UNIVERSITY OF SOUTH ALABAMA
IRB GUIDELINES

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Policies and Guidelines located on the Web:
http://southmed.usouthal.edu/com/research/humansubjects.html
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PART I: MANDATE OF THE INSTITUTIONAL REVIEW BOARD

A. HISTORY

Since 1966, the United States Department of Health and Human Services (DHHS), formerly called the department of Health, Education and Welfare (DHEW) has required prior review and approval of all research using human subjects that is funded by federal agencies. DHEW issued its "Institutional Guide to DHEW Policy on Protection of Human Subjects" in December 1971. Between 1974 and 1978, the National Commission on Protection of Human Subjects of Biomedical and Behavioral Research met and issued a series of reports and recommendations resulting in revised regulations issued by DHHS in January 1981. The United States Food and Drug Administration (FDA) was simultaneously developing its own regulations, which were also issued in January 1981 and have since been revised, most recently in September 1998. DHHS issued revised regulations in March 1983 and most recently in September 2001. These regulations, which provided standards for review of human research activities by institutional review boards (IRBs) now apply to all activities involving human subjects within the University.

The University of South Alabama (USA) holds a Federal Wide Assurance (FWA) from the DHHS. This is a written agreement in which USA describes the jurisdiction, composition, and methods of procedure by which the IRB will function. The Office for Human Research Protections (OHRP) in the DHHS approves it. This FWA was most recently approved in 2002. The IRB is regularly audited by the FDA and may be audited by other offices at DHHS.

B. Composition

Committee members are nominated by a Committee on Committees with input from the chair, vice-chair, and IRB administrator and appointed by the Institutional Signatory (Vice-President for Medical Affairs/Dean of the College of Medicine). The committee consists of:

- At least five members of sufficiently diverse backgrounds, including consideration of racial and cultural backgrounds of members and sensitivity to issues such as community attitudes;
- Persons who are able to ascertain the acceptability of research applications in terms of institutional commitments, applicable law, and professional standards;
- Members of both sexes;
- At least one member whose primary area of expertise is with handicapped and/or retarded children;
- At least two members whose primary concerns are in behavioral disciplines;
- At least one member whose primary concerns are in non-scientific areas;
- Members representing more than one profession;
- A member who is not affiliated or related to a person who is affiliated with the institution;
- Persons who are primarily concerned with the welfare of vulnerable subjects;
- When needed, individuals with competence in special areas to assist in the review of complex issues;
- Participants in the initial or continuing review of projects who do not have a conflicting interest.

C. JURISDICTION

1. What Research Must Be Reviewed?

It is the policy of the University of South Alabama that all faculty and staff, both full-time and part-time, and students (whose research is conducted under the sponsorship of a faculty member) using human subjects to conduct research within the course and scope of their duties, regardless of the source of funding or even when no funds are involved, are required to have prior approval from the IRB before research is initiated. This includes medical record reviews, surveys, studies of pathological and/or diagnostic specimens, compassionate use studies, and exempt studies.

Research

... a systematic investigation including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute "research" for purposes of these regulations, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities as a component of the program.

Human Subject

... a living individual 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.

Standard Diagnostic or Therapeutic Procedures

Clearly, an established and accepted diagnostic or therapeutic procedure done solely for the benefit of the patient is not usually subject to IRB review. However, collection of data about a series of such procedures or treatments requires IRB review if information identifying individuals (even code numbers) is recorded. If patient care or assignment to care is altered for research purposes in any way (for example, if subjects are randomized to one or two standard treatments or if a cohort of patients are assigned to different standard treatments) the activity must be submitted to the IRB for review. A diagnostic procedure for research purposes added to a standard treatment requires IRB review.

Innovative Procedures or Treatments

Innovations in diagnosis or therapy are not necessarily subject to IRB review if they are applied to a patient for the sole purpose of aiding that individual, although such innovations are governed by the customary ethics of medicine (for example, consultation with peers, obtaining informed consent from the patient or family). However, IRB review is required when a "systematic investigation" of such innovations is contemplated (for example, when a physician plans to accumulate information about the innovation for scientific purposes or will repeat the innovation in other patients in order to compare it to standard treatment).

Emergency Use of an Investigational Drug or Device

When innovative diagnosis or therapy for one patient involves emergency use of an investigational new drug or device, or a new use of an approved drug or device, the physician must follow the FDA regulations which allow one-time use at an institution of an investigational drug or device for emergency purposes, and require reporting this use to the IRB within five working days.

D. CHARGE

The Institutional Review Board (IRB) at the University of South Alabama (USA) is responsible for the review of all research projects involving human subjects which are carried out on the campuses of the University of South Alabama, its hospitals and clinics, or any of its affiliated institutions, regardless of source of funding.


These codes empower the IRB and the University research community in their primary responsibility to protect human subjects from undue risk and from deprivation of personal rights and dignity. This protection is assured by consideration of three principles that are the basis of ethical research:

- That voluntary participation by the subjects, indicated by free and informed consent, is assured;

- That an appropriate balance exists between potential benefits of the research to the subject or to society and the risks assumed by the subject;

and
That there be fair procedures and outcomes in the selection of research subjects.

These principles are summarized as respect for persons, beneficence, and justice in “The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research.”

E. RESPONSIBILITIES OF THE IRB
The IRB will:

1. Conduct initial and continuing review of research involving human subjects at intervals appropriate to the degree of risk, but at least once a year and report IRB findings and actions to the investigator and the institution.

2. Determine which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

3. Review proposed changes in research activities to insure that changes in approved research, during the period for which IRB approval has been given, has not been initiated without IRB review and approval.

4. Require or waive documentation of informed consent.

5. Follow procedures to insure that the IRB and Office for Human Research Protections (OHRP) of the Department of Health and Human Services (DHHS) receive reports of unanticipated problems involving risks to subjects and others.

6. Monitor additional safeguards when vulnerable subjects (minors, mentally incompetent, prisoners, economically and educationally disadvantaged, pregnant females) are involved in the research in order to protect against coercion or undue influence.

7. Conduct its review of research, except when an approved exempt review procedure is used, at convened meetings at which a majority of the members of the IRB are present.

8. Approve research only with the concurrence of a majority of those members in attendance.

9. Report to the institution and OHRP any continuing or serious matters of non-compliance by investigators with the requirements and determination by the IRB.

10. Have authority to suspend or terminate approval of research that is not in compliance with the IRB’s determinations or has been associated with unexpected serious harm to subjects.

The IRB will maintain:

1. Copies of all research proposals reviewed, scientific evaluations, if any, that accompany proposals, approved sample consent documents, approved advertising or other solicitations for subjects, progress reports and injuries to subjects.

2. Minutes of meetings.

3. Records of continuing review activities.

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

5. A list of all members.

6. A compendium of written procedures.

7. Statements of significant new findings provided to subjects.

8. Records required by regulations, which shall be retained for at least three years after completion of the research. The records shall be accessible for inspection and copying by authorized representatives of DHHS, or any agency subscribing to the Common Rule (56.117).
PART II: APPLICATION FOR IRB REVIEW GENERAL INFORMATION

A. TYPES OF APPLICATIONS

There are four types of IRB applications. These are:

1. A new project full board review application
2. A new project expedited review application
3. A new project exempt review application
4. A continuing review, annual renewal application (full board or expedited)

Descriptions, submission requirements and other information for each type of application or submission are described in detail in the following sections. Samples of the appropriate forms can be found in Appendix I.

B. PROCEDURES

The Institutional Review Board (IRB) meets on the second Tuesday of each month. Applications for full board review are seen by all members of the IRB, however two committee members are assigned as primary discussants. Applications for expedited review are seen by a subcommittee of the IRB. Expedited protocols are subsequently approved by the full board at the monthly meeting. Exempt applications are reviewed by the IRB administrator who either confirms exempt status or recommends expedited or full board review. An agenda that lists all items that have been circulated and/or reviewed since the previous meeting is distributed one week prior to the monthly meeting.

Applications about which there are no questions are given approval as of that meeting’s date. Investigators will be promptly notified in writing.

For each application where the IRB has unanswered questions, a letter explaining the issues or problems is sent from the IRB administrator. The principal investigator must then address a response and/or revise the consent documents in order to obtain approval. The IRB may:

- Defer approval pending administrative review (requires a written response to the chair or IRB administrator only);
- Defer approval pending primary discussant’s review (requires a written response which is forwarded to the discussant(s)); or
- Defer approval pending full committee review (full IRB review required).

On very rare occasions, the IRB may encounter major difficulty in making a risk/benefit assessment, and an outside reviewer may be asked to consider the protocol, and/or the principal investigator may be invited to attend a meeting to discuss the issues in question.

Upon acceptance of an original protocol, or a response and/or revision, IRB approval is given for a maximum period of one year. To continue work on the study, a renewal application must be submitted and approved. Renewal approval is also for a maximum of one year from the date of approval. Approval for any modification request is given only to the expiration date of the full year’s approval.

The IRB administrative staff reviews all applications for completeness and suitability for presentation to the IRB. The IRB compliance specialist is available to answer all questions about submission requirements, status of protocols and correspondence with the IRB, and to provide consultation for investigators submitting applications to the IRB. For any matters pertaining to IRB business, the investigator should contact the IRB office (rather than contacting the IRB Chair or members directly), where these matters can be referred appropriately and handled as expeditiously as possible.

Application forms and information can be found in Appendix I, and are available at the IRB Website (http://www.southalabama.edu/com/research/humansubjects/index.shtml) and the IRB office CSAB 138.
The IRB mailing address is:

CSAB 138, University of South Alabama, Mobile, AL 36688-0002

Telephone: 251-460-6308
FAX: 251-461-1595

C. SUBMISSION SCHEDULE

The monthly deadline for applications is approximately two weeks prior to the meeting (see IRB website for specific dates). Items for full board review will be distributed during the week before the monthly meeting.

For applications requiring full board review, investigators should allow at least six weeks from the time an application is received in the IRB office for review and approval. Applications requiring expedited review may be approved in as few as ten days provided the application is complete, ethical questions are addressed in the protocol, the reviewer has no questions, and there is no backlog. When changes are requested by the Expedited Subcommittee, applications may take up to four weeks for approval. To obtain up-to-date information regarding approximate turnaround time for IRB review to be completed, call the IRB office (at 460-6308). Applications qualifying as exempt are typically approved in about a week, but may be approved as quickly as one or two days.

If an investigator has an emergency situation or an unanticipated urgent deadline, the IRB office can be contacted to request expedition of the correspondence and review and processing of the response. Every effort will be made to assist the investigator in such a situation. However, in general, it is considered the investigator’s responsibility to make submissions early enough to meet deadlines such as those of granting agencies, sponsoring companies, or IRB expiration dates. Factors such as University holiday periods or major granting agency deadlines (when the volume of applications submitted to the IRB increases greatly) should be taken into consideration to allow a sufficient amount of time for IRB review.

D. GENERAL SUBMISSION REQUIREMENTS

1. The investigator must be USA faculty or staff.

2. All study personnel should be listed.

   All co-investigators or others involved in the conduct of the study should be listed on the New Projects Application, cover page.

3. Incorrect applications may be returned:

   All submissions are reviewed for completeness by the IRB staff before distribution to the IRB members. Submissions must meet all requirements (for example, forms completed, consent forms and all attachments included) or they may be returned to the investigator for correction or completion prior to IRB review.
PART III: NEW PROJECTS IRB APPLICATION FULL BOARD REVIEW

A. GENERAL INFORMATION

This type of application is used for studies that involve more than minimal risk to the subjects and is reviewed by the full committee membership. A New Projects Application Form is to be submitted with the protocol to facilitate review. The application form contains a set of questions that must be addressed for any submission (see sample form, Appendix I).

B. SPECIFIC SUBMISSION REQUIREMENTS

Four copies of the protocol (including investigator’s brochure, questionnaire or survey if applicable), thirty copies of the New Projects IRB Application Form, and thirty copies of the consent form must be submitted for an initial, full board review. The sets should be individually stapled and collated in the order listed below.

1. Cover letter (optional)
2. New Projects IRB Application Form (30 copies)
3. Protocol (four copies)
4. Consent Form (30 copies)
5. Special Requirements/Attachments

   a. Disclosure of Financial Conflict of Interest

   A Disclosure of Financial Conflict of Interest Form (Appendix I) is to be submitted with each proposal for funded research, either through the Office of Sponsored Projects (for most federally funded applications), or through the College of Medicine Business Office (for grants that are processed through the Medical Sciences Foundation). If a significant financial interest is felt to present a possible conflict of interest the application may be given to the University Conflict of Interest Committee to determine appropriate management following review by the University’s Senior Vice President for Academic Affairs or the Office of the Vice-President for Medical Affairs.

   b. Approval of the Radiation Safety Committee

   If x-rays or isotopes are to be used specifically in support of the research, approval of the Radiation Safety Committee must be obtained.

   c. Approval of the Institutional Biosafety Committee

   If a biological hazard may exist for either subjects or investigators, approval of the Institutional Biosafety Committee must be obtained. Under Federal Regulations, this includes all handling of human blood or tissues for research (not clinical) purposes.

   d. IND (Investigational New Drug) Number and Investigator’s Brochure

   When a study involves use of an unapproved drug, or an approved drug for a new use, the investigator must submit an IND number obtained from the FDA, and one copy of the Investigator’s Brochure for the drug, which provides background information such as information from animal research and toxicity data.
e. IDE (Investigational Device Exemption) Number and Investigator’s Brochure

When a study includes an unapproved device, or an approved device for a new use, and a “significant risk” device is involved, the investigator must submit an IDE number obtained from the FDA, and one copy of the Investigator’s Brochure for the device. If the investigator believes that the device poses a non-significant risk, FDA regulations allow the option of requesting a “non-significant risk” IDE determination from the local IRB. The Investigator must submit this request to the IRB with an explanation of why the study should be considered of non-significant risk, and other supporting information. This request and justification should be presented separately or distinctly from the application for approval of the protocol. The IRB will make a determination based on the criteria described in the FDA “Guidance on Significant and Non-Significant Risk Device Studies.” Depending on the circumstances of the study, additional safety or liability assurances may be required on an individual, case-by-case basis.

f. Approvals from other IRBs

When a study is being carried out at a non-USA site, and approval from other institutional review boards must be sought, the IRB recommends that a copy of each IRB approval be submitted.

g. Questionnaires/Other Instruments

Any questionnaires, tests, survey instruments or data collections sheets which are not standard and well-known must be submitted as part of the application.

h. Advertisements/Notices/Recruitment Flyers

The text of any advertisement, video display, notice, sign, brochure or flyer used to recruit subjects should be included as an attachment.

C. THE NEW PROJECTS IRB APPLICATION FORM—FULL BOARD REVIEW

The following are explanations given for each of the sections of the application form.

1. Purpose of Research

This section should discuss the purpose of the investigation, defining the problem to be investigated. Whenever possible, it should state the specific hypothesis to be tested. If specific hypotheses are not being tested, the questions to be answered, data to be tested, description to be made or the information hoped to be gained should be explained. For pilot or exploratory studies, this section should discuss the way in which the information obtained will be used in future studies, so that the potential long-range benefits of the pilot work can be assessed.

2. Relevant Background and Rationale for the Research

This section should present the context of the work by explaining the relation of the proposed research to previous investigations in the field. Relevant laboratory and animal studies should be summarized. If the study involves an investigational new drug or device, the summary in the protocol must be supplemented with detailed information in the Investigator’s Brochure for the drug or device. This section should present clear justification for participation of human subjects at this stage of the investigation.

3. Procedures and Agents (if applicable) to Be Used

This should give an explanation of what will done to each subject for research purposes, and how this compares with what would be done were the individual not in the study. Agents used in the study should be included in this section.

4. The Experimental Design and Methodology

The purpose of this section is to acquaint the IRB with the specific nature of the procedures to be carried out on human subjects so that the risks of the study may be evaluated. This section
should also present an explanation of how the methods employed will, in fact, allow the investigator to evaluate the hypotheses posed or gather the data sought.

5. What incentives will be offered, if any?

This section should indicate whether or not subjects are to be paid for their participation in the study and how and when they will be paid. If they will be paid, it should clearly state how much subjects will receive, and the rationale for that amount. This section should note whether payment is pro-rated if a subject does not complete the entire study, and whether a bonus payment is offered for completion. A reimbursement schedule should be provided if appropriate.

The proposed payment should be commensurate with the time required for participation, travel expenses, and/or inconvenience assumed by the subject, but should not be so great as to constitute undue influence on an individual to assume risks of study participation that would not otherwise be undertaken.

6. Risks/Benefits to Participants and Precautions to Be Taken

This section should discuss all possible risks and discomforts from participation in the study, indicating both severity and likelihood of occurrence for each. Risks may range from the physical to the psychological. Inconvenience, travel or boredom may also be considered risks of participation in the study. The methods that will be used to minimize these risks should also be discussed. Many studies hold the potential for loss of privacy and confidentiality. These concerns should be noted in this section.

7. Privacy/Confidentiality

This section should indicate whether or not research records will be anonymous. If not, there should be discussion of how records will be coded, and where and how they will be stored. It should also note where and how signed consent forms will be maintained. If video or audio tapes will be made as part of the study, disposition of these tapes should be addressed. In general, the IRB recommends that research tapes be destroyed as soon as the needed data are transcribed, and that only restricted study personnel be allowed access to the tapes. If other procedures are proposed (for example, retaining tapes for future use, allowing individuals other than study investigators access to the tapes) justification should be presented, and separate consent may be required.
PART IV: NEW PROJECTS IRB APPLICATION EXPEDITED REVIEW

A. GENERAL INFORMATION

In November 1998, DHHS issued a list of “expedited review categories,” categories of research that pose no more than minimal risk and are eligible for “expedited” IRB review. This 1998 list replaced and expanded on the original list published by the agency in 1981.

Investigators may apply to the IRB for expedited review if their research falls into one of the nine categories on the new list. The first step in applying is to review the Expedited Review Categories section below. Both the “Applicability” and the “Research Categories” sections of the regulations need to be considered, and the expedited review category must be noted on the IRB Application form. Investigators are encouraged to call the IRB office at 460-6308 with any questions about the regulations and about the specific review categories.

If expedited review seems to be appropriate, the next step is to prepare and submit an IRB Application for New Projects (see sample form, Appendix I). The expedited review regulations allow for review by a member of the Expedited Review Subcommittee of the IRB. If any of the reviewers believes that the research does not fit into an expedited category, or believes the study should be reviewed by additional members, he/she may refer the application to the Full IRB for further review.

Turnaround time for review of Expedited applications is two to four weeks depending on whether review occurs in the office or at a full board meeting.

B. EXPEDITED REVIEW CATEGORIES

The 1998 expedited review regulations are quoted on the following pages. The first section of the regulations is titled “Applicability” and discusses concepts that apply to all types of expedited review research. The second section is titled “Research Categories” and lists the specific categories that are eligible. One or more of these categories must be cited in your application. Each of the nine categories is labeled with a short descriptive heading in **bold and italicized text**; these headings were added for explanation and are not quoted from the regulations. Parts of the regulations are followed by *Comments* sections; again, these comments are provided for explanation and are not quoted from the regulations.

Following the list of categories is an explanation of the specific requirements for submitting an expedited application.

Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure (published in the Federal Register, 63FR60364, effective November 9, 1998):

An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

**Applicability**

- Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involved no more than minimal risk to human subjects.

- The categories in this list apply regardless of the age of subjects, except as noted.

- The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are not greater than minimal.
The expedited review procedure may not be used for classified research involving human subjects.

IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Comments: If as part of the study subjects will be randomized to a treatment group, then the study does not qualify for expedited review.

Research Categories

1. **A very limited number of studies of approved drugs and devices:** Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

   a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

   b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

   Comments: The drug or device must be approved and used exactly according to its labeling. All study procedures other than use of the drug or device must themselves be of minimal risk for the study to qualify for expedited review. Few studies fit this category.

2. **Blood sampling:** Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

   a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

   b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

   Children are defined in the HHS regulations 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.” 45 CFR 46.402(a). In Alabama, minors are less than 19 years old.

3. **Noninvasive specimen collection:** Prospective collection of biological specimens for research purposes by non-invasive means.

   Examples: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. **Noninvasive clinical procedures:** Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)
Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. **Use of data or specimens collected for non-research purposes**: Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

**Comments** (a) This category refers to materials collected for “non-research purposes,” but can be used to cover research materials if the investigator’s role is simply to analyze them. That is, if an investigator is receiving materials from colleagues who have separate approval to collect them, and the materials are handled with code numbers and other protections for confidentiality, he or she may apply for expedited review for the analysis; (b) This type of research is exempt from review only if the data collected has no link whatsoever to identifiers (not even a code number).

6. **Use of recordings**: Collection of data from voice, video, digital, or image recordings made for research purposes.

7. **Low risk behavioral research**: Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

**Comments**: Only very specific types of behavioral research are exempt from review. Again, there usually must be no link whatsoever to identifiers (not even a code number).

8. **Renewal of inactive research protocols or protocols that are essentially complete**: Continuing review of research previously approved by the convened IRB as follows:

   a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

   b. where no subjects have been enrolled and no additional risks have been identified; or

   c. where the remaining research activities are limited to data analysis.

8. **Renewal of other minimal risk research protocols**: Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

C. **SPECIFIC SUBMISSION REQUIREMENTS**

Three copies of the protocol (including questionnaire or survey if applicable), three copies of the New Projects IRB Application Form (see sample form, Appendix I), and three copies of the consent form must be submitted for an initial, expedited review. The sets should be individually stapled and collated in the order listed below.

1. Cover letter (optional)
2. New Projects IRB Application Form (three copies)
3. Protocol (three copies)
4. Consent Form (three copies)
5. Special Requirements/Attachments

a. Disclosure of Financial Conflict of Interest

A Disclosure of Financial Conflict of Interest Form (Appendix I) is to be submitted with each proposal for funded research, either through the Office of Sponsored Projects (for most federally funded applications), or through the College of Medicine Business Office (for grants that are processed through the Medical Sciences Foundation). If a significant financial interest is felt to present a possible conflict of interest the application may be given to the University Conflict of Interest Committee to determine appropriate management following review by the University's Senior Vice President for Academic Affairs or the Office of the Vice-President for Medical Affairs.

b. Approval of the Radiation Safety Committee

If x-rays or isotopes are to be used specifically in support of the research, approval of the Radiation Safety Committee must be obtained.

c. Approval of the Biohazards Committee

If a biological hazard may exist for either subjects or investigators, approval of the Biohazards Committee must be obtained. Under Federal Regulations, this includes all handling of human blood or tissues for research (not clinical) purposes.

d. (IND) (Investigational New Drug) Number and Investigator’s Brochure

When a study involves use of an unapproved drug, or an approved drug for a new use, the investigator must submit an IND number obtained from the FDA, and one copy of the Investigator’s Brochure for the drug, which provides background information such as information from animal research and toxicity data.

e. IDE (Investigational Device Exemption) Number and Investigator’s Brochure

When a study includes an unapproved device, or an approved device for a new use, and a “significant risk” device is involved, the investigator must submit an IDE number obtained from the FDA, and one copy of the Investigator’s Brochure for the device. If the investigator believes that the device poses a non-significant risk, FDA regulations allow the option of requesting a “non-significant risk” IDE determination from the local IRB. The Investigator must submit this request to the IRB with an explanation of why the study should be considered of non-significant risk, and other supporting information. This request and justification should be presented separately or distinctly from the application for approval of the protocol. The IRB will make a determination based on the criteria described in the FDA “Guidance on Significant and Non-Significant Risk Device Studies” Depending on the circumstances of the study, additional safety or liability assurances may be required on an individual, case-by-case basis.

f. Approvals from other IRBs

When a study is being carried out on a non-USA site, and approval from other institutional review boards must be sought, the IRB recommends that a copy of each IRB approval be submitted.

g. Questionnaires/Other Instruments

Any questionnaires, tests, survey instruments or data collections sheets which are not standard and well-known must be submitted as part of the application.

h. Advertisements/Notices/Recruitment Flyers

The text of any advertisement, video display, notice, sign, brochure or flyer used to recruit subjects either should be included as an attachment.
D. THE NEW PROJECTS IRB APPLICATION FORM—EXPEDITED REVIEW

The following are explanations given for each of the sections of the application form.

1. Purpose of Research

   This section should discuss the purpose of the investigation, defining the problem to be investigated. Whenever possible, it should state the specific hypothesis to be tested. If specific hypotheses are not being tested, the questions to be answered, data to be tested, description to be made or the information hoped to be gained should be explained. For pilot or exploratory studies, this section should discuss the way in which the information obtained will be used in future studies, so that the potential long-range benefits of the pilot work can be assessed.

2. Relevant Background and Rationale for the Research

   This section should present the context of the work by explaining the relation of the proposed research to previous investigations in the field. Relevant laboratory and animal studies should be summarized. If the study involves an investigational new drug or device, the summary in the protocol must be supplemented with detailed information in the Investigator’s Brochure for the drug or device. This section should present clear justification for participation of human subjects at this stage of the investigation.

3. Procedures and Agents (if applicable) to be Used

   This should give an explanation of what will be done to each subject for research purposes, and how this compares with what would be done were the individual not in the study. Agents used in the study should be included in this section.

4. The Experimental Design and Methodology

   The purpose of this section is to acquaint the IRB with the specific nature of the procedures to be carried out on human subjects so that the risks of the study may be evaluated. This section should also present an explanation of how the methods employed will, in fact, allow the investigator to evaluate the hypotheses posed or gather the data sought.

5. What incentives will be offered, if any?

   This section should indicate whether or not subjects are to be paid for their participation in the study and how and when they will be paid. If they will be paid, it should clearly state how much subjects will receive, and the rationale for that amount. This section should note whether payment is pro-rated if a subject does not complete the entire study, and whether a bonus payment is offered for completion. A reimbursement schedule should be provided if appropriate.

   The proposed payment should be commensurate with the time required for participation, travel expenses, and/or inconvenience assumed by the subject, but should not be so great as to constitute undue influence on an individual to assume risks of study participation that would not otherwise be undertaken.

6. Risks/Benefits to Participants and Precautions to Be Taken

   This section should discuss all possible risks and discomforts from participation in the study, indicating both severity and likelihood of occurrence for each. Risks may range from the physical to the psychological. Inconvenience, travel or boredom may also be considered risks of participation in the study. The methods that will be used to minimize these risks should also be discussed. Many studies hold the potential for loss of privacy and confidentiality. These concerns should be noted in this section.

7. Privacy/Confidentiality

   This section should indicate whether or not research records will be anonymous. If not, there should be discussion of how records will be coded, and where and how they will be stored. It should also note where and how signed consent forms will be maintained. If video or audio
tapes will be made as part of the study, disposition of these tapes should be addressed. In
general, the IRB recommends that research tapes be destroyed as soon as the needed data
are transcribed, and that only restricted study personnel be allowed access to the tapes. If
other procedures are proposed (for example, retaining tapes for future use, allowing individuals
other than study investigators access to the tapes) justification should be presented, and
separate consent may be required.
PART V: NEW PROJECTS IRB APPLICATION

EXEMPT PROTOCOL REVIEW

A. GENERAL INFORMATION
All research involving human subjects must be reviewed at some level by the Institutional Review Board (IRB). The term “exempt” means a protocol may not require full board review, but it still must be approved by the IRB.

Exempt categories of research are defined by the Department of Health and Human Services (DHHS) regulations for protection of human subjects in 45 CFR 46.101. These categories, with the exception of research involving certain survey or interview procedures, are listed in Section E below. If an investigator believes his or her study qualifies as exempt from IRB review, then the New Projects Applications Form should be completed appropriately and submitted to the IRB office for review and approval (see sample form, Appendix I). Funding agencies do not allow investigators to make this determination on their own; nor does the University of South Alabama.

B. INSTRUCTIONS
If you believe a research project falls into the exempt categories, you should do the following:

- Review the exempt categories listed below in Section E very carefully to make sure the study fits one of the federally-designated exempt categories.
- Call the IRB Office at 460-6308 if you have any questions about whether your study qualifies as exempt.
- Fill out the New Projects Application Form (see sample form, Appendix I; instructions follow).
- Submit two copies of the protocol (including questionnaire or survey if applicable), two copies of the consent form, and two copies of the New Projects Application Form.

C. REVIEW PROCESS
The review process typically takes about one week, though possibly longer during crunch periods. The completed form will be reviewed by the IRB Coordinator. If there are no questions raised, a letter of approval and a stamped copy of your informed consent and survey (if applicable) will be returned to you. If the information on the Application seems incomplete or raises any concerns (e.g., regarding eligibility for exempt status, invasion of the subjects’ privacy, or confidentiality of research records) the investigator will be contacted. If the study does not qualify as exempt, the investigator will be notified as soon as possible and asked to submit an application for the appropriate level of IRB review, either Expedited or Full Committee Review.

D. IMPORTANT DETAILS ABOUT EXEMPT APPROVAL
A letter of approval from the IRB Compliance Specialist must be received by the investigator before the proposed research may proceed. The turnaround time for this review process is typically a week to ten days, but a study may be approved in less time if needed by the funding agency.

If the investigator plans any modification of the procedures that will affect the information given on a previously approved Exempt Application, a new form should be submitted for reconsideration. Approval is valid for one year.

E. EXEMPT CATEGORIES
As described and numbered in DHHS regulations (45CFR46.101(b)), research activities in which the only involvement of human subjects will be in one or more of the following categories may qualify as exempt if:
1. The research is conducted in established or commonly accepted educational settings, involving normal education practices, such as research on regular and special education instructional strategies, or research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. The research involves the use of educational tests (cognitive, diagnostic, aptitude, achievement) or observations of public behavior, except where any of the following conditions exist:
   a. Information obtained is recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects;
   b. Any disclosure of this information outside the research could reasonably place the subject at risk of criminal liability or civil liability or be damaging to the subject’s financial standing, employability or reputation; or
   c. The research deals with sensitive aspects of the subject’s own behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol.

3. The research involves the use of educational tests, survey or interview procedures, or observations of public behavior when the human subjects are elected or appointed public officials or candidates for public office.

4. The research involves the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

F. THE NEW PROJECTS IRB APPLICATION FORM—EXEMPT REVIEW

The following are explanations given for each of the sections of the application form.

1. Purpose of Research
   This section should discuss the purpose of the investigation, defining the problem to be investigated. Whenever possible, it should state the specific hypothesis to be tested. If specific hypotheses are not being tested, the questions to be answered, data to be tested, description to be made or the information hoped to be gained should be explained. For pilot or exploratory studies, this section should discuss the way in which the information obtained will be used in future studies, so that the potential long-range benefits of the pilot work can be assessed.

2. Relevant Background and Rationale for the Research
   This section should present the context of the work by explaining the relation of the proposed research to previous investigations in the field. Relevant laboratory and animal studies should be summarized. If the study involves an investigational new drug or device, the summary in the protocol must be supplemented with detailed information in the Investigator's Brochure for the drug or device. This section should present clear justification for participation of human subjects at this stage of the investigation.

3. Procedures and Agents (if applicable) to be Used
   This should give an explanation of what will done to each subject for research purposes, and how this compares with what would be done were the individual not in the study. Agents used in the study should be included in this section.

4. The Experimental Design and Methodology
   The purpose of this section is to acquaint the IRB with the specific nature of the procedures to be carried out on human subjects so that the risks of the study may be evaluated. This section should also present an explanation of how the methods employed will, in fact, allow the investigator to evaluate the hypotheses posed or gather the data sought.
5. **What incentives will be offered, if any?**

   This section should indicate whether or not subjects are to be paid for their participation in the study and how and when they will be paid. If they will be paid, it should clearly state how much subjects will receive, and the rationale for that amount. This section should note whether payment is pro-rated if a subject does not complete the entire study, and whether a bonus payment is offered for completion. A reimbursement schedule should be provided if appropriate.

   The proposed payment should be commensurate with the time required for participation, travel expenses, and/or inconvenience assumed by the subject, but should not be so great as to constitute undue influence on an individual to assume risks of study participation that would not otherwise be undertaken.

6. **Risks/Benefits to Participants and Precautions to Be Taken**

   This section should discuss all possible risks and discomforts from participation in the study, indicating both severity and likelihood of occurrence for each. Risks may range from the physical to the psychological. Inconvenience, travel or boredom may also be considered risks of participation in the study. The methods that will be used to minimize these risks should also be discussed. Many studies hold the potential for loss of privacy and confidentiality. These concerns should be noted in this section.

7. **Privacy/Confidentiality**

   This section should indicate whether or not research records will be anonymous. If not, there should be discussion of how records will be coded, and where and how they will be stored. It should also note where and how signed consent forms will be maintained. If video or audio tapes will be made as part of the study, disposition of these tapes should be addressed. In general, the IRB recommends that research tapes be destroyed as soon as the needed data are transcribed, and that only restricted study personnel be allowed access to the tapes. If other procedures are proposed (for example, retaining tapes for future use, allowing individuals other than study investigators access to the tapes) justification should be presented, and separate consent may be required.
PART VI: ANNUAL RENEWAL/FINAL REPORT

A. General Information

The Department of Health and Human Services (DHHS), The Food and Drug Administration (FDA) and the University of South Alabama (USA) require at least annual review of all projects involving human subjects. As a courtesy, the IRB office sends out renewal reminders six to eight weeks before the studies expire. However, it is ultimately the investigator’s responsibility to initiate a renewal application, allowing sufficient time for the review and re-approval process to be completed before the current approval expires. If any project activity occurs or continues after the expiration date, the investigator is out of compliance with both federal and university policy.

The Guidance on Continuing Review (7/11/02), the Dept. of Health and Human Services (DHHS) notes that:

Continuing review of research must be substantive and meaningful.

In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including:

- Total number of subjects enrolled since study opened;
- Number of subjects screened and enrolled in past year;
- Number of subjects by race screened for entry into study since the start of the project;
- Number of subjects screened by gender since the start of the project;
- Number of subjects by race entered into the study since last IRB review;
- Number of subjects by gender entered into the study since last IRB review;
- List of any amendments/revisions since last IRB review;
- A summary of adverse events and any unanticipated problems involving risks to subjects or others and any withdrawal of subjects from the research or complaints about the research since the last IRB review;
- A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review;
- A copy of the current informed consent document and any newly proposed consent document.

Previously approved questionnaires or survey instruments should be submitted only if they have been revised in the previous year or modifications are being proposed for the coming year. Any new questionnaires should be submitted.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) at 63FR60364-60367. Under Category (8), an expedited review procedure may be used for the continuing review of research previously approved by the IRB as follows:

(a) Where:

the research is permanently closed to the enrollment of new subjects;

all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects; OR

(b) Where no subjects have been enrolled and no additional risks have been identified; OR

(c) Where the remaining research activities are limited to data analysis.

Under Category (9), an expedited review procedure may be used for continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

B. Specific Submission Requirements for IRB Annual Renewal and Final Reports (see sample form, Appendix I)

Submit two copies of the Annual Renewal/Final Report Form, two copies of the most recent version of the stamped approved consent and two copies of the current protocol and investigator brochure (if applicable).


Submit thirty copies of the Annual Renewal/Final Report Form, thirty copies of the most recent version of the stamped approved consent, and three copies of the most current protocol and investigator’s brochure (if applicable)

NOTE: Only the above information should be included. Previous approval letters and correspondence and other extraneous materials should not be attached as they needlessly increase the volume of paperwork and the amount of time required to approve an application.

A final report should be submitted when the study is officially closed to new patient enrollment and follow up. If patients continue to be actively followed the study is not considered closed and requires annual renewal.

The IRB office is required by Federal regulations to maintain records for three years following the closure of a study.
PART VII: ADDENDUM / REVISION REPORTING

A. GENERAL INFORMATION

All modifications in the protocol, including changes in recruitment, must be approved by the IRB before they are initiated. Requests for approval of modifications may be submitted at any time or they may be incorporated into the yearly renewal application.

Major modification/addendum requests are considered through the full IRB review process, minor modification requests through the Expedited Committee review process. The initial evaluation as to whether an addendum/modification is major or minor starts with the principal investigator, who should assess the degree of change in procedures and risks. If an IRB member reviewing a “minor” modification request feels that it is too substantive to receive this type of review, the application may be referred for full committee review. An addendum is given approval only to the expiration date that was received at the most recent annual review.

Changes or additions in study sites or investigators should also be reported to the IRB office. These requests involve simply sending a letter to the IRB administrator, informing him/her of the change. In the case of a change in principal investigator, the letter should be signed by the investigator who holds the approval.

Minor changes may be eligible for expedited review; for example:

- Changes that do not adversely alter the overall harm-benefit profile of the study;
- Changes that would not potentially affect the willingness of current subjects to remain on the study, or the willingness of potential subjects to enroll in the study; or
- Changes that would not alter the scientific validity of the study design.

If the addendum significantly modifies the protocol, it is important to update the informed consent to reflect the change(s). The revised consent form should be clearly labeled as such and the revisions should be highlighted on the revised form. In this way the revisions can be easily distinguished.

B. SPECIFIC SUBMISSION REQUIREMENTS FOR IRB REVIEW

1. If no subjects are actively enrolled

   Submit two copies of the Addendum report form (see sample form, Appendix I), two copies of the most recent version of the stamped approved consent, and two copies of the current protocol and investigator brochure (if applicable).

2. If subjects are actively enrolled:

   Submit thirty copies of the Addendum Report Form, two copies of the most recent version of the stamped approved consent, and three copies of the most current protocol and investigator’s brochure (if applicable)
PART VIII: ADVERSE EVENT REPORTING

The Common Rule (45 CFR 46) states that investigators conducting research on human subjects have a responsibility to report any “unanticipated problems” involving risks to study participants and others. The responsibilities of all University of South Alabama investigators conducting research on human subjects includes two types of incident reporting: a) any injuries or adverse events associated with the study procedures, and/or problems involving the conduct of the study which may occur during the course of his or her own research projects and b) any possible breach of human subject protection in other research activities at USA of which the investigator may become aware.

As the standard approval letter for the IRB applications states, “All problems involving risks and serious adverse events must be reported to the IRB immediately.” Specifically, the following must be reported, in writing:

- All serious adverse events associated with the study procedures,
- All unexpected adverse events,
- Multicenter trial adverse events occurring at other institutions, and/or
- Any incidents or unanticipated problems involving the conduct of the study or patient participation, including problems with the recruitment and/or consent process.

The information below is provided to clarify IRB policy regarding reporting of adverse events as well as problems involving the conduct of the study. The “Adverse Event Report Form” (see sample form, Appendix I) should be used for reporting such events. All reports should be signed by the Principal Investigator.

A. Types of Events to Report

- **Adverse Events**
  
  The University's policies on adverse events are based on Food and Drug Administration regulations. According to the FDA, a "serious adverse drug experience" with respect to human clinical experience includes "any experience that suggests a significant hazard, contraindication, side effect, or precaution," including "any experience that is fatal or life-threatening, is permanently disabling, requires inpatient hospitalization, or is a congenital anomaly, cancer, or overdose."

  An **unexpected** adverse experience is any adverse experience whose nature, severity, and frequency of risk are not described in the information provided for IRB review or in the consent form.

- **Events at other institutions**
  
  If the project is a multicenter trial and the event on the same protocol occurred at another institution, the investigator must write a memo to the IRB describing the nature of the event, its severity, the likelihood that it will occur at the University, and the implications for future subjects.

- **Unanticipated Problems**
  
  Unanticipated problems in a study, which might affect subject risk benefit analysis, confidentiality, or subjects' willingness to continue in a project are to be reported to the IRB. The IRB will consider the effect of the problem on the study and on the subjects already enrolled.

  In some instances, revisiting the consent process with already enrolled subjects may be necessary. If the problem prompts a change in the study, the consent process and documentation may require alteration for future study subjects.
The investigator should use his/her own judgement when determining if an event is considered reportable beyond the scope of this policy. If there is a question, investigators are encouraged to err on the side of “over-reporting” or contact the IRB Office at 460-6308 or Office of Research Compliance and Assurance at 460-6625 for guidance.

In general, any serious or recurring problem, any unanticipated side effect, any adverse event reported to a study sponsor and/or to the FDA, any adverse event requiring treatment, or any side effect about which a subject is concerned, should be reported to the IRB.

Any deviations from the approved protocol should be reported in writing. Examples of a more serious nature include incidents of a person being enrolled in a study before signed consent has been obtained, an investigational drug being given prior to signed consent, or a subject being given a higher or lower dose of the drug than stated in the approved protocol.

Non-serious and expected adverse events do not have to be reported to the IRB. This means any adverse events that occur with the same frequency or severity as expected or described in the investigator brochure, package inserts, protocol and/or informed consent.

B. All Serious Adverse Events Require a Report

A serious adverse event is defined as an adverse experience that results in any of the following outcomes:

a. death;
b. a life-threatening adverse experience;
c. inpatient hospitalization or prolongation of existing hospitalization;
d. a persistent or significant disability such to disrupt a person’s ability to conduct normal life functions;
e. a congenital anomaly/birth defect;
f. causes cancer;
g. significant overdose or protocol error; or
h. certain medical events that may not result in death, be life-threatening, or require hospitalization, may also be considered a serious adverse event when appropriate medical or surgical intervention is necessary to prevent one of the outcomes listed above.

All serious adverse events that are unexpectedly associated with the study procedures must be reported to the sponsor and the IRB immediately but no later than 7 working days upon learning of the event using the USA Adverse Event Report Form. All deaths, whether or not they are directly related to study procedures, must be reported. For the purpose of this policy, death is never expected. In addition, any unexpected hospitalization of a research subject must be reported, even if the hospitalization is unrelated to the study medication.

C. What is an Adequate Adverse Event Report?

The Adverse Event Report Form was created to help ensure that sufficient information concerning the adverse event is submitted. A separate report should be completed adverse event. Adverse event reports submitted to study sponsors and/or to the FDA may not be sufficient to meet this requirement since they rarely include an assessment of whether changes in the protocol or consent form should be made as a result of the adverse event. If the adverse event results in a revision of the informed consent document, a amendment/revision form and two copies of the revised consent form must also be submitted to the IRB. If revisions are required please provide one revised copy of the protocol and/or consent indicating the revisions by highlighting or underlining, and two clean copies. If applicable, a copy of the FDA adverse event report form should also be submitted to the IRB. (Pursuant to 21 CFR 312.32, adverse events that are both serious and unexpected must be reported to the FDA). The investigator must sign all adverse event reports to verify it has been reviewed by the investigator overseeing the research study. If a study sponsor sends updated drug or device brochures, safety
D. Responsibility of Investigator

It is the responsibility of the investigator for understanding and adhering to this policy on adverse event reporting. Also, investigator is responsible for accurate documentation, investigation and follow-up of all possible study-related adverse events. The investigator should make the initial assessment as to whether changes should be made in the informed consent and/or research design to minimize risks. The IRB relies on the expertise and decision of the investigator, who is required to analyze the adverse event in terms of its relationship to the study and to address the minimization of risks and the adequacy of the informed consent document in reflecting those risks. It is the investigator who bears the ultimate responsibility for protecting subjects enrolled in clinical trials and for appropriate conduct of the study.

Once a clinical trial is officially closed and reporting of adverse is no longer required, it remains the responsibility of the investigator to notify the IRB of the occurrence of any adverse events related to the study with long term consequences to the subjects. The IRB will review the report and recommend appropriate action.

E. Special Requirements for Research Involving the Transfer of Genes

In accordance with Appendix M-I-C-4 of the NIH Guidelines, investigators who have received authorization from the FDA to initiate a human gene transfer protocol must immediately report in writing any serious adverse event (SAE to the IRB, the Institutional Biosafety Committee (IBC), and NIH Office of Biotechnology Activities (OBA)(formerly the Office of Recombinant DNA Activities), and Office for Human Research Protections (OHRP) if applicable.

F. Internal vs External Reporting Requirements

An internal adverse event is an adverse event affecting a research subject who is at a USA study site. For internal events, the USA IRB requires all serious adverse events and all unexpected adverse events to be reported to the IRB office within the time table outlined below. Furthermore, any problems involving the conduct of the study or subject participation at an USA study site, including problems with the recruitment and/or consent processes, require reporting. Adverse events judged to be the result of progressive disease need not be reported.

An external adverse event is an adverse event in a subject that is not at an USA study site. All investigational drug and device studies that are industry-sponsored, the study sponsor typically provides information regarding non-USA adverse events to the investigator. Therefore, the definition of an external adverse event is defined according to the sponsor’s federal reporting requirements, pursuant to 21 CFR 312.32 and 21 CFR 812.150. Study sponsors are required to notify investigators regarding adverse events related to the study drug occurring at other study sites (external events). Notification of these events are provided by the sponsor in an IND Safety Report or a MedWatch Report. These safety reports which describe adverse events from different study sites should be forwarded to the IRB along with a cover memorandum from the investigator or study coordinator outlining the pertinent information.
<table>
<thead>
<tr>
<th>TYPE OF EVENT</th>
<th>Report to IRB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild or Moderate and unexpected – on-site (if related, possibly related, probably not related)</td>
<td>14 working days</td>
</tr>
<tr>
<td>Serious and unexpected – on-site</td>
<td>7 working days</td>
</tr>
<tr>
<td>Serious and unexpected – external site</td>
<td>10 working days after receipt from sponsor</td>
</tr>
<tr>
<td>Serious and expected – on-site</td>
<td>14 working days</td>
</tr>
<tr>
<td>Life-threatening – on-site (if related, possible related, probably not related)</td>
<td>7 working days</td>
</tr>
<tr>
<td>Death – on-site</td>
<td>3 working days from notification</td>
</tr>
<tr>
<td>Death – external site</td>
<td>10 working days after receipt from sponsor</td>
</tr>
</tbody>
</table>

This timeframe is considered the maximal time for reporting a death.

Title 45 and Title 21 of the Code of Federal Regulations, the USA IRB require that a report be submitted in writing for all unanticipated events.

G. What is the Effect of Reporting?

A report is not an admission of any liability. However, for adverse events, the investigator should make an initial determination as to whether any changes are needed in the discussion of the risks and/or benefits in the consent form. In response to incidents, the investigator may need to re-evaluate the recruitment or consent process and modify existing procedures appropriately.

H. How are Adverse Events and/or Incidents Reports Reviewed?

An Adverse Events Subcommittee of the IRB will review all adverse event reports and/or incident reports in order to re-evaluate the risks/benefits of the study and/or the appropriateness of the recruitment/consent process to determine if any changes should be made in the protocol or consent form. If the investigator has already modified the protocol or consent form in response to these events, the appropriateness of these changes is also reviewed. The Adverse Events Subcommittee may recommend additional review by the full IRB. The IRB office will provide acknowledgement of receipt of this information and request additional information if follow-up or clarification is needed. The full committee has the right to request additional information from the investigator, note the occurrence of the adverse event but take no action, ask the investigator to modify the protocol or the informed consent or suspend or terminate the project.

The IRB is responsible for continuing review of all human subject research. This is done through the annual renewal process required for any ongoing study. Thus, all reported adverse events should also be described in detail in the Annual Renewal Report Form when a renewal application is submitted for the study, so that the IRB may consider renewal of the protocol in light of such information.

If the FDA or DHHS is involved, and if the problem is of sufficient magnitude, the appropriate agency officials will be informed.

I. What is the Effect of Failure to Report?

Failure to report is a breach of the conditions under which IRB approval is given, and could result in suspension or revocation of approval. Suspension or revocation of approval could result in loss of support by funding agencies and loss of right to publish.
J. Incident Reports Related to Other Research Activities

The IRB requires annual review of all approved protocols and performs internal audits on approximately ten percent of open protocols per year. In addition, the IRB will conduct an inquiry following any report of possible misconduct related to human research activities that may come from subjects, study personnel, staff, students, or faculty. If, for instance, a research project is being conducted without IRB approval, or an improper method of recruiting subjects is being used, or undue influence is being placed upon prospective subjects to participate in a study, the IRB has no means of learning about such situations and rectifying them unless it is informed that they are taking place. Thus, in order to fulfill its obligation to protect human subjects in research, the institution depends upon concerned individuals, including investigators, to inform the IRB of any possible misconduct related to research activities of which they become aware.

Such incidents are usually reported by telephone or in writing to the Manager of Research Compliance and Assurance (251-460-6625) or to the IRB Coordinator (251-460-6308). An inquiry is made to the investigator conducting the research activity, maintaining requested anonymity of the individual submitting the report whenever possible. Depending upon the outcome of the IRB’s initial inquiry, information about the incident may be forwarded to the Institution Signatory, i.e. Vice-President for Medical Affairs, for appropriate resolution.
PART IX: CONSENT GUIDELINES

A. PURPOSE OF THE CONSENT DOCUMENT

Just as the informed consent process is a vital component of research on human subjects, so is the documentation of that informed consent through use of a signed consent form, or information sheet (an unsigned consent document) a most important part of the consent process.

The consent document is not meant to be merely a legal record of the consent process. Nor is it meant to be the only communication between researcher and prospective subject. On the contrary, the document should be one part of the overall process. The prospective subject may first be contacted in writing or by personal, verbal communication between investigator and subject. The individual will be told about the purpose, procedures, risks and benefits of that study, the subject’s rights in participating in research, the freedom to decline to participate without any jeopardy. If applicable, the alternative treatments available will be explained. The individual will also be given the opportunity to obtain further information and answers to questions related to the study.

The consent form or information sheet should serve as a written summary of the exact information that was presented to the prospective subjects before their agreement to participate in the study. As such, it will provide a useful reference for both the subject and the investigator.

B. ELEMENTS OF CONSENT

Federal regulations on informed consent stipulate eight basic required elements of consent, and note six additional elements that may be added to a standard consent form when appropriate (see Appendix A). The Standard Format that follows has been developed to incorporate these informed consent regulations, as well as institutional and IRB requirements.

C. AUTHORIZATION FOR THE USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

The University of South Alabama is committed to complying with all local, state and federal laws relating to the privacy of health information and to consistently operate with the highest standards of business and professional ethics. In that regard, we have implemented a HIPAA Privacy Compliance Plan for Clinical Research to safeguard the confidentiality and privacy of protected health information (“PHI”) as required by the Federal Standards for Privacy and Individually Identifiable Health Information at 45 CFR Parts 160 and 164, subparts A and E, as may be amended and applicable state privacy laws. The compliance date for the HIPAA privacy rule became effective on April 14, 2003 and are administered by the HHS Office of Civil Rights. The HIPAA Privacy Compliance Plan for Clinical Research and other HIPAA compliance forms are available on the IRB website at http://southmed.usouthal.edu/com/research/HumanSubjects/hipaa.html

Specific written authorization is required for the use and disclosure of PHI in research studies. The University of South Alabama IRB Office has adopted the option of including the authorization in the consent form for research studies. Core elements of information must be provided in writing to prospective subjects in securing authorization for the research use of their PHI. These elements are provided in the HIPAA authorization template provided in the HIPAA Privacy Compliance Plan as Appendix B. This template must be inserted into the confidentiality section of the informed consent form.

D. WAIVER OF SIGNED CONSENT

The federal regulations allow the IRB to waive the requirement for the investigator to obtain a signed consent form if it finds either: 1) that the only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality; or 2) that 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.

Thus, the IRB will usually approve a request for waiver of signed consent in the following situations:

1. When the identities of subjects will be completely anonymous if the consent form is not signed, and there is minimal risk involved in the study;
2. When obtaining a signed consent is not appropriate or feasible according to the cultural standards of the population being studied, and there is minimal risk involved in the study;

3. When there is a possible legal, social, or economic risk to the subject entailed in signing the consent form, e.g., for HIV antibody-positive individuals who might be identified as such by signing the consent form.

4. Retrospective chart review or use of pathological specimens where the patients need not be contacted as part of the study, and appropriate precautions to protect the confidentiality of the data are described;

5. Use of extra unidentifiable blood which is taken at the time of a venipuncture being done for clinical reasons;

6. Use of leftover anonymous biological material taken from another study for which consent was obtained.

If an investigator does request a waiver of signed consent, then the application should provide a written justification for doing so and cite one of the above categories.

As the regulations note, “in cases where the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.” The IRB is likely to require use of such a written statement, in the form of an information sheet, which includes most or all of the same elements as a consent form, but does not require the signature of the subject.

D. GENERAL INFORMATION

Each part of the standard format of a consent form is explained and discussed below. See Appendix J for examples of the USA standard formats that should be used in writing any consent form.

1. Eighth Grade Reading Level

The primary goal of a consent form is to provide all required information about a study in language and format that is easily comprehensible, and presented at the most likely level of understanding of the subject population. For most studies, it is recommended that the consent forms be written at an eighth grade reading level. Everyday vocabulary and simple sentence structure should be used throughout the form. While investigators always have the option of describing the study in more detail and in more scientific language during the consent process itself, the initial written description of the study should be simple and straightforward so that subjects will have an easily understood consent form to take home with them and refer to.

2. Lay Language

Unless the subjects are themselves medical professionals, scientific or technical terms should either be replaced with or defined in lay language. For example, “blood draw” is preferable to “venipuncture, “x-ray” to “radiographs,” “upset stomach” to “GI upset,” “obstruction” to “occlusion.”

3. No Legalistic Language

Legalistic sounding language such as “You hereby agree,” “You certify that,” “You, the undersigned, do acknowledge that” should not be used. Nor should any phrases similar to the following be used: “You understand that,” “You realize that,” “You have been told that,” “It has been explained to you that.” Not only do these phrases not insure a subject’s comprehension but they also lend the appearance of a legal document to the consent form.
4. Proofreading

The entire form should be carefully proofread for correct spelling and grammar before it is submitted for IRB review.

E. DISCUSSION OF EACH CONSENT FORM SECTION

1. Heading and Title

Reference to the University of South Alabama and the information that a research project is being discussed should be included in the consent form heading. For example:

UNIVERSITY OF SOUTH ALABAMA
CONSENT TO BE A RESEARCH SUBJECT

or,

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

The study title must be included in the heading of the form. If the official title is technical and difficult to understand, a simplified non-technical title should be used in addition to the official title.

The consent should be printed on USA departmental letterhead or formatted with a header to include institution, name of investigator, address and contact information.

If a study has more than one consent form, each form should be labeled or titled appropriately, and the same references used within the protocol, in order to avoid confusion.

2. Purpose and Background

This section should present the introduction to the study, indicating who is conducting the research, stating the aim of the study, giving a brief summary of the background or reason for the project, and explaining why the individual has been asked to participate. The reason a person has been asked to participate should be simply but specifically stated (e.g., “because you have tried to quit smoking in the past but have not been successful,” “because you’re undergoing surgery and will be given a general anesthetic,” “because you are a healthy person”) and should not include a discussion of the inclusion/exclusion criteria. The study sponsor should be named.

The first and last names of the principal investigator(s) should be used and the investigators identified with titles and department at the beginning of the form, so that it is clear who is carrying out the study. If an investigational drug or device is being used in the study, this should be mentioned in this section and the drug or device should be named. The name the drug or device referred in this section should be used consistently throughout the form. This section should not begin with such phrases as “You agree to participate ...” since the prospective subject has not yet had a chance to read the form, and could not yet make an informed decision about whether or not to participate.

The number of subjects expected to participate in the study should be included here.

3. Procedures

To emphasize the voluntary nature of participation in research, this section should begin with a phrase like, “If I agree to be in this study, the following will happen.”

Each procedure should then be listed, preferably in the order in which it occurs, and discussed. If the study involves screening procedures, these should be mentioned first and identified as tests that will determine eligibility to continue in the study. The Procedures section should clearly state what will be done to the individual as a result of participation in the study, and, where appropriate, how this differs from standard treatment or what would happen to the individual if he/she did not participate in the study.
When a study involves randomization, it should be described as a study procedure, and the term "randomization" explained in lay language. Information about the probability of assignment to each treatment or condition should be given. Other terms which might not be familiar to the average layperson (e.g., "placebo") should be defined the first time they are mentioned in the form or the lay term used (e.g., "group" rather than "arm").

If a standard medical procedure is being done as part of the study, it should not be referred to as "standard" or "routine," since this could easily imply that the procedure would be done anyway for clinical reasons. Rather, what should be conveyed is that this procedure is an extra laboratory test that is commonly done for clinical purposes, but is being done here for research purposes.

If patient records will be reviewed for purposes of the study, this should be listed as a procedure.

Amounts of blood or tissue to be taken for study purposes should be specified, using lay equivalents (e.g., teaspoons, ounces) for metric terms.

The number of times a procedure will be done, the time involved for each procedure, and the total amount of time for participation in the study should be specified. The location(s) where the procedures will be done should also be stated.

4. Risks and/or Discomforts

The risks and/or possible discomforts of all study procedures should be listed and explained in this section. It is usually best to describe the risks of each procedure in a separate point. Risks should be arranged and described according to their severity and the likelihood of their occurrence. Where appropriate, it should be indicated what precautions will be taken to avoid certain side effects or outcomes from occurring, and what will be done should they occur. A statement should be included 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.

To the extent possible, consent forms should characterize the likelihood of risks using words like "likely," "frequent," "occasional," and "rare." The first time these words are used in a form they should be defined using percentages, as follows:

- Likely events: Expected to happen to more than 50% of subjects
- Frequent events: Will probably happen to 10-50% of subjects
- Occasional events: Will happen to 1-10% of subjects
- Rare events: Will happen to less than 1% of subjects

5. Confidentiality

Since one of the risks of participating in research is a loss of privacy, a discussion of confidentiality issues should be included in the Risks section. It should describe briefly how the confidentiality will be protected, i.e., coding of records, limiting access to the study records, not using any individual identifiers in publications or reports resulting from the study.

Food and Drug Administration regulations require a consent form statement about the extent of confidentiality of records. For studies involving investigation of drugs or devices, both officials from the sponsoring company and the FDA have at least some limited right to review individual records; subjects in such studies must be forewarned about this intrusion into their privacy.

For all statements regarding confidentiality of research records, it should be kept in mind that there is no legal privilege between investigator and subject as there is between physician and patient or counselor and client. Thus, a guarantee of complete confidentiality, or "strictest
NOTE: The one way to protect research records from subpoena is through a Federal Certificate of Confidentiality. More information about this Certificate may be obtained by contacting the federal funding agency (see web-link http://grants1.nih.gov/grants/policy/coc/index.htm) or by calling the IRB Compliance Specialist (460-6308). If such a certificate is obtained, it is recommended that the consent briefly discuss the added degree of protection that this certificate provides.

For studies involving investigational agents, or experimental doses or combinations of drugs and/or treatments, subjects should be warned that there may be as yet unknown risks associated with the drug/treatment but that they will be advised if any new information becomes available that may affect their desire to participate in the study.

6. Compensation for Injury

The consent document must explain whether there is compensation available in case of injury but must not waive or appear to waive the rights of the subject or release or appear to release those conducting the study from liability for negligence. When no system has been set up to provide funds, the preferred wording is: “no funds have been set aside for,” “[the cost] will be billed to you or your insurance,” or similar wording that explains the provisions or the process. Wording such as: “will be your responsibility or that of your third-party payor” has been erroneously interpreted by some subjects to mean the insurance company is required to pay. [FDA Guidance for Institutional Review Boards and Clinical Investigators, 1998 Update.]

7. Benefits

Any potential direct benefits to the subject should be described first, followed by potential general benefits (e.g., the group of patients to which the individual belongs, to medical knowledge, etc.). It is usually recommended that the description of possible direct benefits be qualified with the phrase, “... but this cannot be guaranteed.” If there is no direct benefit to the subject anticipated from the study, this should be stated at the beginning of the section.

The FDA recommends that possible benefits such as medical or societal benefits resulting from a research study be considered separately from payment for participation in the study. Thus, the discussion of payment or reimbursement should be separated from the benefits statement and placed in its own separately labeled section.

8. Alternatives

This section should discuss the various alternatives to participation in the study. This can be a short statement, but it should make clear the possible choices (e.g., no treatment, standard therapy, other experimental treatments, or some or all of the protocol treatment, but without participating in the study) that are available if the individual chooses not to participate in the study. When alternative therapies are available, brief objective descriptions of their important benefits and risks should be included.

When the only alternative is to decline participation in the study (e.g., if the study involves only normal, healthy volunteers), this need not be mentioned in a separate section, since the individual’s right to choose not to participate will be made clear in the last section of the form.

9. Costs/Financial Considerations

When there are no costs at all to be charged to the subject, this should be clearly stated in the form. However, a simple statement that there are no costs is usually not sufficient and could be misleading. The more typical situations are that the subject will have to pay for the usual costs of his or her medical care but will not be charged any extra for participating in the study or the cost of the study medication will be covered by the study but the subject will have to pay all other charges.
When participation in the study may result in any costs whatsoever to subjects, clear information must be provided in the consent form regarding these costs. Special attention must be paid to this issue in studies in which the subjects are also patients. In such cases, where individuals may be undergoing various procedures, tests, or hospitalizations that are part of their clinical diagnosis and treatment, and others that are part of the research study, the costs section of the consent form should clearly distinguish which costs will be charged to the patient or his third party carrier, and which costs will be covered by the study. In addition, when appropriate, a statement should be included warning subjects that because the therapy is experimental, the insurance carriers may not cover the costs involved.

Whenever substantial costs to the subject are involved (e.g., for many oncology, cardiology, and MRI studies) you may wish to consider referring subjects to a financial counselor. The consent form, then, should state that such a counselor is available and ask that subjects take advantage of this service.

10. Reimbursement/Payment

When referring to money that subjects will receive in return for participation in a study, either “reimbursement” or “payment” may be used. However, the term “compensation” should not be used, since it is used on consent forms to designate compensation for injury. Investigators should avoid connotations of undue influence to participate or that the subject is being employed by the investigator. Rather, the sense should be that subjects will be reimbursed for their time, travel expenses, and the inconvenience of being a research subject. However, unless the subject has actual receipts (e.g., parking, taxi, babysitting), the person is not being reimbursed in the strictest sense of the word, for either accounting or tax purposes.

This section should state the total dollar amount that the subject will be paid for participation in the study, and should give any other relevant information such as pro-rating if a subject does not complete the study, or bonus payment at the end of the study. If appropriate, a payment schedule should be included in this section. Subjects should not be required to complete the entire study in order to be reimbursed and bonus payments for study completion should be modest.

Subjects should be informed how payment will be made (e.g., in cash, by check) and when they will be paid (e.g., immediately after the interview, approximately six weeks after individual completion of the study).

Payments for research participation in excess of $600 per calendar year are considered taxable income. If subjects will be paid more than $600, the Reimbursement section should explain that the University will report this income to the IRS.

If there will be no payment or reimbursement of subjects for the study participation, this information should be so stated in this section.

11. Questions

This section should provide contact information for the subject in case of questions about the study. At least one permanent name and telephone number of one investigator, usually the principal investigator, must be typed into this section as submitted. Blank lines to be filled in later may be included for additional contact persons. Even if the principal investigator is faculty/advisor only, his or her name and phone number should be included in this section as subjects often wish to contact the person who is supervising the project.

If the person explaining the study and obtaining consent is not the principal investigator, a blank line in this section may be filled in with the person’s name, and telephone number, if different, at the time consent is obtained.
12. Tissue and/or blood banking or storage

Some studies include the option to have tissue specimens or blood stored (or banked) for studies that may come available in the future, future diagnostic testing, or other purposes not yet determined. Subjects should have the option to participate in the study whether or not they agree to tissue banking. The specific language to provide for this option can be found in Appendix H.

13. Consent

This section should state that the subject has been given (not just “offered”) a copy of the consent form.

Voluntary Nature of Participation in Research: This section should then state the information that participation in research is voluntary, and explain the individual’s right to decline to participate, or withdraw from the study at any time. If the subjects are patients, students, or employees, a phrase may be added indicating that refusal or withdrawal will be without jeopardy to status or care.

The investigator may also wish to advise subjects that they may be withdrawn from the study if the investigator deems it in the best interests of the subject or for other reasons that should be specified (e.g., medical interests, failure to keep appointments).

Consent to Participate: In this section, the IRB discourages such wording as “You have read this form and understand it; based on this understanding, you hereby agree to participate,” since this does not guarantee an individual’s comprehension, legally or otherwise. Rather it is recommended that investigators simply state that if the person wishes to participate in the study, he or she should sign the form; signature will then indicate agreement to participate.

NOTE: All biomedical research studies should adhere to the practice of presenting research subjects with a Bill of Rights at the time of the consenting process. The intent of this document is to inform potential subjects as to their rights when being recruited for clinical research studies. The Medical Research Subjects Bill of Rights should be reviewed prior to the consent document. In addition, there should be a reference at the end of the consent form that the subject has acknowledged receiving and reading the Medical Research Subject’s Bill of Rights.

14. Signature Section

Signature of Subject: Unless waiver of signed consent is approved by the IRB, this should include lines for the subject’s signature and the date of signature.

Signature of Person Obtaining Consent: In order that subjects have a record of who explained the study to them, the consent form should include a signature line for the specific individual obtaining consent.

Third Party Signatures: If the study involves subjects who cannot give consent for themselves (e.g., minors, unconscious patients, individuals with Alzheimer’s Disease), and the IRB accepts the justification for their inclusion in the study, a separate signature should be obtained. For studies involving minors, this signature lines will be for parent(s) or guardian(s). In other studies where a legally authorized representative will give consent for the subject, an appropriately labeled signature line should be used. Note that only parents, guardians, conservators or those who have power of attorney for health care are so authorized.

Assent Signature: If the study involves minors (in Alabama, individuals less than 19 years of age), this line should be signed when appropriate.
15. **IRB Consent Form Stamp**

Once an application has been reviewed and approved by the IRB, the bottom of each page of an approved consent form is stamped. The stamp indicates that the study has been approved by the IRB of the University of South Alabama. It also includes the date the consent was approved and the date the approval will expire. A 1.5 inch margin should be maintained to provide an area for this stamp.
Appendix A

DHHS General Requirements for Informed Consent

The following is quoted directly from Title 45, Code of Federal Regulations, Part 46, Protection of Human Subjects, Revised June 18, 1991:

S46.116 GENERAL REQUIREMENTS OF INFORMED CONSENT

Except as provided elsewhere in this or other subparts, no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

(1) 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;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained [Please note: Title 21, Code of Federal Regulations, Ch.1, April 1, 1992 Edition, which are Food and Drug Administration regulations that apply if an investigational new drug or device is being studied, further stipulates "and that notes the possibility that the Food and Drug Administration may inspect records"];

(6) 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;

(7) 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; and

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

(b) Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) 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;
(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study.

c) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that:

(1) 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: (i) programs under the Social Security Act, or other public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in methods or levels of payment for benefits or services under those programs; or (iv) possible changes in methods or levels of payment for benefits or services under those programs, and

(2) The research could not practicably be carried out without the waiver or alteration.

d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

e) The informed consent requirements in these regulations are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.

(f) Nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, State, or local law.

S46.117 DOCUMENTATION OF INFORMED CONSENT

(a) Except as provided in paragraph (c) of this section, informed consent shall be 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. A copy shall be given to the person signing the form.

(b) Except as provided in paragraph (c) of this section, the consent form may be either of the following:

(1) A written consent document that embodies the elements of informed consent required by S46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or
(2) A "short form" written consent document stating that the elements of informed consent required by S46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the "short form." [Please note: This type of "short form" consent documentation is not used at UCSF.]

(c) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That 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.

In cases where the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.
Appendix B
FDA Guidance on Significant and Non-significant Risk Device Studies

The Investigational Device Exemption (IDE) regulations [21 CFR part 812] describe two types of device studies, "significant risk" (SR) and "nonsignificant risk" (NSR). An SR device study is defined [21 CFR 812.3(m)] as a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. An NSR device investigation is one that does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the Institutional Review Board (IRB) regulations [21 CFR part 56] to identify certain studies that may be approved through an "expedited review" procedure. For both SR and NSR device studies, IRB approval prior to conducting clinical trials and continuing review by the IRB are required. In addition, informed consent must be obtained for either type of study [21 CFR part 50].

Distinguishing Between SR and NSR Device Studies

The effect of the SR/NSR decision is very important to research sponsors and investigators. SR device studies are governed by the IDE regulations [21 CFR part 812]. NSR device studies have fewer regulatory controls than SR studies and are governed by the abbreviated requirements [21 CFR 812.2(b)]. The major differences are in the approval process and in the record keeping and reporting requirements. The SR/NSR decision is also important to FDA because the IRB serves, in a sense, as the Agency's surrogate with respect to review and approval of NSR studies. FDA is usually not apprised of the existence of approved NSR studies because sponsors and IRBs are not required to report NSR device study approvals to FDA. If an investigator or a sponsor proposes the initiation of a claimed NSR investigation to an IRB, and if the IRB agrees that the device study is NSR and approves the study, the investigation may begin at that institution immediately, without submission of an IDE application to FDA.

If an IRB believes that a device study is SR, the investigation may not begin until both the IRB and FDA approve the investigation. To help in the determination of the risk status of the device, IRBs should review information such as reports of prior investigations conducted with the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures. The sponsor should provide the IRB with a risk assessment and the rationale used in making its risk determination [21 CFR 812.150(b)(10)].

SR/NSR Studies and the IRB: The NSR/SR Decision

The assessment of whether or not a device study presents a NSR is initially made by the sponsor. If the sponsor considers that a study is NSR, the sponsor provides the reviewing IRB an explanation of its determination and any other information that may assist the IRB in evaluating the risk of the study. The sponsor should provide the IRB with a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of patient selection criteria and monitoring procedures, as well as any other information that the IRB deems necessary to make its decision. The sponsor should inform the IRB whether other IRBs have reviewed the proposed study and what determination was made. The sponsor must inform the IRB of the Agency's assessment of the device's risk if such an assessment has been made. The IRB may also consult with FDA for its opinion.

The IRB may agree or disagree with the sponsor's initial NSR assessment. If the IRB agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to FDA. If the IRB disagrees, the sponsor should notify FDA that an SR determination has been made. The study can be conducted as an SR investigation following FDA approval of an IDE application.

The risk determination should be based on the proposed use of a device in an investigation, and not on the device alone. In deciding if a study poses an SR, an IRB must consider the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, could result in
permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure should be considered SR. Also, if the subject must undergo a procedure as part of the investigational study, e.g., a surgical procedure, the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device. Two examples follow:

The study of a pacemaker that is a modification of a commercially—available pacemaker poses a SR because the use of any pacemaker presents a potential for serious harm to the subjects. This is true even though the modified pacemaker may pose less risk, or only slightly greater risk, in comparison to the commercially-available model. The amount of potential reduced or increased risk associated with the investigational pacemaker should only be considered (in relation to possible decreased or increased benefits) when assessing whether the study can be approved.

The study of an extended wear contact lens is considered SR because wearing the lens continuously overnight while sleeping presents a potential for injuries not normally seen with daily wear lenses, which are considered NSR.

FDA has the ultimate decision in determining if a device study is SR or NSR. If the Agency does not agree with an IRB's decision that a device study presents an NSR, an IDE application must be submitted to FDA. On the other hand, if a sponsor files an IDE with FDA because it is presumed to be an SR study, but FDA classifies the device study as NSR, the Agency will return the IDE application to the sponsor and the study would be presented to IRBs as an NSR investigation.

IRB and Sponsor Responsibilities Following SR/NSR Determination

If the IRB decides the study is Significant Risk:

1. IRB Responsibilities:
   Notify sponsor and investigator of SR decision
   After IDE obtained by sponsor, proceed to review study applying requisite criteria [21 CFR 56.111]

2. Sponsor Responsibilities:
   Submit IDE to FDA or, if electing not to proceed with study, notify FDA (CDRH Program Operations Staff 301-594-1190) of the SR determination;
   Study may not begin until FDA approves IDE and IRB approves the study.
   Sponsor and investigator(s) must comply with IDE regulations [21 CFR part 812], as well as informed consent and IRB regulations [21 CFR parts 50 and 56]

If the IRB decides the study is Nonsignificant Risk:

1. IRB proceeds to review study applying requisite criteria [21 CFR 56.111]

2. If the study is approved by the IRB, the sponsor and investigator must comply with "abbreviated IDE requirements" [21 CFR 812.2(b)], and informed consent and IRB regulations [21 CFR parts 50 and 56].

The Decision to Approve or Disapprove

Once the SR/NSR decision has been reached, the IRB should consider whether the study should be approved or not. The criteria for deciding if SR and NSR studies should be approved are the same as for any other FDA regulated study [21 CFR 56.111]. The IRB that risks to subjects are minimized and are reasonable in relation to anticipated benefits and knowledge to be gained, subject selection is equitable, informed consent materials and procedures are adequate, and provisions for monitoring the study and protecting the privacy of subjects are acceptable. To assure that the risks to the subject are reasonable in relation to the anticipated benefits, the risks and benefits of the investigation should be compared to the risks and benefits of alternative devices or procedures. This differs from the judgment about whether a study poses a SR or NSR which is based solely upon the seriousness of the harm that may result from the use of the device. Minutes of IRB meetings must document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.
FDA considers studies of all significant risk devices to present more than minimal risk; thus, full IRB review for all studies involving significant risk devices is necessary. Generally, IRB review at a convened meeting is also required when reviewing NSR studies. Some NSR studies, however, may qualify as minimal risk [21 CFR 56.102(i)] and the IRB may choose to review those studies under its expedited review procedures [21 CFR 56.110].

Examples of NSR/SR Devices

The following examples are provided to assist sponsors and IRBs in making SR/NSR determinations. The list includes many commonly used medical devices. Inclusion of a device in the NSR category should not be viewed as a conclusive determination, because the proposed use of a device in a study is the ultimate determinant of the potential risk to subjects. It is unlikely that a device included in the SR category could be deemed NSR due to the inherent risks associated with most such devices.

NONSIGNIFICANT RISK DEVICES

Low Power Lasers for treatment of pain
Caries Removal Solution
Daily Wear Contact Lenses and Associated Lens Care Products not intended for use directly in the eye (e.g., cleaners; disinfecting, rinsing and storage solutions)
Contact Lens Solutions intended for use directly in the eye (e.g., lubricating/rewetting solutions) using active ingredients or preservation systems with a history of prior ophthalmic/contact lens use or generally recognized as safe for ophthalmic use
Conventional Gastroenterology and Urology Endoscopes and/or Accessories
Conventional General Hospital Catheters (long-term percutaneous, implanted, subcutaneous and intravascular)
Conventional Implantable Vascular Access Devices (Ports)
Conventional Laparoscopes, Culdoscopes, and Hysteroscopes
Dental Filling Materials, Cushions or Pads made from traditional materials and designs
Denture Repair Kits and Realigners
Digital Mammography [Note: an IDE is required when safety and effectiveness data are collected which will be submitted in support of a marketing application.]
Electroencephalography (e.g., new recording and analysis methods, enhanced diagnostic capabilities)
Externally Worn Monitors for Insulin Reactions
Functional Electrical Neuromuscular Stimulators
General Biliary Catheters General Urological Catheters (e.g., Foley and diagnostic catheters)
Jaundice Monitors for Infants
Magnetic Resonance Imaging (MRI) Devices within FDA specified parameters
Manual Image Guided Surgery
Menstrual Pads (Cotton or Rayon, only)
Menstrual Tampons (Cotton or Rayon, only)
Nonimplantable Electrical Incontinence Devices
Nonimplantable Male Reproductive Aids with no components that enter the vagina
Ob/Gyn Diagnostic Ultrasound within FDA approved parameters
Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain
Wound Dressings, excluding absorbable hemostatic devices and dressings (also excluding Interactive Wound and Burn Dressings)

SIGNIFICANT RISK DEVICES

General Medical Use

Catheters:

Urology - urologic with anti-infective coatings
General Hospital - except for conventional long-term percutaneous, implanted, subcutaneous and intravascular
Neurological - cerebrovascular, occlusion balloon
Cardiology - transluminal coronary angioplasty, intra-aortic balloon with control system
Collagen Implant Material for use in ear, nose and throat, orthopedics, plastic surgery, urological and dental applications
Surgical Lasers for use in various medical specialties
Tissue Adhesives for use in neurosurgery, gastroenterology, ophthalmology, general and plastic surgery, and cardiology

Anesthesiology
Breathing Gas Mixers
Bronchial Tubes
Electroanesthesia Apparatus
Epidural and Spinal Catheters
Epidural and Spinal Needles
Esophageal Obturators
Gas Machines for anesthesia or analgesia
High Frequency Jet Ventilators greater than 150 BPM
Rebreathing Devices
Respiratory Ventilators
Tracheal Tubes

Cardiovascular
Aortic and Mitral Valvoplasty Catheters
Arterial Embolization Devices Cardiac Assist Devices: artificial heart (permanent implant and short term use), cardiomyoplasty devices, intra-aortic balloon pumps, ventricular assist devices
Cardiac Bypass Devices: oxygenators, cardiopulmonary non-roller blood pumps, closed chest devices
Cardiac Pacemaker/Pulse Generators: antitachycardia, esophageal, external transcutaneous, implantable
Cardiopulmonary Resuscitation (CPR) Devices
Cardiovascular/Intravascular Filters
Coronary Artery Retruperfusion Systems
Coronary Occluders for ductus arteriosus, atrial and septal defects
Coronary and Peripheral Arthrectomy Devices
Extracorporeal Membrane Oxygenators (ECMO)
Implantable Cardioverters/Defibrillators
Laser Coronary and Peripheral Angioplasty Devices
Myoplasty Laser Catheters
Organ Storage/Transport Units
Pacing Leads
Percutaneous Conduction Tissue Ablation Electrodes
Peripheral, Coronary, Pulmonary, Renal, Vena Caval and Peripheral Stents
Replacement Heart Valves
RF Catheter Ablation and Mapping Systems
Ultrasonic Angioplasty Catheters
Vascular and Arterial Graft Prostheses
Vascular Hemostasis Devices

Dental
Absorbable Materials to aid in the healing of periodontal defects and other maxillofacial applications
Bone Morphogenic Proteins with and without bone, e.g., Hydroxyapatite (HA)
Dental Lasers for hard tissue applications
Endosseous Implants and associated bone filling and augmentation materials used in conjunction with the implants
Subperiosteal Implants
Temporomandibular Joint (TMJ) Prostheses

Ear, Nose, and Throat
Auditory Brainstem Implants
Cochlear Implants
Laryngeal Implants
Total Ossicular Prosthesis Replacements

Gastroenterology and Urology
Anastomosis Devices
Balloon Dilation Catheters for benign prostatic hyperplasia (BPH)
Biliary Stents
Components of Water Treatment Systems for Hemodialysis
Dialysis Delivery Systems
Electrical Stimulation Devices for sperm collection
Embolization Devices for general urological use
Extracorporeal Circulation Systems
Extracorporeal Hyperthermia Systems
Extracorporeal Photopheresis Systems
Femoral, Jugular and Subclavian Catheters
Hemodialyzers
Hemofilters
Implantable Electrical Urinary Incontinence Systems
Implantable Penile Prostheses
Injectable Bulking Agents for incontinence
Lithotripters (e.g., electrohydraulic extracorporeal shock-wave, laser, powered mechanical, ultrasonic)
Mechanical/Hydraulic Urinary Incontinence Devices
Penetrating External Penile Rigidity Devices with components that enter the vagina
Peritoneal Dialysis Devices
Peritoneal Shunt
Plasmapheresis Systems
Prostatic Hyperthermia Devices
Urethral Occlusion Devices
Urethral Sphincter Prostheses
Urological Stents (e.g., ureteral, prostatG)

General and Plastic Surgery
Absorbable Adhesion Barrier Devices
Absorbable Hemostatic Agents
Artificial Skin and Interactive Wound and Burn Dressings
Injectable Collagen
Implantable Craniofacial Prostheses
Repeat Access Devices for surgical procedures
Sutures

General Hospital
Implantable Vascular Access Devices (Ports) - if new routes of administration or new design
Infusion Pumps (implantable and closed-loop - depending on the infused drug)

Neurological
Electroconvulsive Therapy (ECT) Devices
Hydrocephalus Shunts
Implanted Intracerebral/Subcortical Stimulators
Implanted Intracranial Pressure Monitors
Implanted Spinal Cord and Nerve Stimulators and Electrodes

Obstetrics and Gynecology
Antepartum Home Monitors for Non-Stress Tests
Antepartum Home Uterine Activity Monitors
Catheters for Chorionic Villus Sampling (CVS)
Catheters Introduced into the Fallopian Tubes
Cervical Dilation Devices

Contraceptive Devices:
Cervical Caps
Condoms (for men) made from new materials (e.g., polyurethane)
Contraceptive In Vitro Diagnostics (IVDs)
Diaphragms
Female Condoms
Intrauterine Devices (IUDs)
New Electrosurgical Instruments for Tubal Coagulation
New Devices for Occlusion of the Vas Deferens
Sponges
Tubal Occlusion Devices (Bands or Clips)

Devices to Prevent Post-op Pelvic Adhesions
Embryoscopes and Devices intended for fetal surgery
Fallopian Scopes and Falloposcopic Delivery Systems
Intrapartum Fetal Monitors using new physiological markers
New Devices to Facilitate Assisted Vaginal Delivery
Thermal Systems for Endometrial Ablation

Ophthalmics
Class III Ophthalmic Lasers
Contact Lens Solutions intended for direct instillation (e.g., lubrication/rewetting solutions) in the eye using new active agents or preservatives with no history of prior ophthalmic/contact lens use or not generally recognized as safe for ophthalmic use
Corneal Implants
Corneal Storage Media
Epikeratophakia Lenticules
Extended Wear Contact Lens
Eye Valve Implants (glaucoma implant)
Intraocular Lenses (IOLs) [21 CFR part 813]
Keratoprosthesis Retinal Reattachment Systems: fluids, gases, perfluorocarbons, perfluoropropane, silicone oil, sulfur hexafluoride, tacks
Viscosurgical Fluids

Orthopedics and Restorative
Bone Growth Stimulators
Calcium Tri-Phosphate Hydroxyapatite
Ceramics Collagen and Bone Morphogenic Protein Meniscus Replacements
Implantable Prostheses (ligament, tendon, hip, knee, finger)
Computer Guided Robotic Surgery
Radiology
Boron Neutron Capture Therapy
Hyperthermia Systems and Applicators

Your comments and suggestions for additional examples are welcome and should be sent to:
Program Operation Staff (HFZ-403)
Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850
(301) 594-1190
Appendix C

Emergency Use of an Investigational Drug or Device

Circumstances of Use

Although FDA regulations require that, in general, clinical investigations of test articles must be reviewed and approved by the Institutional Review Board before they are conducted, the regulations provide for an exception to this rule in the case of an emergency use of a test article. For any given institution, this type of exception can be made for emergency use of an investigational drug or device on a one-time, one-patient basis only.

Any such emergency use (or "compassionate use," as it is sometimes referred to) of a test article is subject to the following conditions, specified in the Code of Federal Regulations, Title 21: Food and Drugs:

1. Section 56.102.d. defines "emergency use" as "the use of a test article on a human subject [1] in a life-threatening situation [2] in which no standard acceptable treatment is available, and [3] in which there is not sufficient time to obtain IRB approval."

2. Section 56.104.c. allows for the emergency use of a test article "provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review."

3. Section 50.23 requires the obtaining of informed consent before the use of the test article unless "both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing..." that four conditions have been met. (See Information Concerning Consent below.)

4. Section 99 states that even for the emergency use of an investigational drug, an Investigational New Drug (IND) exemption is still necessary. In addition, the FDA requires notification for the emergency use of an unapproved Investigational Device.

The FDA expects the physician to follow as many subject protection procedures as possible. These include:

1. obtaining an independent assessment by an uninvolved physician;
2. obtaining informed consent from the patient or a legal representative;
3. notifying institutional officials as specified by institutional policies;
4. notifying the Institutional Review Board (IRB); and
5. obtaining authorization from the IDE holder, if an approved IDE for the device exists

Procedures for Use

In order to approve the emergency use of a drug or device as expeditiously as possible, while maintaining compliance with federal regulations, the USA IRB asks that the following procedures be followed:

1. The investigator should call the office of the IRB (251-460-6308) to inform the office that he/she is requesting permission for the emergency use of a test article. The IRB Compliance Specialist will confirm with the investigator that the request meets the requirements for emergency use (point #1 above), will record the pertinent information required for record-keeping purposes, and then refer the investigator to either the Chair or Vice Chair of the Committee so that the emergency use may be approved.

NOTE: If in order for the investigational drug to be released, the investigator needs a letter informing the drug company that the request for emergency approval has been granted, the IRB staff contact should be informed at this time, and a letter can be faxed to the sponsor.

2. The investigator must then contact the IRB Chair, or Vice Chair, to discuss the emergency use of the test article.
3. Once approval has been received from the Chair, and an IND exemption number obtained (the drug company or sponsor should have this number) or the IDE number obtained from the sponsor or from the FDA, the drug or device may then be used on an emergency basis, for one time, one patient, only. If at all possible, informed consent should be sought from the patient before this use.

4. Within 5 working days after the approved use of the drug or device, a written report must be submitted to the IRB. The report should include at least the following information:

   a. Name of Physician(s) as well as department address and phone number;
   b. Name of Investigational Drug or Device;
   c. Name of Sponsor;
   d. Date of Request for Permission;
   e. Date of Actual Use of Drug or Device;
   f. Name of Patient;
   g. Description of Rationale for Use; and
   h. Results of Use.

   NOTE: If the results of use cannot be submitted within 5 working days, they may be submitted later, but in no case more than 14 days after use.

   i. Copy of Consent Form (if signed consent is possible).

   If in addition to the letter confirming IRB emergency use approval, other letters are needed from the IRB office affirming that the investigator is in compliance with FDA regulations, that documentation will be provided once the above conditions have been met.

Information Concerning Informed Consent

The investigator is required to obtain informed consent of the subject prior to the emergency use; this consent should contain all the elements of consent that are contained in the usual USA IRB consent process. However, an exception to this rule may be made if, as stated in Section 50.23:

"... [B]oth the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

1. The human subject is confronted by a life-threatening situation necessitating the use of the test article.
2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from the subject.
3. Time is not sufficient to obtain consent from the subject's legal representative.
4. There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject."

Considerations for Future Requests

Because the FDA expects physicians "to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements...far enough in advance," the USA IRB recommends that once a drug or device has been used on an emergency basis, a protocol should be developed for future use. The IRB will help physicians handle emergency situations as quickly as possible; however, the Committee is restricted by the federal regulation that allows approval for emergency use of a test article for one patient, one time only, per institution.
Appendix D

Guidance for Institutional Review Boards and Clinical Investigators
1998 Update

Significant Differences in FDA and HHS Regulations
for Protection of Human Subjects

The Department of Health and Human Services (HHS) regulations [45 CFR part 46] apply to research involving human subjects conducted by the HHS or funded in whole or in part by the HHS. The Food and Drug Administration (FDA) regulations [21 CFR parts 50 and 56] apply to research involving products regulated by the FDA. Federal support is not necessary for the FDA regulations to be applicable. When research involving products regulated by the FDA is funded, supported or conducted by FDA and/or HHS, both the HHS and FDA regulations apply.

<table>
<thead>
<tr>
<th>Section Numbers</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ß 56.102 (FDA)</td>
<td>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 in the FDA regulations.</td>
</tr>
<tr>
<td>ß 46.102 (HHS)</td>
<td>FDA provides exemption from the prospective IRB review requirement for &quot;emergency use&quot; of test article in specific situations. HHS regulations state that they are not intended to limit the provision of emergency medical care.</td>
</tr>
<tr>
<td>ß 56.104 (FDA)</td>
<td>FDA provides for sponsors and sponsor-investigators to request a waiver of IRB review requirements (but not informed consent requirements). HHS exempts certain categories of research and provides for a Secretarial waiver.</td>
</tr>
<tr>
<td>ß 46.116 (HHS)</td>
<td>Unlike HHS, 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 which would fall into that category of research. (Both regulations allow for IRB waiver of documentation of informed consent in instances of minimal risk.)</td>
</tr>
<tr>
<td>ß 46.116(c)(HHS)</td>
<td>The FDA list of investigations eligible for expedited review (published in the Federal Register) does not include the studies described in category 9 of the HHS list because these types of studies are not regulated by FDA</td>
</tr>
<tr>
<td>ß 56.114 (FDA)</td>
<td>FDA does 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.)</td>
</tr>
<tr>
<td>ß 46.114 (HHS)</td>
<td>FDA has neither an assurance mechanisms nor files of IRB membership. Therefore, FDA does not require the IRB or institution to report changes in membership whereas HHS does require such notification.</td>
</tr>
<tr>
<td>ß 56.115 (FDA)</td>
<td>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. HHS has no such provision because it does not issue research or marketing permits.</td>
</tr>
<tr>
<td>ß 46.115 (HHS)</td>
<td>FDA regulations provide sanctions for non-compliance with</td>
</tr>
<tr>
<td>Section Numbers</td>
<td>Description</td>
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<tr>
<td>β 50.23 (FDA)</td>
<td>FDA, but not HHS, provides for an exception from the informed consent requirements in emergency situations. The provision is based on the Medical Device Amendments of 1976, but may be used in investigations involving drugs, devices, and other FDA regulated products in situations described in β 50.23.</td>
</tr>
<tr>
<td>β 46.116(c)&amp;(d)</td>
<td>HHS provides for waiving or altering elements of informed consent under certain conditions. FDA has no such provision because the types of studies which would qualify for such regulated by FDA or are covered by the emergency treatment provisions (β 50.23).</td>
</tr>
<tr>
<td>β 50.25a(5)(FDA)</td>
<td>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 when they pertain to the study. While HHS has the right to inspect records of studies it funds, it does not impose that same informed consent requirement.</td>
</tr>
<tr>
<td>β 50.27(a)</td>
<td>FDA explicitly requires that consent forms be dated as well as signed by the subject or the subject's legally authorized representative. The HHS regulations do not explicitly require consent forms to be dated.</td>
</tr>
</tbody>
</table>
Appendix E

Medical Records Review

All research involving human subjects must be reviewed at some level by the Institutional Review Board (IRB) and, as evidenced at the end of this appendix, a medical record falls under the federal definition of "human subject."

Department of Health and Human Services (DHHS) regulations for protection of human subjects identify several categories of research activities which may be exempted from review by the Institutional Review Board (IRB) or which may be reviewed by the IRB through an expedited procedure. The level of review required depends on whether the research falls into one of these categories. The three types of review for research in which the use of medical records constitutes the only involvement of human subjects are described below. The turn around time for approval depends on the level of review and is also discussed below.

1. Exempt Review

Medical records review qualifies as exempt from IRB review if and only if the information retrieved from the records is recorded by investigators in such a manner that subjects cannot be identified, directly or through identifiers linked to subjects and the records are reviewed retrospectively. In addition, if investigators are not reviewing medical records directly but rather reviewing secondary data which does not include patient identifiers or links to medical records, the research also qualifies as exempt. In these cases the research may be determined to be Exempt from Full Board Review in the IRB office. This is accomplished by completing and submitting an New Projects Application Form for Exempt Review. A copy of the signed approval may be required for federally-funded studies.

If investigators maintain any links, even coded links, between their research records and the medical records or the subjects themselves, the research cannot be certified by the IRB as exempt, but may qualify for expedited review (see below). In addition, prospective review (that is, a plan to review data not yet created) of medical records does not qualify as exempt, whether or not links are maintained.

Please review PART V of these Guidelines for information about exempt categories of research and see Appendix I for a copy of the New Projects Application Form. Turn around time for this level of review is typically one week but may be in as little as a day upon request and available time in the IRB office.

2. Expedited Review

A New Projects Application Form should be submitted for research where investigators maintain links between study records and subjects or subjects' medical records, or where medical records are reviewed prospectively.

These applications will be reviewed by the IRB in one of two ways.

a. Retrospective review of medical records falls under Expedited Review Category 5, "Use of Data or Specimens Collected for Non-Research Purposes," of the DHHS categories of low-risk research activities (See PART IV for further information). This type of application is reviewed by the Expedited Review Subcommittee of the IRB. Turn around time for this level of review is approximately two to four weeks if the application is complete and no questions are raised by the reviewer.

b. Prospective review of medical records, the Subcommittee’s recommendations may need to be reviewed at a convened meeting. Turn around time for this level of review is typically two to four weeks if the application is complete and if no questions are raised by the reviewer.

When there will be no contact with the patient, the main issue to be addressed in these applications is the protection of confidentiality. This is particularly important since obtaining information for research purposes creates a record that does not have the legal protection of a medical record. If issues of
confidentiality are satisfactorily addressed, request for waiver of individual consent will usually be approved by the IRB.

3. Informing Subjects or Potential Subjects

If medical records are reviewed as part of a study for which written consent is obtained, then subjects must be informed in the procedures section of the consent form that their records will be reviewed as a procedure of the study.

If medical records are used to identify potential subjects for a study, then this must be described in the study protocol and explained appropriately to the subject. Please review Part III.C or Part IV.D.3.a for additional discussion of subject recruitment issues.

4. Exceptions

Use of medical records information for purposes of individual patient treatment, or in-house or program evaluation (e.g., Grand Rounds presentations) is not considered to be "research" within the definitions given below, and IRB approval need not be obtained. However, if the medical records information will be gathered with the intent of publication or presentation to an outside group, this is considered to be within the IRB's jurisdiction, and requires review.

5. Definitions

Section 46.102 of DHHS regulations (45 CFR 46) provides the following definitions (emphasis added):

"Research" means a systematic investigation designed to develop or contribute to generalizable knowledge . . . Activities which meet this definition constitute 'research' for purposes of these regulations. "Human subject" means a living individual 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.

"Private information" includes information about behavior that occurs in a context which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects."

"Existing" means collected (i.e., on the shelf) prior to the research for a purpose other than the proposed research. In terms of medical records, the records must exist at the time the application is reviewed by the CHR.

Since, in all cases, the individual identity of a patient whose medical record is used to gather information for research purposes "is or may be readily ascertained by the investigator," any such use of medical records fits under this broad definition of "research."
Appendix F

Special Subject Populations

1. HIV-INFECTED INDIVIDUALS
2. FETUSES, PREGNANT WOMEN AND IN VITRO FERTILIZATION
3. MINORS
4. PRISONERS
5. THOSE WHO CANNOT READ OR SPEAK ENGLISH OR WHO ARE ILLITERATE
6. THOSE UNABLE TO CONSENT FOR THEMSELVES

   a. Obtaining Consent from an Authorized Representative or Relative
   b. Waiving Consent in Studies Involving No More Than Minimal Risk
   c. Waiving Consent in Emergency Settings

1. HIV-INFECTED INDIVIDUALS

Individuals who are infected with the Human Immunodeficiency Virus (HIV) are a particularly vulnerable subject group. The fact that they suffer or may eventually suffer from a fatal disease with no currently known cure may compromise their ability to freely give or refuse consent to participate in research projects. The IRB will therefore give special attention to certain issues for these individuals, such as assessing the potential risk/benefit balance of the study and assuring that the consent process clearly distinguishes experimental procedures from clinical care.

Testing for HIV-antibody, which establishes that an individual has been exposed to the HIV virus, involves unique concerns when it is done for research purposes. The primary concerns for the IRB revolve around two sets of issues. One is the complex set of risks associated with a subject learning that he or she is HIV positive, particularly if the results are unexpected. The other issue is the risk of loss of confidentiality of the research record that is created when such testing is done as part of a study. Thus, if HIV-antibody testing is to be performed for research purposes, the following should also occur:

   a. Both the protocol and the consent form must state that the HIV testing is being performed for purposes of the study.

   b. The protocol must include a justification as to why this testing is being performed.

   c. Pre- and post-test counseling of the subjects by qualified personnel must be performed and the subjects must be informed in person of their test results. The subjects should be counseled as to the various risks associated with HIV testing as well as the risks associated with being HIV positive. If the person is HIV positive, the various options available for treatment should be discussed.

   d. The details of this counseling, where, when and by whom it will be done, should be included in the Procedures section of the consent form.

   e. The protocol should discuss how the confidentiality of the HIV-antibody test results will be maintained (see discussion below).

Alabama State Code

In 1987, additions were made to the State Health and Safety Code to establish certain requirements regarding blood testing, reporting, and confidentiality to protect public health. The current Code contains several points that must be addressed by any investigator doing a research study which include HIV-antibody testing.
Title 22, Section 22-11A-14 provides for special protection of results of sexually transmitted diseases, and prescribes penalties for the negligent or willful disclosure of identified results, unless there is written authorization by the subject to do so.

Because the statute refers to individually identified test results, it is assumed that none of the protections apply to research records in which no individual is identified.

2. FETUSES, PREGNANT WOMEN AND IN VITRO FERTILIZATION

Based on federal regulations in Title VII of the Civil Rights Act of 1964 and Pregnancy Discrimination Act of 1978, it is illegal to discriminate against individuals on the basis of sex and/or pregnancy. By implication and logical extension, the automatic exclusion of pregnant women from research protocols is discriminatory and therefore illegal.

Sections of the Code of Federal Regulations (45 CFR 46, Subpart B) also address some issues concerning the inclusion of pregnant women in clinical research. These regulations were amended effective 11/13/01.

A pregnant woman cannot be excluded from a protocol if saving her life is even a remote possibility and there are no other equivalent therapeutic alternatives.

A pregnant woman may be excluded from a research protocol IF appropriate studies on animals and non-pregnant individuals have not been completed. The exceptions to this stipulation are as follows:

1. The purpose of the activity is to meet the health needs of the mother and the fetus will be placed at risk only the minimum extent necessary to meet such needs; OR

2. The risk to the fetus is minimal.

When considering the health needs of the mother, the risk-benefit ratio of the research activity for the individual and the fetus must be considered in the context of available alternatives.

Each protocol must be reviewed individually to determine whether the decision to include or exclude pregnant women in that particular study is appropriate in the context of available alternatives. The automatic exclusion of pregnant (i.e. without a stated rationale) is not acceptable. Reviewers should ask the investigator for an explanation of the rationale for inclusion or exclusion if not given or if it is not clear. The rationale must be scientifically justifiable.

The following information is quoted from these regulations:

45 CFR 46, Subpart B: Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (as of 11/13/01)

46.203 Duties of IRBs in connection with research involving pregnant women, fetuses, and human in vitro fertilization

In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research that satisfies the conditions of all applicable sections of this subpart and the other subparts of this part.

46.204 Research involving pregnant women or fetuses prior to delivery

Pregnant women or fetuses may be involved in research if all of the following conditions are met:

(a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

(b) 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 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;

(c) Any risk is the least possible for achieving the objectives of the research;

(d) 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, her consent is obtained in accord with the informed consent provisions of subpart A of this part;

(e) 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 subpart A of this part, 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.

(f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

(g) For children as defined in Sec 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of Subpart D of this part;

(h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

(i) 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

(j) Individuals engaged in the research will have no part in determining the viability of a neonate.

46.205 Research involving neonates

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

(1) Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

(2) Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

(3) Individuals engaged in the research will have no part in determining the viability of a neonate.

(4) The requirements of paragraph (b) or (c) of this section have been met as applicable.

(b) Neonates of uncertain viability. Until is has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:

(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 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 in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

(c) Nonviable neonates. After delivery, a nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

(1) Vital functions of the neonate will not be artificially maintained;
(2) The research will not terminate the heartbeat or respiration of the neonate;
(3) There will be no 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 in accord with subpart A of this part, except that the waiver and alteration provisions of Sec. 46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

(d) Viable neonates. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of subparts A and D of this part.

46.206 Research involving, after delivery, the placenta, the dead fetus, or fetal material

(a) Research involving, after delivery, the placenta, the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities.

(b) If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable.

46.207 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

The Secretary will conduct or fund research that the IRB does not believe meets the requirements of Sec. 46.204 or Sec. 46.205 only if:

(a) The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and

(b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:

(1) That the research in fact satisfies the conditions of Sec. 46.204, as applicable; or
(2) The following:

(i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;

(ii) The research will be conducted in accord with sound ethical principles; and

(iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.
## Additional DHHS Protections for Children Involved as Subjects in Research

For all research protocols that involve children an initial determination of the appropriate risk category must be made. As required by OHRP the final decision of the risk category will be established at the IRB meeting and reflected in the letters and minutes.

<table>
<thead>
<tr>
<th>45CFR46</th>
<th>Category</th>
<th>Explanation</th>
<th>Parental Consent</th>
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<tbody>
<tr>
<td>46.404</td>
<td>Research not involving greater than minimal risk*</td>
<td>The IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.</td>
<td>Consent from one parent is sufficient</td>
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</table>
| 46.405 | Research involving greater than minimal risk* but presenting the prospect of direct benefit to the individual subjects | a. The risk is justified by the anticipated benefit to the subjects;  
b. The relation of the anticipated benefit to the risk is as least as favorable to the subjects as that presented by available alternative approaches; and  
c. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth below. | Consent from one parent is sufficient |
| 46.406 | Research involving greater than minimal risk* and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition | a. The risk represents a minor increase over minimal risk;  
b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations;  
c. The intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition which is of vital importance for the understanding or amelioration of the subjects’ disorder or condition; and  
d. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth below | Consent must be obtained from both parents if they have custody and are reasonably available |
| 46.407 | Research not otherwise approvable which presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children (very rarely if ever used) | a. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and  
b. The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:  
1. That the research in fact satisfies the above requirements of this section, as applicable, or  
2. The following:  
i. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children;  
ii. The research will be conducted in accordance with sound ethical principles;  
iii. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians. | Consent must be obtained from both parents if they have custody and are reasonably available |
<table>
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<tr>
<th>Requirements for permission by parents or guardians and for assent by children</th>
<th>46.408</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waiver of assent and consent conditions</td>
<td>a. IRB shall determine that adequate provisions are made for obtaining assent when in judgement of the IRB the children are capable of assenting. This determination shall be made by taking into account the ages, maturity, and psychological state of the children involved. This assessment can be made for all children under a research protocol or for each child, as the IRB deems appropriate.</td>
</tr>
</tbody>
</table>
|Waiver of assent conditions | b. **Waiver of assent conditions**  
If the IRB determines the capability for all or some of the children is so limited that they cannot reasonably be consulted or the intervention or procedure involved in the research holds out direct benefit that is important to the health or well-being of the children and is available only in the context of research the assent of the children is not a necessary condition for proceeding with the research.  
Even where the IRB determines the subjects are capable of assenting the IRB may waive assent in accord with the waiver of consent guidelines. |
|Waiver of parental consent conditions | c. **Waiver of parental consent conditions**  
If the research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subject (e.g. neglected or abused children) waiver of consent is allowed if:  
1. An appropriate mechanism for protecting the children is implemented and the waiver is consistent with Federal, State or local law.  
d. Permission by parents or guardians shall be documented per the Federal Regulations. |
|  | e. When the IRB determines that assent if required, it shall also determine whether and how assent must be documented. |

* “Minimal risk means that 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,” 45CFR46.102

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<tr>
<th>Requirements for consent or assent if the study falls under:</th>
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<tr>
<td>46.404 &amp; 46.405</td>
<td>IRB may find that consent of one parent is sufficient</td>
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<tr>
<td>46.406 &amp; 46.407</td>
<td>Consent must be obtained from both parents if they have custody and are reasonably available</td>
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3. MINORS

Special considerations apply when minors (in Alabama, those under the age of 19 years old) are involved as subjects in research. The IRB assesses each study that includes minors on the basis of DHHS requirements for involvement of children as subjects in research (see Section 3.b. below). Relevant issues of risk, benefit, permission of the parent(s) or guardian, and assent of the child should be clearly addressed by the principal investigator in submissions to the IRB.

a. Obtaining Minors’ Assent to be in a Study

Although minors do not have the legal capacity to consent to participate in research, children and adolescents should be asked for their agreement to be in research whenever they are capable of giving their assent (i.e., capable of having a study explained to them and/or reading the consent form and giving verbal or written assent if they decide to participate in the study). The IRB respects and relies upon the expertise of investigators in determining the capabilities of particular subject populations and individuals.

Preferably, the language used in the consent form is clear and straightforward, written at an eighth-grade reading level. If this is the case, both the adolescent and the parents may then be asked to sign the form, with a signature line for the subject and an additional signature line for a parent or parents, to be used if the subject is a minor.

b. Additional Protections for Minors

Subpart D of the Code of Federal Regulations on Protection of Human Subjects (45 CFR Part 46) provides additional protections for children involved as subjects in research. These regulations impose added responsibilities depending on the degree of risk involved in the research and the extent to which the research is likely to benefit the subject or relate to the subject's illness. The regulations also set forth requirements for obtaining permission by parents and guardians, and, except under certain circumstances, assent by the children themselves.

Most notably, if the research is of more than minimal risk and there is no prospect of direct benefit to individual subjects, the consent of both parents must be obtained if both parents have custody and are reasonably available. If the research involves more than a minor increase over minimal risk and there is no prospect of direct benefit, the research cannot be approved without special approval from the Secretary of the Department of Health and Human Services.

The regulations classify studies involving minors into four groups, each with specific added responsibilities. The following information is adapted from these regulations, 45 CFR 46, Subpart D: Additional Protections for Children Involved as Subjects in Research:

The IRB may approve only research that satisfies the following conditions:

46.404 Research not involving greater than minimal risk, if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians. Consent from one parent is sufficient.

46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects, only if:

(a) The risk is justified by the anticipated benefit to the subjects;

(b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and

(c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth below.

Consent from one parent is sufficient.

46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, only if:

(a) The risk represents a minor increase over minimal risk;
(b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations;

(c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and

(d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth below.

Consent must be obtained from both parents if they have custody and are reasonably available.

46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children, which the IRB does not believe meets the above requirements of this section, only if:

(a) The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

(b) The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:

(1) That the research in fact satisfies the above requirements of this section, as applicable, or

(2) The following:

(i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children;

(ii) The research will be conducted in accordance with sound ethical principles;

(iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

Consent must be obtained from both parents if they have custody and are reasonably available.

NOTE: Complete copies of these regulations, 45 CFR 46, Subpart D: Additional Protections for Children Involved as Subjects in Research, which include discussion of wards of the state or any other agency, or institution, may be obtained from the IRB office.

4. PRISONERS

Prisoners may be under constraints because of their incarceration, which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research. Therefore federal regulation (45 CFR 46) provides additional protection for prisoners involved in research. These are outlined in Subpart C—Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects.

All biomedical and behavioral research involving prisoners, regardless of funding source, either as the subject population or subjects who become prisoners after enrollment, must be reviewed and approved by the IRB. Research funded by the DHHS must also be approved by the OHRP (Office for Human Research Protections). Research involving prisoners is limited to the categories of permissible research defined under the Federal regulations and applies to both domestic and international research.
Definitions:

Prisoner -

Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass 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.

Minimal Risk Research as it Applies to Research Involving Prisoners -

The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. (45 CFR 46.303(d))

The risks to which prisoners may be exposed are those compared with routine daily life and not those to which prisoners would normally encounter as prisoners.

Categories of Research Permissible Under the Federal Regulations -

I. The research is minimal risk and no more than an inconvenience to subjects AND the research is a study of the possible causes, effects, and processes of incarceration and of criminal behavior. (45 CFR 46.306(a)(2)(A))

II. The research is minimal risk and no more than an inconvenience to subjects AND the research is a study of prisons as institutional structures or of prisoners as incarcerated persons. (45 CFR 46.306(a)(2)(B))

III. The research is a study on conditions particularly affecting prisoners as a class (i.e., vaccine trials relating to hepatitis and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults). 45 CFR 46.306(a)(2)(C)

IV. The research is a study on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health and well being of the subject. (45 CFR 46.306(a)(2)(D))

If the proposed research does not fall under categories A-D above, the research involving prisoners is not allowable under the Federal regulations.

Review Process

Research Involving Prisoners as the Subject Population:

If prisoners are proposed as part of the inclusion criteria in a new project application, at the time of initial review, the project will be reviewed with special consideration given to the 7 additional findings outlined under 45 CFR 46305(a). The investigator must complete the ‘Checklist for Studies Involving Prisoners’ and attach it with the new project application.

Research Involving Subjects Who Become Prisoners After Enrollment:

If the investigator becomes aware of a subject who becomes a prisoner after enrollment, the investigator should notify the IRB immediately by submitting a memorandum requesting an amendment to the project for inclusion of prisoners, along with a completed ‘Checklist for Studies Involving Prisoners’. The IRB will re-review the protocol based on the 7 additional findings as outlined in the checklist.

Upon IRB approval of the research, the Research Compliance Office will send a certified letter to the OHRP, if applicable, for final approval. NOTE: The OHRP must approve all DHHS research involving prisoners.

5. THOSE WHO CANNOT READ OR SPEAK ENGLISH OR WHO ARE ILLITERATE

Subjects Who Are Unable to Read or Speak English

A researcher will need to give thought to whether it is likely that those unable to speak English will be approached to be included in a study and, if so, plan how to accommodate these potential subjects to insure that they are
consented in a language they understand, as is required by federal regulation. The relevant sections of the protocol should discuss these points.

If a study is designed to take place in or recruit from a clinic or hospital setting, it can be assumed that some of the patients who present for treatment may not speak English. In these cases, unless the researchers are fluent in the language of the patients, a qualified translator must be included in the consent process and then sign his or her name at the end of the consent form. A relative who speaks English does not usually qualify as an official translator unless the person has some training in medical terminology or has a medical background. In addition, the subject must be given a well-translated version of the consent form.

Those unable to speak English may not be excluded from participating in a study merely because they present an inconvenience to the researcher. Since one of the three ethical principles for the protection of human subjects in research, as described in The Belmont Report, is for both the risks and benefits of research to be shared in a society, it would be inappropriate to categorically exclude non-English speakers from most of the studies being conducted.

Subjects Who Are Illiterate

If an investigator wishes to include a subject who happens to be illiterate, then appropriate arrangements will have to be made to obtain verbal consent. The information presented to the subject should be at least as much as that in the already-prepared written consent form. If a relative is available, it might be appropriate for that person to take part in the consent process and then sign the consent form. The person who is illiterate may also be asked to sign an X on the signature line.

If a study is expected to include subjects who are unable to read, the investigator must discuss in the protocol how the verbal consent process is to be carried out and present a written version of what will be said to the prospective subjects. This information should include all the required elements of consent.

6. THOSE UNABLE TO CONSENT FOR THEMSELVES

For some research, some or all of the proposed subject population may be unable to consent for themselves or their ability to consent for themselves may be compromised. These subject groups may include, for example, unconscious patients, persons with Alzheimer's, patients with diagnosed psychoses, and those institutionalized as mentally disabled. (Minors are discussed above in Appendix F, Section 3). Clearly, special considerations must be provided for the protection of these populations and the investigator must provide in the protocol written, detailed justification for including such subjects in a study as well as a careful analysis of the relative risks and benefits of the study to the individual subject as well as to the particular group of subjects. When research involves persons whose autonomy is compromised, it is expected that the research bear some direct relationship to the conditions or circumstances of the subject population.

a. Obtaining Consent from an Authorized Representative or Relative

Federal regulations require the use of a written consent form approved by the Institutional Review Board and signed "by the subject or the subject's legally authorized representative," except under certain circumstances where the IRB may waive the requirement to obtain signed consent. (See the sections below which discuss studies involving no more than minimal risks and/or emergency care research activities. (Appendix A includes a more general discussion.)

Who May Consent

In practice, a "legally authorized representative" may be interpreted to include parents, legally appointed guardians, people with medical power of attorney, and other family members or individuals with associations equivalent to family membership. The range of acceptable representatives depends to some extent on the risks and potential benefits of each specific research proposal. If a research procedure has potential for great therapeutic or diagnostic benefit for the individual subjects, the IRB would be more inclined to permit third-party consent than if there is no direct benefit for subjects. The exact determination of who may give third-party consent depends on both legal definitions and standard medical practice.
Common Medical Practice

The IRB considers common medical practice. If an emergency situation exists, treating an incompetent patient without anyone’s express consent is considered acceptable; this applies when the treatment itself is standard and it may apply in limited circumstances when the treatment is experimental. (See below for research in which emergency situations are expected). In non-emergency medical care situations involving those who are unable to consent for themselves, providers often seek a spouse's or relative's consent or the consent of an individual whose close association with the subject is the equivalent of a family member, even though such individuals do not have express legal authority to consent on behalf of their incompetent relative. This practice has the distinct advantage of involving a person close to the patient who might know more about the patient's values and concerns and be better able to assess whether the patient would consent to undergo the treatment were he/she able to do so. As patients often are eager to have access to experimental treatments, it may be appropriate to consult with a person close to the subject when a research procedure has potential for direct benefit to the individual subjects. It is always preferable to involve spouses or relatives rather than to waive consent.

b. Waiving Consent in Studies Involving No More Than Minimal Risk

Four Criteria for Waiving Consent:

The IRB will consider a specific request to waive consent for patients who cannot consent for themselves and for whom no family member nor legal guardian is available provided certain conditions are met. A request for such a waiver of consent must be made within the study protocol. In order to waive consent for such studies, federal regulations require that the research meet the following four criteria:

1. The research involves no more than minimal risk (see discussion below);
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The research could not practically be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

These four criteria for waiving consent must be addressed in the Consent Process and Documentation section of the protocol with details specific to the study.

Definition of Minimal Risk:

Please note that the definition of a minimal risk is limited by federal regulations to mean A) that 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 (45 CFR 46 paragraph 102.i). For studies involving more than minimal risks to the subjects, different criteria apply. See Appendix F.6.c below.

Providing Subjects with Additional Information:

The additional information provided to subjects after participation should be in written form. If all study procedures will be completed before the subjects can be informed, they should be given an information sheet which explains what procedures occurred without the subject's consent and why they were performed. If any procedures are ongoing (blood draws, tests, collection of information from records) or if the researchers want the subjects to participate in follow-up procedures (interviews, office visits, or additional tests or medical record review) then consent must be obtained for the ongoing or additional research procedures and a consent form must be signed before research on that subject may continue. The consent form should clearly describe what procedures occurred without the subject's consent, why they were performed, and what additionally will be done if consent is given to continue the subject in the study. The subject must also be given the option of refusing to allow the researchers to use the data already collected. In addition, if a guardian or relative of the subject becomes available before the subject is able to consent to ongoing procedures, provision should be made to obtain the consent of that person to continue the study until the subject can be asked for consent.
Types of Consent Documents Needed:

As the preceding paragraphs suggest, three separate types of consent documents may be needed for research in which consent can be waived:

(1) a consent form for subjects who in fact are able to consent and/or for subjects who have relatives available to consent for them prior to their enrollment in the study; (2) a consent form for subjects or relatives to be used after the subject has been enrolled and if the subject becomes alert or a relative becomes available while the study is still going on; and, (3) an information sheet for subjects or relatives that explains what has occurred, to be used after the study procedures have been completed.

Specific information that needs to be in these documents is discussed in the paragraph above. The appropriate consent documents should be submitted with the application and should follow the standards and formats described in Part VII of these Guidelines.

c. Waiving Consent in Emergency Settings

Revised Federal Regulations:

Federal regulations that allow research activities to be conducted in emergency settings were put into effect in October 1996. These regulations are a result of years of considerable and protracted debate at the national level about how to facilitate potentially life-saving and life-enhancing research while protecting the rights and welfare of subjects. These revised regulations were developed with the input from several national organizations and physicians, including those interested in and involved in the treatment of cardiac arrest, stroke, head trauma, spinal cord injury, gunshot wounds, and poisoning. The result of this national interest is that both the FDA and the OHRP have agreed that in very carefully controlled situations, as described below, research may be allowed that includes subjects unable to consent for themselves when there may be more than minimal risk (see Appendix D).

The actual regulations that allow for exception from informed consent requirements for emergency research are adapted or quoted from 21 CFR Part 50 and should be read there in their entirety.

Researchers who wish to conduct research in an emergency setting when there may be more than minimal risk (as defined above in F.6.b) but participation in the research holds out the prospect of direct benefit to the subject should review the federal regulations very carefully to make sure that the proposed research qualifies for a waiver of consent. In addition, researchers are encouraged to consult with the IRB Chair and/or IRB Compliance Specialist in preparing their applications.
Appendix G

Use of Biological Materials (Tissue or Blood) for Research

Until recently, researchers often gathered human biological samples for research purposes without informing patients or obtaining their consent. However, national standards have changed during the last few years. The Office for Human Research Protections has clearly ruled that for all Federally funded research, a patient’s informed consent must be obtained before identifiable tissues may be collected for research purposes. Under the University of South Alabama’s agreement to receive Federal funds, USA researchers are obliged to follow human subject rules for all research, regardless of funding source.

In addition to the regulatory and ethical considerations for obtaining consent, tissue and blood collections are more valuable if they have been gathered with the full consent of the donors. Offers to purchase collections and associated information are routinely accompanied with requests for written assurance that patients’ consent to gather biological materials has been obtained in accord with all applicable Federal and state regulations.

Research involving use of human specimens may be done as an isolated project, as part of the establishment of a permanent repository of tissue and medical information, or as part of a clinical trial or other type of study. Obtaining permission for the collection of biological materials that are collected in connection with sponsored or other clinical studies for undefined future purposes from subjects enrolled in clinical research will be allowed when the IRB determines that the rights and welfare of potential research subjects are adequately protected by the process of informed consent. Such consent must assure that potential research subjects:

- Are not coerced to agree to banking in order to participate in the research project,
- Know where the material would be stored and who would be responsible for security,
- Are advised of the intended general future uses of the material and be allowed to limit the uses,
- Are given the option of having all identifying information removed from the banked material, and
- Are allowed to limit purposes of future contact if identifying information is maintained.

The IRB has also established the following procedures for implementation of this policy.

- Permission for tissue banking must be obtained as part of the informed consent process for the protocol being reviewed.
- The permission must be documented in the consent form prior to the signatures which indicate completion of the consent process.
- Subjects must be allowed to write in any modifications without jeopardizing their participation in the research.

The format in Appendix H was approved by the USA IRB as of 1/16/01 and is required for use of biological materials.
Appendix H
Language to be Included for Tissue and/or Blood Banking

The following language was adopted as policy by the USA IRB for all protocols when blood or tissue is to be stored. This section should be included exactly as written within the body of the consent form (see STANDARD CONSENT FORM FORMAT #1BIOMEDICAL STUDY for example).

Tissue and/or blood banking or storage

1. Stored samples have been used in research activities for many years. These samples allow investigators to make important new measurements that were not possible at the time that the original research was planned and conducted. It is possible that some of the biological material (for example: blood, urine or tissue) collected to diagnose your condition or to conduct this research project may remain unused when the research is completed. Normally such samples would be destroyed. We ask your permission to retain and store this for an indefinite period of time so that it might be used for future, as yet undefined, purposes. Future uses may include, but may not be limited to, research, education and commercial development.

IF YOU DO NOT WISH TO HAVE YOUR MATERIAL STORED FOR FUTURE USE YOU MAY STILL PARTICIPATE IN THIS STUDY.

If you agree to allow storage, the samples will be stored by:

______________________________
(name/location of site)

Security will be provided by:

______________________________
(Responsible person/agency and methodology)

Do you wish to allow storage of your remaining biological material?

Yes _____  No _____

2. If you agree to storage of your samples, you may choose how this material is to be used or you may limit its use.

Do you wish to limit the use of your stored biological material?

Yes _____  No _____

If “yes” specify the limitations:

______________________________

3. If you agree to allow your samples to be stored, they will initially be identified with you (for example, your name, your initials, or a number) that could lead back to you. You may choose to have information that could identify you removed. If such identification is removed it will be impossible for you to be contacted in the future regarding any important new or additional information which may be of benefit to you or your family and might lead to further research.

Do you wish to have all information that could identify you removed from the stored material?

Yes _____  No _____

4. If you agree to allow your samples to be stored with identifying information, you may choose to allow someone to contact you in the future to ask you questions about your health, to ask you to participate in more research or for any other reason
Do you wish to allow personal contact in the future regarding the stored material?
Yes _____  No _____

If “Yes,” specify any limitations you wish to impose:
Appendix I
Sample Forms
Institutional Review Board
University of South Alabama

PROTOCOL APPLICATION FOR HUMAN SUBJECTS RESEARCH

NEW PROJECTS

Investigator’s Assurance: By submitting this protocol, I attest that I am aware of the applicable principles, policies, regulations, and laws governing the protection of human subjects in research and that I will be guided by them in the conduct of this research.

To submit a protocol application please complete the following.

For exempt protocols: Submit two copies of this application, two copies of the consent form and two copies of the protocol (including questionnaire or survey if applicable).

For expedited protocols: Submit three copies of this application, three copies of the consent form, and three copies of the protocol (including questionnaire or survey if applicable).

For full board review: Submit thirty (30) copies of this application, thirty (30) copies of the consent form and four copies of the protocol. Sponsored drug studies also require four copies of the investigator’s brochure, one copy of the FDA Form 1572, and three copies of the drug summary sheet.

In the following judgment of the Principal Investigator, this research qualifies for which of the following:

(please note: protocols involving children <19 years of age cannot be submitted as exempt)

Exempt ______   Expedited ________   Full Board ________
Category _________   Category _________   (See Guidelines Part III)
(See Guidelines Part IV)
(See Guidelines Part V)

Date of submission

Title of Research

Principal Investigator   Dept/College/Bldg.   Room #   Phone   Email

Other Investigator   Dept/College/Bldg.   Room #   Phone   Email

Other Investigator   Dept/College/Bldg.   Room #   Phone   Email

Site(s) of Human Subject Data Collection (If sites are separate from the University, please submit approval letter)

Funding Agency (if applicable)


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PURPOSE OF RESEARCH:

Relevant Background and Rationale for the Research:

Subject Population: NOTE: Federal guidelines require selection of subjects be equitable within the exclusions, and subjects meeting the criteria cannot be discriminated against for gender, race, social or financial status, or any other reason.

Approximate number of subjects _________   Male/Female Ratio _________

Vulnerable Subjects: Identify all categories of vulnerable subjects to be recruited - (check only if applicable):

☐ Minors ( < 19 years )
☐ Pregnant Women
☐ Fetuses
☐ Prisoners (adjudicated youth / adolescents detained in a juvenile detention facility is considered a prisoner)

NOTE: Submission of the Investigator Checklist for Studies Involving Prisoners is required with this application. The federal regulations for inclusion of prisoners as research subjects and investigator checklist are located on IRB website at: http://southmed.usouthal.edu/com/research/IRB.html

☐ Cognitively Impaired Persons
☐ Economically or educationally disadvantaged persons
☐ Other vulnerable population (identify): ________________________________
Procedures and Agents (if applicable) to be Used:

The Experimental Design and Methodology:
Please limit this description to the portions dealing directly with the use of human subjects.

What incentives will be offered, if any?

Risk/Benefits to participants and precautions to be taken
Identify possible risks to subjects. These may be of a physical, psychological, social or legal nature. If subjects are vulnerable populations, or if risks are more than minimal, please describe what additional safeguards will be taken.
There are several acceptable options for fulfilling the human participant research requirement. Options include completion of an NIH on-line training program available at http://cme.cancer.gov/c01/ Other acceptable on-line modules are available through UCLA at http://www.ucla.edu/research (click on “Research”, then go to “Protection of Research Subjects” for the certification program) or University of Michigan at http://www.irb.research.umich.edu/ (click on non-UM Faculty and Staff and Students). Once you have finished, a computer generated certificate is provided. Preferably, a copy of the certificate should be attached with submission of this application form. However, you may also fax a copy to 461-1595 or forward to the IRB Office at CSAB 138. NOTE: Investigators will not receive final approval for human subjects’ research until the training requirement is completed.

List all study team members (sub-investigators, coordinators, and other key personnel involved with the conduct of the study.

<table>
<thead>
<tr>
<th>Name</th>
<th>Role</th>
<th>Human Subjects Training Current Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>☐ Yes ☐ No</td>
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<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>☐ Yes ☐ No</td>
</tr>
</tbody>
</table>

In your opinion, do benefits outweigh risks? Yes _____ No _____

Privacy/Confidentiality

Please describe whether the research would involve observation or intrusion in situations where subjects have a reasonable expectation of privacy. If identifiable existing records are to be examined, has appropriate permission been sought, i.e. from institutions, subjects, and physicians? What provision has been made to protect the confidentiality of sensitive information about individuals?

Human Subjects Protection Training

As a condition of the University’s Federal Wide Assurance of Protection for Human Subjects, principal investigators and key research personnel are required to complete appropriate training before conducting human subject research
Other Requirements (if applicable)

A Disclosure of Financial Conflict of Interest Form is to be submitted with each proposal for funded research.

If x-rays or isotopes are to be used specifically in support of the research, approval of the Radiation Safety Committee must be obtained.

If a biological hazard exists for either subjects or investigators, approval of the Biohazards Committee must be obtained. Under Federal Regulations, this includes all handling of human blood or other tissues for research (not clinical) purposes.

If a medical procedure is to be performed in the hospital using human subjects, the investigator must have been approved for such procedures by the Office of the Senior Hospital Administrator.

Consent for Participation Instructions (see Guidelines Part IX)
The University of South Alabama Clinical Trials Database is accessible via the world-wide web at http://southmed.usouthal.edu/com/trials/ and serves as a useful tool to recruit subjects for the study protocols, enhance physical referral, and address patient inquiries.

Please indicate your preference for inclusion below. Unless you indicate “no” your protocol will be listed on the website.

Yes _____  No _____

IRB Protocol Number ____________________________
(to be filled in by IRB administrator)

Title of Protocol

Principal Investigator

Sponsor

Participants:

Male/Female  _ ___/____  A ge range ____

Eligibility:

Exclusions:

______________________________________________________________________________

Brief description of research in lay terms

Primary Disease Category _________________

Keyword(s):  ___________________ _____________________ _____________________

Experimental Drug/Device:  ______________________________________________________
Contact/Referral Information

<table>
<thead>
<tr>
<th>Physician referrals are encouraged</th>
<th>Yes _____</th>
<th>No _____</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient inquiries are encouraged</td>
<td>Yes _____</td>
<td>No _____</td>
</tr>
</tbody>
</table>

For additional information about this research please contact:

Principal Investigator

Address

<table>
<thead>
<tr>
<th>Phone</th>
<th>Email</th>
<th>Fax</th>
</tr>
</thead>
</table>
Title of Research

Principal Investigator

Department/Campus Address

Sponsor

Sponsor’s Agent (if applicable)

Will this protocol use hospital staff, resources or facilities?  Yes _____  No _____

If no, please sign and obtain department chair’s signature and submit protocol to the IRB.

If yes, review is required by the Office of the Senior Hospital Administrator prior to review by the IRB. Note: Please answer the following questions and attach to this application.

1. Please provide a detailed description of the hospital resources to be used (e.g., lab studies, radiology studies, cardiology studies, etc.)
2. Who will be financially responsible for hospital charges incurred as part of this study? Is there separate funding or is the patient’s insurance responsible?
3. Approximately how many subjects will be enrolled in this study within the USA Hospital System?

My signature, as Principal Investigator, certifies that I will:

► Conduct all aspects of the project as approved by the IRB,
► Promptly report any revisions or amendments to the research activity for review/approval by the IRB prior to commencement of the revised protocol, with the only exception to this policy would be to eliminate apparent, immediate hazards to the subject,
► Promptly report any unanticipated problems or adverse advents,
► Assume full responsibility for selecting subjects in strict accordance with the inclusion/exclusion criteria outlined in the application materials, and,
► Where consent form(s) have been approved for the research activity, only IRB-approved, stamped consent forms will be used in the consent process.

Signature, Principal Investigator       Date

Signature, Departmental Chair       Date

Signature, Senior Hospital Administrator      Date

This signed form and investigator checklist (next page) must accompany your protocol submission to the IRB.
Investigator Checklist for Expedited and Full IRB Submission

The purpose of the checklist is to facilitate the application approval process and is intended to be utilized as a pre-review evaluation which may help identity and resolve issues that may delay approval.

☐ New Projects Application for Human Subjects is filled out in its entirety. This includes signatures of the Principal Investigator, Department Chair and Hospital Administrator, if applicable.

☐ Are risks greater than “minimal risk”? If so, has the investigator cited appropriate references listing potential adverse reactions?

☐ If data is acquired at site other than USA, is permission statement included?

☐ Is subject selection equitable (e.g., subject population included/excluded; risk of coercion in recruitment)?

☐ Is informed consent appropriately documented? All basic elements, and additional elements as appropriate, for informed consent as specified by federal regulations –
  - Research purpose and procedures
  - Risks and Discomforts
  - Potential Benefits
  - Alternative Procedures or Treatments
  - Provisions for Confidentiality
  - Research-related injury
  - Contacts for additional information
  - Voluntary participation and the right to discontinue participation without penalty

When appropriate, the consent document should include the following additional information:

  - Unforeseeable risks
  - Termination of participation by the investigator
  - Additional Costs
  - Consequences of discontinuing research participation
  - Notification of significant new findings
  - Approximate number of subjects

☐ The consent document should include a statement “you will be given a copy of this consent”.

☐ Is clear, concise, non-technical language uses throughout the informed consent document?

☐ Are the provisions for maintaining confidentiality adequate?

☐ Have additional safeguards for subjects vulnerable to coercion or undue influence been included?

☐ Does the research setting (e.g., location of research, facilities) provide adequate safeguards for protection of human subjects?

☐ Are children (under the age of 19) involved? If so, include a assent line for minors.

☐ Consent should be printed on USA departmental letterhead or formatted with a header to include institution, name of investigator, address and contact information.

☐ If applicable, the tissue banking form should be incorporated within the informed consent document prior to the final signature page.

☐ All supporting documents have been attached, including protocol, survey instruments, interview schedules, solicitation letters, advertisements, consent forms, etc. Supporting documents must be in final form as you intend to distribute them. Your application will be returned if these documents are in outline or first draft form.

I have reviewed the relevant items above. I understand that the IRB Office can not accept incomplete packets and will not forward them to the IRB for review. In addition, studies are not to be implemented prior to receiving an IRB approval letter.

__________________________   _________________________
Investigator Signature          Date
ANNUAL RENEWAL / FINAL REPORT FORM

☐ Annual Renewal – study is ongoing
☐ Final Report – no further contact with participants will occur (no copies required)

Protocol IRB# ____________________________  Principal Investigator: ________________________________
Date Submitted: __________________________  Date of prior approval: ___________________________
Project Title: ______________________________

If Annual Renewal, please check the appropriate category below and attach the required copies for each submission:

☐ For expedited review (See Guidelines Part VI for explanation of expedited review):
   Submit two copies of this form, two copies of the most recent version of the IRB approved stamped consent, and two copies of the most current protocol and investigator’s brochure (if applicable).

☐ For full board review (See Guidelines Part VI for explanation of full board review):
   Submit thirty copies of this form, thirty copies of the most recent version of the IRB approved stamped consent, and three copies of the most current protocol and investigator’s brochure (if applicable).

The IRB is required by the federal government to obtain the following information in order to approve a request for a renewal of approval and/or conduct a continuing review of a research project.

1. Total number of patients enrolled since study opened
   Screened  Enrolled

2. Number of patients screened and enrolled in past year

3. Number of subjects by race screened for entry into study since the start of the project

4. Number of subjects screened by gender since the start of the project
   Male  Female

5. Number of subjects by race entered into the study since last IRB review

6. Number of subjects by gender entered into the study since last IRB review
   Male  Female

7. Has there been any amendments/revisions since the last IRB approval?  ☐ NO  ☐ YES
   If yes, briefly explain.

8. Have there been any serious adverse event (on-site) reports since the last IRB approval?  ☐ NO  ☐ YES
   If yes, briefly explain.

9. Brief summary to date. What preliminary findings or evaluations of the study have you received?
Addendum / Amendment / Revision
REPORT FORM

Protocol IRB# ____________________________ Principal Investigator: ____________________________
Date Submitted: ____________________________
Project Title: ____________________________
Addendum number/date: ____________________________
(if applicable)

Please attach the required copies for each submission:

☐ If no subjects are enrolled since the last IRB renewal:
Submit two copies of the following: this form, the addendum, current protocol and investigator brochure (if applicable), the most recent version of the stamped approved consent and the revised consent.

☐ If subjects are enrolled since the last IRB renewal:
Submit thirty copies of the following: this form, the addendum, the most recent version of the approved IRB stamped consent, the revised consent and three copies of the most current protocol and investigator’s brochure (if applicable)

NOTE: CHANGES SHOULD BE HIGHLIGHTED OR OTHERWISE NOTED ON THE CONSENT FORM AND

1) List requested changes to the protocol and/or consent form being requested at this time. Please explain; attach additional pages if necessary.

2) Have there been any serious adverse event (on-site) reports since the last IRB approval? ☐ NO ☐ YES
If yes, briefly explain.
INSTITUTIONAL REVIEW BOARD ADVERSE EVENT FORM
UNIVERSITY OF SOUTH ALABAMA
Investigator Adverse Event Report Form

IRB Protocol #:              Date:
Investigator:               Phone number:
Contact person:             Phone number:
Project title:

*** ATTENTION: A copy of the adverse event form reported to the sponsor must be included with this report, along with a copy of the latest version of the protocol and/or investigator's brochure. ***

If you have exceeded the maximum time allowed for reporting this event, please explain:

Date of Event:     Subject ID#:

Description of adverse event (please avoid abbreviations):

Follow-up scheduled?   □ No   □ Yes

Grade of event:

☐ Mild  (Transient or mild discomfort; no limitation in activity; no medical intervention/therapy)
☐ Moderate  (Mild to moderate limitation in activity, some assistance may be needed; no or minimal medical intervention/therapy required)
☐ Severe  (Marked limitation in activity, some assistance required; medical intervention/therapy required, hospitalization possible)
☐ Life-Threatening  (Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required; hospitalization or hospice care probable)
☐ Fatal  (Subject died)

Relationship to drug/device/procedure:

☐ No study drug or device was ever received by the subject (If none, please provide your signature on the last page of this form and return to the IRB Office.)
☐ Related  (Relationship is likely)
☐ Possibly related  (Relationship may exist)
☐ Probably not related  (Relationship is not likely)
☐ Not related  (No relationship to drug)
Date subject enrolled into the study:

Concurrent illnesses/medications:

Date the first investigational drug/device used:

Dosing schedule (dose/frequency) for each investigational agent/device used:

Any changes/interruptions to the dosing schedule and reasons for these changes?

Was the event anticipated in the protocol?  
No ☐  Yes ☐

Was the risk described in the consent?  
No ☐  Yes ☐

Revision to Protocol or consent required?  
No ☐  Yes ☐

If revisions are required please provide one revised copy of the protocol and/or consent indicating the revisions by highlighting or underlining, and two clean copies.

Will revision require information that will affect all research subjects?  
No ☐  Yes ☐

if yes, have the research subjects been informed? Please provide documentation.

______________________________     _________________________
Principal Investigator's Signature           Date

---

IRB OFFICE USE ONLY:

Serious adverse event/injury report form reviewed by:  
Adverse Event Reviewer ___________________________ Date ____________

Submit report to Full IRB
Write to investigator with concerns
Discussed with investigator – No further action required
File with protocol – No further action required
Additional comments 

_____________________________________________________________________

_____________________________________________________________________

_____________________________________________________________________
Disclosure of Financial Conflict of Interest for Extramurally Funded Research and Educational Activities

The South Alabama Medical Sciences Foundation receives substantial funds from commercial pharmaceutical companies for drug testing. In order for these funds to be treated as nontaxable income, one of the following criteria has to be met:

1. The drug test must be “for benefit.” Those studies in which drugs are offered to patients who have the disease or injury for which the eventual commercial use of the drug is intended are considered to be “for benefit” tests.

2. The test involves nonpatient laboratory testing (of specimens) which is required for the conduct of teaching activities.

To protect our tax exempt status, our external auditors recommended that we sufficiently document that one or both of the above conditions are present for the testing which we conduct. The attached questionnaire must be completed by the Principal Investigator in order to meet the documentation requirement.

Please return to:

Steve Hadley, CPA, MBA
Associate Business Manager
CSAB 104
Mobile, AL 36688-0002

Phone: 251-460-7195
South Alabama Medical Science Foundation
Clinical Trial Agreement Questionnaire

Principal Investigator _________________________________________________________
Project Title ________________________________________________________________
Name of Sponsor ____________________________________________________________
Project Number ______________________   IRB Number (If applicable )_______________

Location of Activity
☐ Hospital           ☐ Health Services Bldg.   ☐ Other (Specify) _________________

Are students receiving training? (Check all that apply)
☐ Medical students
☐ Other graduate students
☐ Interns
☐ Residents
☐ Post Doctoral Fellows
☐ Nurses
☐ Medical technicians
☐ Other (specify) ___________________________

Approximate number trained ______________________
List two names of individuals trained: _________________ _________________

Check all applicable type of training activities
☐ Screening of test subjects
☐ Observation of testing
☐ Administration of drugs
☐ Monitoring drug effects
☐ Interpretation of results
☐ Other (specify) ___________________________

Are results used in instruction? ☐ Yes ☐ No
Are results available for publication? ☐ Yes ☐ No

Type of subjects (check all that apply)
☐ Hospital patients
☐ Clinical outpatients
☐ Health subjects
☐ Other (specify) _________________________

Are tests “for benefit” tests? ☐ Yes ☐ No
Note: “For benefit” definition: Those studies in which the drug/product is offered to patients who have the disease or injury for which the eventual commercial use is intended.
University of South Alabama—Medical Science Foundation
Disclosure of Financial Conflict of Interest for
Extramurally Funded Research and Educational Activities

PROJECT TITLE_______________________________________________________

AGENCY______________________________ LOG #______________ COM #________

This disclosure is a(n) _____ new statement _____ annual renewal _____ report of new financial interest

☐ I have no significant financial interests
   (a) that are related to or would reasonably appear to be affected by the research proposed for funding; or
   (b) in external entities whose financial interest would reasonably appear to be affected by such activities.

☐ I am disclosing the following significant financial interest in the form of:*
   (See the Fact Sheet on Conflict of Interest Disclosure for Definitions and Exclusions.)
   ☐ Salary or other payments for services
   ☐ Equity or ownership
   ☐ Intellectual property rights
   ☐ Other significant financial interests that could affect or be perceived to affect the results of research or
     educational activities proposed for funding.

* If you are disclosing a significant financial interest, this form must be accompanied by other documentation
   available from the College of Medicine Business Office, CSAB 140, 251-460-7195.

In submitting this statement, I affirm that:

I will comply with any conditions or restrictions imposed by the University of South Alabama to manage, reduce, or
eliminate any conflict of interest identified through USA's oversight procedures. Such conditions will be specified in a
written Memorandum of Understanding that is mutually satisfactory to me and the University. Furthermore, I understand
that if the University and I cannot arrive at a satisfactory Memorandum of Understanding, the sponsor will be notified of
the existence of a conflict of interest which could not be managed by institutional measures, and I understand no funds
may be expended from this award pending further review/ action by the sponsor.

I agree to update this Disclosure during the period of the award, either on an annual basis, or as new reportable significant
financial interests are obtained.

_______________________________ _______________________
Signature     Date

☐ Co-PI ☐ Key Personnel

All investigators involved in the project (including subcontractors, subgrantees, etc.) have been informed of their
obligations under federal regulations governing disclosure of significant financial interests and have no conflicts of
interest or potential conflicts of interest that have not been disclosed.

_______________________________ _______________________
Signature     Date

☐ PI
University of South Alabama—Medical Science Foundation
Disclosure of Financial Conflict of Interest for
Extramurally Funded Research and Educational Activities

Fact Sheet

Under federal regulations governing objectivity in research, investigators are required to disclose a listing of Significant Financial Interests that would reasonably appear to be affected by the research or educational activities proposed for funding.

Procedures

1. Investigators submitting proposals to the College of Medicine Business office through the Medical Science Foundation for review must attach form, "USA Disclosure of Financial Conflict of Interest for Extramurally Funded Research and Educational Activities."

2. Please refer to the "Significant Financial Interests" section below to determine if you have financial interests that must be reported. Disclosure is made by submitting a detailed written statement describing the significant financial interest when the proposal is presented for review.

3. If a conflict of interest is identified, the conflict must be resolved through the University or, if not resolved with the University, through the sponsoring agency prior to expenditure of any awarded funds.

4. It is the Principal Investigator’s responsibility to ensure that the Disclosure of Financial Conflict of Interest forms for all investigators are obtained on a timely basis in order to meet proposal application deadlines. The COM Business Office requires that the final review of proposals cannot begin until the proposal package includes this form for all investigators (investigators as defined below).

Definition of Investigators:

"Investigator" is any individual listed on the proposal who is responsible for the design, conduct, or reporting of the research or educational activity. This includes, but is not limited to, the principal investigator/project director and co-principal investigator(s). Other faculty investigators, staff, students, subcontractors, and subgrantees are also included if they have responsibilities for the design, conduct, or reporting of the research or educational activity.

Each investigator must disclose all of his/her significant financial interests that are related to or would reasonably appear to be affected by the research funded or proposed for funding; or, in external entities, whose financial interests would reasonably appear to be affected by such activities.

Investigator Responsibility:

Each investigator must disclose all of his/her significant financial interests:

• that are related to or would reasonably appear to be affected by the research funded or proposed for funding; or
• in external entities whose financial interests would reasonably appear to be affected by such activities.

Each investigator must also certify to the institution that he/she:

• understands the obligations imposed by federal regulations governing disclosure of significant financial interests related to the research for which funding is requested;
• will comply with any conditions or restrictions imposed by USA to manage, reduce, or eliminate conflicts of interest;
• will update the disclosure information throughout the life of the project any time new significant financial interests are obtained, or at least annually.

Definition of Significant Interest

"Significant Financial Interest" refers to: salary or other payments for services, such as consulting fees and honoraria; equity interests, such as stocks and stock options; and intellectual property rights, such as patents, copyrights, and royalties. A Significant Financial Interest does not refer to salary or other remuneration from the university; income derived from seminars, lectures or teaching engagements sponsored by public or nonprofit entities; income derived from service on advisory committees or review panels for public or nonprofit entities; or salary, royalties or other payments that, when aggregated for the investigator and his or her spouse and dependent children, is not expected to exceed $10,000 over a 12 month period, and does not represent more than a five percent ownership interest in any entity.
Significant Financial Interests must be disclosed at the time of the submission of the proposal, but approval of the outside activities and financial interests (with conditions if warranted) need not occur until the project has been funded. The federal regulations require that the disclosures be made annually during the course of the research, which is consistent with the university’s requirement that any material changes to outside activities and financial interests must be reported during the academic year. Review and approval or disapproval of the interests disclosed during the course of a research project must be accomplished within 60 days.
Disclosure of Relationships with External Entities

For each response of "Yes," provide the name of the entity or entities in the space following the question.

I. Identification of Relationships with External Entities

1. Are you currently participating, or do you expect to participate in the next 12 months, in funded or unfunded research on a technology, process or product development related to activities for which you are entitled to receive royalties under USA’s royalty-sharing policies?
   - YES

2. Are you currently participating, or do you expect to participate in the next 12 months, in clinical trials or evaluation or development of a technology, process, or product owned or controlled by a business in which you have a financial interest?
   - YES

3. Are you currently receiving, or do you expect to receive in the next 12 months, USA-supervised sponsored research support or gifts (whether in dollars or in kind) for research from a business in which you or a member of your immediate family ("immediate family" means your spouse and dependent children) has a financial interest, other than royalty income to which you are entitled?
   - YES

4. Are you currently receiving, or do you expect to receive in the next 12 months, research support (sponsored research or gift) from a business in which you or a member of your immediate family serves on the board of directors or advisory board?
   - YES

5. Do you currently hold, or do you expect to hold in the next 12 months, an executive position or serve on a governing board in business engaged in commercial or research activities related to your research or administrative responsibilities? Please attach extra pages to answer the following a - d:
   - YES
   a. Name of enterprise:
   b. Describe your responsibilities, and how much time you expect to dedicate to them.
   c. Does the business or organization plan to submit proposals for federal funding? If so, please describe.
   d. Does the proposal cover research that could be performed in your facilities at USA?

6. Excluding consulting activities that conform to USA’s consulting policies, do you expect that in the next 12 months, while acting in the context of your USA responsibilities, you will make professional referrals to a business in which you or a member of your family has a financial interest?
   - YES

7. Are you currently taking, or do you expect to take in the next 12 months, administrative action on behalf of USA with respect to any supported research activity (sponsored research or gift) in which you or a member of your immediate family has a financial interest?
   - YES
Disclosure of Relationships with External Entities--Continued

8. Are any of your trainees (including students, post-doctoral fellows and other trainees) currently assigned, or do you expect to assign any trainees in the next 12 months, to research projects related to activities for which you are entitled to receive royalties under USA’s royalty-sharing policies?
   □ NO    □ YES

9. Are any trainees (including students, post-doctoral fellows, and other trainees) currently assigned, or do you expect to assign any trainees in the next 12 months, to a business in which you have a financial interest, other than royalty income or the entitlement to future royalty income under USA’s royalty-sharing policies?
   □ NO    □ YES

10. Are you currently employing, or do you intend to employ within the next 12 months, any graduate students in a business in which you or a member of your immediate family has a financial interest? If so, for each student, please set forth a) the nature of the work to be performed, b) how the work relates to the student’s studies or thesis, and c) the expected number of hours per month. (Please provide a complete statement on an additional page).
    □ NO    □ YES

11. Are there any other activities in which you may have a potential for conflict of interest that should be disclosed? (Please provide a complete statement on an additional page.)
    □ NO    □ YES

II. Evaluation of Financial Interest in External Entities

Use the "Financial Disclosure Worksheets" to determine whether you, according to the federal policy, have a significant financial interest regarding any external entity.

III. Disclosure of Relationships with External Entities and Significant Financial Interests Related to Extramurally Funded Research and Educational Activities

Federal regulations and USA policy require investigators to disclose significant financial interests
(a) that are related to or would reasonably appear to be affected by the research or educational activities funded or proposed for funding; or
(b) in external entities whose financial interests would reasonably appear to be affected by such activities.

1. List below the entities in which you have significant financial interests and attach Financial Disclosure Worksheets for each entity.

2. If you answered "Yes" to any question in Part I, "Relationships with External Entities," send this form to the COM Business Office along with documentation.

3. If you wish to apply for extramural funding and you have significant financial interests related to the research or educational activities proposed for funding, this form and the Financial Disclosure Worksheets must be included with the proposal package when presented to the COM Business Office for final review. (Please place in sealed envelope marked "Confidential Disclosure Documentation.")

_______________________________  _____________________
Signature     Date

☐ PI    ☐ Co-PI ☐ Key Personnel

Page 90 of 112
# University of South Alabama—Medical Science Foundation
## Financial Disclosure Worksheet

**Name___________________________________________  Date_______________________________**

**Name of Entity______________________________________ Calculated for Period________________**

Instructions: This worksheet will help you determine whether or not you must report a significant financial interest to the University Conflict of Interest Review Committee. A separate worksheet should be filled out for each entry named in your Disclosure of Relationships and External Entities form. You may retain this form for your records if your financial interests do not qualify as significant.

## I. Financial Interests Related to Payments And Intellectual Property Rights

### A. PAYMENTS  Salary/dividends  Consulting/Honoraria/Services  Total Payments

1. You __________ + ___________ = ____________
2. Your spouse __________ + ___________ = ____________
3. Dependents __________ + ___________ = ____________

Subtotal, A1-A3

### B. PATENTS  Patents  Royalties  Total Payments

1. You ___________ + ___________ = ____________
2. Your spouse ___________ + ___________ = ____________
3. Dependents ___________ + ___________ = ____________

Subtotal, B1-B3

### C. COPYRIGHTS  Copyrights  Royalties  Total Payments

1. You ___________ + ___________ = ____________
2. Your spouse ___________ + ___________ = ____________
3. Dependents ___________ + ___________ = ____________

Subtotal, C1-C3

## II. Financial Interests Related to Equity And Ownership

### D. STOCK  Number of Shares  Price Per Share  Market value of shares

1. You ___________ × ___________ = ____________
2. Your spouse ___________ × ___________ = ____________
3. Dependents ___________ × ___________ = ____________

Date and Source______________________________ Subtotal, D1-D3

### E. STOCK OPTIONS

1. You ___________ × ___________ = ____________
2. Your spouse ___________ × ___________ = ____________
3. Dependents ___________ × ___________ = ____________

Subtotal, E1-E3

### F. OTHER (INCLUDE OWNERSHIP OF PRIVATELY-HELD ENTITIES)


Subtotal, F1-F3

If TOTAL exceeds $10,000 your financial interests are significant and must be disclosed.

G. Check this box if your ownership in this entity exceeds 5% of its worth.
   If so, your financial interests are significant and must be disclosed.  

   ☐
For information and required disclosure forms for research that is routed through the Office of Sponsored Programs see http://www.southalabama.edu/osp/index.html, go to Budget Assistance, then E-forms.
Appendix J
Standard Consent Form Formats
Purpose and Background

Laura Smith, M.D., and Mark Jones, Ph.D. from the Department of ..., are conducting a study to learn ... This study is being funded by ... (the manufacturer of) ...

You are being asked to participate in this study because you are [have] ...
XXX human subjects are expected to participate in this study.

Procedures

If you agree to be in this study, the following will happen:

1. You will have a physical examination, your medical chart will be reviewed, and blood and urine will be collected for laboratory tests. Approximately ___ teaspoons [or other commonly understood units such as tablespoons or cups] of blood will be drawn for these tests.

2. If the physical examination and test results show that you are eligible for study treatment, you will be randomly assigned to one of two groups. This means you have a 50/50 chance (like flipping a coin) or being in either group and that neither the researchers nor you will make the choice of which group you are in. The two groups are Group A (Drug XXX) and Group B (placebo, an inactive substance).

3. Group A will receive XXX, the investigational drug, in tablet form ___ times a week for ___ weeks, for a total of ___ weeks. Group B will receive placebo, also in tablet form, according to the same schedule.

4. An x-ray of your lungs will be done once at the beginning of the study and again at the end of the study, in order to check ___. Each x-ray procedure will take about ___ hour(s).

5. Once every two weeks, you will have a Magnetic Resonance Imaging (MRI) exam. For the MRI exam, you will lie down on a narrow bed which will then be placed in a tunnel that is 6 feet long by 22 inches wide and open at each end. You will lie there quietly for about one hour, during which time you will hear a loud noise. You may feel warm during this procedure.

6. Once a week, a blood sample will be drawn from a vein in your arm. Each sample will be approximately ___ teaspoons; a total of about ___ tablespoons will be drawn for the whole study.

7. The researchers will check your medical records to gather information about ___

8. You may be withdrawn from the study without your consent if the researchers believe it is in your best interest or if you fail to follow study procedures.

9. Participation in the study will take a total of about ___ hours over a period of ___ weeks.

10. All study procedures will be done at ___ at the University of South Alabama Medical Center.
Risks and/or Discomforts

1. **Drug XXX:** If you are in the group that receives Drug XXX, the following side effects are possible: ... These side effects are serious, but have occurred in less than ___ of previous human studies of XXX using comparable doses. If ___ occurs, it will be treated by ___, (and you will be taken off the study). Other side effects which are less severe but may occur more frequently are ...

2. **Randomization:** You will be assigned to a treatment program by chance. The treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

3. **Placebo:** If you are in the group that receives placebo, your condition will go without active treatment for ___ weeks.

4. **Radiation:** The amount of radiation you will be exposed to is relatively small. Such doses of radiation may be potentially harmful, but the risks are so small that they are difficult to measure. If you have already had many x-rays, you should discuss this with the researchers before agreeing to be in the study.

   OR [when larger doses of radiation are involved]

   As a result of participating in this study, you will receive a significant amount of radiation. The amount is similar to that received in many standard x-ray procedures, but is far more than you would receive from natural daily exposure or in the normal course of treatment, and carries at least a theoretical risk. If you are especially concerned with radiation exposure, you should discuss this with the researchers.

5. **MRI**

   Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination, which could in the process possibly harm you. Precautions have been taken to prevent such an event from happening; loose metal objects, like pocket knives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysm clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have an MRI.

   Having an MRI may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia and by the loud banging noise during the study. Temporary hearing loss has been reported from this loud noise. This is why you will be asked to wear ear plugs. At times during the test you may be asked to not swallow for a while, which can be uncomfortable.

   Because the risks to a fetus from MRI are unknown, pregnant women must not participate in this study.

6. **Venipuncture:** The risks of drawing blood include temporary discomfort from the needle stick and bruising.

7. **Unknown risks:** The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

8. **Confidentiality:** Participation in research will involve a loss of privacy, but information about you will be handled as confidentially as possible. [Use this sentence only when appropriate: Representatives from the sponsoring company [insert company name in parentheses] and the Food and Drug Administration and the University Institutional Review Board (IRB) may review information about you to check on the study.] If you sign this consent form, you are allowing the study sponsor, the FDA, and the IRB to review our medical records. Your name will not be used in any published reports about this study.

9. If you experience any discomfort or injury that you think is related to this study, contact one of the physicians listed in this consent. In the event of a physical injury, which may result from research procedures, the University will provide first-aid medical treatment, but no funds have been set aside for this. The cost will be billed to you or your insurance. You do not give up any legal rights by signing this consent form.
**Benefits**

[If subject is randomized] The potential benefit to you is that the treatment you receive may prove to be more effective than the other study treatment or than other available treatments, although this cannot be guaranteed.

If you are in the group that receives Drug XXX and it proves to treat your condition with fewer side effects than the current standard therapy, you may benefit from participating in the study; however, this cannot be guaranteed.

OR

There will be no direct benefit to you from participating in this study. However, it is hoped that the information gained from the study will help in the treatment of future patients with conditions like yours/will help the researchers learn more about ___.

**Alternatives**

If you choose not to participate in this study, you could receive no treatment for your condition/the standard therapy for your condition, which is ___/another experimental treatment/Drug XXX, but without having to undergo the tests involved in the study.

**Costs/Financial Considerations**

[Example #1] You will not be charged for any of the study treatments or procedures. The costs of Drug XXX, the administration of the study drug, the x-rays, MRI exams, all tests associated with this study, and all office visits will be covered by the study.

[Example #2] You or your insurance company will be billed for the clinic visits, and all standard laboratory tests (for example, routine blood counts and blood chemistry tests). Drug XXX will be provided free of charge and you will not be billed for tests required for purposes of research, like extra blood tests, x-rays, or MRI exams. Because this treatment is experimental, your insurance company may refuse to pay for costs related to this treatment, in which case you will be held financially responsible. Financial counselors are available through the hospital accounting department to discuss this with you.

[Example #3] The costs associated with this treatment program will be charged to you or your insurance carrier; however, because this treatment is experimental your insurance company may refuse to pay for it. It is possible that your insurance company will refuse to pay for this treatment program after you have already received your treatment and you will have to pay for your care. You have met with a financial advisor from the hospital, who has provided you with the maximum dollar amount that you will be expected to pay.

**Reimbursement/Payment**

You will not be paid for participating in this study.

OR

In return for your time, effort and travel expenses, you will be paid $___ for your participation in this study. If you do not complete the study, you will receive $___ for each week of participation. A check will be mailed to you approximately six weeks after your participation in the study has ended.

**Questions**

This study has been explained to you by Dr. Smith or the person who signed below and your questions were answered. If you have any other questions about the study, you may call Dr. Smith at (251) 460-XXXX, or his associate at (251) 460-XXXX.
If you have any comments or concerns about participation in this study, you should first talk with the researchers. If for some reason you do not wish to do this, you may contact the Institutional Review Board, which is concerned with the protection of volunteers in research projects. You may reach the IRB office between 8:00 and 5:00, Monday through Friday, by calling (251) 460-6308.

**Tissue and/or blood banking or storage**

Stored samples have been used in research activities for many years. These samples allow investigators to make important new measurements that were not possible at the time that the original research was planned and conducted. It is possible that some of the biological material (for example: blood, urine or tissue) collected to diagnose your condition or to conduct this research project may remain unused when the research is completed. Normally such samples would be destroyed. We ask your permission to retain and store this for an indefinite period of time so that it might be used for future, as yet undefined, purposes. Future uses may include, but may not be limited to, research, education and commercial development.

**IF YOU DO NOT WISH TO HAVE YOUR MATERIAL STORED FOR FUTURE USE YOU MAY STILL PARTICIPATE IN THIS STUDY.**

If you agree to allow storage, the samples will be stored by:

__________________________
(name/location of site)

Security will be provided by:

__________________________
(Responsible person/agency and methodology)

**Do you wish to allow storage of your remaining biological material?**

Yes _____   No _____

5. If you agree to storage of your samples, you may choose how this material is to be used or you may limit its use.

**Do you wish to limit the use of your stored biological material?**

Yes _____   No _____

If “yes” specify the limitations: __________________________________________________________

6. If you agree to allow your samples to be stored, they will initially be identified with you (for example, your name, your initials, or a number) that could lead back to you. You may choose to have information that could identify you removed. If such identification is removed it will be impossible for you to be contacted in the future regarding any important new or additional information which may be of benefit to you or your family and might lead to further research.

**Do you wish to have all information that could identify you removed from the stored material?**

Yes _____   No _____

7. If you agree to allow your samples to be stored with identifying information, you may choose to allow someone to contact you in the future to ask you questions about your health, to ask you to participate in more research or for any other reason.
Do you wish to allow personal contact in the future regarding the stored material?

Yes _____  No _____

If “Yes,” specify any limitations you wish to impose:

______________________________________________________________

Consent

You will be given copies of this consent form.

Participation in research is voluntary. You have the right to decline to participate or to withdraw at any point in this study without risk to [your medical care/employment/student status; only the appropriate category or categories should be indicated].

I acknowledge receiving and reading the Medical Research Subject’s Bill of Rights.

If you wish to participate, you should sign below.

_______________________________________  ______________
Subject’s Signature      Date

_______________________________________  ______________
Person Obtaining Consent     Date

_______________________________________  ______________
Parent or Guardian’s Signature     Date

_______________________________________  ______________
Assenting Minor’s Signature (<19 yrs)    Date

_______________________________________  ______________
Witness Signature      Date
(Required only if legal representative signs on behalf of subject)
Research involving sensitive aspects of the subject's own behavior

The Procedures section should discuss in detail the kinds of sensitive questions that will be asked during interviews, in questionnaires, or in focus groups (i.e., you should specify that questions about sexual activity, drug or alcohol use, domestic violence or child abuse, or other illegal activities will be asked).

In studies in which you think it is likely that subjects will reveal actions that you are legally or morally obligated to report to authorities (e.g., when child, spousal, or elderly abuse is suspected), a statement should be added to the consent form’s discussion of confidentiality, briefly saying that such circumstances may arise.

When questions about drug use or other illegal activities are involved, research subjects are placed at risk since research discussions and records do not enjoy the same legal privilege as medical records. In order to protect your subjects better, you may wish to obtain a Federal Certificate of Confidentiality through your funding agency (see http://grants1.nih.gov/grants/policy/coc/index.htm). This Certificate prevents courts from compelling researchers to reveal information about their subjects. Whether or not you obtain a Certificate, subjects should be warned in the consent form about the risk of loss of confidentiality. Wording like the following is recommended:

Participation in research will cause a loss of privacy. In this study you will be asked about drug use and other possibly illegal activities. The researchers will keep information about you as confidential as possible, but complete confidentiality cannot be guaranteed. On rare occasions, research records have been subpoenaed by a court.

If you obtain a Certificate of Confidentiality for the study, the end of the statement can be revised as follows:

... On rare occasions, research records have been subpoenaed by a court, but the National Institute of Health [or other issuing agency] has given the researchers a Federal Certificate of Confidentiality which says courts cannot force the researchers to reveal information about your participation in the study.

Collecting long-term tracking information

If relatives, neighbors, co-workers, employers, or government agencies will be contacted during the study to provide information on subjects’ whereabouts, you should explain so in Procedures. Subjects should be reminded that they can ask to have these tracking procedures stopped at any time.
STANDARD CONSENT FORM FORMAT #2
BEHAVIORAL STUDY

CONSENT TO BE A RESEARCH SUBJECT
UNIVERSITY OF SOUTH ALABAMA

[Study Title]
[Name of Investigator]
[Contact Number]

Purpose and Background

Ricardo Brown, M.D., and Marcia White, Ph.D. from the Department of ..., are conducting a study to learn how men and women communicate pleasant and unpleasant feelings. [If appropriate] This study is being funded by ... You are being asked to participate in this study because you are a healthy volunteer. XXX volunteers are expected to participate in this study.

Procedures

If you agree to be in this study, the following will happen:

1. You will view two 15-minute videotapes; one will be of pleasant and the other of unpleasant content.
2. After viewing both videotapes, you will be asked to take part in a focus group discussion led by Dr. Brown or Dr. White. Everyone in this focus group will have viewed the tapes. During the focus group, you and the other group members will be asked to discuss reactions to scenes in both tapes. An audiotape will be made of this discussion. This discussion is expected to last about thirty minutes.
3. You will respond to a questionnaire about your reaction to the videotapes. It should take approximately fifteen minutes to complete the questionnaire.
4. You will answer questions on a standard paper and pencil personality test. It should take about an hour to complete this test.

These procedures will be done at Dr. Brown’s laboratory at ___ and will take a total time of about two and one-half hours.

Risks and/or Discomforts

1. Some of the videotapes are likely to produce unpleasant feelings, but you will be able to stop watching at any time if you feel too uncomfortable.
2. Some of the focus group discussions may make you uncomfortable or upset, but you are free to decline to answer any questions you do not wish to answer or to leave the group at any time.
3. Confidentiality: Participation in research will involve a loss of privacy; however, your records will be handled as confidentially as possible. The researchers will ask you and the other people in the focus group to use only first names during the group session. They will also ask group members not to tell anyone outside the group what any particular person said in the group. However, the researchers cannot guarantee that everyone will keep the discussions private. Only Dr. Brown, Dr. White and their assistant will have access to your study records and audiotapes. After the group discussion has been transcribed from the tapes, the tapes will be destroyed. No individual identities will be used in any reports or publications that may result from this study.

If you experience any discomfort or injury that you think is related to this study, contact one of the physicians listed in this consent. In the event of a physical injury, which may result from research procedures, the University will provide first-aid medical treatment, but no funds have been set aside for...
this. The cost will be billed to you or your insurance. You do not give up any legal rights by signing this consent form.

**Benefits**

There will be no direct benefit to you from participating in this study. However, the information that you provide may help health professionals better understand the differences in how males and females communicate pleasant and unpleasant feelings.

**Costs/Financial Considerations**

There will be no costs to you as a result of taking part in this study.

**Reimbursement/Payment**

You will be paid $20 for your participation in this study. If you decide to withdraw prior to study completion, you will receive $10. You will be paid in cash immediately after you complete your participation in this study.

**Questions**

You have talked to Dr. Brown, Dr. White, or the person who signed below about this study and have had your questions answered. If you have further questions, you may call him/her at (251) 460 xxxx.

If you have any comments or concerns about participation in this study, you should first talk with the researchers. If for some reason you do not wish to do this, you may contact the Institutional Review Board, which is concerned with the protection of volunteers in research projects. You may reach the IRB office between 8:00 and 5:00, Monday through Friday, by calling (251) 460-6308.

**Consent**

You will be given copies of this consent form.

Participation in research is voluntary. You are free to decline to be in this study, or to withdraw from it at any point. Your decision as to whether or not to participate in this study will have no influence on your present or future status as a ([patient, student or employee at USA—complete only as appropriate]).

If you wish to participate, you should sign below.

Subject’s Signature ___________________________ Date ____________

Person Obtaining Consent ___________________________ Date ____________

Parent or Guardian’s Signature ___________________________ Date ____________

Assenting Minor’s Signature (<19 yrs) ___________________________ Date ____________

Witness Signature ___________________________ Date ____________

(Required only if legal representative signs on behalf of subject)
NOTES:

Research involving sensitive aspects of the subject's own behavior

The Procedures section should discuss in detail the kinds of sensitive questions that will be asked during interviews, in questionnaires, or in focus groups (i.e., you should specify that questions about sexual activity, drug or alcohol use, domestic violence or child abuse, or other illegal activities will be asked).

In studies in which you think it is likely that subjects will reveal actions that you are legally or morally obligated to report to authorities (e.g., when child, spousal, or elderly abuse is suspected), a statement should be added to the consent form's discussion of confidentiality, briefly saying that such circumstances may arise.

When questions about drug use or other illegal activities are involved, research subjects are placed at risk since research discussions and records do not enjoy the same legal privilege as medical records. In order to protect your subjects better, you may wish to obtain a Federal Certificate of Confidentiality through your funding agency (see http://grants1.nih.gov/grants/policy/coc/index.htm). This Certificate prevents courts from compelling researchers to reveal information about their subjects. Whether or not you obtain a Certificate, subjects should be warned in the consent form about the risk of loss of confidentiality. Wording like the following is recommended:

Participation in research will cause a loss of privacy. In this study you will be asked about drug use and other possibly illegal activities. The researchers will keep information about you as confidential as possible, but complete confidentiality cannot be guaranteed. On rare occasions, research records have been subpoenaed by a court.

If you obtain a Certificate of Confidentiality for the study, the end of the statement can be revised as follows:

... On rare occasions, research records have been subpoenaed by a court, but the National Institute of Health [or other issuing agency] has given the researchers a Federal Certificate of Confidentiality which says courts cannot force the researchers to reveal information about your participation in the study.

Collecting long-term tracking information

If relatives, neighbors, co-workers, employers, or government agencies will be contacted during the study to provide information on subjects' whereabouts, you should explain so in Procedures. Subjects should be reminded that they can ask to have these tracking procedures stopped at any time.
James Williams, M.D. and his associates from the Department of ___ are conducting a study to learn ___. You are being asked to participate in this study because you are [have] ___.

If you agree to be in this study, a little less than one teaspoonful (4 milliliters) of blood will be taken from a vein in your arm. This blood will be drawn at ___ [location]. The procedure will take about five minutes.

The risks of blood drawing include temporary discomfort from the needle stick and bruising.

Participation in research will involve a loss of privacy. However, your records will be kept as confidential as possible. No individual identities will be used in any reports or publications resulting from this study.

If you experience any discomfort or injury that you think is related to this study, contact one of the physicians listed in this consent. In the event of a physical injury, which may result from research procedures, the University will provide first-aid medical treatment, but no funds have been set aside for this. The cost will be billed to you or your insurance. You do not give up any legal rights by signing this consent form.

There will be no direct benefit to you from participating in this study. However, it is hoped that the information gained from the study will help researchers learn more about ____.

You will be paid $10 for your participation. A check will be issued in about four weeks [or, You will not be paid for your participation, nor will you be charged].

This study has been explained to you by Dr. Williams or the person who signed below and your questions were answered. If you have any additional questions you can call Dr. Williams at (251) 460-xxxx.

If you have any comments or concerns about participation in this study, you should first talk with the researchers. If for some reason you do not wish to do this, you may contact the Institutional Review Board, which is concerned with the protection of volunteers in research projects. You may reach the IRB office between 8:00 and 5:00, Monday through Friday, by calling (251) 460-6308.

You will be given a signed copy of this consent form.

**Consent**

Participation in research is voluntary. You are free to decline to be in this study, or to withdraw from it at any point. Your decision as to whether or not to participate in this study will have no influence on your present or future status as a ([patient, student or employee at USA—complete only as appropriate].

If you wish to participate, you should sign below.

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<th>Subject’s Signature</th>
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<th>Person Obtaining Consent</th>
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</tbody>
</table>
Parent or Guardian’s Signature  Date

Assenting Minor’s Signature (<19 yrs)  Date

Witness Signature  Date
(Required only if legal representative signs on behalf of subject)

Note: This study is not sufficient for genetic studies, tissue banking, or blood banking.
Appendix K

HIPAA* Research Guidelines

(*Health Insurance Portability and Accountability Act)
Background

The Privacy Rule establishes the conditions under which protected health information (PHI) may be used or disclosed by covered entities for research purposes. A covered entity may always use or disclose for research purposes health information which has been de-identified (in accordance with §§ 164.502(d), 164.514(a)-(c) of the rule) without regard to the provisions below.

The Privacy Rule also defines the means by which individuals/human research subjects are informed of how medical information about themselves will be used or disclosed and their rights with regard to gaining access to information about themselves, when such information is held by covered entities. Where research is concerned, the Privacy Rule protects the privacy of individually identifiable health information, while at the same time, ensuring that researchers continue to have access to medical information necessary to conduct vital research. Currently, most research involving human subjects operates under the Common Rule (codified for the Department of Health and Human Services (HHS) at Title 45 Code of Federal Regulations Part 46) and/or the Food and Drug Administration's (FDA) human subjects protection regulations, which have some provisions that are similar to, but more stringent than and separate from, the Privacy Rule's provisions for research.

Using and Disclosing PHI for Research

In the course of conducting research, researchers may create, use, and/or disclose individually identifiable health information. Under the Privacy Rule, covered entities are permitted to use and disclose PHI for research with individual authorization, or without individual authorization under limited circumstances set forth in the Privacy Rule.

Research Use/Disclosure Without Authorization:

To use or disclose PHI without authorization by the research participant, a covered entity must obtain one of the following:

- Documentation that an alteration or waiver of research participants' authorization for use/disclosure of information about them for research purposes has been approved by an Institutional Review Board (IRB) or a Privacy Board. This provision of the Privacy Rule might be used, for example, to conduct records research, when researchers are unable to use de-identified information and it is not practicable to obtain research participants' authorization.

  or

- Representations from the researcher, either in writing or orally, that the use or disclosure of the PHI is solely to prepare a research protocol or for similar purposes preparatory to research, that the researcher will not remove any PHI from the covered entity, and representation that PHI for which
access is sought is necessary for the research purpose. This provision might be used, for example, to
design a research study or to assess the feasibility of conducting a study.

or

- Representations from the researcher, either in writing or orally, that the use or disclosure being
  sought is solely for research on the PHI of decedents, that the PHI being sought is necessary for the
  research, and, at the request of the covered entity, documentation of the death of the individuals about
  whom information is being sought.

A covered entity may use or disclose PHI for research purposes pursuant to a waiver of authorization by an
IRB or Privacy Board provided it has obtained documentation of all of the following:

- A statement that the alteration or waiver of authorization was approved by an IRB or Privacy Board
  that was composed as stipulated by the Privacy Rule;
- A statement identifying the IRB or Privacy Board and the date on which the alteration or waiver of
  authorization was approved;
- A statement that the IRB or Privacy Board has determined that the alteration or waiver of
  authorization, in whole or in part, satisfies the following eight criteria:

  - The use or disclosure of PHI involves no more than minimal risk to the individuals;
  - The alteration or waiver will not adversely affect the privacy rights and the welfare of the individuals;
  - The research could not practicably be conducted without the alteration or waiver;
  - The research could not practicably be conducted without access to and use of the PHI;
  - The privacy risks to individuals whose PHI is to be used or disclosed are reasonable in relation to the
    anticipated benefits, if any, to the individuals, and the importance of the knowledge that may reasonably be
    expected to result from the research;
  - There is an adequate plan to protect the identifiers from improper use and disclosure;
  - There is an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the
    research, unless there is a health or research justification for retaining the identifiers or such retention is
    otherwise required by law; and
  - There are adequate written assurances that the PHI will not be reused or disclosed to any other person or
    entity, except as required by law, for authorized oversight of the research project, or for other research for
    which the use or disclosure of PHI would be permitted by this subpart.

- A brief description of the PHI for which use or access has been determined to be necessary by the
  IRB or Privacy Board;
- A statement that the alteration or waiver of authorization has been reviewed and approved under
  either normal or expedited review procedures as stipulated by the Privacy Rule; and
- The signature of the chair or other member, as designated by the chair, of the IRB or the Privacy
  Board, as applicable.
Research Use/Disclosure With Individual Authorization:

The Privacy Rule also permits covered entities to use and disclose PHI for research purposes when a research participant authorizes the use or disclosure of information about him or herself. Today, for example, a research participant's authorization will typically be sought for most clinical trials and some records research. In this case, documentation of IRB or Privacy Board approval of a waiver of authorization is not required for the use or disclosure of PHI.

To use or disclose PHI created from a research study that includes treatment (e.g., a clinical trial), additional research-specific elements must be included in the authorization form required under § 164.508, which describe how PHI created for the research study will be used or disclosed. For example, if the covered entity/researcher intends to seek reimbursement from the research subject's health plan for the routine costs of care associated with the protocol, the authorization must describe types of information that will be provided to the health plan. This authorization may be combined with the traditional informed consent document used in research.

The Privacy Rule permits, but does not require, the disclosure of PHI for specified public policy purposes in § 164.512. With few exceptions, the covered entity/researcher may choose to limit its right to disclose information created for a research study that includes treatment to purposes narrower than those permitted by the rule, in accordance with his or her own professional standards.

Frequently Asked Questions

Q: Will the rule hinder medical research by making doctors and others less willing and/or able to share information about individual patients?

A: We do not believe that the Privacy Rule will hinder medical research. Indeed, patients and health plan members should be more willing to participate in research when they know their information is protected. For example, in genetic studies at the National Institutes of Health (NIH), nearly 32 percent of eligible people offered a test for breast cancer risk decline to take it. The overwhelming majority of those who refuse cite concerns about health insurance discrimination and loss of privacy as the reason. The Privacy Rule both permits important research and, at the same time, encourages patients to participate in research by providing much needed assurances about the privacy of their health information.

The Privacy Rule will require some covered health care providers and health plans to change their current practices related to documenting research uses and disclosures. It is possible that some covered health care providers and health plans may conclude that the rule's requirements for research uses and disclosures are too burdensome and will choose to limit researchers' access to PHI. We believe few providers will take this route, however, because the Common Rule includes similar, and more stringent requirements, that have not impaired the willingness of researchers to undertake federally-funded research. For example, unlike the Privacy Rule, the Common Rule requires IRB review for all research proposals under its purview, even if informed consent is to be sought. The Privacy Rule requires documentation of IRB or Privacy Board approval only if patient authorization for the use or disclosure of PHI for research purposes is to be altered or waived.

Q: Are some of the criteria so subjective that inconsistent determinations may be made by IRBs and Privacy Boards reviewing similar or identical research projects?

A: Under the Privacy Rule, IRBs and Privacy Boards need to use their judgment as to whether the waiver criteria have been satisfied. Several of the waiver criteria are closely modeled on the Common Rule's criteria
for the waiver of informed consent and for the approval of a research study. Thus, it is anticipated that IRBs already have experience in making the necessarily subjective assessments of risks and benefits. While IRBs or Privacy Boards may reach different determinations, the assessment of the waiver criteria through this deliberative process is a crucial element in the current system of safeguarding research participants' privacy. The entire system of local IRBs is, in fact, predicated on a deliberative process that permits local IRB autonomy. The Privacy Rule builds upon this principle; it does not change it.

In addition, for multi-site research that requires PHI from two or more covered entities, the Privacy Rule permits covered entities to accept documentation of IRB or Privacy Board approval from a single IRB or Privacy Board.

Q: Does the Privacy Rule prohibit researchers from conditioning participation in a clinical trial on an authorization to use/disclose existing PHI?

A: No. The Privacy Rule does not address conditions for enrollment in a research study. Therefore, the Privacy Rule in no way prohibits researchers from conditioning enrollment in a research study on the execution of an authorization for the use of pre-existing health information.

Q: Does the Privacy Rule permit the creation of a database for research purposes through an IRB or Privacy Board waiver of individual authorization?

A: Yes. A covered entity may use or disclose PHI without individuals' authorizations for the creation of a research database, provided the covered entity obtains documentation that an IRB or Privacy Board has determined that the specified waiver criteria were satisfied. PHI maintained in such a research database could be used or disclosed for future research studies as permitted by the Privacy Rule - that is, for future studies in which individual authorization has been obtained or where the rule would permit research without an authorization, such as pursuant to an IRB or Privacy Board waiver.

Q: Will IRBs be able to handle the additional responsibilities imposed by the Privacy Rule?

A: Recognizing that some institutions may not have IRBs, or that some IRBs may not have the expertise needed to review research that requires consideration of risks to privacy, the Privacy Rule permits the covered entity to accept documentation of waiver of authorization from an alternative body called a Privacy Board-which could have fewer members, and members with different expertise than IRBs.

In addition, for research that is determined to be of no more than minimal risk, IRBs and Privacy Boards could use an expedited review process, which permits covered entities to accept documentation when only one or more members of the IRB or Privacy Board have conducted the review.

Q: By establishing new waiver criteria and authorization requirements, hasn't the Privacy Rule, in effect, modified the Common Rule?

A: No. Where both the Privacy Rule and the Common Rule apply, both regulations must be followed. The Privacy Rule regulates only the content and conditions of the documentation that covered entities must obtain before using or disclosing PHI for research purposes.

Q: Is documentation of IRB and Privacy Board approval required before a covered entity would be permitted to disclose PHI for research purposes without an individual's authorization?
A: No. The Privacy Rule requires documentation of waiver approval by either an IRB or a Privacy Board, not both.

Q: Does a covered entity need to create an IRB or Privacy Board before using or disclosing PHI for research?

A: No. The IRB or Privacy Board could be created by the covered entity or the recipient researcher, or it could be an independent board.

Q: What does the Privacy Rule say about a research participant's right of access to research records or results?

A: With few exceptions, the Privacy Rule gives patients the right to inspect and obtain a copy of health information about themselves that is maintained in a "designated record set." A designated record set is basically a group of records which a covered entity uses to make decisions about individuals, and includes a health care provider's medical records and billing records, and a health plan's enrollment, payment, claims adjudication, and case or medical management record systems. Research records or results maintained in a designated record set are accessible to research participants unless one of the Privacy Rule's permitted exceptions applies.

One of the permitted exceptions applies to PHI created or obtained by a covered health care provider/researcher for a clinical trial. The Privacy Rule permits the individual's access rights in these cases to be suspended while the clinical trial is in progress, provided the research participant agreed to this denial of access when consenting to participate in the clinical trial. In addition, the health care provider/researcher must inform the research participant that the right to access PHI will be reinstated at the conclusion of the clinical trial.

Q: Are the Privacy Rule's requirements regarding patient access in harmony with the Clinical Laboratory Improvements Amendments of 1988 (CLIA)?

A: Yes. The Privacy Rule does not require clinical laboratories that are also covered health care providers to provide an individual access to information if CLIA prohibits them from doing so. CLIA permits clinical laboratories to provide clinical laboratory test records and reports only to "authorized persons," as defined primarily by state law. The individual who is the subject of the information is not always included as an authorized person. Therefore, the Privacy Rule includes an exception to individuals' general right to access PHI about themselves if providing an individual such access would be in conflict with CLIA.

In addition, for certain research laboratories that are exempt from the CLIA regulations, the Privacy Rule does not require such research laboratories if they are also a covered health care provider to provide individuals with access to PHI because doing so may result in the research laboratory losing its CLIA exemption.

Q: Do the Privacy Rule's requirements for authorization and the Common Rule's requirements for informed consent differ?

A: Yes. Under the Privacy Rule, a patient's authorization will be used for the use and disclosure of PHI for research purposes. In contrast, an individual's informed consent as required by the Common Rule and FDA's human subjects regulations is a consent to participate in the research study as a whole, not simply a consent for the research use or disclosure of PHI. For this reason, there are important differences between the Privacy Rule's requirements for individual authorization, and the Common Rule's and FDA's requirements for
informed consent. Where the Privacy Rule, the Common Rule, and/or FDA's human subjects regulations are applicable, each of the applicable regulations will need to be followed.
# Appendix L

## USA Decision Tree for Determining if IRB Approval is Needed for the Use of Human Tissue or Cell Lines

<table>
<thead>
<tr>
<th>Type of Cell Line/Tissue Sample</th>
<th>Are samples identifiable? (i.e., do you have access to information that would enable you to determine the donor’s name?)</th>
<th>Were samples leftover or collected specifically for research purposes?</th>
<th>IRB Requirement</th>
<th>Turnaround Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Established cell lines publicly available to qualified scientific investigators [e.g., cell lines commercially available from the American Type Culture Collection (ATCC)], including cell lines that have been published and are available by request from the investigator.</td>
<td>NA</td>
<td>NA</td>
<td>None. Not covered under definition of “human subject.”</td>
<td>NA</td>
</tr>
<tr>
<td>Cell lines originally obtained from a commercial source (e.g., ATCC) and subsequently modified in the investigator’s laboratory</td>
<td>NA</td>
<td>NA</td>
<td>None. Not covered under definition of “human subject.”</td>
<td>NA</td>
</tr>
<tr>
<td>Samples from deceased individuals or cadaverous tissue</td>
<td>NA</td>
<td>NA</td>
<td>None. Not covered under definition of “human subject.”</td>
<td>NA</td>
</tr>
<tr>
<td>Self-sustaining, cell-free derivative preparations including viral isolates, cloned DNA, or RNA</td>
<td>NA</td>
<td>NA</td>
<td>None. Not covered under definition of “human subject.”</td>
<td>NA</td>
</tr>
<tr>
<td>Existing tissue (“on the shelf” when the research is proposed), including cell lines derived from living individuals.</td>
<td>No</td>
<td>NA</td>
<td>Submit Exempt Application</td>
<td>~ 1 day</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>NA</td>
<td>Additional consent* usually not required provided that minimum risk criteria are met. Submit application for Expedited review.</td>
<td>~ 1 week</td>
</tr>
<tr>
<td>Prospectively gathered tissue</td>
<td>No (Please note: Removing identifiers from banked samples reduces their value and in the future it is likely that potential sponsors, both public and private, will avoid funding research using samples for which consent has not been obtained.)</td>
<td>NA</td>
<td>Consent not required. Submit Exempt Application Form.</td>
<td>~ 1 day</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>Leftover samples (i.e., originally taken for clinical or diagnostic purposes)</td>
<td>Consent required. Submit application for Subcommittee review.</td>
<td>~ 4 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tissues taken specifically for research purposes</td>
<td>Consent required. Submit application for Full Committee review.</td>
<td>~ 4 weeks</td>
</tr>
</tbody>
</table>

- The research must adhere to the conditions specified in the previously obtained consent, even if all identifiers have been removed.