

Policies and Procedures of the Institutional Review Board of the University of South Carolina

In order to protect the rights, well-being and personal privacy of individuals, to assure a favorable climate for the conduct of scientific inquiry, and to protect the interests of the University of South Carolina, the policies and procedures described below have been established for the conduct of investigations involving human subjects at The University of South Carolina (“University”). The policies and procedures shall be in compliance with regulations promulgated by the Department of Health and Human Services (DHHS) in 45 CFR 46, and when applicable shall be in compliance with the Food and Drug Administration (FDA) regulations in 21 CFR 50 and 56.

These policies and procedures, taken together with the guidance provided on the website and related application forms, define the procedures and responsibilities for the Institutional Review Board (IRB) and principal investigators for the protection of the rights and welfare of human research subjects.

I. General Principles and Policies

The following general principles apply equally to all investigations involving human subjects at the University and to activities carried out at other sites under the aegis of faculty and professional staff of the University, whether supported solely by institutional resources or with the assistance of outside funds:

A. The University and the individual members of its faculty, staff, and student body engaged in research recognize their responsibility for safeguarding the rights and welfare of human subjects.

B. No investigation shall be undertaken which exposes subjects to unreasonable risks to health or well-being.

C. The confidentiality of information received from or learned about subjects in experiments, or respondents to questionnaires or interviews, shall be fully protected both during and after the conduct of an investigation, subject to the requirements of the law.

D. Before a human subject participates in an investigation, informed consent must be obtained from the subject. The basic elements of informed consent as required under 45 CFR 46.116-117 must be included in every informed consent document. The research procedure(s), its purpose and any anticipated risk or substantial stress or discomfort, shall be described in lay language in the consent document. The explanation of the procedures to be followed should identify those which are experimental. In addition, the benefits reasonably to be expected should be described, and appropriate alternative procedures that might be advantageous for the subject should be disclosed. The investigator shall offer to answer any questions, and further, he/she shall be satisfied that the individual, or his/her legally authorized representative, understands all aspects of the procedure(s) or

treatment(s) he/she is to undergo. In giving consent, the subject must be able to exercise free power of choice without the intervention of any elements of constraint or coercion.

E. A consent form, which has been approved by the University of South Carolina Institutional Review Board (IRB), is to be presented to the potential research subject and signed by the subject or his/her legally authorized representative in a manner approved by the IRB. The consent form shall be kept as a matter of record that the required disclosure was made. When appropriate, time will be allowed to elapse between the explanation of the study and disclosure of risks, and the signing of the consent form, to permit due consideration by the subject. The consent form shall contain no exculpatory language through which the subject is made to waive, or appear to waive, any of his/her legal rights, or to release the institution from liability for negligence. If the subject is under 18 years of age or otherwise legally incompetent, the consent of the parent(s) or legally authorized representative is required. Signed written consent is mandatory unless the IRB specifically determines that oral consent or other procedure is acceptable or waives the requirement for consent.

F. Compensation to volunteer subjects should never be such as to constitute an undue inducement to participate in investigative work and should be limited to nominal amounts, including reimbursement for out-of-pocket expenses.

G. A request by any subject to withdraw his/her consent and to discontinue participation in the investigation shall be honored promptly and unconditionally.

H. Whenever possible, the subjects of an investigation shall come from various income and ethnic groups, and excessive representation of the indigent, disadvantaged or other vulnerable subject population is to be discouraged unless the research involves questions specifically related to these groups.

I. It shall be the obligation of the investigator to bring any proposal involving the use of human subjects to the IRB for review and approval prior to initiation of the study. All research studies involving human subjects conducted by students must also be reviewed and approved by the IRB prior to initiation. It is the responsibility of the faculty member who is supervising the student investigator to ensure that the research is approved by the IRB and that informed consent is appropriately obtained from all research subjects.

J. No investigation involving the use of human subjects shall be initiated until the IRB has reviewed and approved the study or determined that the study is exempt from IRB review.

K. All study personnel who are engaged in human research must complete human subjects research training before the IRB approval will be released.

L. Each Chairperson or head of an academic or clinical department or

division shall be responsible to the IRB for the supervision and proper conduct of research involving human subjects in his/her department or division in accordance with procedures prescribed by the IRB.

II. The University of South Carolina Institutional Review Board (IRB)

A. Responsibilities

The IRB has as its primary concern the protection of the rights and welfare of human subjects involved in research and is responsible for the review and approval, in accordance with the procedures set forth below, of all investigations involving human subjects. No study involving human subjects may be undertaken at the University or by faculty of the University at other sites without prior approval of the IRB. In addition, the IRB will be responsible for:

(1) initial review and approval of all research involving human subjects to be conducted at the University or by the faculty of the University at other sites;

(2) conducting continuing review of all research approved by the Committee;

(3) reviewing on a continuing basis the University's policies and procedures with respect to the utilization of human subjects in research;

(4) providing advice and guidance to investigators regarding the rights and welfare of subjects and the IRB review procedures;

(5) reporting any serious or continuing non-compliance by an investigator with the requirements and determinations of the IRB to the Director of the Office of Research Compliance, to the Office of Human Research Protections (OHRP), and to the Food and Drug Administration (FDA) when the investigation is an FDA regulated study.

(6) ensuring required human subjects research training by study personnel is completed prior to release of IRB approval.

B. Membership

(1) The IRB members shall be sufficiently qualified through maturity and diversity to ensure respect for their advice and counsel for safeguarding the rights and welfare of human subjects, and be able, in addition to professional competence, to ascertain acceptability of proposals in terms of organizational commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. Members will therefore be appointed from among individuals in the fields of medicine, law, ethics, religious studies, biological and physical sciences, behavioral sciences, philosophy, health administration and public affairs, as well as individuals

representative of the larger community served by the University.

(2) The IRB shall have a minimum of 5 members.

(3) The IRB shall have at least one member who is not otherwise affiliated with the University and who is not part of the immediate family of a person affiliated with the University.

(4) The IRB shall have at least one member whose primary area of expertise is in a non-scientific area.

(5) The IRB members shall include both males and females and shall have diverse backgrounds and varied areas of professional expertise so as to assure competence necessary to review the range of research activities conducted at the University as well as to assure sensitivity to racial and cultural issues as well as community attitudes.

(6) Designated and trained alternates are used to supplement membership. The IRB roster will list the regular member and specify alternate(s) who are authorized to substitute for each regulator member. Alternate members will have qualifications comparable to those of the regular members and will serve in the same representative capacity as the member for whom they substitute. Alternates may attend any IRB meeting, but their vote will only count when serving as the substitute for the regular member.

(7) When deemed necessary by the IRB Manager, the IRB chair, and/or any voting member, may seek advice from consultants within or outside the University to supplement the expertise of the Board members. The IRB Manager is responsible for securing this expertise. The IRB Manager will ensure the consultant has all the materials required to review and address the concerns/questions. Depending on the request and need for additional expertise, the IRB Manager may ask the consultant(s) to discuss concerns/questions with a Board member, document his/her review, and/or attend the relevant convened Board meeting, but the consultant will not be allowed to vote.

(8) When research is reviewed involving a category of vulnerable subjects (e.g., prisoners, children, individuals institutionalized as mentally disabled), the IRB shall include in its reviewing body one or more individuals who have as a primary concern the welfare of these subjects.

(9) Members shall be appointed by the President.

(10) Members shall serve for terms of three years and may be reappointed for successive terms. Terms shall be staggered to ensure continuity.

C. Meetings

The IRB shall meet regularly, usually once a month. Additional meetings

may be called at the discretion of the Chairperson.

D. Quorum

All members of the IRB are expected to attend meetings. A majority of the voting members of the IRB, including at least one member whose primary concerns are in non-scientific areas, shall constitute a quorum during the process of review. Meetings shall be canceled if a quorum is not present. Approval or disapproval of an application requires a majority of the members present.

E. Minutes and Other Records

(1) Minutes

Written minutes shall be prepared for all IRB meetings. The minutes shall include: (1) attendance at the meeting; (2) actions taken by the IRB; (3) the IRB vote on the actions taken, including indication of any dissenting votes or abstentions; (4) a summary of discussion of controverted issues and their resolution; and (5) the basis for requested changes in research proposals or consent documents or for disapproval of research proposals.

(2) Other Records

The following additional records shall be maintained to document IRB activities:

(a) copies of research proposals reviewed and evaluations of them; (b) copies of approved consent documents; (c) progress reports by investigators; (d) reports of adverse events; (e) records of continuing review of research; (f) copies of all correspondence between IRB and investigators; (g) a list of IRB members; and (h) statements of significant new findings provided to subjects.

All of these records shall be maintained for a period of at least three (3) years after completion of the research. Minutes and other records shall be available for inspection by authorized representatives of the Department of Health and Human Services.

F. Review Procedures

(1) Application Submission

Investigators who wish to conduct a research project involving human subjects shall submit an application describing the research on forms prepared for that purpose. The application shall include: a complete description of the research procedures and methods to be employed; the background to the proposed research; the current state of knowledge in the field; the significance of the research proposed; all risks to the subjects which can be anticipated as a consequence of their participating in the research; procedures to be employed to

minimize risks to subjects; any benefits to the subjects which might reasonably be expected from their participation in the study; procedure for obtaining informed consent and informed consent document; nature of the research subject population, including sex, age, racial and ethnic characteristics; procedures for recruiting subjects; number of subjects to be studied; alternative procedures for diagnosis and/or treatment and their benefits and risks; procedures to be employed to maintain confidentiality of subject-related data; source of funding to support the research; and financial compensation, if any, for the research subjects.

If the research is to be supported by a grant from an external agency a copy of the complete grant application, as submitted to the granting agency, must accompany the application and consent document. If the research is to be supported by an industrial sponsor a draft of the proposed contract between the industrial sponsor and the University, as well as any sponsor developed research protocol must be submitted to the IRB together with the application and consent document. The consent document shall normally contain all of the basic elements of informed consent as per 45 CFR 46.116- 117.

(2) Conflict of Interest

If an IRB member believes that he/she might have, or be perceived as having, a conflict of interest in reviewing a given application, or if one member of the IRB suggests that another member might have such a conflict then, the member who might have a conflict of interest will absent himself/herself from the meeting during the discussion and voting of that application. If a disagreement arises as to whether the potential for a conflict of interest exists, it shall be resolved by vote of the IRB after discussion of the issues involved.

(3) Application Review

As part of its review, the IRB shall determine whether investigations involving use of human subjects will place these subjects at risk of injury, including physical, psychological or social injury. If so, the review will determine if the risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks. In addition, the review will determine if the risks and possible benefits are adequately described in the consent document to assure that the subject is fully and fairly informed in accordance with 45 CFR 46.109.

The IRB will also consider the proposed procedures for recruitment of research subjects and for obtaining informed consent from potential research subjects to ensure that the procedure and document are consistent with 45 CFR 46.116-117. The IRB will also consider whether appropriate protections are provided for vulnerable populations such as prisoners, children and mentally impaired as per 45 CFR 46.305-306 and 45 CFR 46.404-407.

The IRB may request additional information, clarifications or revisions in the application or consent document.

Each committee member shall receive a copy of all applications and informed consent documents at least one week in advance of the meeting date. A primary reviewer system will be employed. One member of the IRB will be assigned to each application as primary reviewer. The primary reviewer will be responsible for an in-depth review of all pertinent materials and preparing a critique of the application that will be presented to the convened IRB. The primary reviewer will also review the written responses by investigators to the requests by the IRB for information, clarification or substantive changes in a protocol or consent document and will report their findings to the convened IRB.

Each application will be discussed by the convened IRB. The convened IRB will approve or disapprove an application by majority vote of those members present. Except in the case of non-substantive revisions (see Section II.F.(4)(a) below), if the IRB requests additional information, clarifications or revisions in the protocol or consent documents, approval or disapproval will be deferred. For any research protocol that is approved the IRB will state the duration of approval, which shall not exceed one year.

Before approving a research proposal the IRB shall determine that the following requirements are satisfied: (a) that risks to subjects are minimized; (b) that risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result; (c) that selection of subjects is equitable, taking into account the purposes of the research and the setting in which it will be conducted; (d) that informed consent will be sought from each prospective subject or subject's legally authorized representative in accordance with 45 CFR 46.116; (e) that informed consent will be appropriately documented in accordance with 45 CFR 46.117; (f) that the research plan appropriately monitors the data collected to ensure the safety of subjects; (g) that subjects' privacy is appropriately protected and confidentiality of subject related data maintained; and (h) that appropriate additional safeguards are included to protect the rights and welfare of subjects who are likely to be vulnerable to coercion.

Investigators are notified in writing of the results of the IRB review. When the IRB requests modifications or defers action, the investigator is informed in writing of the reasons for the IRB's actions, and the substance of such correspondence is included in the meeting minutes. Upon approval of the research proposal, whether by expedited review or by the convened IRB, the investigator is sent a certification of approval notifying him/her of his/her responsibilities related to reporting and continuing review.

If the IRB votes to disapprove a research proposal it shall notify the principal investigator in writing of the disapproval and the reasons for it. The principal investigator or his/her representative may respond to the IRB in writing or in person at a convened meeting of the IRB.

The Institutional Official (or his/her designee) is notified of all IRB actions

by receipt of a copy of meeting minutes and all related correspondence.

(4) Review of Responses to IRB Requests for Additional Information, Clarification or Revision

(a) Non-substantive Revisions

Non-substantive revisions refer to specific revisions which are stipulated by the convened IRB and which require simple concurrence by the investigator. The appropriate inclusion of such revisions as stipulated by the IRB will be confirmed by the Chairperson of the IRB or his/her designee who can approve the research on behalf of the IRB. If the convened IRB has stipulated non-substantive revision(s) and has voted for approval of the research, then after confirmation by the Chairperson/designee of the inclusion of the stipulated revisions the investigator will be sent written notification of approval.

(b) Substantive Revisions

Response to requests by the IRB for additional information, clarification or revisions of protocol or consent document, other than non-substantive revisions discussed in Section II.F.(4)(a) above, will be reviewed by the IRB at a convened meeting. The written response of the investigator will be sent to all members of the IRB one week in advance of the meeting, except in those cases where the convened IRB stated without dissent that the response should be sent only to the primary reviewer(s). In the latter case, a copy of the response will be available at the IRB meeting in the event that any member wishes to see it. The same primary reviewer(s) who were assigned the application at the time of its initial consideration by the IRB will be responsible for reviewing the response in detail and presenting their critique of the response to the convened IRB. The convened IRB will approve or disapprove of the proposed research by majority vote of the members present. If additional information, clarification or revision of protocol or consent document is required by the IRB, approval or disapproval will be deferred pending subsequent review of the new response by the convened IRB.

(5) Review of Requests by the Investigator for Changes in an Approved Application

a) Minor Changes

The expedited review procedure by the IRB Chairperson (described below, Section II.F. (8)) will be used to review minor changes in previously approved research during the period for which approval is authorized. A minor change is defined as one that does not change the risk/benefit ratio of the study, does not increase the risk presented by the study above minimal risk, or, in and of itself, does not present more than minimal risk. The IRB Chairperson shall determine if the proposed change is minor and can therefore be approved by this procedure. If the IRB Chairperson approves the requested minor change

he/she shall notify the investigator in writing. The IRB Chairperson shall also inform the IRB during its next convened meeting of the approval of the requested minor change.

(b) Substantive Changes

All requests for changes in previously approved research (other than minor changes discussed above) shall be reviewed by a primary reviewer, who shall prepare a written critique of the proposed change(s) and present this critique to the convened IRB for its discussion. After discussion the IRB shall vote to approve or disapprove the proposed change or request additional information, clarification, or revisions in which case approval of the proposed change shall be deferred. The decision of the IRB shall be communicated to the principal investigator in writing.

(c) Administrative Changes

Some modifications, such as study staff changes (other than the PI) or correcting typos or formatting errors in study documents, are not changes in the research. The revisions must be submitted through the IRB system for administrative purposes but may be approved by IRB staff. The following are considered administrative changes which can be approved by IRB staff:

- 1) Deletion of study staff or addition of study staff other than principal investigator
- 2) Change in contact information
- 3) Title change that does not reflect a change in the study
- 4) Corrections of typographical errors/reformatting of unchanged text
- 5) Errors in the IRB application as confirmed by the study team and IRB staff

(6) Continuing Review of Research

(a) The IRB shall conduct continuing review of approved research at intervals determined by the IRB as being appropriate to the degree of risk but not less than once a year. In determining the frequency of review, the IRB considers the nature of the study, the degree of risk and the vulnerability of the study participants. The letter of approval issued to the investigator and the minutes specify the required frequency for review and the deadline for re-approval of the study. The IRB shall have the authority to observe or to designate a third party to observe the conduct of the research and the consent process. It may also determine that a study needs verification from sources other than the investigator that no material changes have occurred since the previous

IRB approval or that an independent committee is required to monitor the research. Continuing review will be conducted at a convened meeting of the IRB unless eligible for expedited review.

(b) The principal investigator shall submit, at the time interval determined by the IRB, a summary of the aims and objectives of the research; a summary of the protocol and the status of the research, including the number of subjects accrued; a description of any adverse events or unanticipated problems involving risks to subjects or others and any withdrawal of subjects from the research or complaints by subjects; summary of recent literature related to the study; summary of findings obtained to date; description of modifications to research since the last review; summary of any new information regarding risks to the subjects since the last review; and a copy of the current informed consent document. If the aims, objectives or research procedures employed have changed since the last review by the IRB, such changes should be clearly indicated.

(c) Failure of the principal investigator to submit an application for continuing review by the date stipulated by the IRB will result in automatic expiration of IRB approval.

(7) Duration of IRB Approval and Termination of Research

(a) Duration of IRB Approval

IRB approval of research is always for a limited period of time not to exceed one year from the date of the IRB meeting at which the research was approved. The duration of approval will be stated in the approval letter from the IRB to the principal investigator. If the study is to continue beyond the period of approval stated by the IRB, then continuing review and approval of the project is required as indicated in Section II.F.(6) above. If continuing review information is not received in time for IRB review prior to the end of the period of approval, then the IRB may require a new application be submitted and approved by the IRB if the study is to be continued.

(b) Termination of Approved Research by Investigator

Normally research terminates at the time when the period of IRB approval expires. If for unusual circumstances, such as new information about adverse events or efficacy or a decision by the sponsor of the research, the research is to be terminated before the end of the approval period, the principal investigator should notify the IRB and provide information regarding the reasons for the termination.

(c) Suspension of Approved Research by the IRB

1) Studies that have not received re-approval before the expiration date of IRB approval will be automatically suspended until re-approval is given or the study is terminated.

2) The IRB has the authority to suspend approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any such suspension of approval shall be reported promptly to the investigator and shall include a written statement of the reasons for the IRB's action. The Office of Research Compliance will notify appropriate University officials, and appropriate funding and/or federal officials. Such suspension will normally be made at a convened meeting of the IRB unless immediate suspension is indicated. In this case, the IRB Chairperson may suspend approval.

3) Subjects may not be enrolled or research interventions conducted during the period of suspension.

(8) Expedited Review

(a) An expedited review procedure may be used for certain kinds of research involving no more than minimal risks and for minor changes in approved research (45 CFR 46.110 or 21 CFR 56.110). The specific categories of research for which this procedure is applicable are listed in 45 CFR 46.111.

(b) If the principal investigator believes that the research that he/she is proposing to conduct involving human subjects is appropriate for expedited review, he/she will submit a completed Application for IRB Review to the IRB. The IRB Chairperson or his/her designee will conduct the review of the research. The IRB Chairperson or his/her designee shall confirm that the research is in a category appropriate for expedited review and that the research involves no more than minimal risk for the research subjects. In his/her review of the proposed research the Chairperson may exercise all of the authorities of the IRB except that he/she may not disapprove the research. If the Chairperson believes that the research should be disapproved then he/she shall refer the research proposal for review at a convened meeting of the IRB and the research shall then be reviewed in a manner consistent with the IRB's usual review procedures as described above (Section II.F.(3)). If the Chairperson approves the research (initially or after revision) he/she shall provide written notification to the principal investigator of his/her action and of the duration of the approval. Approval shall be effective as of the date of the letter of approval.

(c) The IRB Chairperson shall report actions taken in regard to research proposed for expedited review to the IRB at its next convened meeting. A copy of the research proposal and consent document shall be present at the IRB meeting so that members may review it if requested.

(9) Monitoring of Adverse Events

Principal investigators are responsible for reporting to the IRB serious and unexpected adverse events that impact the safety of or risk to their

subjects. These reports should be completed in a timely fashion. If an unexpected death occurs, the report should be sent to the Office of Research Compliance immediately. Serious, unexpected events (e.g., treatment requiring hospitalization) are to be reported within 48 hours, and all others within 10 working days.

Any proposed changes in the consent form or research procedures resulting from the report are to be prepared/identified by the principal investigator and submitted with the report to the IRB for approval.

The following definitions apply:

A **serious event** refers to any event in which the outcome is fatal or life threatening, causes permanent disability, requires inpatient hospitalization or is a congenital anomaly, cancer, or overdose.

An **unexpected adverse event** refers to those not identified in their nature, severity, or frequency in the current risk documents (e.g., investigator's brochure) or through clinical practice.

The Chairperson will review the report and, if appropriate, bring it to the attention of the IRB.

Based on the frequency and seriousness of adverse events, the IRB may deem it necessary to suspend or terminate a research study or studies. The IRB will involve the investigator in making such a decision.

(10) Research Involving Human Subjects which is Exempt from Review by the IRB

A study is exempt from IRB approval and other requirements of federal policy if all of the research activities fall into one or more of the categories designated by federal regulation (45 CFR 46.104). Exemptions 2(i) and (ii) for research involving survey or interview procedures or observations of public behavior does NOT apply to research in children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed. Exemption 2(iii), where identifiable information is obtained and the IRB conducts a limited IRB review, is NOT applicable to research in children. Exemption 3 does NOT apply to research involving children. Exemptions do not apply to prisoners.

To qualify for exempt status, the study must be reviewed and approved by the IRB. Upon approval by the IRB a certification of exemption will be issued to the principal investigator.

All exempt research involving human subjects must maintain an adequate standard of informed consent and confidentiality of data.

(11) Approval for Compassionate Use of Research Drugs
(a) Concept

Occasionally a physician may wish to use an experimental (unapproved) drug, device or procedure in the treatment of a specific patient in situations where no standard acceptable treatment is available or all standard therapies have been tried and have failed. It should be emphasized that “compassionate use” is for therapeutic or diagnostic (that is, patient care) purposes only. Patients receiving medication, device or procedure approved for “compassionate use” may not be included as research subjects for a subsequently approved protocol dealing with this medication, device or procedure. “Compassionate use” of drugs, devices or procedures should be strictly for patient benefit and should not involve any additional tests, procedures or data collection for research purposes.

(b) Approval for “Compassionate Use”

Therapeutic use, in an individual patient, of drugs, devices or procedures which have not been approved by the FDA must be approved by the IRB. Request for approval, together with the proposed informed consent form, should be submitted either to the Office of Research Compliance or directly to the IRB Chairperson. The request will be reviewed by the IRB Chairperson and a decision will be rendered in writing within 24 hours. In emergency circumstances (see definition below) requests may be made orally, by telephone or in person, to the IRB Chairperson, who can give oral approval, or where time does not permit prior approval by telephone the procedure described in II. F.(10)(c) below should be followed. However, in such cases a detailed written description of the circumstances and copy of the consent form used must be submitted to the IRB within five (5) working days.

(c) Emergency Use of a Test Article

Emergency use is defined (in FDA regulations) as “the use of a test article (e.g., investigational drug or biologic) on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval for the use.” If an unapproved drug or device is used for patient care under emergency circumstances then the IRB must be informed of the use and the circumstances justifying the use, in writing, within five (5) working days of the occurrence. The IRB Chairperson shall review each report of emergency use of a test article to confirm that the emergency use was justified. The IRB Chairperson shall inform the physician, in writing, and shall report to the IRB at its next convened meeting his/her findings with regard to instances of “emergency use.”

(d) Repeated Emergency Use of a Test Article

It is intended that normally there will be only a single emergency use of a test article for treatment of one patient by one physician in the University. If it can be anticipated that similar emergencies will require subsequent use of the test article at the University, an application should be written (or the sponsor’s application should be signed on to) and in either case

submitted to the University IRB for its review and approval by its usual procedures (Section II.F.(3))

(e) Informed Consent

Written informed consent, signed by the patient or appropriate legal guardian, should be obtained for compassionate use of an unapproved drug, device or procedure even in emergency use situations. Compassionate use of an unapproved drug or device without informed consent is permitted when the following four conditions all prevail: (1) life threatening situations necessitating the use of the test article; (2) patient is unable to provide effective consent because of inability to communicate; (3) insufficient time to obtain consent from patient's legal representative; (4) no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the patient's life. Under these circumstances two physicians (at least one of whom is not involved with research on the test article in any manner) must certify in writing that the four (4) conditions listed here all exist (21 CFR 50.23(a)). If in the physicians' opinion immediate use of a test article is required to preserve the patient's life, and time is not sufficient to obtain an independent physician's determination that the above four (4) conditions apply then the physician may use the test article, but must within five (5) working days of use of the test article have the determination reviewed and evaluated in writing by an independent physician who is not involved in studies related to the test article. The physician using the test article must notify the IRB within five (5) working days after use of the test article (21 CFR 50.23(c)).

(12) Notification of Investigations of Determinations or Requests of the IRB

All official notification of IRB actions shall be in writing and sent to the individual listed as "Principal Investigator." With the exception of Compassionate Use requests of an emergency nature, oral communications shall not be regarded as valid. In the case of Compassionate Use requests in emergency situations, oral requests for approval must be followed up by a written summary within three working days.

(13) Institution and Departmental Review of Research

Research involving human subjects that has been approved by the IRB may be subject to prior or further review and approval or disapproval by divisional, departmental, or institutional officials or committees. These officials or committees may not override IRB disapproval of or restrictions on research proposals.