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| <b>California Pacific Medical<br/>Center (CPMC)</b> | <b>IRB Policies and<br/>Procedures</b> |                      |
| <b>Institutional Review Board<br/>(IRB)</b>         |  | <b>July 22, 2010</b> |

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1. Document

- 1.1 This document replaces the *Guide for Human Subjects Research at California Medical Center*, February 2008.
- 1.2 The Institutional Official or IO [also known as the Federalwide Assurance (FWA) Official] must approve this document.
- 1.3 Minor administrative changes and clarifications may be made to this document without seeking the approval required above.

2. Definitions

See the *CPMC IRB Master Glossary* located at the following URL:  
[www.cpmc.org/research/irb/](http://www.cpmc.org/research/irb/)

3. Statement of Purpose and Principles

- 3.1 California Pacific Medical Center (referred to hereafter as “CPMC”) acknowledges and accepts responsibility for the protection of the safety, rights and welfare of human subjects (also referred to as research participants or study subjects) involved in research.
- 3.2 CPMC has formally designated two Institutional Review Boards (IRBs)—IRB Panel #1 and IRB Panel #2---to ensure the protection of the safety, rights and welfare of human subjects participating in research conducted under the auspices of CPMC.
- 3.3 The IRB is guided by the ethical principles regarding all human subjects’ research as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research titled *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, also known as the “*Belmont Report*.”
- 3.4 Federal regulations and CPMC policy prohibit the involvement of human subjects in research until the IRB has reviewed and approved the research, including the protocol and informed consent process.
- 3.5 The policies in this document are written to comply or align with:
  - Department of Health and Human Services (DHHS) 45 CFR 46, 160, 164, and others as appropriate;
  - Food and Drug Administration (FDA) 21 CFR, Parts 50, 56, and others as appropriate;
  - Other applicable federal regulations relevant to human subjects research; and
  - CPMC’s FWA.

#### 4. Institutional Authority and Responsibility

- 4.1 California Pacific Medical Center has entered into a Federalwide Assurance agreement with the Health and Human Services Office for Human Research Protections (OHRP):
  - CPMC FWA#00000921;
  - CPMC IRB Panel #1 is registered with OHRP as IRB00000239;
  - CPMC IRB Panel #2 is registered with OHRP as IRB00005842.
- 4.2 Attempts of undue influence on the IRB or its members by researchers, administrators, or other individuals or groups should be reported to the FWA Official (also known as the Institutional Official—or IO).
- 4.3 CPMC assigns the responsibilities and authorities listed below to the IRB.
- 4.4 CPMC requires that research conducted on CPMC property or that uses CPMC services have a CPMC Principal Investigator (PI) and use the CPMC IRB.
  - 4.4.1 CPMC property includes: CPMC hospitals (Pacific campus, California campus, Davies campus, and St. Luke's Hospital); Brannan Street Building; Coordinating Center (Holly Street) and CPMC-operated outpatient clinics.
  - 4.4.2 Examples of CPMC services include (but are not limited to): CPMC laboratories and radiology and nuclear medicine departments.
- 4.5 Physicians conducting research in their medical office buildings are not required to use the CPMC IRB if **no** hospital services or hospital patients are involved in the study.
  - 4.5.1 CPMC interns, residents and fellows are considered CPMC employees; therefore, they must use the CPMC IRB for any research activity they are involved in (even if this includes research activity in a physician's medical office building or at another institution).
- 4.6 CPMC IRB policy requires the PI to obtain the approval signature of his/her Department Chair acknowledging the research that will be conducted. (Within certain departments, the signature may be obtained from a division chief.)
- 4.7 The CPMC IRB will also be the IRB of record for Novato Community Hospital and Sutter Lakeside Hospital, 2 Sutter-affiliated institutions in CPMC's regional corporate entity. These two organizations are listed on CPMC's FWA.
  - 4.7.1 Studies originating from these two hospitals must have a PI from the respective home institution.

#### 5. Authority and Responsibility of the IRB

- 5.1 The IRB shall review all activities that involve human subjects research, such as when:
  - CPMC's employees or agents intervene or interact with living individuals for purposes of research;

- CPMC's employees or agents obtain, release, or access individually identifiable private information for the purposes of research; or
    - CPMC receives a direct award to conduct human subject research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.
- 5.2 The IRB will comply with DHHS 45 CFR 46, including all of its subparts. All federally-supported research will also comply with any additional human participant regulations and policies of the supporting federal department or agency. The IRB will comply with 21 CFR 50 and 56 and when reviewing research conducted under the authority of the FDA. The IRB will comply with DHHS 45 CFR 164 when making determinations required by the Privacy Rule. The IRB will comply with relevant state law and CPMC policies.
- 5.3 The IRB has the responsibility and authority to:
- 5.3.1 Review, approve, disapprove, or require changes in research activities involving human subjects.
  - 5.3.2 Suspend, terminate, or place restrictions on IRB-approved research in order to protect the safety, rights, and welfare of human subjects.
  - 5.3.3 Request information from investigators, including research applications, progress reports, clarifications, monitor reports and other information as required.
  - 5.3.4 Require and review reports of proposed changes in ongoing research for review and approval prior to initiating those changes, except when necessary to eliminate apparent immediate hazards to research participants. The IRB will notify the PI that federal regulations require that the PI report changes to IRB-approved research implemented without IRB approval in writing to the IRB within five business days of implementation.
  - 5.3.5 Determine which projects need independent verification from sources other than the PI to assure that no material changes have occurred, based on but not limited to:
    - The principal investigator's prior record of noncompliance with federal regulations, CPMC policies, or IRB policies and procedures;
    - Any concern by the IRB about the accuracy or truthfulness of information submitted; or
    - Failure of the principal investigator to provide required information or documentation in a timely manner.
  - 5.3.6 Appoint a representative, who may or may not be an IRB member, to monitor any aspect of any study operating under its authority for the purpose of:
    - Observing the consent process;

- Verifying that no changes have occurred in the study and that the IRB-approved protocol is being followed;
  - Assuring that documentation of IRB and study activities are being adequately maintained;
  - Ensuring and verifying compliance with applicable regulations, good clinical practice guidelines and CPMC policies; or
  - For any other purpose relating to the protection of human subjects.
- 5.3.7 Require, review, and take appropriate action on reports of:
  - Serious Adverse Events (SAE)
    - Unanticipated problems (or adverse events--AE) involving risks to human research subjects; and
    - Instances of serious or continuing noncompliance with the requirements of the IRB, including noncompliance with timeliness of periodic continuing review or the regulations for the protection of human research subjects in any approved project.
- 5.3.8 Verify whether projects qualify as human subjects' research or are exempt from IRB review.
- 5.3.9 Report allegations of research misconduct to the CPMC Research Integrity Officer (RIO).
- 5.3.10 Report to the Institutional Official and appropriate federal regulatory agencies any unanticipated problems involving risk to subjects or others, any instances of serious or continuing noncompliance with the requirements of the IRB or the regulations for the protection of human subjects, and any suspension or termination of IRB approval of any study activity.
- 5.3.11 Communicate IRB requests for information, clarification, and documentation of full committee decisions in writing within two weeks of the meeting to affected parties, including:
  - Requests for additional information from investigators; and
  - Reports of IRB decisions to the investigator.
- 5.3.12 Communicate IRB requests for information, clarification, and documentation of expedited review decisions in writing within two weeks of the review to affected parties, including:
  - Requests for additional information from investigators; and
  - Reports of IRB decisions to investigator.
- 5.3.13 Maintain adequate records and documentation of IRB activities.

5.3.14 Report changes of its membership to OHRP. No new member may vote until OHRP has been notified of the addition.

## 6. Organization of the IRB

### 6.1 IRB Membership

- 6.1.1 The IRB shall be composed of members who are appointed in writing by the IRB Chair in consultation with the Institutional Official.
- 6.1.2 The IRB Chair, in consultation with the Institutional Official, may change the number of members from time to time, but the minimum number of members is five.
- 6.1.3 The IRB Chair, in consultation with the Institutional Official, may remove and replace members upon discovery of failure or inability to:
- Fulfill the duties of IRB membership; or
  - Comply with all policies and procedures and other applicable standard operating procedures.
- 6.1.4 The IRB Chair, in consultation with the Institutional Official, may appoint alternate IRB members.
- 6.1.5 The IRB Chair, in consultation with the Institutional Official, will make appointments to meet the following requirements:
- Inclusion of both male and female members, so long as no IRB selection is made exclusively on the basis of gender.
  - Inclusion of members representing a variety of professions and backgrounds to promote complete and adequate review of research activities commonly conducted by CPMC.
  - Inclusion of at least one member whose primary expertise is in a non-scientific area.
  - Inclusion of at least one physician.
  - Inclusion of at least one member who is not otherwise affiliated with CPMC and who is not part of the immediate family of a person who is affiliated with CPMC.
  - Composition of an IRB sufficiently qualified, through the experience, expertise and diversity of its members including race, cultural backgrounds, sexual orientation and sensitivity to community attitudes.
- 6.1.6 The Institutional Official shall keep the CPMC Chief of Staff informed of IRB appointments.

- 6.1.7 The term of service for each IRB member shall be three years. Consecutive terms are permitted.
- 6.1.8 The renewal of a member's appointment to the IRB is made by the IRB Chair in consultation with the Institutional Official.
- 6.1.9 Duties of IRB membership include:
- Understanding and following these policies and procedures as well as IRB Standard Operating Procedures;
  - Attending at least 2/3 of the IRB's meetings each year;
  - Complying with the Conflicts of Interest Policy for Members of California Pacific Medical Center Institutional Review Boards and alerting the IRB staff and IRB Chair when a conflict exists;
  - Preparing for each meeting by reading study materials, serving as a primary reviewer in his/her area of expertise, preparing questions for, and seeking answers from investigators;
  - Exercising care to maintain the confidentiality of information and materials distributed to him or her under this policy, using and disclosing such information and materials only as necessary for the conduct of IRB business; and
  - Actively participating in the IRB member continuing education program.
- 6.1.10 Alternate IRB Members
- Alternate members may be selected to fill in for an absent IRB member.
  - Selection as an alternate is member specific. Criteria for selection are based on similar education, occupational expertise and institutional affiliation.
  - If both the regular and alternate IRB member attends a meeting, they may both participate in the discussions but only one of the two may vote. In these instances, the IRB meeting minutes will document who is in attendance as a voting member.
- 6.1.11 Non Voting (*ex officio*) IRB Members
- *Ex officio* members do not vote and they do not count towards establishing a quorum. Their presence/absence is reflected in the IRB's meeting minutes.
  - *Ex officio* members may take part in all meetings of the IRB that they are appointed to. These members may participate in the discussions and make recommendations to influence.

- *Ex officio* members may not participate in any discussions/deliberation in which they have a conflict of interest. In these instances, the *ex officio* member must leave the room during the IRB's deliberation and vote.

#### 6.1.12 IRB Member Liability

- IRB members function as employees and agents of CPMC. As such, when acting in accordance with the IRB's policies and procedures and standard operating procedures, their actions are covered by the CPMC general liability coverage.

#### 6.1.13 Consultants/Ad hoc Reviewers

- The IRB Chair or the IRB Administrator/Coordinator may invite scientists or non-scientists with special expertise to function as consultants and ad hoc reviewers for a particular study.
- These individuals, who may be from within or outside of CPMC, will be provided with all documents submitted to the IRB relevant to the specific study under review.
- The consultant/ad hoc reviewer may participate in the IRB's deliberations and make recommendations on the study, but he/she may not vote.

### 6.2 IRB Chair

6.2.1 The IRB Chair will be appointed or reappointed in writing by the Institutional Official in consultation with the CPMC Chief of Staff.

6.2.2 The term of office for the Chair shall be the balance of the calendar year in which the appointment is made, plus up to two calendar years thereafter. Consecutive terms are permitted.

6.2.3 Criteria used for the selection of the IRB Chair include reputation among the research community for fairness and ethical behavior, reputation among CPMC leadership for commitment to CPMC compliance goals, sensitivity to community issues, excellent communication and leadership skills, knowledge of applicable federal regulations and CPMC policies and experience with human subjects' research.

6.2.4 In addition to duties assigned to every IRB member, duties of the Chair include:

- Assuring that the IRB follows its policies and procedures and applicable federal regulations;
- Conducting the IRB meetings according to applicable federal regulations;
- Recommending IRB members and assisting in their training and development; and

- Reporting to the Institutional Official when studies before the IRB raise significant financial, legal, ethical, or business concerns, which may place CPMC at risk.

6.2.5 The IRB Chair may delegate, in writing, specific tasks to individuals, including:

- Signing IRB correspondence and meeting minutes;
- Conducting expedited review;
- Determining exemption from IRB Review;
- Acting as Chair when the Chair will be absent; and
- Other duties as appropriate.

6.2.6 The IRB Chair may be removed from this position by the Institutional Official, in consultation with the CPMC Chief of Staff, if he/she:

- Does not comply with the Conflicts of Interest Policy for Members of California Pacific Medical Center Institutional Review Boards; or
- Is unable or fails to perform his/her duties as IRB Chair or as an IRB member.

## 7. IRB Meetings

7.1 Convened meetings of each of the CPMC IRBs are generally scheduled to occur once per month. IRB Panel #1 meets on the second Tuesday of each month. IRB Panel #2 meets on the fourth Tuesday of each month. Scheduled meetings may be cancelled because of a lack of quorum or advance notice of unavailability to a sufficient number of members.

7.2 The IRB Chair may call a meeting when he/she determines that such a meeting is necessary to protect the safety, rights or welfare of one or more research participants.

7.3 Meetings convened by telephone conference call are allowed in certain circumstances, such as when the timing of IRB review may affect the safety, rights or welfare of one or more research participants, or as determined by the Chair.

7.3.1 When convening an IRB meeting by telephone, each member must have received all review materials in advance of the telephone meeting and be in a location where he/she can speak freely.

7.3.2 Meetings conducted by telephone are subject to the same federal regulations, CPMC policies, IRB policies and procedures and Standard Operating Procedures.

## 8. IRB Quorum and Voting

8.1 A quorum is defined as a majority (i.e., greater than 50%) of its total membership (i.e., the official IRB roster) and must include at least one member whose primary experience is in a non-scientific area.

- 8.2 A quorum must be present in order to conduct IRB business.
- 8.3 An IRB member with a conflict of interest in a project under consideration by the IRB will leave the room during the deliberation and vote on that project and will not count towards the quorum.
- 8.4 When the IRB reviews investigational drugs, devices or biologics, a quorum must include at least one physician.
- 8.5 Each voting IRB member in attendance at the convened meeting will have one vote, which he or she can exercise to express his or her personal opinion to approve, disapprove, or abstain from voting on the research project or project-related motion or item under consideration by the IRB. Voting by proxy is not allowed.
- 8.6 An alternate member may vote with the IRB if he/she is in attendance at the meeting and is replacing a regular IRB member who is absent from the meeting and who has a comparable profession and/or area of expertise. (For example, a physician/alternate may vote in place of a physician/regular member but not in place of a non-scientific/regular member.)
- 8.7 No IRB member will be involved in the initial or continuing review of a study or be allowed to vote on a project in which the member has a role in the project or a financial conflict of interest that has not been reviewed by the CPMCRI Conflict of Interest Committee, except to provide information requested by the IRB.
- 8.8 An investigator or other non-IRB member who attends an IRB meeting to present or answer questions about his/her project will not be in the room during the vote or deliberation on that project.
- 8.9 For a research project or project-related item to be approved, it must receive the approval of the majority of those members present at the convened meeting, unless it received approval by expedited review according to federal regulations.

## 9. Administrative Operations of the IRB

### 9.1 Meeting Preparation

The IRB Administrator, Coordinator or designee is responsible for meeting preparation, including the following:

- 9.1.1 Providing and publishing the IRB's monthly meeting schedule for each upcoming year.
- 9.1.2 Sending a **courtesy** reminder to project coordinators and principal investigators of upcoming IRB-approval expiration and continuing review requirements.
- 9.1.3 Preparing and distributing meeting materials that include but are not limited to: meeting agenda, minutes of the previous meeting, expedited review report, initial and continuing review materials, modification requests, serious adverse event reports, protocol violation reports and member education handouts.
- 9.1.4 Distributing materials to committee members and scientific merit reviewers at least one week prior to the meeting.
- 9.1.5 Assuring all study materials are available to the members at each meeting.

## 9.2 IRB Member Education Program

9.2.1 The IRB Administrator will coordinate the IRB member orientation and continuing education program.

9.2.2 Upon appointment to the IRB, each new member will receive the following:

- Terms of the CPMC FWA;
- The Belmont Report;
- Nuremberg Code;
- Declaration of Helsinki;
- IRB Policies and Procedures and Standard Operating Procedures;
- 45 CFR 46 Subpart A, B, C, and D;
- 21 CFR 50 and 56 including FDA information sheets;
- IRB forms; and
- Other documents as appropriate.

9.2.3 An IRB member continuing educational component will be included in each regularly scheduled IRB meeting

9.2.4 Newly appointed IRB members are required to complete the following trainings before they are added to the official IRB roster:

- IRB Member Orientation with the IRB Administrator; and
- On-line education tutorial.

9.2.5 The IRB Chair, Administrator and Coordinator will complete the relevant on-line OHRP Assurance Training within one month of assuming his/her role. The URL is: [http://ohrp-ed.od.nih.gov/CBTs/Assurance/module1qset1\\_4.asp](http://ohrp-ed.od.nih.gov/CBTs/Assurance/module1qset1_4.asp)

9.2.6 It is recommended that the IRB Chair obtain the Certified IRB Professional (CIP) and/or Certified IRB Manager (CIM) certification within two years of his/her appointment.

9.2.7 The IRB Administrator will obtain the Certified IRB Professional (CIP) and/or Certified IRB Manager (CIM) certification within two years of his/her appointment.

9.2.8 The IRB Coordinator will obtain the Certified IRB Professional (CIP) and/or Certified IRB Manager (CIM) certification within two years of his/her appointment.

### 9.3 IRB Communication with Investigators and Others

9.3.1 Within two weeks after the IRB meeting, IRB staff will notify the investigators in writing of the IRB's decision to approve, approve with modifications, or disapprove the proposed research activity. The notification may be an electronic communication from, or a letter signed by, the IRB Chair, IRB Administrator, IRB Coordinator or designee.

9.3.1.1 The notification will be sent to the PI and the appropriate research coordinator or research staff member as applicable.

9.3.2 The notification to the investigator will specify the action taken by the IRB including approval, approval with conditions, disapproval, or other action. The notification will specify the modifications or stipulations the investigator must satisfy before final approval of the study can be given, and will indicate that the study cannot be initiated until the stipulations are submitted, reviewed and approved by the IRB.

9.3.3 If the IRB disapproves a research activity, the written notification will include a statement of the reasons for its decision.

9.3.4 The IRB Chair or the IRB Administrator will notify the Institutional Official of any unanticipated problems involving risks to participants or others, serious or continuing noncompliance, suspension or termination of IRB approval.

### 9.4 IRB Meeting Minutes

9.4.1 The IRB will prepare and approve IRB meeting minutes according to all applicable federal regulations.

9.4.2 The IRB staff will keep the Institutional Official notified of the IRB's actions by sending him/her a copy of the minutes of all IRB meetings.

9.4.3 The IRB staff will keep the Director of the Medical Staff Services Office notified of the IRB's actions by sending him/her a copy of the minutes of all IRB meetings.

### 9.5 IRB Documentation

9.5.1 The IRB will maintain records of each study to include:

- All submissions to the IRB, including Initial Research Application and Protocol Summary, progress and final reports, modification requests, adverse events reports, and reports of protocol deviations/violations.
- Research Protocol (all versions, if more than one);
- Grant Proposal (when CPMC PI is the primary awardee);
- Investigator's Brochures, if applicable;
- IRB-approved Informed Consent Documents;

- Recruitment materials (e.g., flyers, advertisements, etc.);
- All communications between the IRB and the Investigator(s); and
- Any other documents relevant to the IRB's review of the study.

9.5.2 The IRB shall maintain records (either on site or in storage) relating to a specific research activity for at least three years after completion of the research.

9.5.3 IRB member appointment or reappointment documentation will be maintained by the IRB Administrator or designee for a minimum of five years following the last term served.

9.5.4 The IRB Administrator or designee will maintain a current IRB member roster, as well as all previous IRB member rosters.

9.5.5 IRB records shall be accessible for inspection and copying by authorized representatives of the OHRP and the FDA at reasonable times and in a reasonable manner, or shall be copied and forwarded to OHRP and the FDA when requested by authorized representatives.

## 9.6 IRB Authorization Agreements

9.6.1 The CPMC IRB may cede review authority to an outside (or non-CPMC) IRB, or conversely, the CPMC IRB may act as the IRB of record for an outside IRB only in the presence of an appropriate agreement (e.g., an IRB Authorization Agreement or a memorandum of understanding).

9.6.1.1 To act as the IRB of record for a Sutter-affiliated hospital located in the same corporate entity as itself, the CPMC IRB will need to revise its FWA. The generation of an IRB authorization agreement and/or a memorandum of understanding will not be necessary.

## 9.7 Unaffiliated Individual Investigators

Individual investigators not affiliated with an institution covered by a DHHS Assurance must be covered under the CPMC FWA when conducting research under the authority of the CPMC IRB. This is accomplished by a written agreement stating a commitment to abide by CPMC's policies and procedures and oversight. The agreement is between the individual investigator and CPMC, and signed by the Institutional Official.

In addition to the above, an unaffiliated individual investigator must have a Principal Investigator for the study who is formally affiliated with CPMC.

## 10. Operations of the IRB

### 10.1 Initial IRB Review of Proposed Research

The IRB will conduct initial review according to the *Initial IRB Review of Proposed Research* Standard Operating Procedure (SOP).

## 10.2 Verifying Exemption from IRB Review

The IRB will follow federal regulations outlined in 45 CFR 46.101(b) and 56.110 when considering whether a research project is exempt from IRB review.

## 10.3 Expedited Review

The IRB will conduct expedited reviews according to the *Expedited IRB Review SOP*.

## 10.4 Study Modifications

The CPMC Investigator and IRBs will follow the *Study Modifications SOP* when requesting changes in IRB-approved research.

## 10.5 Adverse Events (AEs), Serious Adverse Events (SAEs) and Investigational New Drug (IND) Safety Reports: Principal Investigators Reporting Requirements

The CPMC Investigator will follow the *Adverse Events, Serious Adverse Events and IND Safety Reports: Principal Investigators Reporting Requirements SOP* when evaluating AEs, SAES and IND reports.

## 10.6 Adverse Events (AEs) and Investigational New Drug (IND) Safety Reports: IRB Review Process

The CPMC IRBs will follow the *Adverse Events and IND Safety Reports: Principal Investigators Reporting Requirements SOP* when reviewing AE and IND Safety Reports.

## 10.7 Protocol Violations, Deviations and Exemptions

The CPMC Investigator and IRB will follow the *Investigator Reporting and IRB Review of Protocol Violations and Deviations SOP* when evaluating, reporting or reviewing protocol violations, deviations or exemptions.

## 10.8 Continuing Reviews

The CPMC Investigator and IRB will follow the *Continuing Review of IRB-Approved Research SOP* when submitting or evaluating progress reports and final reports.

## 10.9 Research Involving Vulnerable Populations

Federal regulations consider certain groups of human subjects to be particularly vulnerable in a research setting. These groups include: pregnant women, fetuses, children and prisoners. The CPMC IRB will follow regulatory criteria in 45 CFR 46 Subparts B, C and D in carrying out its responsibilities to protect these groups.

In addition to pregnant women, fetuses, children and prisoners, the CPMC IRB may also include other groups to the list of vulnerable populations. These may include (but are not limited to) the educationally or economically disadvantaged, the cognitively impaired, and the terminally ill.

## 10.10 Suspending and Terminating IRB-Approved Research

The IRB has the authority to suspend or terminate approval of human subjects' research that is not being conducted in accordance with federal regulations and IRB policy and procedures or that has been associated with unexpected serious harm to subjects.

10.10.1 When the IRB suspends or terminates a study or a study activity (i.e., enrollment), it may:

- Require actions to protect the safety, rights and welfare of currently enrolled research subjects.
- Require the PI to develop and implement a corrective action plan before the suspension is lifted.
- Terminate a suspended study if the corrective action plan is not completed within 60 days.
- Consider whether research subjects should be informed of the suspension or termination.

10.10.2 The IRB will notify the study's PI of any study suspensions or terminations within five working days.

10.10.2.1 It is the PI's responsibility to notify all sub-investigators of the suspension or termination within five working days of his/her receipt of IRB notification.

10.10.3 The IRB will notify the Institutional Official of any study suspensions or terminations within five working days.

10.10.4 The IRB will notify the appropriate federal regulatory agencies (e.g. FDA, OHRP) of any study suspensions or terminations.

10.10.5 Suspensions of IRB-approved research by the IRB Chair will be reported to and reviewed by a convened IRB.

## 10.11 Noncompliance Investigations and Actions

Investigations of noncompliance by the IRB focus on the protection of study subjects. Information regarding noncompliance in human subjects' research may come to the attention of the IRB through several pathways that include: information contained in application forms, IRB reporting forms, monitoring reports, or reports from collaborators, CPMC employees, study subjects or others not directly involved in the research.

10.11.1 When information comes to the attention of the IRB outside of a full-board meeting, the IRB Chair, Administrator and/or Coordinator will review the allegations of noncompliance. The Chair (or a designee) will make an initial

determination as to whether the alleged practices appear to (1) cause injury or any other unanticipated problems involving risks to subjects or others, or (2) constitute serious or continuing noncompliance with IRB determinations or federal regulations. In such cases, the Chair may suspend any or all study procedures, taking into consideration the welfare of currently enrolled subjects, pending an investigation and review by the full IRB. Such suspension is reported according to procedures in section 10.9. If the Chair determines that the potential noncompliance did not involve any risk to subjects or others, and did not constitute serious or continuing noncompliance, the Chair (or designee) may resolve the issue directly with the Principal Investigator and research team.

- 10.11.2 When potential noncompliance is first identified during a full-board review, the IRB makes a determination as to whether the alleged practices appear to (1) cause injury or any other unanticipated problems involving risks to subjects or others, or (2) constitute serious or continuing noncompliance with IRB determinations or federal regulations. In such cases, the full board may suspend any or all study procedures, taking into consideration the welfare of currently enrolled subjects, and determine how further investigation will be conducted according to the procedures indicated below.
- 10.11.3 In cases that involve allegations of research misconduct, the Chair (or his/her designee) contacts the Institutional Official and the CPMC Research Integrity Officer (RIO). This does not preclude the Chair or any member of the IRB from independently contacting the Institutional Official and/or RIO about any allegation of scientific misconduct. Inquiries or investigations into research misconduct do not preclude IRB review and actions.
- 10.11.4 Procedures for investigating and resolving alleged noncompliance:
- 10.11.5 When made aware of an allegation of noncompliance, the IRB staff immediately notifies the IRB Chair for the IRB of record and works with the Chair to compile any required background file information. The IRB Chair, Administrator or Coordinator may seek advice of legal counsel.
- 10.11.6 The IRB Chair makes a determination as to whether to pursue the matter with the Principal Investigator (PI) via telephone call, e-mail, paper memo, or in person based on the nature and seriousness of the alleged noncompliance. The Chair may also send the IRB Administrator/Coordinator to meet with research team members and review study materials as appropriate. The purpose of such contact is to determine if there is noncompliance. Care must be taken to maintain confidentiality in all communications.
- 10.11.7 The IRB Chair and/or IRB staff will document the outcome of any and all communications and discussions in writing, either by e-mail or paper memo with a copy to the IRB files. Such documentation should be factual and objective, and include timelines for resolution (e.g., meeting dates, response deadlines).
- 10.11.8 The IRB Chair makes a decision based on the information gathered as to whether the allegation is credible. The advice of the CPMC legal counsel may be sought.

10.11.8.1 If the Chair believes the allegation is credible, the Chair determines whether the noncompliance a) meets the definition of serious or continuing noncompliance; and b) involves unanticipated risk to subjects or others.

10.11.8.2 If the Chair determines that the noncompliance is not serious or continuing, and does not involve unanticipated risk to subjects or others, the Chair and PI work together to create an acceptable corrective action plan. If the Chair and PI cannot come to an agreed-upon plan, the matter is referred to the full board for review as well as the Institutional Official.

10.11.8.3 If the Chair determines that the noncompliance is serious, or continuing, or involves unanticipated risk to subjects or others, the Chair refers review of the noncompliance to the next appropriate IRB meeting. If the Chair believes that the noncompliance is serious or continuing and that there is continuing risk of harm to current or future subjects, the Chair may suspend research activities, taking into consideration the welfare of currently enrolled subjects, until reviewed by the full board.

10.11.8.4 The Chair or IRB staff will notify the Institutional Official of these determinations.

10.11.9 A primary reviewer is assigned to lead the discussion at the full board meeting. All IRB members including the primary reviewer receive appropriate materials such as monitoring report(s), communications with the PI or other relevant individuals. In addition, approved IRB applications, consent documents, and other documentation from the project file may also be included as reference materials during the review and are distributed to all IRB members prior to the full board meeting. All IRB members are expected to review and be familiar with all materials as well as maintain confidentiality of the issues discussed.

10.11.10 When a quorum of IRB members is present, and after discussion, the IRB shall vote on when recommended actions.

10.11.11 Possible actions the IRB may take include one or more of the following:

- Suspension or termination of IRB approval of protocols that are found to be noncompliant with CPMC policies and procedures, state laws, and/or federal laws or regulations, taking into consideration the welfare of currently enrolled subjects;
- Institutional Official involvement;
- Legal Counsel involvement;
- Compliance audits;
- Letters of reprimand;
- Restrictions on serving as an investigator on human subjects protocols;

- Notification of currently enrolled subjects;
- Providing additional information to past subjects;
- Modifications to research protocols;
- More frequent continuing review or monitoring;
- Monitoring of the consent process;
- Changes in consent process or documents;
- Requirement that current subjects re-consent to participation;
- Request more information prior to making a final decision;
- Referral of the issue to other organizational entities such as Legal Counsel, Risk Management, the CPMC Research Integrity Officer and the Institutional Official.
- Other actions as appropriate.

The IRB sends written notification of actions to be taken to the PI.

#### 10.12 Emergency Use of Investigational Drugs and Devices

##### Emergency Use Defined:

The FDA human subjects' regulations allow for an investigational drug/device to be used in emergency situations without prior IRB approval. Emergency use is defined as a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval for the use.

##### PI Responsibilities

In Emergency Use situations, the PI:

1. Is required to obtain informed consent unless the FDA requirements allowing an exception to the requirement for informed consent are met.
2. Should, whenever feasible, notify the IRB of the proposed emergency use in advance either verbally or in writing.
3. Must report within 5 working days the emergency use of an investigation drug, biologic or device to the IRB in writing (complete the One-Time Emergency Use form).

All emergency use reports are reviewed by a convened meeting of the IRB.

##### Emergency Use of Investigational Drugs/Biologics

1. Emergency use of an investigational drug or biologic requires that an IND application be on file with the FDA.

2. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.
3. Exception: The need for an investigational drug may arise in an emergency situation that does not allow time for submission of an IND by the sponsor.
  - a. In this instance, the FDA may authorize shipment of the test article in advance of IND submission.
  - b. Requests for such authorization may be made to the FDA by telephone or other rapid communication means.

### Emergency Use of Investigational Medical Devices

Emergency use of an investigational medical device may arise when 1) an Investigational Device Exemption (IDE) for the device does not exist, 2) when a physician wants to use the device in a way not approved under the IDE, or 3) when a physician or institution is not approved under the IDE. Each of the following conditions must exist to justify emergency use:

1. The subject is in a life-threatening condition that needs immediate treatment.
2. No generally acceptable alternative for treating the patient is available.
3. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

The FDA expects the physician to determine whether such an emergency exists, and to have substantial reason to believe that the subject will benefit from the use of the device. The physician is further expected to obtain the following for subject protection:

1. An assessment by an independent physician.
2. Informed consent from the subject or a legal representative.
3. Chair of the IRB's concurrence.
4. If an approved IDE for the device exists, approval from the holder of the IDE. If an IDE does not exist, the physician must notify the FDA of the emergency use of the device and provide the agency with a written summary of the conditions constituting the emergency, patient protection measures taken, and any scientific results.

### Waiver of Informed Consent in Emergency Use Situations

Waiver of informed consent requires a signed statement from an independent physician who is not participating in the clinical investigation to certify in writing to all of the following [21 CFR 50.23]:

1. The subject is confronted by a life-threatening situation necessitating the use of the test article;
2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent;
3. Time is not sufficient to obtain informed consent from the subject's legal representative; and

4. There is no available method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the patient's life.

#### 10.13 Humanitarian Use Device (HUD) Studies

Humanitarian use of investigational drugs/devices is prospectively reviewed by the convened IRB. The investigator is required to submit the *Request to Treat Using Humanitarian Use Device* application to the IRB for review. Included in the application must be evidence that the investigator/sponsor has obtained a Humanitarian Device Exemption (HDE) from the FDA. These projects are subject to the same new and continuing review requirements for research projects as required of all non-exempt research. The FDA does allow for an expedited continuing review of HUD studies. Informed consent is not required by the FDA in HUD studies; however, the IRB may require that an informed consent document be used.

### 11. Appeal Process

11.1.1 The decisions of the IRB are not negotiable. No person or other group may override the IRB's decision.

11.1.2 The Institutional Official may decide that an IRB-approved study cannot be conducted at CPMC but he/she may not approve a study that the IRB has voted to not approve.

11.2 An investigator may request the IRB to reconsider a negative IRB decision by submitting a letter to the IRB Chair within 60 days.

11.2.1 The PI's letter should include the reasons for asking for an override of the IRB's decision.

11.3 The IRB Chair will decide whether the convened IRB will rehear the study (e.g., new information, explanation).

11.4 The convened IRB may reverse a previous decision if its findings are consistent with federal regulations, these policies and procedures, and the IRB's standard operating procedures.

### 12. Other Committees

#### 12.1 Conflict of Interest [in Research] Committee (COI Committee)

The COI Committee must review those studies in which an investigator has disclosed a significant financial conflict of interest. Review of a study by the IRB and COI Committee is concurrent.

As part of their review, the COI Committee will develop a management strategy to:

- Address the investigator's financial interest;
- Assure that the investigator may satisfy his/her research obligations in an objective manner;
- Avoid and/or mitigate concerns of bias; and
- Protect the rights and welfare of research subjects.

Management strategies that may be considered in addressing conflicts can range from:

- No action required other than disclosure
- To that of disqualification of the investigator from participating in the study.

Once developed, the COI Committee will provide the IRB with their management strategy for review.

The IRB will place a contingency on the study until it receives the COI Committee management strategy. If the IRB approves the submitted management strategy, the IRB will lift its contingency and notify the investigator and the COI Committee of its approval. The IRB has the authority to revise the management strategy if it determines that such a modification will increase protection for research subjects. The IRB will communicate any such revisions to the COI Committee and the Institutional Official.

If the investigator of a study brought to the COI Committee is a member of the IRB, he/she may answer questions but must then leave the room for the IRB's deliberation and vote.

## 12.2 Human Stem Cell Research Oversight (SCRO) Committee

Studies involving human stem cell research must be reviewed by the SCRO Committee as well as the IRB. The IRB and the SCRO may conduct their reviews concurrently; however, the IRB's final approval is contingent on the SCRO's approval of the study. Please contact the Director of Research Program Development for further information.

## 12.3 Institutional Biosafety Committee (IBC)

Human subjects' research conducted within CPMC involving biohazardous agents, select agents and toxins, recombinant DNA, gene transfer and gene therapy must be reviewed and approved by the CPMC Institutional Biosafety Committee (IBC). The IBC is responsible for ensuring that recombinant DNA activities are aligned with the National Institutes of Health (NIH) DNA guidelines.

The PI is required to submit a registration document to the IBC staff for all recombinant DNA experiments that are not exempted from the NIH guidelines. Please contact the Director of Research Program Development for further information. The registration document must be reviewed and approved by the IBC prior to the initiation of the research.

The IBC notifies the IRB of its approval of projects using recombinant DNA, but deliberations of the IBC are not shared with the IRB unless there are specific subject protection issues raised by the IRB.

At its discretion, the IRB may review a study concurrent to the IBC's review; however, the IRB's approval of the study would be contingent upon receipt of the IBC's approval.

If the IBC review identifies specific subject protection issues after the IRB's contingent review has occurred, the IRB Chair will review the issue. If the Chair (or his/her designee) believes the suggested change(s) are appropriate and qualify as a minor modification, the revision may be reviewed through the expedited process. If the Chair or designee determines that the suggested change exceeds a minor modification, the Chair will refer the application back to the full board for review prior to final approval.

#### 12.4 Radiation Safety Committee

Research protocols exposing human subjects to ionizing radiation greater than routine care are required to be reviewed and approved by the CPMC Radiation Safety Committee. The Committee will review the investigator's plan for the use of radioactive materials as well as the safety precautions that will be implemented.

Review and approval of a study by the Radiation Safety Committee is required prior to the IRB's review. Please contact the Director of Research Program Development for further information.