UNIVERSITY OF CALIFORNIA - SAN DIEGO
HUMAN SUBJECTS RESEARCH GUIDELINES

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INTRODUCTION

In accordance with the Federal Policy on the Protection of Human Subjects (DHHS Policy 45 CFR Part 46, FDA Policy 21 CFR Parts 50 and 56), the University of California, San Diego (UCSD) is responsible for the protection of the rights and welfare of human subjects of research conducted by, or under the supervision of, faculty, staff or students. To conduct this responsibility effectively, the University maintains Institutional Review Boards to review research protocols involving human subjects and to evaluate both risk and protection against risk for those subjects. It is the function of the IRBs to 1) determine and certify that all projects reviewed by the IRBs conform to the regulations and policies set forth by the DHHS and FDA regarding the health, welfare, safety, rights, and privileges of human subjects; and 2) assist the investigator in complying with federal and state regulations.

I. Jurisdiction of UCSD Institutional Review Board Review (IRB)

The IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of this institution. The IRB has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified both by federal regulations and institutional policy. Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, those officials may not approve research if it has been disapproved by the IRB.

Independence of IRB. The IRB functions independently of, but in coordination with, other committees. The IRB, however, makes its independent determination whether to approve or disapprove a protocol based upon whether or not human subjects are adequately protected.

The IRB has review jurisdiction over "all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency" that has adopted the human subjects regulations.

Research is defined by the regulations as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

Human Subjects are defined by the regulations as "living individual(s) about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information."

The University of California, San Diego, as part of its **Multiple Project Assurance** (MPA), [the "license" from the NIH to function as an IRB] has agreed to protect the welfare of all human subjects involved in research, whether or not the research is conducted or supported by a federal department or agency. Therefore, the UCSD IRB has jurisdiction over <u>all</u> human subject research conducted at this institution and does <u>not</u> recognize any exemptions.

A. The University of California, San Diego currently has three designated Institutional Review Boards with the authority to review, approve, disapprove, or require changes in research activities involving human subjects. These IRBs have been established in accordance with the requirements of current federal rules.

B. The UCSD IRBs shall review all human subject research:

   1. sponsored by UCSD;

   2. conducted by any UCSD or San Diego Veterans Affairs Medical Center (SDVAMC) employee or agent in connection with his or her institutional duties;

   3. conducted by any UCSD or SDVAMC agent or employee using any property or facility of UCSD or the SDVAMC;

   4. that involves the use of UCSD's or SDVAMC's non-public information to identify or contact human research subjects.

C. Any questions regarding the necessity of UCSD IRB review should be addressed to the Director, Human Subjects Program, (HSPO), UCSD, at (619) 534-4520.

II. Committee Structure

A. One of the **School of Medicine (SOM) IRBs** shall review all medically-oriented research proposals involving human subjects. The School of Medicine IRB may refer proposals to the Social and Behavioral Sciences IRB.

B. The **Social and Behavioral Sciences (SBS) IRB** shall review all non-medical research proposals involving human subjects. The Social and Behavioral Sciences IRB may refer proposals to the SOM IRB.

C. Composition of the IRBs

1. Membership

Each UCSD IRB will include at least one member whose primary concerns are in the scientific areas and at least one member whose primary concerns are in the non-scientific areas.

Each UCSD IRB will include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

UCSD faculty, who constitute some of the **membership of the IRBs**, come from a variety of academic disciplines necessary to provide expertise relevant to the studies being evaluated. The **Director, Human Subjects Program** is a voting member of the IRB. The Investigational Pharmacist will be an *ex officio* member of the School of Medicine IRB. Additional members will also consist of a non-scientific person representing the San Diego Community and a person or persons knowledgeable in areas of institutional commitments and regulations, standards of professional conduct and practice, and applicable law.

2. Selection of IRB Members

a. The IRB and/or the HS Program Office identifies a need for a new or replacement member, or alternate member. The IRB nominates candidates and sends the names of the nominees to the UCSD Human Subjects Program Office, (HSPO).

b. For faculty members, the UCSD HSPO contacts the nominee. If there are no nominees, then appropriate Department Chairs will be contacted in writing by the UCSD Institutional Official for Human Subjects, or the HSPO, concerning the vacancies and solicits nominees from the Department Chair.

c. The final decision in selecting a new member is made by the UCSD Designated Institutional Official for Human Subjects Research, the Human Subjects Committee members and the Director of Human Subjects Program. Appointments are made for a renewable two-year period of service.

d. The UCSD Designated Institutional Official for Human Subjects Research, in consultation and approval with the HS Committee members, and the Director, HSPO, appoints a chair and vice chair of each IRB to serve for renewable two-year terms.

3. **Membership Lists**

   a. The HS Program Office shall keep IRB membership lists current.

   b. IRB Membership lists shall identify the members by name, earned degrees, areas of professional competence, indications of experience, and relationship with UCSD.

   c. Changes in IRB membership shall be promptly reported to the Office of Protection from Research Risks, Departments of Health and Human Services (OPRR, DHHS).

D. **Schedule of IRB Meetings**

All IRBs shall meet on a regular basis throughout the year. Currently, the SOM IRB has two HS Committees. Committee A will meet the first Thursday of the month and Committee B will meet the third Thursday of the month. Both Committees meet for approximately 3-4 hours. The SBS IRB meets on the first Monday of each month for approximately 2 hours.

E. **Human Subjects Program Office (HSPO)**

The HSPO is supervised by the Director, Human Subjects Program, and is an administrator with experience and training in regulatory issues regarding human subjects.

III. Overview of IRB Review Process

The primary concern of the IRBs is the protection of the rights and welfare of human subjects in research. The efforts of the IRBs are directed at: 1) identification of the risk; 2) evaluation of the risk (i.e., a determination of whether or not the risk/benefit ratio is acceptable/ appropriate); 3) evaluation of procedures to minimize risk; and 4) evaluation of the informed consent document which adequately explains the risks.

A. **Initial Review**

1. Applications will be screened by the HSPO staff. Those qualifying for "expedited review" as established by the Secretary, DHHS, (see Appendix 12, Item 2, "Research Activities That May Be Considered For Expedited Review") will be sent to the appropriate IRB Chair or Vice Chair (or her/his designee) for review. The IRB will be apprised of all such "expedited approvals" by means of the agenda for the next scheduled meeting under the section entitled: "Applications Given Expedited Review & Approval." The agenda is provided to all IRB members approximately one week prior to each meeting.

2. The IRB will use the **"expedited review"** process to review some or all of the research appearing in Appendix 12, Item 2, "Research Activities That May Be Considered For Expedited Review." Copies of the research will be made available for any optional review at the request of any IRB member.

3. All other applications will be reviewed by the IRB at a convened meeting at which a quorum (simple majority) is present, including at least one member whose primary concerns are in a non-scientific area.

B. **IRB Review**

1. **Preparation for Review**

The HSPO will assign **a primary and a secondary reviewer** from the members of the IRB for all protocols requiring full IRB review. All protocols and supporting documentation will be provided to the reviewers by the HSPO approximately two weeks prior to the meeting.

2. **Review by the Full IRB**

Before the meeting, each **application** (including background information, project protocol, and informed consent) will be carefully reviewed by the primary and secondary reviewers. At the meeting, the primary reviewer will present an overview of the goals, design, study procedures, safety procedures, and qualifications of the investigators. Particular attention will be paid to the "**Risk:Benefit Ratio**" of the investigation and the adequacy of the Consent Form in conveying Human Subjects concerns. The secondary reviewer will provide an independent view of the application. Problems identified by the primary and secondary reviewers or by other IRB members will be discussed and suggestions for any necessary changes will be agreed upon by the IRB. These issues are considered in the vote to decide IRB action. Length of discussion can vary from a few minutes to over an hour when formal presentations are made by investigators or information from outside experts is required.

3. **Discretionary Utilization of Outside Experts**

The IRB may establish subcommittees or invite individuals with special expertise outside the IRB to assist in the evaluation of complex issues. These experts are non-voting consultants to the IRB.

4**. Voting on Disposition**

a. Disqualification of members with potential **conflicts of interest**.

No IRB member with a conflict of interest may participate in the IRB's initial, continuing review or vote on an IRB action for a project except to provide information requested by the IRB.

b. Possible **IRB actions** taken by vote:

i. **Approval**: Action taken if no more than one dissenting vote is cast.

ii. **Approval Pending:** Action taken if the IRB requires minor additional information and/or modifications. The needed revisions are agreed upon at the meeting. The investigator is required to concur and provide written revision of the documents. When revisions are made by the investigator, the IRB Chair or her/his designee(s) approves the revised documents and allows the study to begin.

iii. **Deferral**: Action taken if substantial modification is required or if insufficient information is at hand to judge the application adequately (e.g., the risks and benefits cannot be assessed with the information provided). The

study is deferred and the investigator is informed of the reason(s) for the action. In order to receive approval for a deferred protocol, it must be submitted for full IRB review at a subsequent, convened meeting. The IRB's determination concerning the subsequent amended submission will be documented in the minutes of that meeting. (See Section III.D, of the guidelines.)

iv. **Disapproval**: Action taken if two or more dissenting votes are cast that would not be altered by the proposed modifications.

5. Investigators are informed in writing of all IRB decisions, including any changes required for approval. For applications that have received Approval Pending status, the HSPO will review the changes that are simple and routine to ensure that the investigator has made the modifications required by the IRB. When the issues or changes are more involved, but still minor, the primary reviewer assigned to the protocol will review the revised documents to ensure that the necessary change(s) have been made. The IRB will approve the protocol only when the required changes have been made and received by the HSPO.

6. Along with **notification of approval**, investigators are informed that: 1) Changes in approved projects must be reviewed and approved by the appropriate IRB before they are initiated. 2) Unexpected adverse events/reactions must be reported. 3) **Monitoring** will occur. The frequency of monitoring will be determined by the IRB at the time of initial or continuing review, and investigators will be so informed. Approval letters are signed by the Director, Human Subjects Program. (See Appendix 12, Item 9, "Cover Sheet for all IRB Approval Letters.")

7. The IRB will report its findings and actions to the institution in the form of its minutes which are sent to the appropriate institutional officials.

C**.** **Criteria for Approval**

Applications must meet the following **criteria for IRB approval**:

1. Risks to the subjects are minimized by using procedures which: a) are consistent with sound **research design**; b) do not unnecessarily expose subjects to risk; and c) whenever appropriate, utilize procedures already being performed on the subjects for diagnostic or treatment purposes.

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects and the importance to society of the knowledge that may reasonably be expected to result.

3. **Selection of subjects** is equitable. The IRB will consider the purposes of the research, the setting in which research will be conducted, and the population from which subjects will be recruited including special problems of research involving **vulnerable populations** such as pregnant women, children, mentally disabled persons, or economically or educationally disadvantaged persons.

4. IRB approved consent forms must be used for the consent. Informed consent will be sought from each prospective subject or the subject's legally authorized representative in accordance with current federal rules on the protection of human subjects. (See Section VI of these guidelines.)

5. Where appropriate, the research plan makes adequate provision for regular **monitoring of the data** collected to ensure the safety of the subjects. **NOTE:** For blinded or multicentered studies, studies in which mortality or morbidity from underlying disease (e.g., cancer or AIDS) may be high, and phase I or II studies of potentially dangerous drugs or procedures, continuous centralized monitoring of outcomes may be necessary. This may be accomplished by a **data safety monitoring board (DSMB)** or unblinded co-investigator. Specific rules for overwhelming evidence of efficacy or sufficient evidence of toxicity to require changes in protocol may be required. Description of these measures should be included by the PI in the section of the application on risk management.

6. Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

7. Where some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as persons with severe physical disabilities or mental illness, appropriate safeguards have been included in the study to protect the rights and welfare of these subjects.

D. **Further Review of Deferred Protocols (See Section III.B.4.b.iii, of these Guidelines.)**

1. If the application is deferred the following will occur:

   a. HSPO informs the investigator in writing of the IRB's decision, questions and concerns.

   b. Investigator's response is sent to the HSPO.

   c. The HSPO provides the IRB with the response, the revised protocol and the previously submitted protocol. The item is placed on the agenda for the following meeting.

   d. The project is given full IRB review again.

   e. The outcome of the IRB's deliberations is once again communicated to the investigator in writing.

2. Approval of the project will not be granted until all deficiencies are corrected to the satisfaction of the IRB.

3. The IRB may request that an outside consultant review the application.

4. Poor quality and lack of diligence in resubmitting a proposal to the IRB can result in concerns being raised regarding the investigator's ability to engage in research involving human subjects.

5. Investigators who have other individuals write their protocols and responses to the IRB must recognize that the ultimate responsibility of any study lies with the Principal Investigator. It will be incumbent upon the PI to check all material that is submitted to the IRB for review.

6. The IRB will also take under consideration the number of times an investigator resubmits a "deferred" project and it is subsequently rejected based on lack of diligence and attention to the issues raised by the IRB and whether it will allow a PI to continue such submissions. Among the issues that the IRB has found to be problematic are inclusions of drugs or procedures in the consent that are not included in the protocol or vice versa, failure to address all issues raised by the IRB in its correspondence to the PI, failure to address all risks in the consent that are listed in

the either the Master Protocol or the UCSD protocol, etc.

E. **Appeals Process for Disapproved Protocols**

1. If the application is disapproved, the principal investigator will be informed of the IRB's decision in writing by the HSPO. This communication shall include, in detail, the reason(s) for the disapproval. The principal investigator may then provide additional information and/or request to meet with the IRB to discuss the application.

2. A final decision regarding the appeal will be made by a vote of the IRB.

F. **Continuing Review and Monitoring of Active Protocols**

The Department of Health and Human Services (DHHS), the Food and Drug Administration, and the University of California, San Diego under the DHHS Regulations, Title 45 Code of Federal Regulations Part 46 (45 CFR 46), require at Section 46.109 (e), that "an IRB shall conduct continuing review covered by this policy at intervals appropriate to the degree of risk, but **not less than once per year..."** of all projects involving human subjects. OPRR interprets "not less than once per year" to mean review on or before the one-year anniversary date of the previous IRB review required by 45 CFR 46, even though the research activity may not begin until some time after the IRB has given approval. **As a courtesy**, the HSPO will send out reminder notices about six weeks before the approval for a study is due to expire. It is the investigator's responsibility to initiate an appropriate response, allowing for sufficient time for the review and re-approval process to be completed before the current approval expires should continuation of the research be planned.

If any project activity occurs or continues after the expiration date, the investigator is deemed to be out of compliance with both federal regulations and University policy. If patients remain under active study after the expiration date, the IRB should be notified immediately and permission may be obtained to continue **ONLY WHERE NECESSARY TO ELIMINATE APPARENT IMMEDIATE HAZARD TO THE SUBJECT**. E.g., Patients in the middle of an experimental treatment such as cancer chemotherapy for whom interruption of treatment may be harmful, but may apply to other protocol related activities as well.

1. Routine Monitoring

   a. The frequency of continuing review will be determined by the IRB and will be set at the time of initial review and at each subsequent review of a research project. At regular intervals, appropriate to the degree of risk and at least once a year, the IRB will conduct a detailed review of each study based on the IRB Protocol Monitoring Form. (See Appendix 12, Item 3, IRB Protocol Monitoring Form.)

   b. The **IRB Protocol Monitoring Form** will include the following information:

      i. information regarding **activation of study**;

      ii. The number of subjects studied to date;

      iii. Expected accrual completing the study;

      iv. Any changes in the scientific literature;

      v. Serious and unexpected reactions; (NOTE: Both **serious** and **unexpected**, or **unusual** adverse events should be reported to the HSPO, using the UCSD Research Subject Injury Report form, Appendix 12, Item 4, within 10

working days of the occurrence);

vi. Changes to the protocol;

vii. Summary of progress to date;

viii. A copy of the current approved informed consent.

c. The IRB will review the IRB Protocol Monitoring Form for each study at a regularly convened meeting. At the time of each continuing review the IRB will determine if the study should be terminated, amended, or allowed to continue.

d. The IRB minutes will record the IRB actions under the heading entitled **RENEWALS**. The minutes will record the IRB actions on these studies, the numerical results of the voting, as well as the frequency with which continuing review/monitoring will occur as determined by the IRB.

2. Intensive Monitoring of Protocols

Follow-up for rapidly changing or problematic protocols will be more frequent. This will be determined by the IRB when the initial review or a report from an ongoing study shows high risks to the subjects. Other factors such as multiple requests to

amend, the occurrence of unexpected adverse events, or other evidence of problems will trigger more frequent and intensive review. When appropriate, the IRB may require continuing review after a predetermined number of subjects have been treated with the test article. This more intensive monitoring can result in possible audit of research and patient records. When necessary, the Committee shall request verification of facts and verification that no material changes have occurred since the previous IRB review from sources other than the investigators.

3. Unresponsiveness to Information Requests

If a response to Committee requests for information is not received within 60 days of the date of the request, approval of the protocol will be rescinded. Further

unresponsiveness will result in suspension of all protocols for which the principal investigator is responsible. The suspension will also be reported to the FDA and OPRR as required by the regulations.

4. Continuation of Active Protocols

At the end of two years, no further extensions may be granted. Investigators wishing to continue their research must submit the requisite number of copies of the appropriate application for IRB review.

For projects not accruing new subjects, a terminal extension not to exceed 6 months may be granted to complete data gathering.

5. Notification of Completed Study

The School of Medicine and Social and Behavioral Sciences IRBs require that all investigators notify the IRB in writing, when a study is completed.

G. **Modifications/Amendments**

All modifications/amendments to an approved application and/or consent form must be received and approved by the IRB before they are initiated except where necessary to eliminate apparent immediate hazard to the subject. Requests for approval of modifications may be submitted at any time. (See Appendix 12, Item 9, "Cover Sheet for

all IRB Approval Letters. Also refer to Amendments/Modifications/Changes to a Protocol Fact Sheet dated 5/9/95.)

Major modifications/amendments are reviewed through the full committee review process, minor modification requests through the expedited process. Examples of modifications considered to be major in nature include, but are not limited to, escalation in the drugs(s) dosage(s), the introduction of an additional drug(s); the addition of a new invasive procedure. Major modifications may impact on the risk/benefit ratio in the study. It is the investigator's responsibility to assess the degree of change in procedures and risks of the study.

The initial determination as to whether a modification is major or minor is the responsibility of the principal investigator, who assesses the degree of change in procedures and risks. The modification is reviewed by the HSPO and determines whether full IRB review is necessary.

Minor changes in previously approved research during the period (of 1 year or less) for which approval has been authorized will be done under an expedited review process. The review will be carried out by the IRB Chair, or his/her designee(s) from members of the IRB. If the Chair or designee believes that the "minor" modification is too substantive to receive this type of review, the application will be referred for full IRB review. **A modification is given approval only to the expiration date that was received at the most recent review.**

Changes in study sites or investigators or additions should also be reported to the HSPO. These requests involve sending a cover letter, revised face sheet, and may involve a revised protocol to the HSPO of the requested change. In the case of a change in the principal investigator, the letter should be signed by the investigator who holds the approval.

The specific submission requirement for requests for amendments that go the Full Committee are as follows:

1. The REQUISITE NUMBER OF IDENTICAL APPLICATIONS (such as described in 2 below) must be sent to the HSPO by the submission deadline date of the next scheduled meeting.

2. Each of the 20 identical sets must include a **cover letter** that indicates title, principal investigator, HS approval number and specifies that an amendment/revision/modification is being requested. The request should clearly explain what the modification is, and why it is being proposed, and any potential risks or benefits to the subject.

3. An updated Cover Sheet/Face Sheet of the "Application to Committee on Investigations Involving Human Subjects" with the revisions highlighted.

4. The entire revised protocol with all the revisions highlighted. A **revised protocol** will be needed if there are substantive changes. The changes should be clearly identified as such, and should include a revised application face sheet as part of the set.

5. Both the approved and revised consent forms (if any are needed) should be submitted in the sets. Revisions should be clearly highlighted on the revised material.

REMINDER: Investigators **CANNOT INITIATE** the changes proposed until IRB approval is granted except as provided in Subpart C, 56.108(a)(4) of the Federal regulations which state that "...changes may not be initiated without IRB review and

approval except where necessary to eliminate apparent immediate hazard to the human subjects."

H. **Allegations of Protocol Violations**

1. The IRBs shall investigate allegations concerning possible **non-compliance with these guidelines** and federal regulation.

2. **Confidentiality** will be maintained concerning the source of the report to the extent allowed by law.

3. Action taken will include: (a) presentation of the allegation to the person(s) involved with a request for a response; (b) review of the problem by the IRB and communication of its recommendations to the investigator; and (c) presentation to the IRB by the investigator at a full committee meeting, if appropriate.

4. Any instance of serious or continuing non-compliance with federal, state, or UCSD IRB regulations or determinations will be reported promptly to appropriate institutional officials, the Office for Protection from Research Risks (OPRR) and to the United States Food and Drug Administration (FDA) (for FDA-regulated test articles).

IV. Reports of Adverse/Untoward Reactions

The United States Food and Drug Administration under Subpart C - IRB Functions and Operations 56.108 Subpart C(b)(1) requires written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of: (1) Any instance of serious or continuing problems involving risks to human subjects or others. This institution includes the notification of this **REQUIREMENT TO REPORT ANY UNANTICIPATED PROBLEMS INVOLVING RISKS TO HUMAN SUBJECTS OR OTHERS**, on the cover sheet for all IRB approval letters (Appendix 12, Item 9, Cover Sheet for all IRB Approval Letters) as well as in these written Guidelines, which go to all investigators.

A. The Human Subjects Program Office must be notified in writing of any injuries to human subjects and/or any unanticipated problems that involve risks to human subjects or others. Title 21 of the Code of Federal Regulations and the SOM IRB require that a report be made of **unexpected, fatal or life-threatening experiences** in writing no later than 10 working days of the event. The UCSD RESEARCH SUBJECT INJURY REPORT form (Appendix 12, Item 4) will be used for this purpose.

B. Confidentiality, for both subjects and investigators, to the extent allowed by law will be maintained.

C. The written report of the untoward reaction by the investigator will be presented to the appropriate IRB. If additional information is required by the IRB in order to make a final determination concerning the event, the investigator will receive such a request in writing from the Committee. In addition, and if necessary, the IRB may directly audit the research and medical records pertaining to the event or interview witnesses.

D. Any unanticipated problems involving risks to human subjects or others will be promptly reported to OPRR, and University officials.

E. The Director, Human Subjects Program, is responsible for reporting unanticipated problems involving risks to subjects, instances of serious or continuing noncompliance with regulations or committee requirements, and any suspension or termination or committee approval, to the US Food and Drug Administration, OPRR and appropriate

institutional officials.

V. Emergency Use of a Test Article

A. Definition

Emergency use is defined as the use of a test article (e.g., investigational drug or biologic) on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval for the use. Except as noted in Section V.B.3 below, **the investigator is still required to obtain informed consent under these circumstances.**

B. Obtaining Approval for Emergency Use

When an investigator identifies a need for emergency use of a test article, the following procedures must occur:

1. Approval must be obtained from the Chair or Vice Chair, IRB Committee, or in their absence from any other physician member of the IRB. Investigators may call the HSPO at x44520 for assistance in locating IRB members.
2. The investigator provides written documentation to the HSPO that approval was obtained. If urgent documentation of IRB approval is required by the company providing the drug, this may be sent by FAX from the HSPO.
3. The HSPO will provide a letter to the investigator stating that emergency IRB approval has been given to treat one patient.
4. The investigator must report the emergency use of the test article to the IRB within five working days.

Please note: Any subsequent use of the test article is subject to full IRB review. "Subsequent use" means any use of the test article that occurs after its initial emergency use. Should the investigator see a subsequent need to use the test article, a complete, formal application must be made for IRB review at a convened meeting.

C. **Emergencies** for which Informed Consent is not Feasible

In some emergency circumstances, it may not be feasible to obtain informed consent prior to using the test article. The regulations therefore provide an exception for informed consent requirements for such situations. Except as stated below, in order for this exception to apply, both the investigator and a physician who is not otherwise participating in the clinical investigation must certify in writing all of the following: (1) the subject is confronted by a life-threatening situation necessitating use of the test article; (2) the subject is unable to provide effective consent; (3) there is insufficient time in which to obtain consent from the subject's legal representative; and (4) there is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the subject's life.

If, in the investigator's opinion, immediate use of the test article is necessary to save the life of the subject and there is insufficient time to obtain the independent certification

required before using the test article, the investigator is to make his or her own written determinations and, within five working days after the use of the test article, obtain the written review and evaluation of a physician who is not participating in the clinical investigation.

Documentation, in both instances, must be submitted to the IRB within five working days after the use of the test article.

VI. Informed Consent

A. Definition

Informed consent is the knowing consent of an individual or her/his legally authorized representative which is obtained without undue inducement or element of force, fraud, deceit, duress, or other forms of constraint or coercion. A consent form documents informed consent.

One of the most common reasons for delay of approval of a protocol is an inadequate consent form. The consent form should be a statement addressed to the subject and should read as such. It must be in a language the subject or the representative can understand (avoid or define technical terminology, adjust for educational background and ages, provide translations in other languages when subjects do not understand English). Separate forms may be required for different subject groups (parents, children, etc.), as well as for release of particular kinds of information (photographs, audiotapes, videotapes).

B. Obtaining Informed Consent

1. Responsibility for Process

Research investigators are responsible for obtaining the subject's informed consent to participate in the research and for ensuring that no human subjects will be involved in the research **prior** to obtaining their consent.

2. Required Procedures

Unless otherwise authorized by the IRB, investigators are responsible for ensuring that legally effective informed consent shall:

a. be obtained from the subject or the subject's legally authorized representative;

b. be in language understandable to the subject or the representative; (The HSPO will provide a Spanish language translation upon request.)

c. be obtained under circumstances that offer the subject or the representative sufficient opportunity to consider whether the subject should or should not participate; and

d. not include exculpatory language through which the subject or representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the research investigator, the sponsor, the institution or its agents from liability for negligence.

C. Elements of Informed Consent

1. Required Elements of Informed Consent:

Basic elements of informed consent. In seeking informed consent the following

information shall be provided to each subject:

a. A statement that the **study involves research,** an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

b. A description of any **reasonable foreseeable risks or discomforts** to the subject.

c. A description of any **benefits** to the subject or others which may reasonably be expected from the research.

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

e. A statement describing the extent, if any, to which **confidentiality** of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.

f. For research involving more than minimal risk, an explanation as to whether any **compensation** and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

g. An explanation of **whom to contact** for answers to pertinent questions about the research and research subjects' rights and whom to contact in the event of a research-related injury to the subject.

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

2. **Additional Elements of Informed Consent:**

When appropriate, one or more of the following elements of information shall also be provided to each subject:

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) which 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.

c. Any additional costs to the subject that may result from participation in the research.

d. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.

e. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.

f. The approximate number of subjects involved in the study.

Since the **Moore case**, according to UC Legal Counsel, informed patient consent now requires ... that (a) "a physician must disclose personal interest unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgment; and (b) a physician's failure to disclose such interests may give rise to a cause of action for performing medical procedures without informed consent or breach of confidentiality."

3. **Waiver or Alteration of Informed Consent:**

DHHS provides for waiving or altering elements of informed consent under certain conditions. FDA **has no such provisions** because the types of studies that would qualify for waiver or alteration are either not regulated by FDA or are covered by the Emergency Treatment provision of FDA Regulation 50.23.

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirement to obtain informed consent provided one of the following sets of conditions exists and is documented:

a. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine a) programs under the Social Security Act, or other public benefit or service programs; b) procedures for obtaining benefits or services under these programs; c) possible changes in or alternatives to those programs or procedures; or d) possible changes in methods or levels of payment for benefits or services under those programs; and the research could not practicably be carried out without the waiver or alteration.

b. The research involves no more than **minimal risk** to the subjects; the waiver or alteration will not adversely affect the rights and welfare of the subjects; the research could not practicably be carried out without the waiver or alteration, and, whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Investigators at this institution must provide subjects of a medical experiment with a copy of their signed consent form(s) and "The Experimental Subjects' Bill of Rights."

D. **Documentation of Informed Consent**

1. Types of **Consent Documents**

The consent form may be (1) a written document that contains the required elements of informed consent, to be read by the subject or the subject's representative or by the investigator to the subject; or (2) a short written form stating that the basic elements of informed consent have been presented orally to the subject or representative.

a. **Written Consent Document**

When a written document is used, investigators shall be responsible for ensuring that informed consent is documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative, unless this requirement is specifically waived by the IRB. Each person signing the written consent form must be given a copy of that form.

b. **Short Form Consent**

When a short form written consent document is used:

1. a witness must be present at the oral presentation;
2. the person obtaining consent must sign a copy of the summary;
3. the written summary of what is to be said to the subject or the representative must receive the prior approval of the IRB;
4. the subject or representative must sign the short form;
5. the witness must sign both the short form and a copy of the written summary; and
6. a copy of the summary and the short form must be given to the subject or representative.

2. Waiver of Documentation of Informed Consent

Under certain conditions, the IRB can waive the requirement that the subject sign the consent form. However, waiver of documentation of informed consent does not constitute waiver of informed consent. The IRB may waive the requirement to obtain a signed consent form for some or all of the subject if one of the following conditions exists:

a. The consent document is the only record linking the subject and the research and the principle risk would be potential harm resulting from a breach of confidentiality. Subjects will be asked whether or not they want documentation linking them to the research, and their wishes will prevail.

b. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

c. For projects of minimal risk involving the use of questionnaires, the required elements of informed consent may be included in an introductory letter attached to the instrument, which includes a statement that completion and return of the questionnaire will constitute consent to participate.

3. Retention of Signed Consent Forms

Signed consent forms should be stored so as to be available upon IRB request. If subjects are patients, signed consents become a part of their medical records. For subjects who are not patients, consent forms are to be stored in departmental files. In instances where this is not feasible (e.g., off-site locations), they may be stored in the principal investigator's files, but procedures must be developed to ensure that the department can gain physical control over consent forms when necessary.

E. Confidentiality/Anonymity

1. Legal Challenges and Confidentiality

In the informed consent procedure, subjects are often given assurances that the confidentiality of records identifying the subjects will be maintained.

Loss of confidentiality may occur however when a court orders that research files or information be submitted as evidence in a legal matter. The court decides who has access to the files and what information may be required to be provided.

Unless there are no identifiers on project materials and subject lists are not maintained, complete confidentiality of records identifying the subjects may be assured only to the extent that disclosure is not compelled by court order. When FDA regulated products are being studied, the informed consent document should state that the FDA may review and copy the subject's medical records and, if necessary, obtain the identity of the subject.

2. **Inadvertent Disclosure**

Security in storage, limitation of access, and coding constitute the best measure to minimize risk of inadvertent disclosure to unauthorized parties. Measures to prevent this problem should be described in applications for studies in which the data collected is sensitive.

3. **Certificate of Confidentiality**

Certificates of Confidentiality can be obtained by writing to the Director of the Office for Protection from Research Risks, NIH, Suite 3B01, 6100 Executive Blvd., MSC 7507, Rockville, MD 20892-7507.

Persons engaged in biomedical, behavioral, clinical, or other research (including research on mental health, the use and effect of alcohol and other psychoactive drugs) to protect the privacy of individuals who are the subject of such research by withholding from all persons not connected with the conduct of such research the names or other identifying characteristics of such individuals. Persons so authorized to protect the privacy of such individuals may not be compelled in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals. (Public Health Service Act, S 301(d), 42 U.S.C. s 241 (d), as added by Pub. L. No. 100-607, S 163 (November 4, 1988)).

A Certificate of Confidentiality is granted when the research is of a sensitive nature where the protection is judged necessary to achieve the research objectives. Research can be considered sensitive if it involves the collection of information in any of the following categories:

(a) Information relating to sexual attitudes, preferences, or practices;
(b) Information relating to the use of alcohol, drugs, or other addictive products.
(c) Information pertaining to illegal conduct;
(d) Information that if released could reasonably be damaging to an individuals' financial standing, employability, or reputation within the community;
(e) Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonably lead to social stigmatization or discrimination;
(f) Information pertaining to an individual's psychological well-being or mental health.

F. Children Involved as Subjects in Research

1. "Children" are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
2. "Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
3. "Permission" means the agreement of parent(s) or guardian to the participation of

their child or ward in research.

4. "Guardian" means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.
5. "Emancipated Minor" means a legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage or procreation.
6. "Mature Minor" means someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g., consenting to medical care). Note that a mature minor is not necessary an emancipated minor.

Research involving children as subjects must be reviewed by full Committee regardless of the risks involved.

VII. Appeals and Disciplinary Actions

A. Authority of Institution to Review Research

Research that has been reviewed and approved by an IRB may be subject to review and disapproval by officials of the institution. However, those officials may not approve research if it has been disapproved by the IRB.

B. Appeals of IRB Decisions

Investigators are encouraged to communicate with the HSPO or members of the IRB to clarify the reasons for deferral or disapproval of applications. If formal written responses to IRB inquiries fail to resolve disputed issues, investigators may request an **appearance at an IRB meeting** to present their views.

C. Auditing Procedures

1. A determination is made that an **audit** is necessary by the IRB based on several issues that may include but are not limited to:

    a. Subjects' complaint(s) that rights were violated;

    b. Report(s) that investigator is not following the protocol as approved by the IRB;

    c. Unusual and/or unexplained adverse events in a study;

    d. **FDA audit report** of an investigator;

    e. Repeated failure of investigator to report required information to the IRB;

2. A Sub-Committee consisting of IRB members, and non-members if appropriate, to ensure fairness and expertise is appointed.

3. The Sub-Committee is given a charge by the IRB which can include any or all of the following:

    a. Review of protocol(s) in question;

b. Review of FDA audit report of the investigator, if appropriate;

c. Review of any relevant documentation, including consent documents, case report forms, patient's investigational and or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects;

d. Interview of appropriate personnel if necessary;

e. Preparation of either a written or oral report of the findings which is presented to the full IRB at its next meeting;

f. Recommend actions if appropriate.

4. The IRB determines the appropriate action based on its own knowledge and the facts gathered by the appointed sub-committee's investigation.

5. The investigator is informed of the IRB determination in writing.

6. If the determination includes suspension of an investigator, the FDA and OPRR will be notified by the HSPO.

7. All appropriate institutional officials are informed of the IRB's decision.

D. Sanctions and Disciplinary Actions

Failure to abide by the UCSD IRB Guidelines and federal regulations may result in the following sanctions, among others:

1. **Suspension or termination of IRB approval** of specific research protocols or of all research involving human subjects in which the investigator participates. The IRB also has the authority to suspend or terminate approval of research that has been associated with unexpected serious harm to subjects. The IRB shall report any suspension or termination of IRB approval to the investigator, appropriate university representatives, and the OPRR and the FDA, as appropriate. This report will include a statement of the reasons for the IRB's actions.

2. **Institutional or individual action by the FDA or OPRR.** The FDA and OPRR DHHS may (a) withhold approval of all new UCSD studies by the IRB; (b) direct that no new subjects be added to any ongoing studies; (c) terminate all ongoing studies, except when doing so would endanger the subjects; and/or (d) notify relevant state, federal and other interested parties of the violations.

3. **Individual disciplinary action** of the investigator or other personnel involved in a study, up to and including dismissal, pursuant to University policies and procedures. Failure to secure necessary UCSD IRB approval before commencing human subject research will be reported to the Vice Chancellor Academic Affairs for disciplinary action.

4. Suspension or termination of project support by the Department of Health and Human Services.

5. Investigators should also be aware that, in general, the University **indemnifies** them from liability for adverse events that may occur in UCSD studies approved by the UCSD IRBs. Failure to follow approved procedures may compromise this indemnification and make the investigator personally **liable** in such cases.

IMPORTANT NOTE TO INVESTIGATORS: A COPY OF **ALL** FDA, NIH, NCI, DEPARTMENTAL, DIVISIONAL, ORGANIZATIONAL RESEARCH UNITS, OR CENTER AUDITS AND/OR LETTERS OF WARNING MUST BE SENT TO THE HUMAN SUBJECTS PROGRAM OFFICE WITHIN **TWO WORKING DAYS AFTER RECEIPT**.

A COPY OF **ALL RESPONSES** TO AUDITS AND/OR LETTERS OF WARNING MUST BE SENT TO THE HUMAN SUBJECTS PROGRAM OFFICE **PRIOR TO BEING SENT** TO THE REGULATORY AGENCIES.

VIII. IRB Records

The IRB will prepare and maintain for at least 3 years after completion of the research, adequate documentation of IRB activities, including the following:

A. Copies of **all protocols** reviewed (including the most recent master protocol) and their accompanying documentation, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

B. **Minutes of the IRB meetings** in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controversial issues and their resolution.

C. Records of continuing review activities.

D. **A list of IRB members** identified by name; earned degrees; representative capacity; indication of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to the IRB's deliberations; and any employment or relationship between each member and the institution.

E. The IRB's written procedures.

F. Statements of significant new findings provided to subjects.

G. Copies of all correspondence between the IRB and the investigators.

H. All records of the IRB will be made available to authorized representatives of the FDA, OPRR, and the institution upon request.

IX. Comparing FDA and DHHS Human Subjects Regulations.

UCSD has a **Multiple Project Assurance** with DHHS to conduct research supported by DHHS. This institution also engages in research involving products regulated by the FDA. Therefore this institution follows **both** DHHS and FDA regulations. The DHHS regulations (45 CFR 46)

apply to research involving human subjects conducted by DHHS or supported in whole or in part by DHHS. The FDA regulations (21 CFR 50 and 56) apply to all research involving products regulated by the FDA, including research and marketing permits for drugs, biological products, or medical devices for human use, food and color additives, or electronic products. Federal funds do not need to be involved. When research involving products regulated by the FDA is funded by DHHS, both DHHS and FDA regulations apply. Following is a description of the significant differences between FDA and DHHS regulations, including departures from the new Federal Policy as outlined in the OPRR 1993 PROTECTING HUMAN SUBJECTS INSTITUTIONAL REVIEW BOARD GUIDEBOOK.

IRB Regulations

312.120 (FDA)
46.101(h) (DHHS)

The **FDA regulations** provide criteria for accepting foreign clinical studies not conducted under an **Investigational New Drug Application (IND)**. The DHHS regulations allow a department or agency head to determine that if procedures prescribed by a foreign institution afford protections at least equivalent to DHHS regulations, the department or agency head may approve the substitution of foreign procedures

56.102 (FDA)
46.102 (DHHS)

FDA definitions are included for terms specific to the type of research covered by the FDA regulations (**test article**, application for research or marketing permit, clinical investigation). A definition for emergency use is provided. The definition of "IRB approval," added as a result of the Federal Policy, substitutes the term "clinical investigation" for the term "research" used in the Federal Policy [56.102(m)]. FDA also adopted the Federal Policy's new wording for the definition of "minimal risk" ("the probability and magnitude of

harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests") [56.102(i)].

46.103 (DHHS)

DHHS requires that institutions provide an **Assurance of Compliance** with human subjects regulations, which is negotiated with OPRR. FDA does not require Assurance of Compliance, but does require that IRBs have written policies and procedures.

56.104 (FDA)

Unlike DHHS, FDA exempts from prospective IRB review the "emergency use" of a test article in specific situations. FDA added the Federal Policy's new "taste testing" exemption at 56.104(d).

56.105 (FDA)

FDA provides for sponsors and sponsor-investigators to request a waiver of IRB review requirements (not informed consent requirements). DHHS regulations do

not have a similar provision.

56.108 (FDA)
46.108 (DHHS)

DHHS requires prompt reporting of an anticipated problems to the Secretary. FDA does not specify that a similar report be made by the IRB to the FDA Commissioner, but that the IRB have and follow written procedures to ensure that such reporting is done by the sponsor and clinical investigator.

56.109 (FDA)
46.109 (DHHS)
46.117(c) (DHHS)

Unlike DHHS, FDA does **not** provide that an IRB may waive the requirement for signed consent when the principal risk is a breach of confidentiality because FDA does not regulate studies that would fall into that category of research. (Both regulations allow for IRB waiver of documentation of informed consent in instances of minimal risk.)

56.110 (FDA)
46.100 (DHHS)

FDA does not include research on behavior or characteristics of groups or individuals such as studies of perception, cognition, game theory, or test development (DHHS activity #9) in its list of research activities that may be reviewed through expedited review procedures, because those type of studies are not regulated by FDA.

56.114 (FDA)
46.114 (DHHS)

FDA regulations do not discuss administrative matters dealing with grants and contracts because they are irrelevant to the scope of the Agency's regulation. (Both regulations make allowances for review of multi-institutional studies.)

56.115 (FDA)
46.115 (DHHS)

DHHS, but not FDA, requires the IRB or institution to report changes in membership. FDA has neither an assurance mechanism nor files of IRB membership; there is therefore no reason for FDA to be informed about changes in membership.

56.115(c) (FDA)

FDA may refuse to consider a study in support of a research or marketing permit if the IRB or the institution refuses to allow FDA to inspect IRB records. DHHS has no such provision because it does not issue research or marketing permits.

56.120-124 (FDA)

FDA regulations provide sanctions for noncompliance with regulations. There is no parallel DHHS regulation, other than 46.123, which permits early termination of research support and evaluation of applications and proposals in light of prior noncompliance.

Informed Consent Regulations

50.3(j)

FDA adopted the Federal Policy's new wording for the definition of "minimal risk" ("the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests") [56.102(i)].

50.23 (FDA)

FDA, but not DHHS, provides explicit guidance for an exemption from informed consent in emergency situations. The provision is based on a statutory requirement in the Medical Devices Amendment of 1976, and may be used in investigations involving drugs, devices, and other FDA-regulated products in situations describes in 50.23.

46.116(c) and (d) (DHHS)

DHHS provides for waiving or altering elements of informed consent under certain conditions. FDA has no such provision because the types of studies that would qualify for waiver or alteration are either not regulated by FDA or are covered by the emergency treatment provision of 50.23.

50.25(a)(5) (FDA)
46.116(a)(5) (DHHS)

FDA explicitly requires that subjects be informed that FDA may inspect the records of the study because FDA may occasionally examine a subject's medical records as they pertain to the study. While DHHS has the right to inspect records of studies it funds, it does not impose the same informed consent requirement because of the infrequency with which the Department actually inspects subject records.

X. **Fetal Tissue Transplantation**

A. On January 22, 1993, President Clinton issued a directive to the Secretary of Health and Human Services ending a five-year moratorium on federal funding of therapeutic transplantation research that uses human fetal tissue derived from induced abortions. In March 1993, NIH published interim guidelines for research involving human fetal tissue transplantation. On June 10, 1993, the NIH Revitalization Act of 1993 (Public Law 103-43) was enacted, and, because of the superseding provisions regarding fetal tissue transplantation contained in the law, NIH's interim guidelines were withdrawn.

B. The requirements of the law outlined below must be followed by all investigators at this institution who engage in fetal tissue transplantation in humans. Adherence to our OPRR-approved Human Subject Assurance of Compliance requires that this new legislative mandate be met; certification of IRB review and approval in accord with that Assurance is this institution's guarantee that it is abiding and continuing to abide by the statute. The provisions of that act are as follows:

- **Human fetal tissue** means tissue or cells obtained from a dead embryo or fetus after a

spontaneous or induced abortion, or after a stillbirth.

- Human fetal tissue may be used regardless of whether the tissue is obtained pursuant to a spontaneous or induced abortion or pursuant to a stillbirth.

- The Secretary of Health and Human Services may conduct or support research on the transplantation of human fetal tissue for therapeutic purposes.

- The woman donating the human fetal tissue must sign a statement declaring that the tissue is being donated for therapeutic transplantation research, the donation is being made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue, and the donation is being made without her (the donor) having been informed of the identity of those individuals who may be the recipients.

- The attending physician must sign a statement declaring that the tissue has been obtained in accord with the donor's signed statement and that full disclosure has been made to the donating woman of: (1) The attending physician's interest, if any, in the research to be conducted with the tissue, and (2) any known medical risks to the donor or risks to her privacy that might be associated with the donation of the tissue and are in addition to the risks associated with the woman's medical care. In the case of tissue obtained pursuant to an induced abortion, the attending physician's statement must also declare that the consent of the woman for the abortion was obtained prior to requesting or obtaining consent for donation, the abortion was conducted in accordance with applicable state law, and no alteration of the timing, method, or procedures used to terminate the pregnancy was made solely for the purposes of obtaining the tissue.

- The individual with the principal responsibility for conducting the research must sign a statement declaring that the individual is aware that the tissue is human fetal tissue donated for research purposes and may have been obtained pursuant to spontaneous or induced abortion or pursuant to a stillbirth; that the principally responsible researcher has provided such information to other individuals with responsibilities regarding the research; that the principally responsible researcher will require, prior to obtaining the consent of a person to be the recipient of a transplantation of the tissue, written acknowledgement of receipt of the foregoing information by such recipient; and that the principally responsible researcher has had no part in any decisions as to the timing, method, or procedure used to terminate the pregnancy made solely for the purposes of the research.

- Human Fetal tissue may be used only if the head of the agency or other entity conducting the research involved certifies to the Secretary of Health and Human Services that the statements required herein will be available for audit by the Secretary [DHHS].

- Research involving the transplantation of human fetal tissue for therapeutic purposes must be conducted in accord with applicable State law and the Secretary may not provide support for such research unless the applicant for assistance agrees to conduct the research. The conduct of such research by the Secretary must be in accord with applicable state and local law.

  The provisions of section 498B of the Public Health Service Act(42 U.S.C. 298g-2), added by Public Law 1-3-43, the NIH Revitalization Act of 1993 are summarized as follows:

- It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human fetal tissue for valuable consideration if the transfer affects interstate commerce. (Valuable consideration does not include reasonable payment associated with the transportation, implantation, processing, preservation, quality control, or storage of human fetal tissue.)

- It shall be unlawful for any person to solicit or knowingly acquire, receive, or accept a donation of human fetal tissue for the purposes of transplantation of such tissue into another person if the donation effects interstate commerce, the tissue will be obtained pursuant to an induced abortion, and: (1) The donation will be or is made pursuant to a promise to the donating individual that the donated tissue will be transplanted into a recipient specified by such individual; (2) the donated tissue will be transplanted into a relative of the donating individual; or (3) the person who solicits or knowingly acquires, receives, or accepts the donation has provided valuable consideration for the costs associated with such abortion. (Valuable consideration does not include reasonable payments associated with the transplantation, processing, preservation, quality control or storage of human fetal tissue.)

- Any person who violates these provisions shall be (1) Fined in accordance with title 18 United States Code, except that the fine shall be not less than twice the amount of any valuable consideration received, (2) imprisonment for not more than 10 years, or (3) penalized as described in both (1) and (2).

  Your attention to these requirements is essential if you are an investigator conducting or planning to conduct research involving the therapeutic transplantation of human fetal research. The IRB, in reviewing your research requires that all requirements outlined in this section of the guidelines are met. Copies of all the required signed consent documents must be included with the application.

XI. Special Requirements

A. Radioisotope Use in Humans

If radioisotopes are involved in the proposed project, additional approval for their use in humans is required. If research is to be conducted at the UCSD Medical Center, the Radiation Safety Officer must be contacted for instructions (campus 534-1069). If the research is to be conducted at the VA Medical Center, the Radiation Safety Office, VA 552-8585 extension 3911 must be contacted. (Radiation Safety Committee approval may be obtained before, during, or after application to the IRB. Final IRB approval, however, is contingent upon approval of the appropriate Radiation Safety Committee).

B. Use of "Test Articles"

The use of new drugs and/or device in an investigation usually requires clearance from the U.S. (or State of California) Food and Drug Administration in addition to IRB approval.

C. Veterans Affairs Medical Center

If the research project will involve VAMC patients, staff, and/or facilities, approval by

the VAMC Research & Development Committee is needed (in addition to UCSD IRB approval). Only one application need be made (the Application to Committee on Investigations Involving Human Subjects MO1), but investigators must be sure to indicate on the cover sheet that the VAMC is to be involved. It is also necessary that one of the investigators hold a VAMC appointment.

D. **General Clinical Research Center** (GCRC) Facilities

For research projects conducted at a GCRC Facility, a special, joint HSC/CRC application form should be used (MO2).

E. **Medical Risk Management**

In addition to reporting an injury to a subject to the IRB, the investigator also needs to report such an injury to Medical Risk Management (8976), 294-6468.

XII. Availability of Forms

The following application forms are available in the HSPO. To order, call 534-4521.

MO1 Standard application for medically oriented research.

MO2 Application for research that will be carried out in General Clinical Research Center Facilities.

MXP Application for "approval in principle"--to be used **only** for funding proposals in which definite plans for the involvement of human subjects will not be set forth; i.e., training grants, institutional type grants, or projects in which the involvement of human subjects will depend upon completion of instruments, prior animal studies, or purification of compounds.

MXT Application for the use of existing pathological or diagnostic specimens.

SO1 Standard application for social & behavioral science research.

CO1 Application for "blanket" approval of student research conducted as part of a COURSE. (This application is submitted by the COURSE instructor.) Students who propose projects that deviate from the research described by the instructor are required to submit individual applications (MO1 or SO1).

XIII. **Institutional Policies Relating to Human Subjects**

The Institution may institute or amend policies as needed that relate to human subjects as long as they do not violate Federal or State regulations.

A. It is a policy of this institution that **non-salaried faculty** may not serve as the Principal Investigator on a study. This policy, however, does not prohibit non-salaried faculty from submitting an application to the IRB with the non-salaried faculty as a co-investigator.

B. All clinical trials and other human subject activity involving University faculty, staff, and students **must be** reviewed by UCSD's Institutional Review Board regardless if another IRB has reviewed and/or approved the protocol. Use of an "outside" IRB is not permissible.

C. All **clinical trial activity** must be sponsored by and come through the University.

D. All clinical trials must have a **clinical trial agreement** in place, signed by one of the officials authorized to execute UCSD contracts and grants, before initiation of the clinical trial activity.

E. A copy of **all** FDA, NIH, NCI, Departmental, Divisional, Organizational Research Units, or Center audits and/or **letters of warning** must be forwarded to the Human Subjects Program Office, 0052, within **two working days after receipt**. Failure to comply with this policy may result in suspension of human subjects approval for project(s).

A copy of **all** responses to audits and/or letters of warning must be sent to the Human Subjects Program Office prior to being sent to the regulatory agencies.

F. Since the **Moore case**, according to UC Legal Counsel, informed patient consent now requires ... that (a) "a physician must disclose personal interest unrelated to the patient's health, whether research or economic, that may affect the physician's professional judgement; and (b) a physicians' failure to disclose such interests may give rise to a cause of action for performing medical procedures without informed consent or breach of confidentiality."

G. The Counsel of the Regents of the University of California has stated that: "If a principal investigator conducts an activity involving human subjects, but does not obtain the approval of the campus Human Subjects Committee, the Regents would **not** be obligated to defend or indemnify the principal investigator if legal action were instituted by the subject."

XIV. **Appendices**

1. "Experimental Subject's Bill of Rights"

2. Research Activities that may be Considered for Expedited Review

3. IRB Protocol Monitoring Form

4. UCSD Research Subject Injury Report

5. Policy on the Use of Women of Child-bearing Potential in Drug Studies

6. HIV Antibody Testing Policy at UCSD

7. IRB Checklist for Informed Consent

8. Cover Sheet for all IRB Approval Letters