EXPEDITED APPLICATION INSTRUCTIONS & GUIDANCE

This Guidance is to be used in conjunction with the Expedited Application / New Study. Each section below directly corresponds with the order of the Application. Please review carefully.

APPLICATION

Principal Investigator (PI) Information: The IRB establishes an electronic record of each IRB application it receives. This electronic record identifies the principal investigator (name, employee ID number, university position, department, mailing address, phone and fax number, and e-mail address), study information (title of the study), and tracks the entire history of the IRB review and approval process of the study. Your e-mail address is the mechanism used by the IRB Administration to correspond with you. We often communicate with Study Coordinators so the accuracy of their contact information is just as important. Your e-mail address also provides valuable contact information should the IRB Chair/Members try to reach you during their review of your study. Please ensure your e-mail address is a university issued account as private e-mail accounts may not be compatible with university systems. To be able to provide you with important updates and changes, you and your designated contact person will automatically be subscribed to our *Advisory* listserve at the e-mail addresses noted on your application. The application form will give you the option to *opt out* but we strongly encourage you to stay connected.

Do not neglect to include sponsor version numbers or other identifiers such as "CCRC" or "ADC" in the title of your study, as applicable.

Your approval documents will be transmitted to you electronically. However, it's always a good idea to include your "mailing address" should electronic systems fail and we have the need to mail you your approval documents via campus mail.

As correspondence to the PI is generated off of this electronic record, ensure your information is complete and accurate. When preparing your IRB application, use the most current application forms located on the IRB website. A considerable percentage of applications are deficient as a result of using outdated application forms. We strongly encourage you not to save blank application forms on your computer but instead refer to the IRB website for each study you begin to prepare. This will ensure that you are consistently using the most current up to date application forms.

Financial Sponsor: Identify the financial sponsor of the project. If a private, for-profit sponsor, be sure to complete and attach the IRB Fee Form. In investigator-initiated studies, completion of the IRB Fee Form is required if the drug or device is being provided to the PI by the drug / device manufacturer. Although the study may be considered investigator-initiated, in these instances the manufacturer is considered the financial sponsor.

IRB review fees apply to all research involving human subjects, fully, or in part funded by extramural funds, and conducted by UC Davis employees, students, or agents, except for those projects that are fully and directly funded by the following sources:

- Federal government
- State of California and its local governments
- Non-profit foundations

- UC Davis Departmental discretionary funds

If a federal sponsor, HHS regulations require that the IRB review the actual grant or proposal for HHS support. The IRB's review ensures that all research described in the grant or proposal is entirely consistent with any corresponding protocol submitted to the IRB. Therefore, IRB reviewers must have ready access to the entire grant or proposal (exclusive of appendices) because information related to the protection of human subjects sometimes appears only in seemingly peripheral sections. Please submit the entire grant or proposal minus the appendices.

As we may be contacted by the federal sponsor or by the Office of Research, Sponsored Programs (Contracts & Grants Office) to verify IRB approval, it is also important to indicate the title of your federal grant (as it may differ from the IRB application), the federal grant ID number, and grant type.

In collaborative studies, identify whether this involves a subcontract and who the prime grantee is and funding source. The IRB will need to determine whether the entity is engaged in human subjects research and if so, what their role is in the research and verify IRB approval for their scope of the study. If the study is funded by a State of California source, this same assessment will need to be made.

Protocol Development: A regulatory sponsor protects the rights and welfare of human subjects and confirms scientific integrity and data reliability. If this is a study under the jurisdiction of the US Food and Drug Administration, please identify whether the protocol was developed by either: a) a drug or device manufacturer; b) you, the principal investigator; or c) an academic investigator at another institution. Generally speaking, sponsors are the regulatory sponsors; but for investigator-initiated studies usually the holder of the IND and/or the PI is the regulatory sponsor.

Signatures: The signature of the principal investigator is required. The signature certifies to the IRB that the principal investigator has the appropriate credentials and privileges to conduct the study and that the facilities to conduct the study are adequate. The signature of the department chair supports this certification. Faculty signatures are required for all applications submitted by non-faculty PIs (student PI's). The Dean's signature is required for all applications from the School of Medicine.

The IRB Administration does not require the original signed paper copy of the PIs signature as applications are typically received in electronic form. However, investigators are asked to retain the originally signed copy in their research records for quality assurance purposes.

REQUIRED DOCUMENTS

Research Personnel List: The IRB Administration recommends that you review the following two key IRB Standard Operating Procedures (SOPs): *"Education and Training"* and *"Investigator Qualifications"* regarding the required training of research personnel and investigator qualifications. Specifically, the Principal Investigator is required to:

- Understand and be able to apply ethical principles guiding human subjects research as described in The Belmont Report. Investigators also are required to be aware of, and familiar with the requirements of applicable state and federal law, professional standards, as well as UC and UC Davis policies and procedures regarding human subjects research;
- Complete the required initial and continuing IRB training on human research protections;
- Ensure that other Investigators and key study personnel have completed the required initial and continuing IRB training and are familiar with the proposed research;
- Ensure that other Investigators and key study personnel are competent and licensed, if applicable, relevant to the scope and complexity of the research conducted;
- Conduct research in accordance with the ethical principles of *The Belmont Report*, Federal and State laws, UC policies and procedures, UC Davis IRB policies and procedures, IRB

Administration's applicable standard operating procedures, and if applicable, Good Clinical Practice standards.

All research personnel, beginning with the principal investigator, must be listed in the table if they will interact with human subjects or identifiable data. In addition, by signing the IRB application the PI attests that only certain designated research personnel will obtain informed consent, who have the appropriate training and/or credentials, understand the study, are knowledgeable about the study, and are able to respond to questions from research subjects including risks and alternative treatment and therapies. The IRB recognizes physicians and nursing personnel as the most appropriate individuals to obtain informed consent in a clinical trial. Pharmacists who dispense medications or lab personnel who do blood draws as part of their employment, are not considered research personnel and should not be listed.

Principal Investigators are reminded that it is their responsibility to ensure that all research personnel complete the required initial and continuing IRB training on human research protections, prior to submission of the application to the IRB.

Although not mandatory, the IRB highly recommends that the PI identify a member of the research personnel who will assume the role of Principal Investigator, should the PI take official leave from the University. This individual should have the equivalent training and credentials as the PI and have complete understanding of the research study and PI responsibilities. This individual must be UCD personnel.

PI and Co-PI CV/Biosketch: Non-Faculty Principal Investigators and Co-Principal Investigators (if applicable) are required to submit their current Biosketch. This is necessary as the IRB is required to ensure that all Investigators are competent and licensed, if applicable, relevant to the scope and complexity of the research to be conducted. The IRB may request additional information, qualification documentation, or licensure to assure competence in performing proposed research activities. *See IRB Standard Operating Procedure "Investigator Qualifications" for further information.*

Description of Study: Please see pages 8-12 for guidance.

Study Protocol: A study protocol is required for studies greater than minimal risk. The study protocol is a document that describes the objective(s), design, methodology, statistical considerations, and organization of the clinical trial. The protocol usually also gives the background and reason the trial is being conducted and contains a study plan on which the clinical trial is based. The plan is designed to safeguard the health of the participants as well as answer specific research questions. The protocol describes, among other things, what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; resources; and the length of the study.

A protocol provided by an industry sponsor will suffice. If you reference sections of the Study Protocol in the IRB application, you must include the Study Protocol with every future renewal. As some IRB members are non-scientists, it is recommended that you summarize the Study Protocol in lay language in this IRB application. For assistance in developing this document, please visit:

http://healthsystem.ucdavis.edu/clinicaltrials/documents/protocol_shell.doc

Recruitment Materials: The text of all direct advertising for research subjects (i.e., advertising that is intended to be seen or heard by prospective subjects) is required to be reviewed and approved by the IRB prior to distribution, posting, publication, or broadcasting. This is because recruitment of subjects is considered an extension of the informed consent process. Direct advertising includes but is not limited to the use of newspaper, radio, TV, bulletin boards, press releases, in-class announcements, letters, or the internet. Provide all proposed advertisements that

will be used to recruit subjects. *See IRB Standard Operating Procedure "Evaluation of Recruitment and Participant Selection Practices" for guidance on developing these documents.*

Surveys/Questionnaires: Provide a complete copy of all surveys and/or questionnaires, whether they are widely used as standard in the field of study or newly developed by you.

Interview Script: If applicable, provide the script that you will use to interview and screen participants (all in person and/or phone interviews).

Translated Documents: Should your study enroll non-English speaking subjects, regulations require that you provide the consent form in the language understandable to the participants. This will require translation/interpretation of the consent form and pertinent documents. Interpreting Services at UCDMC can assist with this service. The English version of documents will first be approved by the IRB. Translated documents can then be submitted to the IRB for approval through the modification/amendment process. *See IRB Standard Operating Procedure "Informed Consent" for guidance on developing this document.*

Forms for Informed Consent Process : Review the Model Consent Forms, Assent Form/Information Letter, Surrogate and Capacity Assessment Checklists and Debriefing Script on the IRB website to select and develop as appropriate for your study. If your study involves multiple consent forms be sure to label each clearly (i.e., consent/diet plus intervention; consent/diet only). If this study is to be conducted at the CCRC and/or ADC (subjects are seen at the CCRC / ADC), you must use the VA-UCD Joint Model Consent Form. See *Guidance for Drafting an Informed Consent Document.*

The federal Office for Human Research Protections reminds investigators that:

> Informed consent is a process, not just a form. Information must be presented to enable persons to voluntarily decide whether or not to participate as a research subject. It is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act. The procedures used in obtaining informed consent should be designed to educate the subject population in terms that they can understand. Therefore, informed consent language and its documentation (especially explanation of the study's purpose, duration, experimental procedures, alternatives, risks, and benefits) must be written in "lay language", (i.e. understandable to the people being asked to participate). The written presentation of information is used to document the basis for consent and for the subjects' future reference. The consent document should be revised when deficiencies are noted or when additional information will improve the consent process.

SUPPLEMENTS

Multi-Site Research: Multi-site research is a study involving more than one performance site, engaged in research with UC Davis. In instances where UC Davis is the lead institution, the PI must develop a communication plan as part of the protocol to ensure that all sites are made aware of all issues relevant to the study, such as unanticipated problems, protocol modifications, and interim results. This communication plan must be outlined in the *IRB Application Supplement – Multi-Center or Multi-Site Studies*. If UC Davis is not the lead institution, investigators are required to provide the Federalwide Assurance (FWA) number, PI name, and contact information for the lead site.

International Research: Investigators who plan to conduct international research must complete and attach the *IRB Application Supplement – International Research* to their IRB application. In collaborative studies with foreign countries, the UCD principal investigator is required to provide written evidence of IRB approval from the foreign institution where the clinical trial will be taking place. This is done to assure the IRB that adequate provisions are in place to protect the rights and welfare of the subjects. If the foreign institution does not have a fully constituted IRB, the institution may cite the Declaration of Helsinki as their statement on institutional letterhead. The

IRB application should clearly address the entire scope of the study, including the role of the foreign collaborator.

Waiver/Alteration of Informed Consent and/or HIPAA Authorization: To grant a waiver of informed consent, an alteration of the consent elements or procedures, or the requirements to obtain a signed consent document, the IRB must assess and evaluate the potential risks and expected benefits associated with participation in the research and the consent process. In evaluating the risk, the IRB will assess the risk or harms inherent in the informed consent process. Thus, the first step in determining whether a waiver or alteration is appropriate is the IRBs evaluation of the risks.

When the IRB approves a waiver of the requirements for informed consent or a procedure that does not include or alters elements of informed consent, the IRB must determine that the research meets the definition of minimal risk. This is because the waiver or alteration is based on the determination that the research poses no more than minimal risk to subjects. Therefore, the IRB may approve a waiver or alteration of informed consent provided the IRB finds and documents that:

- The research involves no more than minimal risk to the participants; and
- The research is not subject to FDA regulations; and
- The waiver or alteration will not adversely affect the rights and welfare of the participants; and
- The research could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the participants will be provided with additional pertinent information after participation.

Or, 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:

- Public benefit or service programs;
- Procedures for obtaining benefits or services under those programs;
- Possible change in or alternative to those programs or procedures; or possible changes in methods or levels of payment for benefits or services under those programs;
- The research could not practicably be carried out without the waiver or alteration; and
- The research is not subject to FDA regulations.

To make this assessment, the IRB requires that you complete the *IRB Application Supplement – Waiver/Alteration of Informed Consent and/HIPAA Authorization.*

If the study is subject to HIPAA and includes the use of a consent form(s), research participants must also sign the HIPAA Research Authorization Form. The IRB does not require the submission of the Research Authorization Form with your IRB Application Form.

Children/Minors : The inclusion of a vulnerable population in research, such as children, must be justified. In addition, adequate safeguards are required to be in place to minimize the risks unique to the particular vulnerable population. To make this assessment, the IRB requires that you complete the *IRB Application Supplement – Use of Children as Participants.* In the Supplement you will be asked questions about the children in the study, the parental consent and assent process, among other questions and requirements. This information will help the IRB determine whether the research meets the federal regulatory requirements for approval of research involving children.

For your information, DHHS and FDA regulations define "children" as 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. When research is conducted in California, individuals under the age of 18 meet this definition of "children" unless:

- The minor is emancipated (as specifically defined by California law);

- The research procedures are limited to pregnancy care, mental health treatment, drug or alcohol treatment; or
- The minor is a minimum of 15 years of age, not living at home, managing his or her own financial affairs, and legal counsel has determined that they meet the DHHS and FDA definition of "child".

For further information on this population, please see *IRB SOP "Vulnerable Populations (pregnant women, human fetuses and neonates, prisoners, children and cognitively impaired persons)".*

Pregnant Women / Human Fetuses / Neonates: If you plan to involve pregnant women and/or fetuses and/or neonates in your study, you are required to complete the *IRB Application Supplement – Pregnant Women and/or Human Fetuses and/or Neonates as Research Subjects .* Please be aware that federal regulations only allow the involvement of pregnant women and/or fetuses and/or neonates if ALL of the following conditions are met:

- Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or if there is no such prospect of direct benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- Any risk is the least possible for achieving the objectives of the research;
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the woman's consent is obtained in accord with the informed consent provisions outlined in IRB SOP "Informed Consent";
- If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of IRB SOP "Informed Consent", except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- For children who are pregnant, assent and permission are obtained in accord with the provisions of IRB SOP "Informed Consent";
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research will have no part in determining the viability of a neonate.

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

- Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and
- Individuals engaged in the research will have no part in determining the viability of the subject neonate.

a. Neonates of uncertain viability may not be involved in research unless:

1) The IRB determines that: (i) the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability and any risk is the least possible for achieving that objective, or (ii) the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
2) The legally effective informed consent of either parent of the neonate or if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained. However, the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

b. Nonviable neonates may not be involved in research unless all of the following additional conditions are met:

1) Vital functions of the neonates will not be artificially maintained;
2) The research will not terminate the heartbeat or respiration of the neonate;
3) There will be no added risk to the neonate resulting from the research;
4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5) The legally effective informed consent of both parents of the neonate is obtained. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent will suffice. Consent of the father need not be obtained if the pregnancy resulted from rape or incest. Consent cannot be obtained from a legally authorized representative.

c. Viable neonates may be included in research only to the extent permitted by 45 CFR 46 Subpart D – Additional Protections for Children Involved as Subjects in Research.

For further information on this population, please see *IRB SOP "Vulnerable Populations (pregnant women, human fetuses and neonates, prisoners, children and cognitively impaired persons)".*

APPROVAL BY OTHER COMMITTEES

Submit approvals by other committees for each, as appropriate:

Cancer Center Scientific Review: All cancer-related clinical trials require review and approval from the Cancer Center Scientific Review Committee (SRC). For guidance and information, please call 916-734-2596.

Radiation Use: All radiation/radioactive material usage, including x-rays and fluoroscopy procedures require review and approval from the Radiation Use Committee (RUC). For guidance and information, please call 916-734-3355.

Conflict of Interest Committee Review: Provide the approval letter or a copy of the recommended conflict management plan from the Conflict of Interest (COI) Committee. For guidance and information, please call 530-754-1184.

Reportable financial interests include: ownership interests (stock, stock options, or other investments) in the research sponsor or other entity related to the research; consulting or supplemental income from the research sponsor or other entity related to the research; a proprietary interest related to the research such as a patent, trademark, copyright, or licensing agreement; board executive, managerial or employment relationship with the research sponsor or other entity related to the research; or travel outside California paid for, or reimbursed by, the research sponsor.

DESCRIPTION OF STUDY – CLINICAL FULL COMMITTEE

BACKGROUND (Questions 1 – 5)

1. Study Format (Phase I, II, III): In addition to providing the study protocol, investigators are asked to describe the study format. The clinical investigation of a previously untested drug is divided into three phases. Although in general the phases are conducted one after the other, they may overlap. FDA defines the three phases as:

- Phase I includes the initial introduction of an investigational new drug into humans. Phase I studies are typically closely monitored and may be conducted in patients or normal volunteer subjects. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. The total number of subjects and patients included in Phase I studies varies with the drug but in generally in the range of 20-80.
- Phase II studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. Phase II includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase II studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects.
- Phase III studies are expanded controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase III studies usually include from several hundred to several thousand subjects.

2. Aims, Hypothesis, Scientific Problem: The primary goal of a research activity is to learn something for the purpose of benefiting people. In reviewing your IRB Application, the IRB will ask "Why is this research important to conduct?" and "What will be learned from the proposed study?" Provide a clear description of the scientific problem, objectives of the research, and a statement of the study hypothesis. Provide a summary of the study, in layman's terms. This condensed description summarizes the important aspects of the study in a way that facilitates IRB review. The summary is particularly useful for the non-scientific members on the Board as well as the IRB Chairs and Vice Chairs when reviewing serious adverse event reports and requests for modifications/amendments during the year of approval.

3. Rationale for Conducting the Study: Utilizing references and available background information, provide the rationale for the study and the importance of the knowledge to be gained. Provide references, as applicable.

4. Research Methods and Procedures: The IRB must be able to differentiate those procedures that are performed for research purposes from those that are performed for routine care or evaluation and determine whether the research is going to be conducted in a way that minimizes risks to subjects by employing procedures that are already being performed for diagnostic or treatment purposes (45 CFR 46.111.a.1 Criteria for IRB approval of research). Federal regulations and ethical codes such as the Nuremberg Code and the Declaration of Helsinki emphasize that:

> A characteristic of ethical research is that (1) the study is designed so that the risks to subjects are minimized and (2) the potential benefits of the research justify the potential risks. It is these two directives that establish the obligation of the IRB to consider carefully the study design and overall scientific quality of each study.

Researchers are asked to provide a comprehensive outline of the research procedures, including the timing and setting of the procedures, and a clear differentiation between research procedures and standard care and evaluation. If flow charts, tables or schemas are included, it is important that they be consistent with the study protocol and the informed consent document.

5. Resources: All research studies are required to have the resources necessary to protect human participants. These resources may include medical services, adequate personnel, social services, ancillary care if needed, medical monitoring, counseling services if required due to participation, equipment to protect subjects, and psychological care if needed. By identifying and documenting these resources, the researcher provides assurance to the IRB that there are adequate resources available for the safe conduct of the research and that there is a plan to monitor data to ensure subject safety. In addition, by identifying and documenting the names of individuals who will work on the research project, the principal investigator provides assurance to the IRB that all personnel are adequately trained and knowledgeable regarding human participant protections. See *IRB SOP "Provision of Adequate Resources for the Safe Conduct of Research Studies".*

DURATION AND LOCATION (Questions 6-7)

6. Duration of the Study: Provide a brief timeline in periods of months from IRB approval (Month 0), recruitment initiation, end of recruitment, end of interventional research procedures, end of data analyses of identifiable data.

7. Location(s) of the Study: List the specific locations where this study will be conducted, i.e., in what clinics, buildings, etc. will recruitment occur; subjects be consented; and interventional procedures conducted.

SUBJECT RECRUITMENT AND CONSENTING PROCESS (Questions 8-15)

The goal of equitable selection of subjects, is to distribute fairly the risks and benefits of research among the populations that stand to benefit from it. The IRB has the authority and the responsibility to examine the extent to which this goal is achieved or impeded in each protocol it reviews. To make this analysis, the IRB must be able to identify the study population; determine whether the study population is reasonably related to the purpose of the research; have a clear description of the inclusion and exclusion criteria; and the rationale for inclusion and exclusion.

8. Criteria for Including and Excluding Subjects: The selection of subjects must be equitable. An appropriate inclusion and exclusion criteria for research participants is essential in order to justify human subject research ethically. Research that has the potential to benefit men, women, and children or different races should target study subjects that reflect this diversity in sufficient numbers to distinguish differing effects, risks, and benefits. No group should be categorically *excluded* from the research without a good scientific reason to do so. Address your criteria for inclusion and exclusion of research subjects.

9. Age Range: Specify the age range of the research participants and your rationale for this determination.

10. Vulnerable Populations: Identify all that apply. See *IRB SOP "Vulnerable Populations (pregnant women, human fetuses and neonates, prisoners, children and cognitively impaired persons)"* for assistance.

Prisoners: The inclusion of a vulnerable population in research, such as prisoners, must be justified. In addition, adequate safeguards are required to be in place to minimize the risks unique to the particular vulnerable population. This Supplement is required if the individual(s) you plan to enroll meet the following definition:

> 'Prisoner" is defined by federal regulations as "any individual involuntarily confined or detained in a penal institution. This encompasses individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or

commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial or sentencing."

Although federal regulations permit biomedical research, except as provided in Section 1706 of the Welfare and Institutions code, no biomedical research shall be conducted on any prisoner in the State of California. However, behavioral research is permissible. Behavioral research means studies involving but not limited to, the investigation of human behavior, emotion, adaptation, conditioning, and responses in a program designed to test certain hypotheses through the collection of objective data. For further guidance on this vulnerable population, see the following IRB document *Guidance on the Involvement of Prisoners in Behavioral Research.* Complete and attach to your IRB application *IRB Application Supplement – Prisoners as Participants*.

Surrogate Consent Due to Lack of Cognitive Capacity: To include this vulnerable population in research, investigators must apply to the IRB for use of surrogate consent that is specific to the particular study being reviewed. This request is made through this application, by completing the *IRB Application Supplement – Surrogate Consent,* and shall only apply on a case-by-case basis within this protocol. The Supplement must detail a protocol-specific plan for the assessment of the decision-making capacity of the subject that will be conducted by the investigator for any subject who may qualify for surrogate consent. While there are no standardized measures for determining capacity to consent, subjects may be assessed on their ability to understand and to express a reasoned choice concerning the:

- Nature of the research and the information relevant to his/her participation;
- Consequences of participation for the subject's own situation, especially concerning the subject's health condition; and
- Consequences of the alternatives to participation.

The UCD Clinical and Translational Science Center (CTSC) has developed a sample capacity assessment checklist which can be accessed at www.ucdmc.ucdavis.edu/ctsc .

Investigators are strongly encouraged to review the *IRB SOP "Surrogate Consent for Research"* for guidance on determining the decision-making capacity of the subject, investigator responsibilities regarding the surrogate decision-makers, and to obtain a copy of the Self-Certification of Surrogate Decision Makers form.

11. Additional Safeguards/Accommodations for Vulnerable Population(s): Address the additional safeguards / accommodations that will be put into place to protect the rights and welfare of those subjects identified in the question above. Appropriate safeguards might include:

- Formally assessing decision-making capacity;
- Educating participants until they can demonstrate knowledge of consent information;
- Risks to the fetus and to the mother should be discussed individually so that it is clear who is at risk for what;
- Obtaining assent from the participant and consent from the surrogate decision maker;
- Involving a patient advocate to assist in explanations or to provide oversight.

Researchers are encouraged to exercise discretion in determining when a specific accommodation is appropriate for an individual participant. If applicable, address the translation and interpretation efforts that will be employed during the entire conduct of the study for non-English speaking participants.

12. Total Number of Subjects and Statistical Justification: Your protocol must contain well-conceived, well-formulated, and appropriate plans for interpretation of data and statistical analyses. The study protocol must convince the IRB that the proposed design has a reasonable chance of achieving the principal objectives of the research. The IRB should be given enough information to determine that the sample size and statistical power or precision associated with the sample size is

adequate. In addition, thought must be given to developing a sound method of data and statistical analysis, with adequate stratification factors and treatment allocation plans for the study design after study completion. Here is a sample of questions the IRB will consider when reviewing your response to this section of the application/description of study: (1) is the rationale for the proposed number of subjects reasonable? Were formal sample size calculations performed and are they available for review? (2) Are the plans for data and statistical analysis defined and justified, including the use of stopping rules and endpoints? (3) Are there adequate provisions for monitoring data (data and safety monitoring board/plan?

13. Recruitment: Provide a complete description of the recruitment process. Appropriate recruitment process might include:

- Use of flyers in public areas, including clinic offices, publications, on the internet, listserves, etc.
- Eligibility screening by telephone
- Unsolicited phone call or letter
- Direct recruitment of patients (HIPAA applies, attach supplement)
- Identifying patients at already scheduled standard of care clinic visit (HIPAA applies, attach supplement)

14. Consent Methods: Indicate the method you will employ to consent participants and attach the Supplement as appropriate. Please be advised that the consenting method approved by the IRB cannot be altered without prior review and approval of the change by the IRB. Should you deviate from the IRB approved method of obtaining informed consent, this will constitute a deviation from the approved protocol and the study will be determined out of compliance.

15. Consent Process Assurance: please review and check. By doing so, you are providing assurance to the IRB of your agreement to follow these procedures.

BENEFITS AND RISKS OF THE RESEARCH (Questions 16-21)

16. Potential Benefits to Individual Subjects or Group or Community: Address if there are any potential benefits to individual subjects or to the particular group or community. To address this issue, please see the following guidance from the *OHRP IRB Guidebook, Chapter III, Basic IRB Review:*

> "Assessment of Anticipated Benefits - The benefits of research fall into two major categories: benefits to subjects and benefits to society. Frequently, the research subjects are undergoing treatment, diagnosis, or examination for an illness or abnormal condition. This kind of research often involves evaluation of a procedure that may benefit the subjects by ameliorating their conditions or providing a better understanding of their disorders. Patients and healthy individuals may also agree to participate in research that is either not related to any illnesses they might have or that is related to their conditions but not designed to provide any diagnostic or therapeutic benefit. Such research is designed principally to increase our understanding and store of knowledge about human physiology and behavior. Research that has no immediate therapeutic intent may, nonetheless, benefit society as a whole. These benefits take the form of increased knowledge, improved safety, technological advances, and better health. The IRB should assure that the anticipated benefits to research subjects and the knowledge researchers expect to gain are clearly identified. Direct payments or other forms of remuneration offered to potential subjects as an incentive or reward for participation should not be considered a "benefit" to be gained from research. [*See* Guidebook Chapter 3, Section G, "Incentives for Participation."] Although participation in research may be a personally rewarding activity or a humanitarian contribution, these subjective benefits should not enter into the IRB's analysis of benefits and risks."

17. Plan for Protecting Subject Privacy and Confidentiality: Describe how privacy and the confidentiality of the information obtained in the course of the study will be maintained. This

includes how long records will be kept after the study is completed. If you plan to maintain an electronic recordkeeping system to track source documents, describe your recordkeeping system and your plan for securing and maintaining source documents (data management, consent forms, IND or IDE applications and approvals, sponsor notifications, monitor visits, DSMB reports, and documentation of performance and adherence to the trial). Identify who will have access to the electronic system.

18. Recordkeeping Systems: When conducting research, Investigators are entrusted with confidential and privileged human subject information. As a consequence, investigators must take measures to protect the security of this information, ensuring that all research personnel be familiar with information security policies of their department/unit, UCDavis, State Law, and HIPAA privacy laws. In this section of the IRB application, describe your recordkeeping system and plan for securing and maintaining source documents (e.g., password protection; encryption, etc.). In addition, identify who will have access to the system. Also, address your security plan for the following portable devices and the frequency that subject identifiers will be transferred to a secure system, as appropriate: laptops, digital cameras, portable hard drives including flash drives, memory sticks, iPODS or similar storage devices, as these are particularly susceptible to loss or theft. Principal Investigators should work with information security experts to review their data storage and transmission procedures at least annually to minimize the risk of unauthorized access to or exposure of confidential information.

19. Expected Risks of Participation in the Study: Investigators are asked to address those risks that may result from the research, as distinguished from those associated with therapies subjects would undergo even if not participating in the research. The risks to which research subjects may be exposed have been classified as physical, psychological, social, economic, or legal. List the different types of risks and estimate their likelihood and seriousness [e.g., Common (>20%), Less Common (5-20%), Rare but Serious (<5%)]. For examples of toxicity grading scales, please see http://www.ucdmc.ucdavis.edu/clinicaltrials/tools.html .

COSTS AND COMPENSATION TO THE SUBJECTS (Questions 22-24)

20. Costs to the Research Subject or Third Party: If there is the possibility that there will be costs to the subject or to a third party (insurer), identify the specific expenses: drug, tests, procedure, hospitalization, travel, etc.

21. Justification of Costs: Address how the costs to subjects/insurer are justified.

22. Compensation of Research Subjects: The FDA requires prorating payments based on the duration of participation of the subject in the research. Prorated payments should be made regardless of whether withdrawal was voluntarily or involuntarily, that is, whether the withdrawal was based on the decision of the subject to discontinue or based on a withdrawal criteria of the research protocol. Describe your plan for payment of subjects.

FINANCIAL INTERESTS (Question 25)

23. Financial Interests of PI and Key Personnel: Indicate whether you do or do not have a financial interest by check marking the appropriate box. In addition, describe all outside income Industry sources.

References

45 CFR 46 OHRP
21 CFR 56 FDA
University of California, Davis IRB Standard Operating Procedures
OHRP IRB Guidebook
Institutional Review Board, Management and Function by Bankert and Amdur