent

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document(s), the IRB will defer action on the item pending subsequent review by the convened IRB of the clarification provided by the CPMC principal investigator or an outside source as requested by the IRB.

- 3.15 Proposed research will not be approved by the IRB without a:
- Waiver or alteration of authorization as required by the Privacy Rule, or
  - Mechanism for obtaining written authorization from potential research subjects.

**Except when:**

- a. The proposed research does not involve the use or disclosure of Protected Health Information (PHI); i.e., only de-identified information will be used;
- b. The proposed research involves only information that meets the criteria for a Limited Data Set;

When PHI is used by the researcher to create a Limited Data Set for disclosure, the researcher must obtain a waiver or a mechanism to obtain authorization to use the PHI (Data Use Agreement).

- c. Written representation is received from the CPMC PI that the use of PHI is solely to prepare a research protocol or for purposes preparatory to the research (e.g., pilot study or pre-screening of clinical trial enrollees), that access to PHI is sought for research purposes only, and that PHI will not leave CPMC premises;
- d. Written representation is received from the CPMC PI that the use or disclosure of PHI is for research on decedents and that the PHI is necessary for the research; or
- e. The IRB approves a modification of the study that eliminates the use or disclosure of PHI.

**4. Scientific Merit**

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- 4.1 The scientific merit of the protocol must be established in order to justify any potential risks to research participants.
  - 4.1.1 The IRB may require a written report from a separate committee or an individual who evaluated the protocol's scientific merit.
- 4.2 The IRB will consider whether research is designed to produce valid findings.
- 4.3 At a minimum, the IRB should consider the following when conducting an initial review:
  - a. If the research design and methods are adequately described and justified;
  - b. If the research design and methods are adequate to answer the research question; and
  - c. If the research objectives are likely to be achievable within the projected time frame.
- 4.4 The data and statistical analysis section of the research protocol should provide enough evidence to assure the IRB that the proposed research has a reasonable chance of achieving the stated objectives of the research. This requirement may be waived for pilot studies.

**5. Research Subject Recruitment and Selection**

- 5.1 The IRB will assure that the recruitment process promotes voluntary participation, is not coercive, and does not provide inappropriate incentives.
- 5.3 The IRB will assure that special safeguards are provided in the recruitment process as necessary to protect the safety, welfare and rights of members of vulnerable populations who may be recruited to participate in the research.
- 5.4 The IRB should consider the following when reviewing a study's recruitment plan:

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- a. Whether confidential information will be accessed to identify and contact potential study subjects and, if so, whether appropriate measures to protect the privacy of this information are in place;
- b. Who (position, organizational affiliation and relationship to the subjects and the study) will contact potential research participants;
- c. Whether any proposed payments or other compensation to subjects could have a coercive or inappropriate effect on them;
- d. Whether anyone who will be recruiting or enrolling subjects has a conflict of interest with the study;
- e. How, when and where potential subjects will be contacted; and
- f. Whether potential subjects will be given sufficient time to consider participation in the study.

**6. Informed Consent Process**

- 6.1 The IRB will comply with applicable federal and state regulations regarding informed consent, including those pertaining to vulnerable populations.
- 6.2 The IRB will review the process for obtaining informed consent in addition to the consent form and/or any other consent documents.

The informed consent process begins with the identification and recruitment of potential study subjects and continues until the study is complete.

- 6.3 The IRB may require that informed consent to participate in a study involving investigational drugs, biologics or devices or any study that has potentially serious clinical implications (such as research on a surgical procedure) be obtained by a licensed practitioner who is knowledgeable about the research protocol.
- 6.4 The IRB will consider the maturity, language and decisional capacity of the subjects from whom informed consent is being sought and assure that the consent process and associated documents are designed and

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written to enable their maximum understanding of the study and all potential risks and benefits of the study.

- 6.5 The IRB will evaluate the informed consent process to ascertain that the informed consent process is not coercive.
- 6.6 The IRB will assure that potential research subjects are informed of any potential conflict of interest in the study by an investigator or any individual who obtains informed consent.

## **7. Informed Consent Document**

- 7.1 The IRB will require that PIs maintain documentation of informed consent by use of a written consent form approved by the IRB unless the requirement to obtain written consent is waived by the IRB. All decisions concerning consent forms will comply with applicable federal regulations.
  - 7.1.1 Consent forms must not contain language that deprives research subjects of their legal rights; and
  - 7.1.2 Consent forms should be translated into the appropriate language(s) as necessary to enable understanding by potential research subjects who do not read or understand English.
- 7.2 The IRB will assure that the following 13 elements are included in the consent form except when waived or altered by the IRB:
  - (1) A statement that the study involves research;
  - (2) An explanation of the purposes of the research;
  - (3) The expected duration of participation;
  - (4) A description of the procedures to be followed;
  - (5) Identification of any procedures that are experimental;
  - (6) A description of any reasonably foreseeable risks or discomforts to the subject;

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- (7) A description of any benefits to the subject or to others which may be expected from the research;
- (8) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be available and advantageous to the subject;
- (9) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, including the fact that disclosure may be made to the FDA, OHRP or study sponsor as prescribed by federal regulations;
- (10) For research involving more than minimal risk, an explanation as to whether any compensation will be provided 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;
- (11) An explanation of whom to contact (research investigator and the IRB) for answers to pertinent questions about the research and research subject's rights, and whom to contact in the event of a research-related injury to the participant;
- (12) 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
- (13) A statement that the research subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

7.3 When required by the IRB or relevant to the study, the consent form will include one or more of the following additional elements:

- a. 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) that are currently unforeseeable;
- b. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

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- c. Any additional costs to the subject that may result from participation in the research;
- d. Consequences of a subject's decision to withdraw from the research, and procedures for orderly termination of participation;
- e. A statement that significant new findings discovered during the course of the research which may influence the subject's willingness to continue in the research will be provided to the participant; and
- f. The approximate number of subjects involved in the study overall and at CPMC, specifically.

7.4 For protocols that involve children, the IRB is required to determine whether assent is required and, if so, to determine an appropriate mechanism to obtain and document assent.

7.5 For protocols involving pregnant women, the IRB will consider the health and welfare of the fetus.

7.6 For protocols involving persons with a decisional impairment, the IRB will be guided by the principle that every effort should be made to explain the nature of the research, including its potential risks and benefits, in a manner and at a level at which the participant is likely to understand.

## **8. Waiver or Alteration of the Informed Consent Procedure**

8.1 Federal regulations permit the IRB to waive or alter the informed consent procedure. The IRB must find and document that the reason for the waiver or alteration is consistent with federal requirements. The PI must provide adequate justification to the IRB for a waiver or alteration of informed consent.

8.2 To waive the requirement for informed consent, the IRB must find and document that:

- a. The research involves no more than minimal risk to the research subjects; and

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- b. The waiver or alteration will not adversely affect the rights or welfare of the subjects; and
- c. The research could not be practicably carried out without the waiver or alteration; and
- d. If appropriate to the study, the subjects will be provided with additional pertinent information following participation in the research.

8.2.1 The IRB must document the reason(s) for the waiver, and document all findings (a through d above) in the IRB meeting minutes.

8.3 To approve a consent procedure that does not include all of the 13 elements required for a consent form or to approve a consent procedure that alters any of the 13 elements (both of these situations are considered to be an alteration of consent), the IRB must find and document that:

- a. The research involves no more than minimal risk to the subjects; and
- b. The alteration will not adversely affect the rights or welfare of the subjects; and
- c. The research could not be practicably carried out without the alteration; and
- d. If appropriate to the study, the subjects will be provided with additional pertinent information following participation in the research.

8.3.1 The IRB must document the reason for the alteration and whether the entire consent form is being waived or only certain elements and which ones.

8.4 To waive the requirement that the PI obtain a *signed* consent form, the IRB must find and document that:

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- a. The research is determined to be minimal risk and involves no procedures for which written consent is normally required outside of the research context; or
- b. The only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality. In this case, each subject will be asked whether he/she wants any link between him/her and the research to be removed and his/her wishes will govern.

**Note:** When the IRB waives the requirement to obtain a *signed* consent form, the PI will still need to provide subjects with an IRB-approved consent form.

## 9. Privacy Rule Authorization to Use or Disclose PHI

- 9.1 When Privacy Rule authorization from potential research subjects is required, the CPMC IRB will determine the appropriate mechanisms for obtaining and documenting such authorization.
  - 9.1.1 All Privacy Rule authorizations will be in writing unless an alteration of this specific requirement is approved by the IRB.
  - 9.1.2 If there will be a consent form for the study, Privacy Rule authorization language will be included in the informed consent document.
- 9.2 The CPMC IRB will require that all Privacy Rule authorizations to use or disclose Protected Health Information (PHI) for a research study will contain all of the following core elements:
  - a. Specific description of the PHI to be used or disclosed in the conduct of the research;
  - b. Identification of the persons or class of persons authorized to make the requested use or disclosure of the PHI;
  - c. Identification of the persons or class of persons to whom the covered entity (CPMC) may make the use or disclosure;
  - d. Description of each purpose of the requested use or disclosure;

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- e. Expiration date after which use or disclosure is no longer allowed.
    - The expiration date for a study can be listed as either a specific date (month, day, year) or as an event such as "end of study."
    - If the authorization is for the use or disclosure of PHI to create and maintain a research database or specimen repository, no expiration date is required. In this case, the expiration date should be indicated as "none."
  - f. Research subject's signature and date; and
  - g. If signed by the legally authorized representative or surrogate, a description of his/her relationship to the research subject.
- 9.3. The CPMC IRB will require that all Privacy Rule authorizations contain the following notifications:
- a. A statement that the individual may revoke the authorization in writing and the exceptions to the right to revoke (such as when the PHI has been used, disclosed, or de-identified) and a description of how the individual may revoke the authorization.
  - b. A statement that the only consequence of refusing to sign the HIPAA Privacy Rule authorization or revoking the authorization will be the ineligibility to participate in the research or to receive research-related treatment; and
  - c. A statement regarding the potential for the PHI to be re-disclosed to a third party by the individual or entity to which information was disclosed by CPMC.
- 9.4 Unless research subjects provide written authorization to use or disclose their PHI for a particular study, the CPMC IRB will only approve use or disclosure of PHI if such use or disclosure is the minimum necessary to conduct the research.

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- 9.5 If the research is a clinical trial and it is necessary for subjects to waive their right to access and review information collected about them, the authorization will state this.
- 9.6 The Privacy Rule authorization will be written in "plain" language, free of technical terminology and complex phraseology.
- 9.7 The research subject or his/her legally authorized representative (or surrogate) will sign the Privacy Rule authorization and receive a copy of the signed authorization.
  - 9.7.1 If a legally authorized representative or a surrogate signs the authorization on behalf of the research subject, the authority of the personal representative will be described on the authorization form.

**10. Waiver or Alteration of Privacy Rule Authorization**

- 10.1 The CPMC IRB can approve a waiver or alteration of authorization when all of the following criteria are met:
  - a. The use or disclosure of PHI involves no more than a minimal risk to the privacy of the individuals to include at least the presence of the following elements:
    - An adequate plan to protect the identifiers from improper use or disclosure;
    - An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research (unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law); and
    - Adequate written reassurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted by the Privacy Rule.
  - b. The research could not be practicably conducted without the waiver or alteration; and

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- c. The research could not be practicably conducted without access to and use of the PHI; and
- d. Only the minimum necessary PHI will be used or disclosed to the researcher.

10.2 Activities Preparatory to Research

10.2.1 The Privacy Rule permits investigators to use PHI for limited recruitment-related activities (e.g., determining whether there are enough subjects with a particular diagnosis to support a study) before the IRB approves a study (and without authorization or a waiver of authorization). The PI must complete the *Intent to Use PHI Preparatory to Research* form (referred to in the Privacy Rule as a “representation” to use PHI preparatory to research) and submit it to the CPMC IRB Office. Under a Preparatory to Research representation, no PHI may leave CPMC premises, and investigators must use the minimum necessary PHI to conduct the preparatory activity. Investigators must not contact potential research subjects for recruitment or other purposes under a Preparatory to Research representation.

10.2.2 Before investigators can contact potential research subjects, the IRB must approve the study, including the recruitment strategy and associated documents, and a mechanism for obtaining informed consent and privacy authorization (or a waiver of alteration of informed consent or privacy authorization, as appropriate).

10.3 In communicating with CPMC investigators, the IRB will document in writing its decisions regarding the approval, waiver, or alteration of authorization, and the requirements for obtaining authorization.

10.4 The IRB will document waiver or alteration of authorization in the meeting minutes or in other documentation in the IRB’s study file, including:

- a. The date on which the alteration or waiver of authorization was approved;

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- b. A statement that the IRB has determined that the alteration or waiver of authorization satisfies the criteria identified above (see 10.1 a through d);
  - c. A brief description of the PHI for which use or access has been determined to be necessary;
  - d. A statement that the alteration or waiver of authorization has been reviewed and approved under either normal or expedited review procedures; and
  - e. The signature of the Chair or other member of the IRB as designated by the Chair.
- 10.5 The CPMC IRB may approve a waiver of authorization or a mechanism for obtaining authorization through an expedited review process if the study or study modification otherwise qualifies for expedited review under the Common Rule.

## 11. Expedited Review

- 11.1 Expedited review may be conducted on proposed research by the IRB Chair or by an appropriately experienced IRB member designated in writing by the IRB Chair when the study is determined to be minimal risk and the research involves activities that fall within one or more of the following eight categories.
- a. Uses data, documents, records, or specimens that have already been collected, or will be collected, for non-research purposes (e.g., review of medical records, utilization data, etc.);
  - b. Evaluates individual or group characteristics, behaviors, or opinions where the research data are collected by survey, focus group, program evaluation, quality assurance methodologies, interview, or oral history;
  - c. Does **NOT** involve an investigational drug or biologic or an approved drug being used for a non-approved purpose, route, or dosage;
  - d. Does **NOT** involve a significant risk device, unless the device is being used for the approved purpose;

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- e. Collects data only from voice, video, digital, or image recording made for research purposes;
- f. Collects blood samples by finger stick, heel stick, ear stick, or venipuncture in amounts defined by federal rules;
- g. Collects biological specimens for research purposes by non-invasive means; and
- h. Collects data through non-invasive procedures routinely employed in clinical practice, excluding procedures involving x-rays and microwaves.

11.2 The IRB may establish additional criteria for expedited IRB review as long as they do not conflict with these federally approved criteria.

11.3 The IRB will be notified of studies and study-related documents approved by expedited review, e.g., studies will be placed on the subsequent IRB meeting agenda or by an alternative way as determined by the IRB and consistent with federal regulations.

11.4 If a proposed new study is not approved during an expedited review, the study will be reviewed by the full IRB.

11.5 For more information, refer to the *Expedited IRB Review SOP*.

## **12. Proposed Research Involving Investigational Drugs or Biologics**

12.1 For studies evaluating investigational drugs or biologics, and for studies evaluating approved (licensed) drugs or biologics for unapproved indications, dosages or routes of administration, the IRB will assure that an IND has been applied for or is in place.

12.2 The IRB will evaluate the dosage, route of administration, previous use, and safety and efficacy data as summarized in the protocol and the Investigator's Brochure and determine potential risks and benefits to study participants.

## **13. Proposed Research Involving Investigational Devices**

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- 13.1 The IRB will determine whether device studies are "significant risk" (SR) or "non-significant risk" (NSR) in accordance with the Investigational Device Exemption (IDE) regulations.
- 13.1.1 A SR device study is defined as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and
- a. Is an implant;
  - b. Is used in supporting or sustaining human life;
  - c. Is of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise prevents impairment of human health; or
  - d. Otherwise presents a potential for serious risk to the health, safety, or welfare of the participant.
- 13.1.2 A NSR device investigation is one that does not meet the definition for a SR study.
- 13.1.3 The risk determination will be based on the proposed use of the device in an investigation and not on the device alone. The sponsor will make an initial assessment of whether or not a device study presents a SR. The IRB may request the sponsor to provide an explanation of its determination and any other information that may assist the IRB in evaluating the risk of the device study.
- 13.2 If the investigator proposes the initiation of a sponsor-determined NSR investigation to the IRB and the IRB agrees that the device study is NSR and approves the study, the investigation may begin immediately, without submission of an IDE application to the FDA. In these cases, the sponsor and investigator must comply with "abbreviated IDE requirements" and all IRB requirements.
- 13.3 If the IRB determines that the device study is SR, the study may not begin until an IDE application has been approved by the FDA and the study and consent form are approved by the IRB.

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13.4 If a licensed device is used "off label" (for purposes other than those covered under the license) for treatment purposes and no data from the use will be used for research, IRB approval is not required.

**14. Single Patient and Emergency Uses of Investigational Agents**

14.1 Single patient and emergency uses of investigational drugs must reflect requirements issued in the relevant federal regulations.

14.2 The IRB will require and/or review at least the following documents prior to approving a single patient use:

- a. Evidence of a treatment or single patient IND, **or**
- b. Documentation of Group C status from the National Cancer Institute, [*Group C status* refers to a program developed by the FDA and National Cancer Institute (NCI) that permits NCI to distribute certain investigational agents to oncologists for the compassionate treatment of cancer under protocols outside a controlled clinical trial. Safety and effectiveness data are collected although treatment, not research, is the primary objective.] **or**
- c. A copy of a single patient use IND application to the FDA, **and**
- d. A comprehensive research protocol, **and**
- e. An investigator's brochure or equivalent safety information, **and**
- f. A draft consent form with all required elements.

14.3 Single patient use of an investigational drug or biologic requires an IND, prospective IRB approval and documentation of informed consent.

14.4 When the need for the single patient use of an investigational drug is emergent and there is not sufficient time for submission of an IND application, the PI is required to obtain FDA authorization to ship the investigational agent for use prior to the submission of an IND. Prospective IRB approval and documentation of informed consent from the patient or a legally authorized representative are required.

14.5 The treating physician may proceed without IRB approval as an "Emergency Exemption from Prospective IRB Approval" (Emergency

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Use) when use of the investigational agent on a patient is carried out in a life-threatening situation in which no acceptable standard treatment is available, and in which there is not sufficient time to obtain IRB approval. Documentation of informed consent from the patient or a legally authorized representative is required.

- 14.5.1 Emergency Use authority can be used to administer one course of treatment to one individual. Single Patient Use approval by the IRB is required prior to any subsequent administration of the drug to the patient.
- 14.5.2 When Emergency Exemption from Prospective IRB Review (Emergency Use) is invoked, as authorized by FDA regulations, the IRB will require that the treating physician/PI report on the use in writing to the IRB within five business days.
- 14.5.3 The IRB will review the report and acknowledge use. However, this should not be construed to imply approval of the use. The IRB will notify the treating physician/PI that he/she cannot administer a second course of treatment without prior IRB approval for a single patient use.
- 14.6 When emergency medical care involving an investigational drug is initiated without prior IRB approval, the patient may **not** be considered a research subject and no data relevant to this use may be used for research purposes.
- 14.7 In limited emergency situations, the informed consent requirement can be waived (FDA regulations call this an "Informed Consent Exception"). If waived, the treating physician must notify the IRB. The treating physician and a second physician who is not involved in the clinical investigation must determine and document that all of the criteria below have been met:
  - a. The patient is in a life-threatening situation and needs use of the investigational drug emergently;
  - b. Informed consent cannot be obtained because of an inability to communicate with or obtain legally-effective consent from the patient;

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- c. Time is not sufficient to obtain legally-effective consent from the patient's legal representative; and
  - d. There is no alternative method of generally accepted therapy that provides an equal or greater likelihood of saving the patient's life.
- 14.8 In even more limited emergency situations, if the treating physician determines that there is not sufficient time to obtain an independent physician's determination that the necessary conditions apply, the treating physician can make the determination. In this case, the treating physician must have the determination reviewed and evaluated in writing by a physician who is not involved in the clinical investigation and both physicians are required to report the use in writing to the IRB within five business days.
- 14.9 Some institutions conduct research for which they can anticipate uses of investigational drugs in situations in which informed consent will not be possible (such as research pertaining to trauma care in an emergency room setting). The FDA has specific regulations for such situations, which include community review and input. If such research is proposed, consult CPMC IRB Administrator and the FDA Information Sheets.

**15. Investigator-Initiated Clinical Trials**

- 15.1 Investigators will not conduct clinical trials under a protocol developed by them or other investigators without prospective approval by a CPMC IRB. This includes trials involving an herb or other substance not regulated by the FDA, an unlicensed (or not otherwise approved for commercial use) drug, biologic or device, or an approved drug or device being tested for efficacy in an unapproved indication, dosage or route of administration.

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15.2 The IRB will require full disclosure of **any** potential financial or professional benefit relating to the outcomes of the trial by any investigator involved in the trial.

15.2.1 In general, if an investigator(s) has **any** financial interest in the outcome of the trial, CPMC IRB will refer the issue to the CPMC Conflict of Interest Committee for resolution as a condition of IRB approval.

15.3 The IRB will require that the PI conduct a thorough literature review and report all significant findings and their implications for the proposed research in the research application.

15.4 The IRB will require that the PI apply for an IND from the FDA, as appropriate.

16.4.1 The IRB will have a compelling reason for not requiring an IND and will document this reason in the IRB meeting minutes.

15.5 The IRB will require that the PI submit a plan for monitoring subject safety in the trial such as formation of a Data and Safety Monitoring Board (DSMB) that is independent from the study.

15.5.1 The plan will include information on the membership and responsibilities of DSMB members in addition to a description of the monitoring process, access to trial data, reporting to the IRB, stopping rules, and protection of confidential information.

15.6 The IRB will assure that the investigator is sufficiently qualified and has adequate training, infrastructure and staff support to function as both investigator and sponsor for a clinical trial, sufficient to assure compliance with the Guideline for Good Clinical Practice and all applicable federal regulations pertaining to investigators and sponsors.

## **16. Notification and Documentation of IRB Decisions**

16.1 The IRB will notify the PI in writing (e.g., letter, electronic communication) of its decisions, conditions, and requirements on the proposed new research within a reasonable interval following the IRB meeting.

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16.1.1 In the initial review approval communication, the IRB will inform the PI of his/her obligation to seek approval for modifications to research or other IRB-approved documents associated with the research.

16.1.2 The IRB will inform the PI of his/her responsibility to report Adverse Events according to IRB policies and procedures and consistent with federal regulations.

16.2 The IRB Chair may delegate authority to sign letters documenting IRB decisions and actions to the appropriate IRB staff member.

16.3 When a decision is made to disapprove or defer a study, the notice to the PI will include the reason(s) for the decision.

16.3.1 If the decision is to disapprove a protocol involving an investigational drug, device, or biologic, the decision will also be reported to the study sponsor.

16.4 The IRB actions will be documented in the IRB meeting minutes.

16.5 The IRB will assure that Privacy Rule-related decisions and determinations are documented in the IRB meeting minutes.

## **17. Appealing an IRB Decision**

17.1 After being notified of the IRB's decision, the PI may submit a request in writing to the IRB Chair for a hearing to dispute the decision.

17.2 The Chair or designee will determine whether or not to grant an appeal.

17.3 No IRB decision can be rescinded or changed without action from the convened IRB.

17.4 The final decision of the IRB will be communicated in writing to the PI and cannot be appealed to another individual or group.