The University of Chicago Division of Biological Sciences
The Pritzker School of Medicine
and
The University of Chicago Medical Center

Institutional Review Board (IRB) Policies and Procedures Manual

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REVISED: August 6, 2026
Effective: October 27, 2026

Approved by IRB Committee A on August 11, 2026
Approved by IRB Committee B on September 22, 2026
Approved by IRB Committee C on August 19, 2026
Approved by IRB Committee D on September 10, 2026

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"Research with human beings plays an essential part in combating disease and in expanding the frontiers of knowledge."

The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, Protecting Human Subjects -- The Adequacy and Uniformity of Federal Rules and Their Interpretation. (Washington, D.C., December 1981)

I. INTRODUCTION AND IRB OVERVIEW

The University of Chicago Division of the Biological Sciences (BSD) and The University of Chicago Medical Center (UCMC) have previously established an Institutional Review Board (IRB) in accordance with federal regulations governing the use of human subjects in research. Effective January 2002, the Department of Health and Human Services (DHHS) approved the division of the BSD IRB into three independently constituted Committees. Effective April 2026, the Department of Health and Human Services (DHHS) approved the addition of a fourth independently constituted Committee. Unless specified otherwise, "IRB" in this document will refer to the four BSD/UCMC IRB Committees collectively.

The IRB support office is located within the office of the Dean of the Biological Sciences Division.

The Dean of the BSD has the responsibility for enforcing IRB decisions and recommendations based on federal and institutional policies and procedures.

The IRB support office is physically located in the University of Chicago Medical Center. The Director of Regulatory Compliance for Human Subject Research can be reached at (773) 702-6505. If there are questions or concerns related to IRB activities, the IRB staff can also be reached at (773) 702-6505. The IRB office hours are 8:30 AM to 5 PM Monday through Friday.

This manual pertains to the policies and procedures of the BSD/UCMC IRBs. References to "the IRB" in this manual apply to the BSD/UCMC IRBs. Research for which the University of Chicago has ceded review to another IRB should comply with the relevant policies and procedures of that IRB.

A. IRB RESPONSIBILITIES

The IRB is charged by the University with the responsibility for review and surveillance of research involving human subjects carried out in the BSD and UCMC or by a BSD/UCMC investigator. Review and surveillance are conducted to assure the protection of the rights and welfare of all research subjects, including volunteers and patients. The ethical principles which guide the IRB are consistent with *The Belmont*

Report. The IRB policies and procedures comply with the rules and regulations of *The Federal Policy for the Protection of Human Subjects* (56 FR 28003; often referred to as the "Common Rule"), the Department of Health and Human Services (DHHS) (45 CFR Part 46), and the Food and Drug Administration (FDA) (21 CFR Parts 50 and 56, Part 812 Subpart D).

The BSD/UCMC IRB(s) operates under the University's Federalwide Assurance (FWA) (FWA00005565), negotiated with the Office of Human Research Protections (OHRP). This Assurance authorizes the University to conduct human subject research and authorizes the BSD/UCMC IRB(s) to oversee research. To that end, the IRB is granted the authority to approve, modify, or disapprove studies, as well as to require progress reports, oversee the conduct of ongoing research, and suspend, terminate approval, or place restrictions on active studies in the consideration of human subjects protection. The Social and Behavioral Sciences Division IRB of the University of Chicago also operates under this FWA; the Social and Behavioral Sciences Division IRB has its own policies and this IRB is not covered under this policy manual.

On July 14, 2009, DHHS regulations requiring registration of IRBs went into effect. The DHHS regulations at 45 CFR 46, subpart E, and 21 CFR 56.106 require all IRBs to register with HHS if they will review human subjects research conducted or supported by DHHS. All IRBs are to be designated under an FWA. The OHRP IRB registration system is compatible with the requirements of both the OHRP and FDA regulations. Consequently, registration with OHRP fulfills the regulatory requirements for both the OHRP and FDA regulations. The University of Chicago BSD/UCMC IRBs' federal registration numbers are as follows:

IRB Committee A: IRB00000331
IRB Committee B: IRB00000735
IRB Committee C: IRB00002169
IRB Committee D: IRB00015086

The revised Common Rule (known as the "2018 Common Rule") went into effect January 21, 2019. The revised Common Rule applies to research approved or determined to be exempt from review on or after January 21, 2019. Protocols approved or determined to be exempt prior to January 21, 2019 will remain under the 1991 Common Rule unless the IRB determines at time of continuing review that the study will transition to the 2018 Common Rule requirements.

All clinical or behavioral research in the BSD or UCMC conducted by University of Chicago investigators and involving human subjects, regardless of its source of financial support, must be approved by the IRB unless the IRB determines it to be exempt from their review or the University determines that review by another IRB may be accepted in lieu of BSD/UCMC IRB review. In addition, research involving human subjects

conducted elsewhere by BSD and UCMC investigators must also be submitted to the IRB for review except as noted above. Individuals from outside the University of Chicago wishing to conduct research within the BSD or UCMC must have a BSD or UCMC collaborator who is willing to function as the principal investigator responsible for the research at this institution.

Research conducted at an institution for which the BSD/UCMC IRB has been appointed as the IRB for that institution may also fall under the purview of the University's FWA. Human subjects protocols conducted at these institutions require review by the BSD/UCMC IRB so long as they meet the definition of human subjects research and are not otherwise excepted from the policy as noted above.

Investigators wishing to conduct research at the Friend Family Health Center (FFHC) must seek and receive approval from the FFHC to conduct research at that location, in addition to approval from the BSD/UCMC IRB.

Many multi-center research projects will require review and approval of a Central IRB, or "single IRB," of record. In these cases, the University of Chicago may rely upon an external IRB. However, the IRB office should be consulted for assistance in the processing of the reliance agreement. In addition, Institutional sign-off will be needed prior to the start of the research activities at the University of Chicago. Please contact the IRB Reliance team at irbreliance@bsd.uchicago.edu for further assistance.

No institutional committee, office, or official may permit human subjects research to proceed that has not been approved or exempted from review by the IRB or a designated external IRB.

Scientific review is performed at this institution by several committees, including the Protocol Review and Monitoring Committee (PRMC) (formerly the Clinical Trials Review Committee (CTRC)) and the Independent Scientific Advisory Panel (ISAP) of the General Clinical Research Center (GCRC). A GCRC member is invited to be present during the IRB review of any GCRC-reviewed protocols. In addition, IRB approval cannot be granted to protocols requiring PRMC review without the prior approval of the PRMC. A protocol must be reviewed by the PRMC prior to IRB review. However, while the IRB may take the recommendations and advice of other committees into account, the IRB makes the final determination regarding the approval of studies submitted for its review.

In the event that scientific merit is not considered by a Committee external to the IRB, the IRB may assume the responsibility to determine scientific merit of a proposal. The IRB may also determine during its review of a proposed research study that scientific merit must be determined by an external review committee. The IRB may recommend

that the ISAP or another review committee determine scientific validity prior to study approval.

The IRB can make determinations as required by the HIPAA regulations, including approving a waiver of authorization.

B. IRB MEMBERSHIP

The BSD/UCMC IRBs follow the IRB membership requirements as outlined at 45 CFR46.107 and 21CFR56.107. No IRB meeting will be conducted without the necessary quorum, and no Committee decisions will be made lacking the vote of at least one non-scientist and at least one scientist. If a quorum fails for any reason, no further actions are taken until quorum is restored.

The IRB membership in each Committee (Committees A, B, C and D) is comprised of faculty members from a broad range of disciplines and each Committee includes at least one community (unaffiliated) member, a member without scientific expertise, and at least one member with scientific expertise. In addition, non-faculty representatives from University and Medical Center Legal Counsel, Pharmacy, and Nursing serve as members of the IRB Committees. A member is considered "unaffiliated" if neither that person nor a member of the person's immediate family is employed by the University of Chicago or the University of Chicago Medical Center. A member is considered "non-scientific" if that person's primary profession or area of interest is in a non-medical and non-academic field. Alternate members parallel and complement the expertise of the primary members. Unless otherwise noted, "member" in this document will refer to any potential voting member of the IRB, whether designated as a primary or alternate member.

The University of Chicago is in compliance with the statutory requirement that a majority of the members (exclusive of the prisoner representative) have no association with prison(s) involved in research other than their membership on the IRB reviewing prisoner studies [45 CFR 46.304 (a)].

Membership reflects basic federal requirements for expertise and advocacy; additional members are added as necessary or appropriate to ensure protection of subjects of a particular population. The IRB may also call upon outside consultants as necessary for additional expertise on a particular topic. Outside consultants are expected to maintain the confidentiality of the research.

The Dean of the BSD will appoint the IRB Chair. The IRB Chair appoints Vice Chair(s) and appoints IRB members in consultation with Departmental leadership. Office of Clinical Research leadership may be consulted in the appointment of all IRB members, including the Chair. The term of membership is three years. All terms are renewable.

Committees may have a Vice-Chair who is called upon to serve in the Chair's absence. In rare instances, an ad hoc Vice-Chair is appointed by the Chair to allow for presiding authority in the absence of the Chair or Vice-Chairs. The ad hoc Vice-Chair is appointed for a limited time when necessary. Either the Chair or Vice Chair is empowered to lead the convened IRB meetings. Vice-chairs from the other Committees serve as alternates on each Committee; a vice-chair from any other Committee may substitute for an absent chair or vice-chair in presiding over an IRB meeting.

IRB members, both primary and alternate, are given initial training when appointed to the Committee and continuing training over the course of their membership. Primary and alternate members receive the same initial training and identical opportunities for continuing training.

Removal of IRB members and chairs from the Committee will be performed at their request, and a suitable replacement will be appointed as above. Members, including the chair and vice-chairs, may also be removed from serving on the IRB by the Dean, in consultation with the Chair, Dean of Clinical Research, and/or Director of Regulatory Compliance for Human Subjects.

C. APPEAL OF IRB DECISIONS

If an investigator wishes to make an appeal of any IRB decision regarding a protocol proposal or a previously approved protocol, the investigator must submit a formal request in writing to the IRB Committee. The appeal must include details as to the exact nature of the investigator's disagreement with the Committee decision and the basis for making a claim to overturn that decision, including supporting evidence. The thorough review of and discussion on every submission to the IRB by the Committee ensures that the Committee feels confident in decisions they have made; consequently, an investigator wishing to make an appeal must present sufficient evidence to persuade the Committee to reconsider their decision. Assessments regarding whether or not to bring a protocol back to the Committee for further review upon the appeal of the investigator will be made by the Director of Regulatory Compliance and the Chair, in consultation with Vice-Chair(s) and/or the Associate Vice-President for Research Administration.

If an appeal is considered to be insufficient for review by the full Committee, the investigator will be notified in writing. If the Committee does consider an appeal, the Committee's decision regarding the merits of the appeal will be conveyed in writing to the investigator following the meeting.

External institutions or authorities cannot override IRB decisions; only the IRB Committee itself can overturn its decisions.

D. IRB RECORDS

The IRB maintains records of all its proceedings, including minutes of each meeting, all correspondence, and all submitted protocols, amendments, consent forms, continuing reviews, unanticipated problems, and statements of significant new findings provided to subjects, as applicable per protocol, including a copy of the IRB-approved consent form for each protocol currently utilizing a written consent form.

IRB determination letters are issued in electronic format from the online submission system. The IRB staff have processes in place to ensure that determination letters accurately reflect the decisions of the IRB. No physical signature of an IRB representative is required on IRB determination letters.

Current and past rosters showing qualifications of members are maintained by the IRB office. Rosters are provided to OHRP per the requirements of 45 CFR 46 Subpart E and 21 CFR 56.106. Current membership rosters are available on the IRB website.

The IRB maintains records of its policies and practices in its Policies and Procedures Manual, Member's Handbook, and Standard Operating Procedures (SOPs). The IRB staff are responsible for writing and implementing the standard operating procedures for the BSD/UCMC IRB. New SOPs are written and implemented as needs arise.

Revisions to the Policies and Procedures Manual, unless editorial in nature or made at the request of a regulatory auditing body, require review by the IRB Committees prior to implementation. Revisions to the Member's Handbook and SOPs do not require approval by the IRB Committee(s) or other entities prior to implementation, unless otherwise specifically indicated.

The IRB follows all written procedures for:

1. conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution
2. determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review
3. ensuring prompt reporting to the IRB of changes in research activity, and
4. ensuring that changes in the approved research, during the period for which IRB approval had already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazard to the human subjects.

The IRB also follows all written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of:

1. any unanticipated problems involving risks to human subjects or others,
2. any instance of serious or continuing non-compliance with federal regulations or the requirements and determinations of the IRB, or
3. any suspension or termination of IRB approval.

IRB individual protocol records are maintained a minimum of 10 years from the date of IRB expiration or termination of the study. Exceptions may be made on a case by case basis, dependent upon contractual obligations. IRB minutes are maintained indefinitely.

Relevant Federal Register notices, sections of the Code of Federal Regulations, and NIH and FDA policies, procedures, and regulations are available to faculty from the IRB office or from the IRB website. Scholarly and interpretive articles that pertain to research involving human subjects are also kept in the IRB office as reference items. Such materials are utilized by the IRB Chair, staff and the Committee, and are available for reference and educational purposes.

E. ADDITIONAL INFORMATION OR ASSISTANCE

Faculty orientation sessions on the involvement of human subjects in research and IRB policies and procedures are conducted at regular intervals; special instructional sessions can also be arranged. Periodic informational mailings are also sent to the faculty by email. To be added to the IRB list-serve, please contact the IRB office.

For further information concerning guidelines, related topics, or protocol preparation, submission, or management, please call the IRB office at (773) 702-6505 or send an email to bsdirb@bsd.uchicago.edu. The IRB office is open 8:30 to 5:00, Monday through Friday. Messages received outside these hours will be addressed during business hours.

This manual is available on the IRB website at https://biologicalsciences.uchicago.edu/irb-home. Additional materials are also available on this website. The website may be consulted for information at any time, including during non-business hours.

II. PRINCIPAL INVESTIGATORS, CO-INVESTIGATORS, AND OTHER RESEARCH PERSONNEL: ELIGIBILITY AND RESPONSIBILITIES

The Principal Investigator (PI) is responsible for the overall conduct of the study for each human subject research protocol on which the investigator is the named PI. This includes any modifications to the original submission. Investigators may not initiate or change research protocols until they have received IRB approval or exemption and may not continue ongoing programs without satisfying the federally-mandated periodic IRB continuing review requirement to assure that the research remains appropriate for human subjects and that the rights of these subjects remain fully protected.

Correspondence from the IRB is directed to the PI, who is then responsible for sharing any necessary information with study co-investigators or staff.

A. PI ELIGIBILITY

In accordance with University Policy, "Principal Investigator Eligibility," individuals who are eligible to serve as PIs on proposals for external funding may also serve as principal investigators on IRB protocols. In general, these are individuals who have faculty or other academic appointments at the University of Chicago. Please see the University Research Administration (URA) guidelines for more information on this policy.

Individuals who do not have the appropriate faculty appointment may conduct research under two conditions. First, individuals who do not have the appropriate appointment may request special permission to serve as PI on a protocol. There should, however, be a compelling reason why this individual should be allowed to serve as PI. Representative(s) of the BSD Dean's Office review requests for special PI status. Approval to serve as PI is granted by the Dean. To request special PI status, the departmental chair should follow the same procedure used to request special PI status for externally sponsored grants and contracts [please see URA guidelines for more information]. The IRB may require notification from URA indicating that the individual has been approved to be the PI for the research protocol before accepting a submission for review from that individual.

Alternatively, individuals without the appropriate appointment to serve as PI (for example, research associates with the parenthetical rank of Instructor, fellows, residents, nurses, students or other staff members, as well as individuals from outside the University of Chicago) should collaborate with a faculty member who is interested in conducting and overseeing the study. The faculty member must abide by the PI responsibilities outlined in this document, including signature requirements. The faculty member will be designated as PI for the protocol; all others are listed as Co-Investigators or Other Research Personnel. It is the faculty member listed as PI who is

ultimately responsible for the conduct of the study and to whom correspondence will be directed.

B. CO-INVESTIGATORS AND OTHER RESEARCH PERSONNEL

Any investigator engaged in human subjects research (other than the PI) must be designated as a Co-Investigator or Other Research Personnel in the IRB submission. Research personnel should be designated with the original submission or with an amendment if added or removed after original approval. An amendment must be submitted when personnel are added to or removed from the protocol. Only the named and approved research personnel may carry out procedures performed upon research subjects or research with identifiable human data. Accordingly, anyone having direct contact with the subjects or their data (obtaining consent from subjects, recruiting of subjects, administering questionnaires and surveys, conducting clinical interventions, performing data analysis, etc.) must be listed on the protocol. The PI must take direct responsibility for the activities of all research personnel.

C. TRAINING

Investigators who have not previously served as PI on a study at the University of Chicago BSD must complete the required training for all investigators. This should be done prior to submitting a new study to the IRB. New research personnel, including co-investigators and other research personnel, should complete training prior to being added to an approved protocol.

All research personnel listed on non-exempt research studies must abide by the Clinical Research Policy 110 "Faculty and Staff Training Requirements for the Conduct of Clinical Research," effective June 30, 2010. Investigators may complete the human subjects protections training offered online through the CITI program or equivalent training as determined by this policy. In addition, investigators are encouraged to attend a session of the human subjects protections training offered by the IRB office as well as any other training sessions offered on specific research issues that may arise each year.

For any studies funded by the National Institutes of Health (NIH), human subjects protections training is **required** for all key personnel.

The IRB will confirm that an investigator is eligible to be the PI and has completed all necessary training prior to approving any submissions from that investigator.

D. RESPONSIBILITIES OF PRINCIPAL INVESTIGATORS

The principal investigator is held responsible for ensuring that a protocol is conducted

in accordance with the research plan and with all applicable regulations. Consequently, it is the responsibility of the principal investigator to:

- protect the rights and welfare of human subjects and ensure ethical performance of the project;
- provide the IRB with complete and correct information on the research protocol including initial information, notification of subsequent modifications, terminations, and unanticipated problems, and utilize the appropriate IRB format and forms for supplying this information;
- ensure that no research will be initiated until IRB approval is received;
- carry out the protocol as approved, initiating modifications only after the IRB has approved the amendment;
- ensure the timely completion and submission of any continuing review materials;
- report in writing to the IRB any unanticipated problems involving risks to subjects or others in accordance with the IRB policy;
- obtain appropriate informed consent from subject(s), if consent is a requirement;
- ensure that all procedures in approved protocols (including the consent process) are performed by authorized personnel;
- maintain confidentiality of all records;
- keep appropriate records, including if applicable names and access information for all research subjects;
- note subject's participation in a research protocol in the medical record, establish a medical record if none exists, and ensure that the original consent form is inserted, if applicable;
- be aware of current IRB policies and procedures; and
- complete all necessary training and ensure that listed personnel have completed all necessary training, including human subjects protections training as per BSD policy and HIPAA compliance as applicable per UCM requirements.

The IRB will direct original correspondence to the principal investigators, with exceptions on a case-by-case basis. It is the responsibility of the investigator to ensure that copies of IRB letters are distributed to appropriate individuals (e.g., grant and contract administrators, department administrators, granting agencies or pharmaceutical sponsors, other sites, etc.).

If the protocol is externally funded, the PI should receive a fully executed agreement before work on the research project can begin.

Note that while payments to subjects are allowable and appropriate, the BSD/UCMC IRB does not consider special incentive or recruitment payments to physicians or other

study staff appropriate beyond the per patient payments to the University for the conduct of a clinical trial. UCM personnel are also strictly prohibited by the Code of Conduct from offering anything of value to any organization, entity, or individual (including vendors, providers, other hospitals, etc.) with the intent to induce or encourage referrals of any business or patients to or from the UCM or outside facilities.

1. TERMINATION OF A PROTOCOL

Investigators should terminate a protocol when human subjects are no longer being followed or studied. As long as subjects are still being followed at this site, even if the protocol is closed to subject accrual, or if data is still being analyzed, even if not being actively collected, a protocol is considered active and continuing review may be required. If no subjects are being followed and data analysis is complete, the study may be officially terminated. When research has been terminated, the responsible investigator must notify the IRB.

When faculty members leave the University, they should either terminate their protocol(s) or submit an amendment for each approved study indicating that the protocol(s) should be transferred to another investigator who will take responsibility for the research. See next section.

If the IRB discovers that an investigator has left the University of Chicago but that this PI's studies have not been terminated through the IRB, the IRB staff may contact the PI's former department chair or departmental administrator to verify that studies are not currently active. IRB staff will also verify that the study or studies in question are not in the process of being transferred to another investigator through the amendment process. Depending on the departmental response, the IRB will then administratively terminate any remaining studies listed under the name of the departed PI.

2. TRANSFERRING A PROTOCOL TO ANOTHER INVESTIGATOR

When an investigator chooses to transfer a status as principal investigator on an approved protocol to another investigator, the IRB must be notified. The new investigator must be eligible to serve as Principal Investigator (see Section II). To effect this transfer, an amendment should be submitted to the IRB. The new principal investigator should provide adequate documentation to acknowledge that this investigator is now responsible for the study. Appropriate changes to consent forms, advertisements, and other relevant study documents must also be submitted to the IRB when transferring a protocol. The amendment should specify whether the original investigator will remain on the study as a member of the research team.

The new PI will be notified if and when the amendment is approved.

3. UNANTICIPATED PROBLEM REPORTING

Investigators are required to promptly report to the IRB all unanticipated problems involving risks to human subjects or others under Title 21 of the Code of Federal Regulations (21 CFR) part 56 (Institutional Review Boards), part 312 (Investigational New Drug Application), part 21 CFR 320.31(d)(3) (IND-exempt Bioavailability/Bioequivalence (BA/BE) Studies), and part 812 (Investigational Device Exemptions) as well as under 45 CFR 46.108(a)(4). Sponsors and investigators should differentiate those unanticipated problems that must be reported to the IRB and those that do not, under this policy. The University of Chicago policy is consistent with guidance set forth by OHRP (Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, presented January 15, 2007) and the FDA regulations when determining what related events require review by the Institutional Review Board.

FDA guidance provides specific criteria for which events require reporting to the IRB. Please see the IRB website for more information about FDA guidance on this topic.

Unanticipated problems involving risks to subjects or others refer to a problem, event or information item that is not expected, given the nature of the research procedures and the subject population being studied; and which suggests that the research places subjects or others at a greater risk of harm or discomfort related to the research than was previously known. The IRB considers unanticipated problems, in general, to include any incident, experience, or outcome that meets **ALL** of the following criteria:

1. **unexpected** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol, investigator's brochure, drug or device product information, informed consent document, or other research materials; and (b) the characteristics of the subject population being studied, including underlying diseases, behaviors, or traits;
2. **related or possibly related** to participation in the research (possibly related means there is a **reasonable** possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
3. **suggests that the research places subjects or others at a risk of unknown harm or addition/increased frequency of harms** (including physical,

psychological, economic, legal, or social harm) than was previously known or recognized.

Unanticipated problems may be adverse events, protocol deviations, noncompliance or other types of problems, but **must** meet all of the criteria listed above. It is the expectation of the IRB that all approved protocol procedures are being followed without alteration unless the IRB has been informed of a protocol change or deviation.

When reviewing a particular incident, experience, or outcome reported as an unanticipated problem by the investigator, the IRB may determine that the incident, experience, or outcome does not meet the criteria for an unanticipated problem.

Unanticipated problems occurring in research that is federally funded may or may not require further reporting to appropriate institutional officials, the department or agency head (or designee), and OHRP. The IRB has the authority, under HHS regulations at 45 CFR 46.109 and 21 CFR 56.109, to require, as a condition of continued approval by the IRB, submission of more detailed information by the investigator(s), the sponsor, the coordinating center, or DSMB/DMC about any unanticipated problem occurring in a research protocol.

It is the responsibility of the investigator to ensure that written notification of unanticipated problems is submitted to the IRB. The investigator should complete an "Unanticipated Problem" report form with electronic signature and attach any additional information necessary in evaluating the report (such as laboratory or autopsy reports). All other events or adverse events that do not meet reporting criteria can be submitted as a summary at the time of continuing review.

In reviewing the unanticipated problem, in order to ensure adequate protection of the welfare of subjects, the IRB will consider whether the event impacts the risk/benefit ratio and may need to reconsider approval of the study, require modifications to the study, or revise the continuing review timetable. Furthermore, the IRB may suspend or request further changes to an individual study due to safety concerns.

The IRB retains submitted unanticipated problem reports. Notification of review of these reports is sent to the PI.

All internal and external Unanticipated Problems must be reported to the IRB in a timely manner following the investigator's knowledge of the event. For internal events that are fatal or life-threatening Unanticipated Problems, the PI should

notify the IRB Chair by phone immediately and consider voluntarily halting subject enrollment.

For device studies, investigators are required to submit a report of an unanticipated device effect to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event. Unanticipated device effects are defined as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects" (21 CFR 812.3(s)).

4. REPORTING UNANTICIPATED CHANGES TO THE PROTOCOL

The federal regulations require the IRB to review and approve proposed changes to research studies prior to initiation of these changes, except when changes are "necessary to eliminate apparent immediate hazards to the subject" [45 CFR 46.108(a)(3)(iii)/21 CFR 56.108(a)(4)]. The majority of proposed changes are reviewed through submission of amendments. Any changes that are made to eliminate apparent immediate hazards to a subject should be reported as an Unanticipated Problem to the IRB and an amendment should be submitted as soon as possible to change the protocol to eliminate future hazards of this type, as appropriate.

In the event that such a change is implemented to eliminate immediate hazards to a subject, enrollment of new subjects should be halted until the IRB has had an opportunity to consider such changes. The reviewer may also recommend that the subjects on the study be provided specific information about the change and the cause of the change.

5. REPORTING DEVIATIONS

An IRB is asked to ensure prompt reporting of serious or continuing noncompliance with regulations or noncompliance with the IRB's own requirements/determinations [45 CFR 46.108(a)(4)(i) and 21 CFR 56.108(b)]. Deviations from the approved protocol may fall into this category of noncompliance. A protocol deviation occurs when the study departs from the IRB-approved protocol in any way without the investigator first obtaining IRB approval.

Deviations range in seriousness according to how the changes may impact subject safety, the degree of noncompliance with federal and state regulations, and the degree of foreknowledge of the event. Anticipated changes to a protocol should always be reported prior to the event occurrence unless an immediate change is necessary to protect subject safety. Repeated deviations of the same type may be an indication that an amendment is needed to permanently change study criteria.

A major deviation is one that may impact subject safety or alter the risk/benefit ratio, compromise the integrity of the study data, and/or affect subjects' willingness to participate in the study. Major deviations should be reported as Unanticipated Problems. A description of the effect of the deviation on subject safety and a description of how similar events will be avoided in the future should be provided.

A minor deviation is one that does not impact subject safety, compromise the integrity of the study data, or affect subjects' willingness to participate in the study (i.e. non serious and non continuing). Minor deviations should be summarized at the time of continuing review on the continuing review form.

6. REPORTING NONCOMPLIANCE

Investigators and research staff are expected to promptly report any observed serious or continuing noncompliance with approved research procedures, IRB policies, or federal regulations to the IRB. Reports should be made as an Unanticipated Problem within 2 working days of observed serious noncompliance or immediately after continuing noncompliance is observed.

The IRB office will review the report and forward to the IRB chair and Committee, taking into account conflicts of interest, as appropriate. The IRB Chair and/or Committee will review any report of serious or continuing noncompliance and any relevant information prepared by the IRB staff and will make a determination regarding further action. Investigators are advised that the IRB Committee is authorized and required to report noncompliance to the Associate Vice-President for Research Administration who is the University of Chicago's Institutional Official. The Institutional Official, on behalf of the institution, is required to report serious noncompliance directly to federal regulatory agencies.

The IRB will attempt to respect the confidentiality of informants as requested or as the situation warrants.

7. REPORTING CONFLICT OF INTEREST

If there is a known or potential conflict of interest at the time of IRB submission, investigators are asked to detail the nature of the conflict with the initial submission. Any subsequent change to this status as related to a protocol should also be brought to the attention of the IRB. In addition, any new conflicts of interest which arise from the PI or any co-investigator(s) should be brought to the attention of the IRB as soon as possible. The IRB will coordinate with the Institutional Official or designee as to the appropriate measures or protections to be implemented or that may have already been implemented to manage the conflict of interest.

8. RESEARCH RECORDS

It is required that all research records (including a copy of all materials submitted to the IRB) be maintained by the investigator. The permanent record of research done on each subject consists of signed consent forms together with the names and access information for all subjects, other research data, budget and accounting records, and the subjects' medical records, as applicable. If subjects are asked to provide additional documentation of consent during the study, for example, when new risks are discovered that may affect willingness to continue participation, these consent records should be retained in the same manner as the original consent documentation.

Records should be kept confidential to the extent required by the protocol and, as applicable, the consent form. All research records should be stored in a manner compliant with BSD record retention policies. All research records that are subject to HIPAA must be stored in a HIPAA-compliant manner.

If the investigator leaves the University of Chicago, the records must be kept at the University in the hands of the designated investigator taking over the study, and the IRB should be notified of the transfer prior to the investigator's departure.

The records shall be accessible for inspection and copying by authorized representatives of the Department of Health and Human Services, the Food and Drug Administration, funding agencies, and/or the sponsor at reasonable times and in a reasonable manner.

Record retention requirements will vary depending upon the type of research, sponsor requirements, relationship to intellectual property protection, and federal requirements. The research team is required to maintain a copy of each signed consent form for federally-funded studies for a minimum of three years

after the completion of the research (as defined by the last publication related to the study). This minimum requirement may be superseded by other record retention requirements. HIPAA regulations require that authorizations (e.g., any consent/authorization form) be kept for at least six years. For FDA-regulated studies, materials must be maintained for two years following the date of marketing application approval for the device or drug for the indication for which it was being investigated. Finally, the Illinois Hospital Licensing Act recommends retaining records for a "period of 10 years after the most recent patient care usage." In most cases, this 10 year requirement will ensure compliance with federal or industry sponsor requirements.

The HRPP recommends retaining records for at least 10 years following termination of the study.

III. PREPARING A NEW SUBMISSION

A. DETERMINING "RESEARCH INVOLVING HUMAN SUBJECTS"

Activities performed by physicians outside of the clinical context may or may not meet the definition for research involving human subjects. Per 45 CFR 46.102(l), an activity is considered to be "research" if it involves a "systematic investigation designed to develop or contribute to generalizable knowledge." Activities not systematic, not designed to contribute to general knowledge, or done only for personal use (i.e. not shared with anyone else, including other members of the department) do not meet this definition.

Per 45 CFR 46.102(e), research is considered to involve "human subjects" if it entails obtaining information about living individuals, either through intervention or interaction with the individuals or if the research involves the use or receipt of individually identifiable information, including biospecimens, originally obtained in a context in which the individuals could reasonably expect privacy.

In order for research to be subject to FDA regulations, it must be a "clinical investigation," which is defined as "any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit… The terms 'research,' 'clinical research,' 'clinical study,' 'study,' and 'clinical investigation' are deemed to be synonymous for purposes of this part" (21 CFR 56.102(c)). A "human subject" "means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient" (21 CFR 56.102(e)).

The IRB follows the regulatory definitions when considering whether a project is subject to IRB review as research involving human subjects. When defining "individually identifiable information," the IRB considers data to be "de-identified" if all elements of protected health information as defined by HIPAA have been removed. Per institutional practices, use of clinical notes in the medical record for research purposes would be considered use of identifiable data and would be subject to IRB review.

If a research project involves private information or biological specimens obtained from living individuals, please consult NIH guidance of June 6, 2005 as to whether this research requires IRB review.

If it is unclear as to whether an activity meets the regulatory definition of human subjects research, the IRB staff can assist in making this determination. If the IRB staff finds that the activity does not constitute human subjects research, the staff will, upon request, issue documentation stating that the activity does not require IRB review or approval. No further review of the project is required, unless aspects of the project change so that it then becomes research involving human subjects.

If investigators propose a quality improvement (QI) or quality assurance (QA) project, they may also contact the Center for Healthcare Delivery Science & Innovation, who can issue a determination that the project does not involve research.

Quality Assurance (QA) processes often involve reporting on a large number of individuals. Quality Assurance projects are done to verify the quality of current hospital tests or procedures. These are usually designed to contribute to generalizable knowledge, and as such many QA projects could be considered research (per the regulatory definition) and are therefore subject to IRB review if the project involves human subjects.

Note that federal, state, or local laws or regulations may apply to activities whether or not they meet the definition for research involving human subjects as outlined by 45 CFR 46 and 21 CFR 56.

1. DECEASED INDIVIDUALS

   The Health Insurance Portability and Accountability Act (HIPAA) Security and Privacy regulations [45 CFR 160, 164] apply to individuals both living and deceased. Thus, if any protected health information as defined by the HIPAA regulations is collected about deceased individuals, additional protections for subjects may be necessary before beginning a proposed activity (even if the activity does not otherwise qualify as human subjects research) in order to comply with HIPAA.

B. EXEMPT RESEARCH PROTOCOLS

The federal guidelines (45 CFR 46) under which the IRB operates specify certain types of non-FDA regulated protocols that qualify as "exempt" and may be pursued without IRB approval. These protocols involve research with no more than minimal risk to human subjects. Exemptions from IRB review do not typically apply to research involving prisoners.

Institutional policies require that the IRB or its delegates determine whether research qualifies as "exempt." Faculty may not make this determination.

Specific criteria are defined for research in the exempt categories, which are as follows.

1) "Research conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods."

2) "Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review." *Due to the requirement for "limited IRB review," requests for exemption under 2iii will be processed using expedited review procedures. See Section VIII.C.*

Please note: The exemption for research involving survey or interview procedures or observation of public behavior does not apply to research with children covered by Subpart D, except for research under 2(i) or 2(ii) involving educational tests or observations of public behavior when the investigator(s) do not participate in the activities being observed.

3) "Benign behavioral interventions:
(i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(A) the information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
(B) any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
(C) the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to subjects, and an IRB conducts a limited IRB review. *Due to the requirement for "limited IRB review," requests for exemption under 3ic will be processed using expedited review procedures. See Section VIII.C.*

(ii) In addition, benign behavioral interventions must be brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing."

Please note: The exemption for research involving behavioral interventions does not apply to research with children covered by Subpart D.

In addition, research utilizing deceptive techniques is not typically exempt under this category.

4) "Secondary research for which consent is not required: Secondary research uses of identifiable private information or biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;
(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify the subjects;
(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information regulated by HIPAA; or
(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information (subject to additional federal regulations)."

The exemption for research at 4iii that involves only information collection and analysis involving the investigator's use of identifiable health information regulated by HIPAA

would require review by a HIPAA Privacy Board. As the University of Chicago does not have a distinct HIPAA Privacy Board, the exemption at 45CFR46.104(d)(4)(iii) will not be applicable for BSD research.

5) "Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads, and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs."

Please note: The Federal department or agency conducting or supporting the research is required to establish a list on a publicly accessible website of the research that is conducted/supported under this exemption category.

6) "Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for use found to be safe by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture."

To request status as an "Exempt" protocol, an investigator will be asked to indicate the category of exemption to which the researcher believes the research belongs. In addition, documentation should be included to support the assertion that the protocol qualifies for exemption (e.g. description of the data to be used, whether data will have identifiers, etc.). As applicable, the P.I. should submit any surveys to be used in the research and a copy of any consent script or document to be used.

If a protocol is found to be exempt from review, the investigator will be notified in writing. If the protocol does not qualify for the exempt category, the investigator will be notified. A complete protocol submission must then be submitted for consideration for approval by the IRB if the investigator wishes to pursue the project.

C. PROTOCOL SUBMISSION PROCESS

All non-exempt research involving human subjects conducted in the BSD and UCMC or by members of the BSD and UCMC must be submitted to the IRB for approval prior to initiation. IRB submission forms, policies, and procedures are periodically revised to ensure that all current regulatory requirements are met, and that the IRB has information needed for a complete review of the research. The current versions of the IRB submission forms are available by linking through the IRB website to the online

submission system. The IRB website is also regularly updated to include revised or new policies and procedures. When preparing a protocol, it is advisable to consult this website and/or contact the IRB staff for assistance in order to ensure an acceptable submission. Review of a protocol may be delayed if further information is required.

The principal investigator should submit all relevant materials. Protocols may be submitted at any time. When the submission is complete, it will be assigned for review either to an IRB reviewer for expedited review or to an agenda for review at an IRB meeting, as applicable. A schedule of IRB Meeting dates is available from the IRB office and on the IRB website. The IRB Chair and/or IRB Director may remove any submission from an IRB meeting agenda, regardless of submission date, if additional information or documentation is needed, if there is a conflict of interest, or for another stated reason.

If documentation required to complete review of a protocol has not been submitted, administrative staff will inform the research team in writing. Failure by the research team to respond to requests for revisions to meet regulatory or local policy requirements within 60 days may result in withdrawal of the protocol submission from further review.

D. PROTOCOL APPLICATION CONTENTS

To be considered complete, a protocol should include the Protocol Submission Form, a detailed description of the research plan (also known as the written protocol or detailed protocol narrative), written consent form or request for other consent method, and other supplemental documentation as described below.

1. PROTOCOL SUBMISSION FORM

The Submission Form is designed to highlight areas of IRB concern. Therefore, the form should provide an accurate and complete summary of the research project. In addition, consistency between the submission form, protocol, and supporting information is critical. Investigators should also demonstrate, whether in the protocol or a grant application submitted with the new protocol materials, that they have access to the necessary support services and facilities to conduct the research, in addition to the necessary professional qualifications.

If there are additional costs to subjects as a result of participation, such as additional copays as a result of additional charges to their insurance, this should be outlined in the submission.

All new protocol submissions must include the investigator's signature (physical or electronic).

2. DETAILED PROTOCOL NARRATIVE

The protocol narrative must be sufficiently detailed to permit the IRB to evaluate the soundness of the procedures proposed and the potential risks and benefits to research subjects. Please see guidance on the IRB website for an outline of appropriate sections to include in a written protocol narrative. The IRB office may refuse to process a new submission lacking a sufficient protocol narrative until such time as a sufficient protocol is provided.

For clinical trials, the latest version of the sponsor protocol must be provided for review.

It is a policy of the National Institutes of Health that all research involving human subjects includes women, minorities and children. All protocols that explicitly exclude any of these populations must provide sufficient rationale for the exclusion of such. Sufficient rationale might include a discussion of the inappropriateness of the study population with respect to the health of the subjects or the purpose of the research. The expectation that additional costs may be incurred by including women, minorities, and/or children cannot be used as a reason for excluding these populations. Protocols involving children must conform to the requirements of 45 CFR 46 subpart D, "Additional DHHS Protections for Children Involved as Subjects in Research" and, if FDA regulated, 21 CFR 50 subpart D. Under the NIH policy, "child" is defined as a person under the age of 21 (http://grants2.nih.gov/grants/funding/children/children.htm). However, other federal and state regulations define "child" differently. The IRB policy defines children as individuals less than 18 years old.

3. INFORMED CONSENT PROCESS

All protocols must address the process by which both the informed consent and (if applicable) the authorization for use of protected health information of subjects will be sought, either by describing the consent process, including a request for waiver of consent, or a including request for a waiver of some or all of the requirements for consent. Accordingly, all new submissions must include one of the following:

a) a description of the informed consent process;
b) if oral consent is requested, justification for waiver of documentation of consent;
c) a justification for waiver of the consent process; or
d) a request for a non-emergency waiver of consent

AND

a) if the research involves accessing PHI:
   a. a written authorization form (can be combined with the written consent form)
   b. justification for waiver of authorization; or
   c. documentation that research data meet requirements for a limited data set; or
b) explanation as to why HIPAA does not apply to the research.

4. CONSENT FORM OR SCRIPT

For details of types of consent, see Section VI ("Informed Consent") and the IRB consent form template. Note that the IRB consent form template contains all required elements of informed consent as defined in 21 CFR 50.25(a) and 45 CFR 46.116(a-b) as well as required elements of a HIPAA authorization as defined in 45 CFR 164.508. This template is available on the IRB website.

Protocols that meet the criteria for emergency waiver of consent, use an Investigational New Drug (IND), or have an Investigational Device Exemption (IDE) must have written consent forms.

Submissions should include at least one of the following:
a) written consent/authorization form
b) a written summary and oral script for the short form consent process
c) a written script to be used for a waived consent process (such as an email script)
d) request for waiver of consent as described in above section.

5. OTHER RELEVANT MATERIALS

Additional materials may be required by the IRB in order to fully review a proposal. For all studies, other relevant materials may include:

a) entire grant application, if the protocol will be funded by a grant

The revised Common Rule removes the requirement that the IRB formally review the federal grant application or proposal for consistency with the protocol submitted to the IRB. Unless required by the Federal department or agency conducting or supporting the research, or by foreign, state, or local laws or regulations, the IRB will not conduct formal congruency review of Federal grant applications or proposals when research is subject

to the revised Common Rule. The IRB will, however, continue to require notification of the funding source in order to determine if additional requirements and/or regulations apply. The IRB may choose to request a copy of any applicable grant materials.

b) copies of IND/IDE information, if applicable (see Section IV)

c) investigative brochure or other material(s) provided by a sponsor concerning an investigational drug or device, if applicable

d) a copy of the package insert for approved drug(s) or device(s)

e) copies of all advertisements (including print, internet, radio, TV, or other means) or other methods of recruitment to be used

The IRB must review the exact wording to be used in advertisements except for the date and time the research is to be initiated. In most cases, advertisements should include the PI's name, the purpose of the research, brief eligibility criteria, a brief description of the benefits or payments to the subjects in the study, location of the research, its probable duration, and the person and phone number to contact for further information.

Advertisements may NOT include the name of the study drug or corporate sponsor and may not promise free medical care or free medication, emphasize payment or amount to be paid by such means as larger or bolded type, or contain therapeutic claims. With certain multisite studies, exceptions to this policy may be made at the discretion of the IRB.

Note that certain websites such as www.clinicaltrials.gov allow posting of minimal trial information. IRB review and approval of listings of clinical trials on the internet is not required when the system format limits the information provided to basic trial information, such as: the title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s); and how to contact the site for further information. Researchers wishing to list an approved protocol on such a website will not be required to have the IRB Committee review this request prior to posting the approved protocol on the website. In addition, information contained on www.clinicaltrials.gov may be copied and included on the U of C Medical Center Clinical Trials website without IRB approval (if such information is an exact duplicate of that posted on www.clinicaltrials.gov).

f) complete copies of any survey(s), questionnaire(s), interview(s) or other written testing instruments to be used

g) copy of PRMC approval letter, PRMC approval with documentation, or PRMC approved with revisions letter, if PRMC review is required

h) CRI feasibility memo, when applicable

i) other materials considered relevant by IRB staff or Committee. Please also see the next section.

E. PROTOCOL SPECIFICS AND POINTS TO CONSIDER

The protocol submission form should provide an accurate and complete summary of the research project and should be tailored to the specifics of the study. Certain types of research may require detailed documentation as noted below.

1. CHART REVIEWS: DETERMINING RETROSPECTIVE AND PROSPECTIVE DATA USE

Investigators wishing to conduct a review of medical records and/or other clinical records for **research** purposes should submit a proposal to the IRB. This proposal should include details concerning the source of the data, what type of information will be collected, including the identifiers to be used, how data will be recorded, if data will be shared, and the time period from which data originates.

Research use of medical record data requires review by the IRB.

"Existing data" is defined as data that exists at the time the research is approved by the IRB. This may include medical charts, x-rays, medical databases, biological specimens, or other clinically collected materials. This may also include data from another research study, if data collection is now complete on that study, or data originally collected for non-clinical purposes.

Research using only existing patient material is considered a retrospective study. **Retrospective studies should not be conducted without an IRB submission.** If prospective data, including outcomes that have not yet occurred, may be used in the research, investigators should specify in the submission that prospective data will also be used.

The IRB advises the use of written consent for the prospective collection of data from medical records.

2. CASE STUDIES

Data concerning one individual, their family, and/or environment, including medical history and any other information, collected for the purposes of analyzing and diagnosing the individual's condition or for instructional purposes, is considered a "case study." Although this case reporting does involve the intent to publish results, it does not involve a testable hypothesis. Consequently, the wish to publish a single case report is not considered to be research and the IRB does not require the submission of a protocol in order to publish the case report.

If more than one case occurs of the specific condition or medical anomaly, or the investigators begin to formulate a hypothesis or attempt to gather further information on cases of this type with the intent to publish the results, activities cross into what would be considered "research" and it becomes necessary to submit a research proposal to the IRB.

Although publishing a single case report may not require submission to the IRB, investigators should be aware of the use of individually identifiable health information in their publications. Under HIPAA, the disclosure of an individual's protected health information must be authorized by that individual. In other words, if a case report contains any identifiers as defined by the HIPAA regulations, authorization to disclose this information in a publication must be sought from the individual whose information is being disclosed. The subject must sign a consent form (or authorization) to disclose this information. Many journals now require authorization/consent from the subject of the article prior to publication.

Case reports often involve reporting on a rare disorder, condition, or course of treatment. In such cases, individuals may be more easily identified as being the subject of a publication than individuals with a more common disease or condition. Consequently, this rare disorder may fall under the category of "any other unique identifying characteristic" under the HIPAA regulations, and thus be considered Protected Health Information. Researchers must then obtain a subject's authorization before publishing a report, even when no other identifiers are being disclosed, because the subject may be able to be identified by their disorder.

3. GENETIC ANALYSIS

Genetic analysis includes both "genetic testing" done in a certified laboratory and "genetic research," including genetic analysis with unknown applicability. When any genetic analysis will be conducted as part of a research study, investigators should indicate this on the protocol submission form.

Investigators should consider whether results of these analyses are expected to result in genetic information related to the subject's (or relatives') health or susceptibility to a disease or condition currently or in the future, and if so, how this information would or would not be communicated to the subject and relatives, as applicable. If the study is approved with a written consent form, the consent form should describe who will have access to results, including whether results would be shared with the subject. In addition, the consent form should explain in lay language that if genetic material is collected and/or used on study, there is the possibility that whole genome analysis may be done on the sample.

Finally, language similar to the following should be included in the consent form:

"The Genetic Information Nondiscrimination Act (GINA)

The Genetic Information Nondiscrimination Act (GINA) is a federal law that may help protect you from health insurance or employment discrimination based on genetic information. GINA is a federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease."

4. DECEPTION AND WITHHOLDING OF INFORMATION

Deception is a research method that can improve the internal validity of a research study. The intention of deception is to produce a false belief in the participants during the course of the study. Incomplete disclosure of information

may also be used in research where telling the subject about some aspect of the study in detail might interfere with the ability to measure the outcome of interest. The use of deception and incomplete disclosure in human subjects research raises issues for the IRB to consider with regard to informed consent and analysis of risks and benefits. Unethical uses of deception in research can cause distress to those being deceived and may undermine public trust in the research enterprise.

Deception may be defined as an investigator giving false information to subjects or intentionally misleading them about some key aspect of the research. Examples include: participants complete a quiz, and are falsely told that they did very poorly, regardless of their actual performance or a study that includes a researcher's "confederate" (an individual who poses as a participant) but whose behavior in the study is actually part of the researcher's experimental design.

Incomplete disclosure may be defined as an investigator withholding some information about the real purpose of the study or the nature of the research procedures. An example is participants being asked to complete a task for research without being given an explanation of the purpose of the research.

The American Psychological Association's Ethical Principles of Psychologists and Code of Conduct guidelines on the use of deception and debriefing state that psychologists do not conduct a study involving deception unless they have determined that the use of deceptive techniques is justified by the study's significant prospective scientific, educational or applied value and that effective nondeceptive alternative procedures are not feasible. In addition, psychologists do not deceive prospective participants about research that is reasonably expected to cause physical pain or severe emotional distress and psychologists explain any deception that is an integral feature of the design and conduct of an experiment to participants as early as is feasible, preferably at the conclusion of their participation, but no later than at the conclusion of the data collection, and permit participants to withdraw their data.

Therefore, researchers proposing to use deceptive techniques or proposing to withhold information are asked to provide justification in the submission for the design of the study, including references for prior use of the technique and sufficient rationale to document why this method is necessary in order to conduct the research.

For research that plans to use deception or incomplete disclosure, the IRB may approve a waiver or alteration of the general requirements for informed consent if the study meets the regulatory criteria for a waiver or alteration of consent. Please see section VI.A. for these requirements.

Research involving deception or incomplete disclosure is recommended to include a debriefing session to inform subjects of the nature of the deception after they have completed participation in the research. A script for the debriefing session should be provided to the IRB and the submission form should describe who will perform the debriefing and at what time point. The IRB will decide on a case-by-case basis whether it is necessary to re-consent subjects to use study data obtained under deceptive premises. In cases that involve only incomplete disclosure, a debriefing form that gives additional information about the study but does not ask for re-consent may be acceptable. In contrast, when deception at the time of subject enrollment is likely to have influenced the subject's decision about whether to participate in the research, or when the deception would likely be perceived by the subject as an invasion of privacy, the subject's permission to use the research data may be required.

When appropriate, subjects could also be informed prospectively of the use of deception or incomplete disclosure and consent to its use. For example, the consent form could include language similar to the following:

"Some research requires that the full purpose of the study not be explained before you participate. We will give you a full explanation at the end of the study."

F. CONFLICT OF INTEREST

The PI is responsible for disclosure to the IRB at the time a protocol is submitted if any research personnel involved in the protocol have any outside financial interests that are or could be perceived to be related to the research as described in the protocol. See Section II. Please also refer to the URA website (http://ura.uchicago.edu/) for references to applicable University policy and practices, particularly the policy on "Outside Professional and Commercial Interests of Faculty/Conflict of Interest policy" (March 12, 1996), the Ad Hoc Faculty Committee Report on COI Policy (December 2003), and current University policies for disclosure of individual financial conflicts of interest.

The IRB will relay any conflict of interest disclosure to the Institutional Official (IO) and/or the IO's representative and coordinate with URA as to the appropriate measures or protections to be implemented or that may have already been implemented to manage the conflict of interest. Such measures typically include (but are not limited to) disclosure of both the outside interest and the nature of the relationship to the proposed study in the written consent form.

The IRB Committee receives a copy of any management plan prepared by URA for existing potential conflicts in order to aid in its review of the protocol.

The IRB Committee may consult the Deputy Provost for Research and/or the Provost's designee regarding potential conflicts of interest prior to review at a meeting; the Deputy Provost for Research issues a decision regarding appropriate conflict of interest disclosure or research restrictions. The IRB Committee may suggest additional disclosures as necessary. Investigators may respond with changes to conflict of interest recommendations made by the IRB, but the Committee must consult with the Deputy Provost for Research or designee on any changes made by the investigator(s) and may not overturn or modify any recommendations made by the Deputy Provost for Research without approval.

The IRB Committee may also consult the University's Office of Legal Counsel on conflict of interest issues. The IRB Committee has final authority to determine whether the management of a disclosed interest is sufficient to permit the approval of associated human subjects research.

IV. FDA REGULATED RESEARCH

FDA regulations apply to any research involving a drug, device, or biologic conducted in the BSD/UCMC or by a BSD/UCMC investigator.

A. INVESTIGATIONAL NEW DRUG (IND)

All research involving the use of unapproved drugs must be reviewed and approved by the full IRB Committee. This research never qualifies for expedited review and must utilize a written consent form. In addition, investigators or their study sponsors must have an Investigational New Drug (IND) application on file with the FDA and must have received an IND number. FDA IND applications may be obtained directly from the FDA. If the IND is held by a University of Chicago investigator, a copy of the FDA communication approving the IND and containing the assigned IND number should be forwarded to the IRB once received.

The protocol submission form must provide the drug name, IND #, and name of the company manufacturing the drug. The investigator's brochure provided by the company sponsor and any other background information must also be included as part of the original protocol submission.

The consent form must identify the drug as a drug that is not approved by the FDA.

B. USE OF FDA-APPROVED THERAPEUTIC AGENTS FOR UNAPPROVED PURPOSES

While physicians may use approved drugs clinically for unapproved purposes with no special permissions, the use of approved agents for unapproved purposes in research requires approval of the IRB and either an IND number or a specific exemption from the FDA IND regulations. To determine whether the proposed research requires an IND, PIs may consult the guidance on the FDA website. Generally, a new IND number will be needed when:

a) an FDA-approved drug is investigated repeatedly or systematically for new (unapproved) indications,
b) the investigator or sponsor is seeking to change or expand the current FDA-approved labeling of the drug, or
c) the sponsor-investigator is seeking to change the current FDA-approved route of administration or dosage level, change its use in a subject population, or change other factors that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.

The consent form should identify as experimental any approved drug being used for an

unapproved purpose.

Experimental combinations of approved drugs do not require an IND if both drugs are being used in accordance with their FDA-approved indication. Investigators should consult the FDA concerning experimental combinations of approved drugs that involve off label use of drug(s) to determine if an IND may be needed.

C. INVESTIGATIONAL DEVICE EXEMPTION (IDE)

All research involving the use of unapproved investigational medical devices (including devices exempt from FDA requirements, significant risk devices, or non-significant risk devices) must be reviewed by the full IRB Committee; this research never qualifies for expedited review and must always have a written consent form. With the exception of devices exempt from FDA requirements (such as those with Humanitarian Device Exemptions) and non-significant risk devices, investigators must have an Investigational Device Exemption (IDE) application on file with the FDA and have received an IDE number. FDA IDE applications are obtained directly from the FDA.

Unless FDA has already made a risk determination for the study, the IRB must review the sponsor's significant risk (SR) or non significant risk (NSR) determination for every investigational medical device study reviewed. If FDA has already made the SR or NSR determination for the study, the agency's determination is final. Although an IDE is not required for NSR devices, requirements for investigational devices at 21 CFR 812.2(b) must be followed for non-significant risk devices.

The protocol submission form should provide the device name, IDE #, and name of the company manufacturing the device where requested on the form. If the FDA has granted an exemption from IDE requirements, a copy of the FDA letter of exemption must be included in the protocol submission packet.

The consent form must identify the device as a device that is not approved by the FDA.

The investigator's brochure provided by the company sponsor and any other background information on the device should be included as part of the original protocol submission. Sufficient information should be provided for devices considered to present a non-significant risk to ensure that the IRB can adequately assess the device, as the IRB is charged by the FDA with the responsibility of confirming a device study as non-significant risk in the absence of an FDA determination.

1. HUMANITARIAN DEVICE EXEMPTION (HDE)

A Humanitarian Device Exemption (HDE) is granted by the FDA for the use of a Humanitarian Use Device (HUD). An HUD is "a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year" [per FDA final rule on the Safe Medical Devices Act of 1990 effective October 1996]. The Humanitarian Device Exemption must be granted by the FDA prior to submission to the IRB of a protocol involving an HUD. The FDA determination letter should accompany the submission.

If the HUD is used for its intended HDE use, IRB review is required by the FDA. However, the IRB may waive certain of its requirements for research studies for the HUD protocol, as the intended use on protocol is an FDA approved use rather than "research." On the other hand, if a researcher proposes to use an HUD for a purpose other than what is described in the HDE, an IDE may be needed. The researcher should consult the FDA.

E. EMERGENCY USE OF INVESTIGATIONAL DRUGS OR DEVICES

Federal regulations allow physicians to use investigational drugs and/or devices in the provision of emergency medical care for patients who need such care. "Emergency use" is defined as "the use of a test article 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" [21 CFR 56.102(d)]. This use of the investigational drug or device does not, however, constitute research and, according to OPRR guidance, "Whenever emergency care is initiated without prior IRB review and approval, the patient cannot be considered to be a research subject. Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity (OPRR Reports, May 15, 1991)." [The oversight of human subjects in research under OPRR was transferred to the purview of OHRP in 2000; some guidance from OPRR remains in effect under OHRP.]

In cases where a physician wishes to use an investigational drug or device for emergency care, it is advisable to contact the Chair of the IRB or the IRB office prior to use of the test article. Both the Chair and IRB staff can provide help in interpreting the regulations and ensuring that physicians understand the post-administration reporting requirements. If pre-event notification is not required, post-event notification of emergency uses of investigational drugs and devices should be sent to the IRB. See below for details of the notification.

While data from emergency use cases cannot be used for research, data may be shared with the sponsor and/or FDA for safety and reporting purposes only.

Although prior acknowledgement of use an investigational drug or device in an emergency from the IRB is not an "IRB approval," a drug or device manufacturer may require this prior to shipment of the drug or device. The acknowledgment letter has been acceptable to manufacturers in the past and has allowed the shipment of drug or device to proceed.

Subsequent use of this drug or device in similar circumstances should be handled by a formal protocol submission to the IRB, including a protocol narrative and consent form, and review through the normal IRB mechanisms. However, the FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. Again, in these cases, the IRB must be notified within five days after any emergency use of a test article. These data should also not be used for research purposes but may be shared with the sponsor (if applicable) and FDA for safety and reporting purposes only.

Investigators should retain records of emergency use occurrences in the same manner as records of approved studies, with the understanding that this data cannot be used for research. Please see the section entitled "Research Records" in this document for more information on record retention. The IRB also maintains all submitted information and correspondence on emergency use events in its records. Please see the section "IRB Records and Related Materials" for more information.

Please be advised that the terms "interim," "compassionate," "temporary" or other terms for a rapid approval process are not proper terms for emergency use and, therefore, not recognized by the IRB.

If an investigator obtains a single-patient treatment IND and there is sufficient time for the IRB to review and approval a research study involving this patient, the investigator should submit a protocol for the use of this drug or device (also often referred to as "compassionate use").

1. EMERGENCY USE OF DRUGS

Notification to the IRB should include the following information:

- the drug name
- provider of the drug,
- IND number and holder,
- subject's initials and details about the subject's disease or condition,
- justification or rationale for the emergency use and
- copy of the consent form.

Such notification should be provided **within five days** after any emergency use of a test article. The IRB will send a written statement to the investigator acknowledging that the IRB is aware of the use and considers it to meet the requirements of 21 CFR Part 56.104(c) and/or 45 CFR 46.116(j).

2. EMERGENCY USE OF DEVICES

Notification to the IRB should include the following information:

- the device name
- provider of the device, including confirmation that device manufacturer authorized use of the device
- IDE number and holder, if applicable
- subject's initials and details about the subject's disease or condition
- copy of the consent form
- justification or rationale for the emergency use and
- an independent assessment from an uninvolved physician.

Such notification should be provided **within five days** after any emergency use of a test article. The IRB will send a written statement to the investigator acknowledging that the IRB is aware of the use and considers it to meet the requirements of 21 CFR Part 56.104(c) and/or 45 CFR 46.116(j).

"Compassionate use" of medical devices should be performed under a previously-approved IRB protocol which allows for the use of device in cases not otherwise allowed. The emergency use pathway should not be used for compassionate use of a device. If investigators anticipate that there will be instances where a device they regularly use or plan to use on a research protocol will be needed by persons not qualified to receive it on that protocol, the investigators are encouraged to submit a separate protocol for compassionate use of the device.

V. DOD REGULATED RESEARCH

Human subjects research is subject to Department of Defense (DoD) oversight when one or more of the following applies:

- the research is funded by the DoD,
- the research involves cooperation, collaboration or other type of agreement with the DoD (including subawards),
- the research uses property, facilities, or assets of the DoD, and/or
- the subject population will intentionally include military personnel and/or civilian personnel employed by the DoD.

These regulations do not apply when DoD personnel incidentally participate as research subjects where they are not the intended research population.

Involving a detainee as a human subject is prohibited in DoD-regulated research.

In addition to its Common Rule regulations at 32 CFR 219, DoD provides specific instructions for human subjects research in DoD Instruction 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research." Investigators are encouraged to consult the granting agency with questions about additional requirements for specific DoD-regulated projects. DoD agencies may provide additional guidance about regulations specific to each agency. After the IRB has approved a research project, the project may also be subject to additional review or approval by the Secretary of Defense.

Investigators intending to survey or interview military or civilian DoD personnel should note that the survey or interview instrument(s) may require specific review and approval by the DoD.

Although classified research is allowed by DoD, per the University of Chicago Policy on Performing Classified Research, no classified work may be undertaken in the name of the University of Chicago or using University facilities or resources.

A. TRAINING REQUIREMENTS

DoD requires continuing research ethics training for research personnel involved in the design, conduct, or approval of humans subjects research. For certain DoD-sponsored research, the BSD training requirements meet the DoD requirements. However, for research specifically sponsored by the Under Secretary of Defense for Personnel and Readiness, training is required on an annual basis. For research specifically sponsored by the Department of Navy, training specific to Department of Navy-Supported Extramural Performers is required. For other military branches, researchers are advised

to consult the appropriate program officer for any applicable training requirements. The IRB may require documentation of appropriate training for personnel, as applicable.

B. SCIENTIFIC REVIEW AND OTHER REVIEWS

Review for scientific merit is required for all non-exempt research regulated by the DoD. Documentation of this review if it has already occurred should be provided with the IRB submission. Scientific review is required for new submissions and for substantive amendments to ongoing research. IRB may provide scientific review on a case by case basis.

For research conducted in an international setting, all applicable national laws and requirements of the foreign country must be met. The IRB may request documentation to this effect from the research team. During its review, the IRB must also consider the cultural sensitivities in the setting where the research will take place.

For multisite research, the research involving human subjects must be approved by all required organizations before human subjects research activities begin. The IRB may approve a protocol contingent upon approval by other organizations.

C. IRB REVIEW REQUIREMENTS

DoD regulations place certain limitations on IRB review of certain research, including that DoD research intending to include prisoners as subjects cannot be reviewed by the IRB through an expedited review procedure.

When evaluating risk to subjects, the IRB must consider the risk to the average person, and not the specific risks of the everyday life of a person inherent in the work environment (e.g., emergency responder, pilot, soldier in a combat zone) or associated with a medical condition (e.g., frequent medical tests or constant pain).

1. CONSENT

Unless specifically agreed to by the DoD, the IRB cannot approve a waiver of consent for research where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Informed consent must be obtained in advance from the experimental subject or the subject's legal representative.

If consent is to be obtained from the experimental subject's legal representative rather than the subject, the research must intend to benefit the individual subject.

The determination that research is intended to be beneficial to the individual experimental subject must be made by the IRB.

For research involving Service members as human subjects that has been determined to be greater than minimal risk and when recruitment occurs in a group setting, the IRB will appoint an ombudsman. The ombudsman shall not be associated in any way with the research and shall be present during the recruitment in order to monitor that the voluntary involvement or recruitment of the Service members is clearly and adequately stressed and that the information provided about the research is clear, adequate, and accurate. For research involving Service members as human subjects that has been determined to be no greater than minimal risk or research involving civilians, when recruitment occurs in a group setting, the IRB shall determine when it is appropriate to appoint an ombudsman. The decision to require the appointment of an ombudsman will be based in part on the human subject population, the consent process, and the recruitment strategy.

2. CONSENT DOCUMENT

The consent documentation must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.

The consent document should include a statement that the DoD (and if applicable the U.S. Army Research and Materiel Command if that Component is involved) will have access to participant records for audit purposes.

If DoD-affiliated personnel will be included as subjects and if the research includes any risks to their fitness for duty (e.g. health, availability to perform job, data breach), the informed consent document must inform DoD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.

For greater than minimal risk research, the consent document should include that participants may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility, and this eligibility for health care services extends beyond participants' participation in the study to such time after the study has ended.

3. COMPENSATION

In general, federal personnel enrolled in DoD-supported research may be compensated up to $50 for a blood draw and may not be otherwise compensated while on duty. If the personnel are off duty, and if the research is not federally

funded, the human subjects may be compensated for blood draws in a reasonable amount as approved by the IRB. Additionally Federal personnel while off duty may be compensated for research participation other than blood draws in the same way as human subjects who are not Federal personnel. However, payment to off-duty Federal personnel for general research participation must not be directly from a Federal source.

Non-Federal personnel may be compensated for participation in DoD-supported research in a reasonable amount as approved by the IRB. Payment for non-Federal personnel for research participation may come directly from a Federal or non-Federal source.

D. SPECIFIC SUBJECT PROTECTIONS: SUBORDINATES

Military superiors and civilian supervisors are prohibited from influencing the decisions of their subordinates regarding participation as subjects in research involving human subjects. In addition, superiors of Service members in the chain of command cannot be present at any human subject recruitment sessions or during the consent process in which members of units under their command are afforded the opportunity to participate as human subjects.

E. LARGE SCALE GENOMIC DATA

Research involving large-scale genomic data from DoD-affiliated personnel is subject to additional requirements.

The disclosure of DoD-affiliated personnel's genomic data may pose a risk to national security; accordingly, written materials must describe administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of deidentified data or specimens.

All research involving large-scale genomic data collected from DoD-affiliated personnel must have a certificate of confidentiality.

Research involving large-scale genomic data collected from DoD-affiliated personnel is subject to DoD Component security review to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of de-identified data or specimens.

F. INSTITUTIONAL REQUIREMENTS

The University of Chicago is required to notify the DoD Human Research Protection Official when significant changes to the research protocol are approved by the IRB, the

results of the IRB continuing review, if the IRB used to review and approve the research changes to a different IRB, when the institution is notified by any Federal department or agency or national organization that any part of its human research program is under investigation for cause involving a DoD-supported research protocol, and all unanticipated problems, suspensions, terminations, and serious or continuing noncompliance regarding DoD-supported research involving human subjects.

Records maintained by the institution that document compliance or noncompliance are accessible for inspection and copying by authorized representatives of the Department of Defense. The DoD Components may rely on the institution to keep the required records that were generated by the institution, or the DoD Components may make arrangements to transfer the records.

There may be additional requirements that the institution must comply with when conducting DoD regulated research.

VI. INFORMED CONSENT

Informed consent of the subject is one of the fundamental principles of ethical research with human subjects. Per 45 CFR 46.116 and 21 CFR 50.20, "… no investigator may involve a human being as a subject in research … unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative," except as specifically allowed by certain exceptions under the waiver of consent regulations. In addition, per 45 CFR 46.116, "an investigator shall seek informed consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence." See also 21 CFR 50.20. Informed consent should be an ongoing discussion between the research team and the subject to ensure that the subject is fully informed about the study. The prospective subject or the legally authorized representative should be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate and be provided an opportunity to discuss that information.

Informed consent "as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates … understanding of the reasons why one might or might not want to participate." (45CFR46.116(a)(5)(ii))

While use of a written consent form including all required elements of consent described in 45 CFR 46.116(a-c) and 21 CFR 50.25(a-c) (if applicable) is the preferred method of documenting the informed consent process, short form consent and oral consent provide alternative methods of conducting the consent process and obtaining consent. The written consent documentation procedures may be modified to include either surrogate consent or a waiver for emergency situations. In certain limited situations, federal regulations and state law allow for a waiver of the consent process in addition to waiver of consent documentation. Each of these categories is described in detail below. Multifaceted studies may include more than one method of consent process and/or documentation.

Often, studies involving written consent will require written authorization pursuant to the HIPAA regulations [45 CFR 160, 164]. Similarly, studies involving a waiver of written consent or a waiver of the documentation of consent will also involve a waiver of authorization pursuant to the HIPAA regulations.

Any proposed consent method and documentation method should be approved by the IRB prior to being used to enroll a research subject.

A. INFORMED CONSENT PROCESS AND DOCUMENTATION CATEGORIES

The requirements for informed consent will depend on the nature of the research protocol. The following sections detail each type of informed consent or alteration of informed consent, the documentation required, and the conditions under which consent must be obtained.

1. INFORMED CONSENT WITH WRITTEN DOCUMENTATION OF CONSENT (WRITTEN CONSENT FORM)

In most circumstances, a written consent form is required. In addition to conducting a consent discussion, the investigator shall give the subject and/or the subject's legally authorized representative adequate opportunity to read a written consent form and ask questions before it is signed. The PI should maintain the original signed document. A copy of the signed document must be given to the subject or the subject's representative with additional copies placed in the subject's medical record, if applicable, and provided to others (e.g., University, Pharmacy, sponsor), as required.

If consent is documented in an electronic system, the IRB must approve the system to be used and the text of the document that will be placed in the electronic system prior to use. It is the expectation of the IRB that the exact electronic document text is being used to consent subjects as was approved by the IRB.

The IRB has prepared a standard format for all consent forms. The IRB requests that investigators utilize the standard format when preparing consent forms. This IRB template consent may be accessed from the IRB website. The template consent form includes statements that address all 45CFR46.116 (a-c) and 21CFR50.25 (a) consent form elements as well as the authorization requirements for HIPAA at 45CFR164.508.

It is recommended that the written consent form be typed in at least 12-point font and written in language easily understood by a person having seventh-grade level reading skills. Exceptions may be made based on the expected subject population. In all cases, the information to be given to a prospective subject should be in language understandable to the subject. Similarly, the consent discussion should be conducted in lay language and the subject given the opportunity to ask questions, as needed.

a) Child Assent/Parental Consent

In general, for research with individuals under the age of 18, unless the individual is pregnant or an emancipated minor, the use of informed consent with a written consent form is required. Permission to participate must be provided by at least one parent or guardian; in instances where the research presents more than minimal risk and/or provides no direct benefit to the subject, permission and signature of both parents is required.

In addition, per the decision of the IRB the assent of the participating child should be obtained for all children with capacity to understand the research, its risks and benefits, and the alternatives to the research. At the discretion of the PI, a separate assent form can be prepared for the child to document assent in addition to the parent/guardian consent form. If a separate assent form is not prepared, the child should be asked to sign the parental consent form on a separate "assent" line.

If subjects are enrolled in a study as minors and reach the age of majority while on study, the researcher should obtain and document consent to continue participation in the study from each competent individual subject who is no longer a minor.

For studies greater than minimal risk enrolling wards of the state, a witness is required to the consent procedure. Foster parents may not sign the consent form for a ward of the state to participate in research, either as parent/guardian or witness.

b) Low literacy subjects

When necessary, the written consent form may be read to the subject or the subject's representative if the subject is unable to read or write. The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study. Low literacy individuals can document consent by "making their mark" on the consent document instead of signing the form, such as making an "X" or placing their fingerprint on the consent signature line.

When enrolling low literacy participants, the IRB recommends that an unbiased witness observe the consent process. The witness should not be a study team member or a family member of the participant. After the subject has agreed to participate, the witness signs and dates the consent form to attest that the consent information was accurately explained, that the subject apparently understood the information, and informed consent

was given freely. The study team member obtaining consent signs and dates the consent form as usual. A video tape recording of the consent interview is recommended in this case.

The study team should document the names of all the individuals who were present for the consent process and any procedures the study team used to enhance the participant's comprehension in the research record.

c) Non-English speaking subjects

If the investigator expects to enroll non-English speaking subjects, a translator fluent in the language of the potential subject should facilitate the consent discussion. It is also recommended that a translated version of the approved English-language consent document be prepared. Document(s) should be translated by a qualified translator and as necessary, qualifications of the translator and/or certification of the translation should be provided to the IRB. Translated documents should be submitted to the IRB for approval prior to use.

d) Physically Disabled

When necessary, the written consent form may be read to the subject or the subject's representative if the subject is physically unable to read or write. As with all informed consent processes, sufficient time should be allowed for the potential subject's questions and concerns to be satisfactorily addressed prior to documenting consent or proceeding with study participation. If the potential subject agrees to participate in the study, the potential subject may indicate their agreement in a predefined manner such as blinking of the eyes or raising an arm.

When enrolling physically disabled participants, the IRB recommends that an unbiased witness observe the consent process. The witness should not be a study team member or a family member of the participant. After the subject has agreed to participate, the witness signs and dates the consent form to attest that the consent information was accurately explained, that the subject apparently understood the information, and informed consent was given freely. The study team member obtaining consent signs and dates the consent form as usual. A video tape recording of the consent interview is recommended in this case.

The study team should document the names of all the individuals who were present for the consent process, the method used to communicate

with the potential subject, and the specific means by which the subject communicated agreement to participate, in the research record.

e) Surrogate/Proxy Consent

Medical circumstances may preclude a subject from participating in the consent process, and thus the IRB will consider requests for surrogate consent in keeping with the *Medical Patients Rights Act* and the *Health Care Surrogate Act of the State of Illinois* for individuals who are unable to consent for themselves and who do not have a pre-determined legally authorized representative.

The federal regulations require that informed consent be provided by the subject or the subject's legally authorized representative, except 1) in cases where the IRB has altered or waived some of the requirements for informed consent and the research presents no more than minimal risk or 2) in cases which meet the criteria for waiver of consent in emergency situations (45 CFR 46 and 21 CFR 50). It is State law that defines who can act as a subject's "legally authorized representative" to make treatment and /or research-related decisions on the subject's behalf. The State of Illinois has two pieces of legislation which provide family members or others with legal authority to provide consent in situations where the patient is unable to provide consent. *The Medical Patient Rights Act* indicates that consent to participate in a research program or experimental procedure may be given by "the patient or, if the patient is unable to consent, the patient's guardian, spouse, parent, or authorized agent." In 1997, the State of Illinois amended the *Medical Patient Rights Act* to align state law with the recently enacted federal (DHHS and FDA) regulations on the waiver of consent in emergency situations.

The *Illinois Health Care Surrogate Act* also provides authority for a surrogate decision maker to act on behalf of patients (minor or adult) who lack decisional capacity. This statute initially applied only in situations concerning withdrawal of life sustaining treatment. Amendments to the statute extend the surrogate's authority to general medical treatment decisions, which can include research-related decisions.

For copies of *The Medical Patient Rights Act* and *The Health Care Surrogate Act*, please contact the Office of Medical Legal Affairs.

Proxy consent should involve all the same considerations that informed consent from a competent patient involves. It also involves identifying the proper surrogate and ensuring that the research decision reflects the

wishes of the subject, if known or, if not known, the best interests of the subject. In addition, the IRB will consider whether the research could be accomplished in situations involving the consent of a competent patient and will consider whether the intervention is likely to offer therapeutic benefit to the subject of the study.

Researchers wishing to utilize surrogate consent should answer the questions concerning subjects who are not able to make decisions for themselves on the protocol submission form and submit a consent form suitable for proxy consent.

Illinois law requires that the following process be followed when obtaining consent from a surrogate decision-maker.

1) The attending physician must determine that the subject lacks decisional capacity.

2) An attempt should be made to determine whether there is an operable and unrevoked living will, durable power of attorney for health care, or declaration for mental health treatment ("Advance Directive") which is applicable to the subject's decision about whether to participate in the research. Surrogate consent should be invoked only in cases when, after reasonable inquiry, no Advance Directive applies or, despite efforts to contact the person authorized in an Advance Directive, that person is unavailable.

3) The researcher must attempt to identify a surrogate of the highest priority. (Note: If there is more than one surrogate of the highest priority and there is a disagreement between them, majority rules. If there is disagreement and no majority, consult with the Ethics Consult Service or the Office of Medical Legal Affairs.)

For the purposes of this law, relevant surrogates in order of priority are as follows:

1) patient's guardian of the person;
2) patient's spouse;
3) any adult son or daughter of the patients;
4) either parent of the patient;
5) any adult brother or sister of the patient;
6) any adult grandchild of the patient;
7) a close friend of the patient;
8) the patient's guardian of the estate.

4) The consent process with the surrogate should include a discussion with the attending physician and an inquiry into the extent to which the surrogate is able to speak for the subject. Following the requirements of the Health Care Surrogate Act, this discussion should emphasize the surrogate's ability to make a decision that would conform as closely as possible to what the subject would have done or intended under the circumstances. The surrogate should take into account evidence that includes the subject's personal, philosophical, religious, and moral beliefs and ethical values relative to the purpose of life, sickness, medical procedures, suffering and death.

5) In circumstances in which the subject's wishes are unknown after reasonable efforts to discern them, the decision shall be made on the basis of the subject's best interests as determined by the surrogate decision maker. In determining the subject's best interests, the surrogate shall weigh the burdens and benefits of the proposed research and shall take into account any other information, including the views of family and friends, that the surrogate decision maker believes the patient would have considered if able to act for self.

6) The surrogate should express a decision to the researcher in the presence of an adult witness (at least 18 years of age).

7) The subject should be made aware of the research and the identity of the surrogate as soon as feasible. If the subject objects and the surrogate is not a court-appointed guardian, the subject should be withdrawn from the research.

8) The surrogate will have the same rights as the subject to receive information on the research, to withdraw consent for further participation, etc.

The IRB requires that the research team maintain documentation that each of the required elements in the surrogate process set forth above has been satisfied, including, but not limited to: a determination by the attending physician that the subject lacks decisional capacity, the identity of the surrogate, and the relationship of the surrogate to the subject.

f) Emergency Waiver of Consent

In 1997, the FDA and DHHS provided a narrow exception to the standard requirements for obtaining informed consent and documentation of

consent from each subject or the subject's legal representative prior to initiation of an experimental intervention. These federal regulations allow the IRB to approve a limited class of research activities involving human subjects in need of emergency medical intervention, but who are unable to consent because of their life-threatening medical condition, to proceed without prior consent from the subject. The intent of the regulation is to allow research on life-threatening conditions for which available treatments are unproven or unsatisfactory, which would ordinarily require informed consent with written documentation of consent in specific instances or populations, where it is not possible to obtain consent in the standard manner while establishing additional protections to provide for safe and ethical studies and protect the rights of vulnerable populations of subjects. Some form of consent is typically needed following the emergency intervention.

Use of this provision requires special justification, community consultation, the preparation of a consent document, the consenting of a subject or the subject's proxy as soon as feasible, and other unique considerations. The IRB will review requests to waive consent in certain emergency research on a case-by-case basis. Please see section VIII.D.

2. INFORMED CONSENT WITH SHORT WRITTEN DOCUMENTATION OF CONSENT (SHORT FORM CONSENT)

If the research activities involve no more than minimal risk to the subjects, the IRB may waive traditional written consent requirements in favor of the short form consent process. All protocols requesting such procedures are carefully reviewed by the IRB to determine whether the short form process and documentation will suffice.

The short form written consent is a document stating that the elements of informed consent (see Section VI.C) have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there must be a witness to the oral presentation. The IRB must approve a written summary or script of what is to be said to the subject or the representative prior to use of this summary. Only the short form itself is to be signed by the subject or the representative. The witness and the person obtaining consent should sign a copy of the summary as well as the short form consent document. A copy of the summary should be given to the subject or the representative in addition to a copy of the "short form."

When appropriate, the person who obtained the consent must also document the obtaining of the short form consent in the subject's medical record in addition to the study record.

The PI should maintain the original, signed short form consent document.

If PHI will be used and/or disclosed as part of the research, the subject should also sign a HIPAA authorization for this use/disclosure written in a language understandable to the subject.

3. INFORMED CONSENT WITH WAIVER OF DOCUMENTATION REQUIREMENTS (ORAL CONSENT)

Under certain conditions, the requirement to provide documentation of the informed consent process can be waived. In this process, the investigator obtains informed consent through a consent process that includes the required elements of informed consent. An oral consent script to be used for the consent process is provided to the IRB. Similar to a written consent form, the script would include information regarding the nature and duration of study procedures, risks and benefits, alternatives, and cost to subjects. The subject will either verbally agree or not agree to participate in the study. Investigators are not required to secure subjects' signatures, but researchers should document in the protocol record that a consent process occurred.

To qualify for oral consent, one of the following criteria must apply:

a) The only record linking the subject and the research would be the consent document and the principal risk to subjects would be the 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 whether such a link is made.
b) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
   or
c) The subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk of harm to subjects, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In these cases, if HIPAA applies to the research data, the investigator should also apply for a waiver of HIPAA authorization, as written authorization is not being obtained. A justification for a "waiver/alteration of authorization" must be submitted for any protocols for which oral consent is requested unless HIPAA does not apply to the research.

4. ALTERATION OF INFORMED CONSENT IN NON-EMERGENCY SITUATIONS

The IRB may also consider an alteration of the informed consent process and/or consent documentation for studies that are no more than minimal risk. Typically, an alteration of the informed consent process would be granted in circumstances in which subjects are provided information about the study but one or more elements are not included, or when subjects are offered but are not required to engage in a full consent discussion. To qualify for altered consent, the research must provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and 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 legally authorized representative must be in language understandable to the subject or the legally authorized representative, and the prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.

The IRB would consider an alteration of the informed consent process for online studies, surveys sent to subjects via the mail, and other types of research for which an informed consent process is not practical for all subjects, but all subjects must be provided the opportunity to discuss the study with a member of the research team.

Although there may be no direct interaction with subjects, subjects should be given a chance to accept or decline participation via responding or not responding to the electronic request. Similar to an oral consent script, the email contact script or mailed contact letter should include information regarding the nature and duration of study procedures, risks and benefits, alternatives, and cost to subjects. In order for the IRB to grant an alteration of the informed consent process, a justification for not obtaining informed consent must be provided to the IRB.

In addition, the consent documentation may be altered such that certain consent elements are not included in the document or a physical signature is not obtained. Again, the research must be minimal risk and a justification provided

to the IRB for altering the consent documentation. Note, if HIPAA applies to the research data, all authorization elements must be present in the consent/authorization document or the researcher must request approval of a waiver of authorization.

For studies employing an alteration of informed consent, the protocol submission should describe how record of subject's consent to participate will be maintained.

To qualify for an alteration, justification must be provided to address the following:

a) the research presents no more than minimal risk to subjects;
b) the research could not practicably be carried out without the alteration;
c) if the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
d) alteration will not adversely affect the rights and welfare of the subjects; and
e) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Alteration of consent may also be used to alter some of the consent form elements described in Section VI.C. An example of this type of alteration is research involving deception. In deceptive research, subjects are not fully informed of the nature or some or all of the components or design of the research, or subjects are falsely informed of the nature or design of the research. Thus, the subjects are not considered to have given fully informed consent. See section III.E for more information.

5. WAIVER OF INFORMED CONSENT IN NON-EMERGENCY SITUATIONS

There are circumstances in which the IRB can consider a waiver of the requirements of informed consent, including the requirements for documentation of consent. This typically occurs when investigators have no physical, vocal, or electronic contact with potential subjects. When the IRB authorizes a waiver of consent, this waiver does not apply to any other consent that may be required by any other committee or institutional procedure. To request approval for waiver of consent, the investigator should provide a written justification, addressing each of the five points listed below.

The IRB may waive the requirements to obtain informed consent provided the IRB finds and documents that:

a) the research presents no more than minimal risk to subjects;
b) the research could not practicably be carried out without the waiver;
c) if the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
d) the waiver will not adversely affect the rights and welfare of the subjects; and
e) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Appropriate procedures for maintenance of confidentiality should be described in the protocol.

6. WAIVER OF AUTHORIZATION

If a waiver or alteration of consent is requested, and HIPAA applies to the research data, the investigator must also apply for a waiver of HIPAA authorization. As per 45CFR164.512, the IRB may waive the requirement to obtain written authorization provided the IRB finds that the use or disclosure of PHI planned in the research involves no more than minimal risk to a subject's privacy and the research includes:

a) "an adequate plan to protect the identifiers from improper use and disclosure; and
b) a plan to destroy identifiers at the earliest opportunity that is consistent with the goals of the study, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law."

In addition, the IRB must also receive:

a) written assurance that PHI "will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study or for other research for which the use or disclosure of PHI would be permitted" by the HIPAA Privacy Rule;
b) a description of why "the research could not practicably be conducted without the waiver,"
c) a description of why "the research could not practicably be conducted without access to and use of the PHI," and
d) a brief description of the PHI and of why the PHI is necessary for the research.

When a waiver of HIPAA authorization is approved for screening, recruitment and/or data collection, disclosures of PHI must be tracked to allow for accounting of disclosures by the UCM Privacy Office. This tracking may be automated for certain studies or the research team may be required to document the disclosures themselves. Please see the Guidance for Tracking of Research Disclosures or contact the UCM Privacy Office for more information.

B. GENERAL CONSIDERATIONS IN OBTAINING CONSENT

The investigator and research personnel are responsible for providing information from the research protocol to the potential research subject, including updated information as necessary and applicable. When obtaining informed consent, as described in this section, research personnel are responsible for maintaining confidentiality within the limits of the law and sponsor requirements.

At the time consent is to be obtained, the subject must be competent to understand the procedure(s) and to freely give consent or the subject must be represented by a legally authorized representative, unless consent is waived or altered as approved by the IRB. Unless an alteration of consent is sought, all subjects must be fully informed of the nature of the procedures to be undertaken and the risks, benefits and alternatives, if any, to the procedure(s).

If a minor subject is enrolled in a study with parental consent and that minor reaches the age of majority while on study and is competent to consent, the researcher should include provisions to obtain consent from that individual to continue participation in the study.

In addition to the requirements concerning the involvement of children in research, there are also federally-mandated special considerations for obtaining the consent of other special populations, such as prisoners. See Section VII in this document for information on enrolling and consenting special populations.

Informed consent should involve, or be based on, one or more conversations between the investigator, the subject(s), and/or the subject's legally authorized representative. The written form signed by the subject serves as documentation that this dialogue has taken place and also as a record that the subject has agreed to participate in the research. It should be noted that signing the consent form is merely documentation that the full informed consent process has taken place and should not be considered the only necessary step in the process.

When changes occur during the study or new information is found that may be applicable to subjects, currently enrolled subjects may be asked to re-consent to the

study and, if applicable, sign a revised written consent form. When submitting an amendment when changes are proposed (see Section IX), researchers should document whether it is necessary to inform subjects who have already consented to participate in the research of the changes proposed in the amendment. If yes, the researchers are asked to state whether subjects will be given and asked to sign the full revised informed consent or asked to sign an addendum to the consent document. In addition, the researchers are asked to explain when this re-consent discussion will occur as well as who will conduct the discussion. If the researchers do not propose to ask currently enrolled subjects to provide additional consent to continued participation, researchers should document why it is not necessary to re-consent subjects. The IRB will review the request and may determine that re-consent is needed, regardless of whether this was proposed by the researcher.

C. ELEMENTS OF INFORMED CONSENT

The term "informed consent" refers to the ongoing consent process, not to the completeness of the consent form document. While it is expected that the required elements of informed consent are present in the written consent form document, it is also expected that these elements are thoroughly discussed with the potential subject prior to any signing of the consent document.

1. REQUIRED ELEMENTS

Informed consent must be in language understandable to the subject and include the following elements:

a) Key Information: the consent should begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject in understanding the reasons why one might or might not want to participate in the research. Key information must be organized and presented in such a way to facilitate comprehension.

b) Statement that the protocol 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, drugs, or devices which are experimental.

c) Description of any reasonably foreseeable risks or discomforts to the subject. OHRP IRB Guidance suggests that the PI think about the risk from the subject's viewpoint and include all the information necessary for the subject to make an informed decision.

d) Description of any benefits to the subject or to others that may reasonably be expected from the research.

e) Disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

f) Statement describing how confidentiality will be maintained.

g) For research involving more than minimal risk, a statement that in the event of physical injury, free emergency care will be provided if necessary. See Section C.5.

h) Statement as to whom to contact (a single individual) for answers to pertinent questions involving the research, whom to contact regarding research subject's rights (including the IRB office and its phone number), and whom to contact in the event of a research-related injury to the subject.

i) Statement similar to "participation is voluntary" or "you may choose not to participate," as well as a statement that "refusal to participate, or discontinuing participation at any time, will involve no penalty, loss of benefits or denial of treatment or services by the University of Chicago and the University of Chicago Medical Center."

   These statements should be included in the alternatives ("other options") section of the written consent or wherever possible alternatives to the research are described.

j) If the research involves the collection of identifiable private information or identifiable biospecimens:
   i. statement that identifiers might be removed from the data and/or specimens and that, after removal, the data and/or specimens could be used for future research or given to other investigators without additional consent; or
   ii. statement that the data and/or specimens collected as part of the research would not be used or distributed for future research, even if identifiers are removed.

k) Provision for the date and time of the subject's consent.

l) Provision for subjects to be given a signed copy of the consent form, if the consent is written.

m) In the case of research involving FDA-regulated products, statement that the FDA and the study sponsor may inspect records that may identify individual subjects.

n) In the case of sponsor-initiated studies, the sponsor's name should be included as having access to the records of the research, including specifying sponsor's access to individually identifiable information.

o) If blood is to be withdrawn, include the standard blood withdrawal information in the description of procedure:
   - amount of blood to be drawn (in teaspoons or tablespoons)
   - number of blood draws
   - period of time to be covered.

   Additionally, in the description of risks, include the potential hazards of a blood draw, such as "a bruise at the site of vein puncture, inflammation of the vein and possible infection" and statement that "care will be taken to avoid these complications."

p) Disclosure of video recording, audio recording and/or photography of subjects and an explanation of how they will be used (i.e., research, diagnostic, or educational). This is mandatory under Illinois law if any recording or photography will occur. Additionally, tape recording and disposal should be discussed.

q) If Protected Health Information is accessed, authorization elements as required by the HIPAA regulations including:

   - A description in a specific or meaningful way of the Protected Health Information (PHI) to be used or disclosed;
   - Who will use or disclose the PHI;
   - To whom the PHI will be disclosed;
   - A description of each purpose of the requested use or disclosure;
   - An expiration date/expiration event that relates to the purpose of the use or disclosure ("end of research study" or "indefinitely" is permissible);
   - A statement of the individual's right to revoke the authorization in writing and the exceptions to the right to revoke, together with a description of how the individual may revoke the authorization, including where the written revocation should be directed;
   - A statement that information used may be subject to re-disclosure by the recipient and no longer be protected by this rule; and
   - A statement of the consequences to the individual of a refusal to sign.

r) For FDA-regulated clinical trials, the following statements are required verbatim:
"A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

2. ADDITIONAL ELEMENTS

When appropriate, one or more of the following additional elements should be included in the informed consent:

a) A statement that the particular study procedure may involve risks to the subject (or to the embryo or fetus, if the subject may become pregnant) which are currently unforeseeable.

b) Anticipated or unanticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

c) Any costs to the subject that might result from participation in the research.

d) The consequence of a subject's decision to withdraw from the research as well as procedures for orderly termination of participation by the subject.

e) Statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject. In certain instances involving minimal or no risk to subjects the IRB has allowed this statement to be removed. This is determined on a case-by-case basis.

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

g) Statement that the subject's biospecimens, even if identifiers are removed, may be used for commercial profit and whether or not there are plans for the subject to share in this commercial profit.

h) Statement regarding whether any clinically relevant research results, including individual research results, will be disclosed to subjects and if so, under what conditions.

i) If research involves biospecimens, whether the research will or might include whole genome sequencing.

Whole genome sequencing is defined here as "sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen" (45CFR46.116(c)(9)).

j) If subjects are being recruited from LaRabida Children's Hospital, include LaRabida after mention of the University of Chicago in the header of the consent form, and include LaRabida as an entity that will use and, if applicable, disclose health information as part of the study.

k) If subjects are being followed for survival, the consent form should indicate the investigator's intent to do so as well as how survival data will be collected, e.g. ongoing review of medical records, contacting subject and/or family, etc.

l) Under the "Other Options" section, statements similar to:

"Alternatives for your disease include treatment with different drugs and drug combinations with similar side effects. You may choose to continue whatever treatment you are currently receiving instead of participating in this study. Another alternative is comfort care, where treatments are directed at reducing symptoms, relieving suffering, and maximizing comfort, dignity, and control. (In comfort care, treatment is not directed at curing, slowing, or reversing your disease.)"

If the study drug is available off-study, a statement should also be included to that effect.

m) If the study is protected by a Certificate of Confidentiality, description of the confidentiality provisions and limitations of this protection should be included.

n) If the study is NIH-funded, any data sharing required by the granting agency should be described.

o) If subjects will be paid, details regarding the payment amount.

Normal volunteers, research subjects acting as control group subjects in an experiment, or research subjects who do not directly benefit from the study may be offered a reasonable, but not coercive, payment to participate in the protocol. The reasonableness of the amount offered will depend on the degree of discomfort the subjects experience, the invasiveness of the procedure or investigation, the character of the research, the population likely

to be attracted by the protocol, the method in which the protocol will be advertised, the amount of time a subject is expected to devote to the protocol, and related considerations.

In addition, the consent form should describe the plan for pro-rated payment to subjects if subjects withdraw voluntarily from the protocol or if, upon the suggestion of a physician or investigator, early withdrawal is necessary. If prorated payment will not be offered to subjects, justification as to why prorated payment is not being offered should be provided to the IRB.

3. ELEMENTS FOR PROTOCOLS WITH SPECIAL POPULATIONS

a) Children

Individuals under the age of 18 cannot legally consent to be involved in research protocols, unless the individual is a legally emancipated minor. The permission of the parent(s) of the child is generally required. A legally emancipated minor may consent for the inclusion of that minor's own child in research.

The consent of both parents is required for research involving greater than minimal risk unless one parent is deceased, unknown, incompetent, or not reasonably available or when only one parent has legal responsibility for the care and custody of the child. One parent may, however, consent when there is no more than minimal risk or if there is more than minimal risk but the research presents the prospect of direct benefit to the individual subject.

Foster parents may not consent to research for children in their custody who are wards of the state. A representative of the state under which the children are wards must consent to the research on the children's behalf.

Additionally, the assent of the participating child must be obtained from all children with a capacity to understand the research to be done. This assent is an indication of agreement by the child to the research protocol, which must be explained to each child in language the child can understand. This personal assent must be documented on the written consent form or assent form and, as appropriate, in the child's medical record.

There are two circumstances in which children with the potential capacity to assent may be enrolled in a research protocol without their assent:

- The IRB (not the investigator) determines that the understanding of some or all of the children involved is so limited that they cannot reasonably be consulted (because of age, maturity, or mental state).

- The IRB determines that a waiver of assent is evident that the intervention or procedure involved in the research shows a prospect of direct benefit that is important to the health or well-being of the specific child (subject) and is available only in this context.

b) Pregnancy

If persons of childbearing age will be recruited as subjects and pregnancy is an exclusion criterion, the protocol and consent form should state that a pregnancy test will be given prior to subjects' entry into the study and, as applicable, that the test may be repeated during the study. In addition, the consent form should state whether subjects must abstain from sexual intercourse or use appropriate contraception after the pregnancy test prior to study initiation and/or throughout the duration of the study.

It should also be stated in the consent form that if the subject becomes pregnant during the course of the study, the subject must notify the principal investigator as soon as possible. As applicable, the consent form should clarify whether subjects should immediately discontinue any study drug or other research intervention if a pregnancy is discovered.

If pregnant persons will be or may be enrolled as study subjects, the IRB must make a determination regarding risk to the fetus as well as risk to the pregnant person. If the research holds out the prospect of direct benefit solely to the fetus and is greater than minimal risk, the federal regulations require that the both parents provide consent to the research, unless the second parent is unable to consent because of unavailability, incompetence, or temporary incapacity or if the pregnancy resulted from rape or incest.

c) Prisoners

If prisoners will be enrolled as study subjects, language similar to the following should be included in the consent form:

> "Your participation (or refusal to participate) in this research project will have no effect whatsoever on any criminal charges pending against you or on any sentence, including imprisonment, parole, probation, or placement in other correctional or treatment program, and will have no effect on your release from custody or likelihood of future incarceration."

If a subject becomes a prisoner while on a research study, the subject-now-a-prisoner should not undergo any study procedures until the protocol has been re-reviewed by the IRB, which may determine that the subject may no longer

participate in the study or that the subject should be reconsented. If the subject may no longer participate, the investigator should consider additional language in the consent form to clarify that any subsequent incarceration will result in removal from the study.

If the subject-now-a-prisoner is allowed to remain on study, that subject should be reconsented using a consent form that includes the language provided above.

4. PROHIBITED ELEMENTS

The consent form may **not** include:

a) Any exculpatory language through which the subject is made to waive or appear to waive any legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence; or

b) Language from study sponsors which details any payment agreement for treatment required for research-related injuries that differs from the IRB-provided template language, unless approval for such language has been specifically requested from the IRB.

5. RESEARCH-RELATED INJURY

For studies that involve more than minimal risk, federal regulations at 45 CFR 46.116/21CFR50.25 require that the consent process include "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." As the wording in consent forms is intended to inform subjects about studies, not to limit liability, the Biological Sciences Division has set the following policy to ensure that all compensation for injury statements meet both Federal and Institutional standards.

a) Commercial Sponsor Statements

It is the policy of the University of Chicago and the Medical Center that commercial sponsors of clinical research at the Medical Center must agree to pay for treatment of injuries that are the direct result of the administration of a study drug or device, or any study procedure required to be performed in the study. This obligation of commercial sponsors is limited to research protocols designed or supplied by the commercial sponsor. The University and the Medical Center's obligations for treatment of research injuries, as expressed in the language below and in Medical Center's Policy on Research-Related Injuries, will be secondary to

the commercial sponsor's obligations under the clinical trial or other sponsored research agreement. University Research Administration is responsible for implementation of this requirement in commercially-sponsored research agreements.

The obligations of commercial sponsors to subjects who suffer a research-related injury must be expressed in the written consent form using the following language, which should immediately precede the applicable statement concerning the Medical Center's obligations discussed below:

"The sponsor of the study, [insert sponsor name], has agreed to pay for the care of certain injuries directly resulting from this research. If you think that you have suffered a research-related injury, you must contact [insert PI/study doctor name] right away. The study doctor can help you obtain more information about the sponsor's agreement to pay for research-related injuries."

Exceptions to this consent form language may be considered by the IRB, in consultation with legal counsel, on a case by case basis if requested by the commercial sponsor, but are not looked on favorably, and must satisfy the requirements of the Medical Center's Policy on Research-Related Injuries.

b) University/Medical Center Statements

One of the following University of Chicago BSD/ University of Chicago Medical Center statements must be included (without any modifications) in the written consent form, immediately following the commercial sponsor statement described above (if applicable). The appropriate statement should be chosen based upon the subject population being recruited. The IRB recognizes that for studies that recruit both individuals with a disorder and condition and healthy controls, the use of both statements may be required. However, a separate consent form should be drafted for each of the populations with the appropriate costs statement included.

(i) For studies with therapeutic intent for the subject (including Phase I and II trials):
If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, you may receive such emergency medical treatment at the University of Chicago Medical Center, UChicago Medicine Ingalls Memorial Hospital, UChicago Medicine Northwest Indiana, UChicago Medicine AdventHealth Bolingbrook, UChicago Medicine AdventHealth Glen Oaks, UChicago Medicine Advent Health

Hinsdale, or UChicago AdventHealth LaGrange at no cost to you. You must notify _____ [insert PI/study doctor name] as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure, and is not the result of your disease or condition. The costs of any non-emergency care for such an injury will be billed to you, your insurance [or the study sponsor*] in the ordinary manner. If you think that you have suffered a research-related injury, you must let _____ [insert PI/study doctor name] know right away.

In the event of an emergency, you should seek care at the nearest emergency room or call 911.

** Include "or the study sponsor" only if study is commercially sponsored and the sponsor designed or supplied the protocol.*

(ii) For studies involving healthy volunteers:
If you suffer an unanticipated injury as a direct result of this research and require emergency medical treatment, you may receive such emergency medical treatment at the University of Chicago Medical Center, UChicago Medicine Ingalls Memorial Hospital, UChicago Medicine Northwest Indiana, UChicago Medicine AdventHealth Bolingbrook, UChicago Medicine AdventHealth Glen Oaks, UChicago Medicine Advent Health Hinsdale, or UChicago AdventHealth LaGrange at no cost to you. Costs of related non-emergency care for an unanticipated research injury will be covered if that care is provided at the University of Chicago Medical Center. You must notify _____ [insert PI/study doctor name] as promptly as possible after your injury in order to receive this care. An injury is "unanticipated" if it is not one of the known effects of a study drug, medical device or procedure. If you think that you have suffered a research related injury, you must let _____ [insert PI/study doctor name] know right away.

In the event of an emergency, you should seek care at the nearest emergency room or call 911.

D. CONSENT FORM RECORDS

It is the expectation of the IRB that if consent documentation is required from a subject, the subject will sign a consent form prior to beginning any study procedures. The

research team member who is obtaining consent should sign the form at the same time as the subject. The signed copy given to the subject would thus contain at least two signatures: the subject's own and the signature of a member of the research team who is designated to obtain consent.

If the consent form contains a signature line for the investigator/physician, the investigator is not required to sign at the same time as the subject (if the investigator is not the person obtaining consent), but the investigator should sign prior to the subject receiving an experimental drug, receiving implantation of an experimental device, or undergoing any more than minimal risk research intervention. Signature line for signature of the investigator/physician may not be required for minimal risk studies. Minimal risk studies approved prior to September 24, 2013 may be revised at time of study renewal or with an amendment to remove signature line of investigator from the approved consent form(s), at the discretion of the IRB.

The original, signed consent forms for each subject must be kept in the subject's research record with the Principal Investigator. A signed copy of the consent form must be given to the subject. For clinical trials, another signed copy should be kept in the subject's medical record. If desirable, medical records can be initiated for all subjects who are not already patients at the University of Chicago Medical Center or its affiliated hospitals, including volunteers participating in research studies.

If consent is documented in an electronic system, the IRB must approve the electronic consent form prior to use. Electronic documentation of consent must comply with University and UCMC requirements for electronic signature.

If subjects are asked to provide additional documentation of consent during the study, for example, when new risks are discovered that may affect willingness to continue participation, these consent records should be retained in the same manner as the original consent documentation.

The research team is required to maintain a copy of each signed consent form for federally-funded studies for a minimum of three years after the completion of the research (as defined by the last publication related to the study). This minimum requirement may be superseded by other record retention requirements.

For studies approved on or after January 20, 2019, for each clinical trial conducted or supported by a Federal department or agency, one IRB-approved consent form used to enroll subjects must be posted on a publicly available federal web site. The consent form must be posted on the web site after the clinical trial is closed to enrollment, and no later than 60 days after the last study visit by any subject as defined by the protocol. For the purposes of this policy, "clinical trial" is defined as "a research study in which one or more human subjects are prospectively assigned to one or more interventions

(which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes." (45CFR46.102(b))

VII. SPECIAL POPULATIONS

OHRP regulations at Subparts B, C, and D require that particular care be taken of subjects who are classified as special, vulnerable populations. These populations are:

- children (under 18);
- pregnant women;
- human fetuses;
- nonviable neonates;
- neonates of uncertain viability; and
- prisoners.

FDA regulations also make provision for children as research subjects (21 CFR 50 Subpart D).

When dealing with any of these populations, investigators are typically required to use a written consent form. Certain studies involving children and/or pregnant persons, including survey studies, may or may not require the use of a written consent form.

Federal and state regulations also make special provision for research involving, after delivery, the placenta, dead fetus, or fetal material, as outlined below.

Research not otherwise approvable under federal regulations for children [45 CFR 46.407/ 21 CFR 50.54] must be submitted to OHRP and the FDA if an investigator intends to pursue the research. Research not otherwise approvable under federal regulations for pregnant women, fetuses, or neonates [45 CFR 46.207] must be submitted to OHRP if an investigator intends to pursue the research. Also, certain categories of research with prisoners require submission to OHRP (see below).

Expedited approvals may not be granted for certain protocols involving illiterate persons or prisoners. Please see the section on "Requests for Expedited Approval of New Protocols" for more details on the expedite review and approval process.

A. CHILDREN

The defined categories of approvable research involving children, including viable neonates, are as follows:

(1) 45 CFR 46.404/21 CFR 50.51 Research not involving greater than minimal risk

(2) 45 CFR 46.405/21 CFR 50.52 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects

(3) 45 CFR 46.406/21 CFR 50.53 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

(4) 45 CFR 46.407/21 CFR 50.54 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children
Category (4) under 45 CFR 46.407 requires review by OHRP prior to approval by the IRB. This category also requires review by FDA prior to approval by the IRB, if FDA regulated.

Research with children may be expedited provided it falls under one of the allowable expedite categories and the IRB determines that the study is of minimal risk to potential child subjects.

When reviewing research involving children, the IRB must determine that adequate safeguards have been included in the study to protect the rights and welfare of the child subjects.

Although the IRB recommends obtaining written parent permission (written consent) to enroll children in research as well as child assent, consent may be altered or waived for research involving children provided the investigator has adequately justified a waiver of consent (parental permission) and fulfilled the necessary waiver requirements. Justification for waiver of assent should also be provided.

The IRB may waive parental consent requirements in a non-FDA regulated study if the study is enrolling a population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), provided an appropriate mechanism for protecting the child subjects is in place [45 CFR 46.116 and 45 CFR 46.408(c)].

When considering studies involving child subjects where consent is required, the IRB will also consider the length of the study and the age range of potential child subjects to determine if consent of the child upon reaching the age of majority should also be obtained for the child (now an adult) to continue on study. In particular, the protocol submission for long term studies such as registries should address how consent for continued participation on study of subjects who were originally enrolled as minors will be obtained when the minors reach the age of majority.

Effective September 1, 2005, all faculty who will be enrolling pediatric populations on research protocols must complete the pediatric research training mandated by the Dean for Clinical Research and Associate Vice President for Research. New faculty will be required to complete the pediatric training (either by attending a training session or

completing online training) prior to the approval of any research protocols involving children. The IRB strongly recommends that all staff involved in research protocols that enroll children also receive training on this topic.

1. WARDS OF THE STATE

Wards of the state may be enrolled in research that is minimal risk or greater than minimal risk with the prospect of direct benefit provided all other conditions for the enrollment of children are met and appropriate consent is obtained from a legal guardian.

Per the federal regulations, children who are wards of the state or any other agency, institution, or entity can be included in research that is greater than minimal risk without the prospect of direct benefit ONLY if such research is:

(1) Related to their status as wards; or
(2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

The IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis for research approved under 45 CFR 46.406/21 CFR 50.53 or 45 CFR 46.407/21 CFR 50.54 (studies of greater than minimal risk without prospect of direct benefit).

B. PREGNANT PERSONS AND FETUSES

Subpart B of 45 CFR 46 sets the following conditions as "Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research":

1. 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.

2. 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.

3. Any risk is the least possible for achieving the objectives of the research.

4. If the research holds out
    - the prospect of direct benefit to the pregnant woman,
    - the prospect of a direct benefit both to the woman and her fetus, or
    - no prospect of benefit for the woman or the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means,

   the consent of the pregnant woman is obtained in accord with informed consent policies.

5. 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 informed consent policies, 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.

6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.

7. For children who are pregnant, assent and permission are obtained in accord with the provisions of federal and state regulations. (Please see Section VI "Informed Consent.")

8. No inducements will be offered to terminate a pregnancy.

9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.

10. Individuals engaged in the research will have no part in determining the viability of a neonate.

These provisions must be addressed with the original protocol for studies which involve pregnant persons and/or fetuses, or with the amendment if this population is being added.

C. NONVIABLE NEONATES AND NEONATES OF UNCERTAIN VIABILITY

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions outlined in 45CFR46 Subpart B 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 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.

These provisions must be addressed with the original submission for studies which involve nonviable neonates or neonates of uncertain viability or with the amendment if a population is being added.

1. NONVIABLE NEONATES

After delivery, nonviable neonates may not be involved in research unless all of the following additional conditions are met.

a) Vital functions of the neonate will not be artificially maintained;

b) The research will not terminate the heartbeat or respiration of the neonate;

c) There will be no added risk to the neonate resulting from the research;

d) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

e) The legally effective informed consent of both parents of the neonate is obtained, except that the provisions for waiver and alteration of informed consent are not applicable. 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 for consent, except that the consent of the second parent 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 these requirements.

2. NEONATES OF UNCERTAIN VIABILITY

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following conditions have been met:

a) The IRB determines that:

(i) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective,

OR

(ii) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

b) 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, except that the consent of the second parent or that person's legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

D. PLACENTA, DEAD FETUS, OR FETAL MATERIAL

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 and Illinois laws and regulations regarding such activities.

If information associated with the placenta, dead fetus, or fetal material 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 considered research subjects and appropriate procedures for enrolling these subjects must be followed.

If tissue will be obtained from a miscarried fetus, Illinois law requires that the consent of the parent be obtained for the use of this tissue. Use of this tissue will therefore require the use of a written consent form to obtain the consent of the parent.

Research on tissue obtained from an electively-aborted fetus is prohibited in Illinois.

E. PRISONERS

Federally-regulated research involving prisoners must meet the following criteria.

1. Research must fall under one of the categories in a-e, below. Note that categories c and d require the review of OHRP prior to approval.

a) It is a study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects.

b) It is a study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects.

c) It is research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after OHRP has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of intent to approve such research.

d) It is research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after OHRP has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research.

e) Effective June 20, 2003, waiver from the requirements at 45 CFR 46.306(a)(2):

   It is research that involves epidemiological studies that meet both of the following criteria:

   1) In which the sole purpose is
      a) to describe the prevalence or incidence of a disease by identifying all cases, or
      b) to study potential risk factor associations for a disease.

   2) Where the institution responsible for the conduct of the research certifies to OHRP in DHHS (acting on behalf of the Secretary) that the IRB approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)-(7) and determined and documented that
      a) the research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and
      b) prisoners are not a particular focus of the research.

The range of studies to which the waiver applies includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiological methods (such as interviews and collection of biological specimens) that generally entail no more than minimal risk to the subjects.

2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired.

3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.

4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project.

5. The information is presented in language which is understandable to the subject population.

6. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.

7. Where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

Federal regulations regarding prisoners in research apply both to cases where the subjects are incarcerated prior to study enrollment and in cases where a human subject becomes a prisoner after being enrolled in a study. When a subject becomes a prisoner after being enrolled into a study, the investigator should immediately inform the IRB of this event. The IRB must then re-review the study with a prisoner representative present to ensure that the additional safeguards for prisoners in research have been met for this subject. The PI and the IRB should also consider whether the subject-now-a-

prisoner can remain in the study. The subject-now-a-prisoner should not participate in any study-related procedures until the IRB has re-reviewed the study.

If it is determined that the prisoner-subject should be withdrawn from the study, the subject should be informed of the specific reason for the withdrawal. At this time, the IRB should also consider whether the consent form for the study should be revised to inform future subjects that any subsequent incarceration would result in their removal from the study without their consent.

The IRB will inform OHRP should it approve any federally-funded studies specifically targeting prisoners in research.

The prisoner representative member of the IRB Committee must review any federally-funded study for which it is expected that a prisoner or prisoners will be a study population, both at the time of original submission of the protocol and at the time of each subsequent continuing review, so long as the investigator indicates that prisoners may still be included on the study. The prisoner representative must also review any amendments to the protocol. Similarly, amendments to add prisoners as a study population are also subject to these review requirements.

Unanticipated problems occurring on a study involving prisoners will be specifically noted and the prisoner representative consulted, as necessary.

F. OTHER POPULATIONS

Federal regulations identify additional populations that may be considered vulnerable. Language regarding these other populations is found at 45 CFR 46.111(b): "When some or all of the subjects are likely to be vulnerable to coercion or undue influence, … additional safeguards have been included in the study to protect the rights and welfare of these subjects." The BSD/UCMC IRB has therefore identified and requires particular care be taken of subjects who are members of certain specific populations. These populations may include:

- persons with intellectual disabilities;
- the decisionally impaired;
- economically or educationally disadvantaged;
- University of Chicago students;
- infants (under the age of one year);
- the elderly (ages 60 and over); and
- illiterate persons.

The protocol submission form must indicate the appropriate category of special population to be included as research subjects. Supplemental documentation may be

required with the protocol submission or with an amendment (if a special population is being added) in certain instances to ensure additional protections are in place for these populations.

1. UNDERGRADUATE STUDENTS AND EMPLOYEES

The Dean of Students of the University of Chicago is particularly concerned with the involvement of undergraduate students at the University of Chicago in research protocols. Protocols involving students will be sent to the Dean of Students for review. The Dean of Students may then contact investigators directly with questions, although in most instances, communication will be handled via the IRB staff or Chair. The Dean must inform the IRB whether the research is or is not appropriate prior to its approval by the IRB.

In addition, published OHRP guidance, while allowing the possibility of enrolling students and employees, emphasizes the need for carefully considering whether the inclusion of students and employees can be justified since the investigator's relationship with students and employees is potentially coercive.

Recognizing that a potential for coercion exists when an employer or faculty member recruits a subordinate to participate in a research study, the IRB may request additional safeguards for proposed research in which investigators will enroll students or employees over whom they have, or they can reasonably anticipate having, a supervisory role. The IRB will consider the inclusion of students and employees in research if the investigator has proposed adequate methods and guidelines for recruitment and participation to minimize coercive elements and risks to privacy and confidentiality.

As a rule, the IRB disapproves of recruiting employees or students as a targeted population merely for the sake of convenience or because of their easy availability. In addition, the IRB recommends that students and employees should be recruited through general announcements, bulletin board postings or advertisements, rather than individual solicitations.

The IRB recommends that employees and students assigned to a particular investigator or laboratory should not be directly recruited for participation in any study conducted by that investigator or laboratory, although such employees and students may, on their own, volunteer to participate.

Investigators seeking to target students and employees for enrollment must describe in their IRB application how they will avoid creating the perception that participation in the research by a student or employee will favorably influence the participant's professional or academic career. Investigators must stress that

the student/employee's performance evaluations, job advancement, or grades will not be influenced by participation or lack of participation in the research study. As appropriate, the IRB may require language to that effect in the consent document.

VIII. IRB PROCEDURES FOR THE REVIEW OF NEW PROTOCOLS

Upon receipt of a protocol, the IRB staff reviews it for completeness and notifies the investigator of any apparent problems. Each protocol is assigned a protocol number by which the protocol will be tracked.

Requests for expedited review for new protocols are reviewed by both the staff and the IRB expedited reviewer for appropriateness. Any protocol not appropriate for expedited review or consideration as "exempt" is reviewed by both the IRB staff and the full IRB. This includes all protocols that involve more than minimal risk to human subjects -- meaning a greater risk than that found in ordinary daily life. If a proposed study does not qualify for the requested level of review, investigators may be asked to resubmit their proposals in more detail.

Results of IRB deliberations are reported to the pertinent investigator in writing. The IRB may also report the results of Committee deliberations to applicable and appropriate institutional officials.

All questions regarding a protocol should be addressed to the assigned staff member; it is helpful to know the applicable protocol number when making inquiries.

A. COMMITTEE REVIEW OF NEW PROTOCOLS

Under federal regulations each IRB shall review protocols at a convened meeting at which a majority of the Committee members (a quorum) is present. All protocols determined to require full review are assigned to one or more primary reviewer(s) who present the protocol to the Committee for discussion. Reviewers are guaranteed anonymity, which they themselves may waive by direct contact with the investigator. The IRB office will not disclose the name(s) of reviewers unless legally required.

The protocol is discussed until consensus for approval, rejection, or revision is reached. Protocols are never assigned to reviewers who are the principal investigator or other member of the research team or who have a reporting relationship with the principal investigator. Committee members attending the meeting who are involved in the protocol being discussed are not involved in the final decision. A simple majority of voting members present is required for all final decisions. Following each IRB meeting, the principal investigator is informed of the protocol status in writing. (See Section B, below, for an explanation of protocol statuses.)

Per 45 CFR 46.111 and 21 CFR 56.111, the IRB must determine that the following requirements are satisfied in order to approve a research study.

1. Risks to subjects are minimized.

The IRB considers whether procedures are consistent with sound research design and whether or not study procedures unnecessarily expose subjects to risk. Whenever possible and appropriate, research studies should involve procedures already being performed on the potential subjects for diagnostic or treatment purposes.

2. Risks to subjects are reasonable in relation to anticipated benefits to subjects, if any, or the importance of the knowledge that may be expected to result from the study.

   The IRB considers only those risks and benefits that may result from the research, as opposed to risks and/or benefits of procedures or treatment that potential subjects would receive even if not participating in the research. The IRB is charged to consider the effects of the research on enrolled subjects and others today rather than the possible long-range effects of applying knowledge gained in the research (for example, effects on public policy).

3. Selection of subjects is equitable.

   The IRB considers the purposes of the research as well as the setting in which the research will be conducted in making this determination. In addition, the IRB must determine whether the enrollment or lack of enrollment of vulnerable populations is appropriate.

4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative.

   The consent process, including the individuals who will conduct the consent process, the timing of the consent process, and the setting will be considered by the IRB.

   This requirement may be waived if the research fulfills the regulatory and institutional requirements for a waiver or alteration of informed consent.

5. Informed consent will be appropriately documented.

   All consent documentation will be reviewed and any deficiencies noted.

   This requirement may also be waived if the research fulfills the regulatory and institutional requirements for a waiver of informed consent.

6. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

   The IRB may recommend that a Data Safety and Monitoring Board (DSMB) be in place before approving a study and may request that DSMB reports be forwarded to the IRB when available. The IRB may also recommend that other monitoring occur on a particular study.

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

   Investigators are asked to clarify measures in place to protect confidentiality, including identifying where records will be stored, who has access to records, and how records will be destroyed. In addition, investigators must clarify whether any samples or tissues to be analyzed will be labeled with identifying or linking information, and how this link and/or identifier will be protected.

   The IRB may consider additional confidentiality protections when vulnerable populations are involved or sensitive information (such as genetic information or HIV/AIDS status) is being collected.

8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

   Where some or all of the subjects are expected to be children, the study must fulfill all requirements of 45 CFR 46 subpart D (and if FDA regulated, 21 CFR 50 Subpart D). Similar requirements for prisoners (45 CFR 46 subpart C) and pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates (45 CFR 46 subpart B) must be met.

   Consideration will be given to whether safeguards may be needed for other potentially vulnerable populations on a per protocol basis.

B. POST REVIEW STATUS

As part of its review of a protocol, the Committee will assign a status to each protocol. It is the policy of the IRB to reflect the comments of the Committee and the primary reviewer(s) in the letters provided to PIs from the review process and to ensure that any conditions given are fully met by investigators prior to study approval. The IRB will not approve a study for which conditions and/or reviewer comments have not been fully addressed.

The IRB staff will communicate that status to the investigators following the IRB meetings. The status will be one of the following:

1. APPROVED or APPROVED WITH STIPULATION(S)

If full approval is granted, the investigator may begin the research proposed in the protocol. If, however, this protocol is a sponsor-initiated clinical trial, a fully executed agreement is needed before work may begin on the study.

If approval with stipulation(s) is granted, no immediate response to the IRB is needed and the research may be initiated to the extent allowed by the stipulation(s).

2. PENDING-CONDITIONAL

A "Pending-Conditional" status may be given, requiring modifications in the protocol and/or consent form before initiation. Pending-conditional status may only be given when the required changes or responses are non-substantive and when the pending issue response will not affect the meaning or the level of risk of the protocol as reviewed. Pending-conditional responses should involve only a simple concurrence from the investigator.

Investigators have 60 days from the date of the pending-conditional letter to respond to the IRB. If these conditions have not been met within 60 days, the protocol submission may be considered withdrawn, unless extensions have been granted as determined by the IRB office. If withdrawn, any future submissions related to the original protocol will then be considered new submissions and given a new protocol number.

No human subjects research may be started until all conditions have been met and formal approval has been obtained from the IRB.

3. PENDING-DEFERRAL ("Deferral")

A deferred protocol must be revised and resubmitted to the IRB. Revisions generally entail substantial modifications to the protocol and/or the consent form. **Revised deferrals require further discussion and review by the committee to which they were originally assigned**. In certain cases, deferred protocols may be reviewed by a Committee to which they were not originally assigned, but this is unusual and will be determined on a case-by-case basis.

To respond to IRB concerns, an investigator should submit a letter to clarify deferral issues along with any revised documents. The response should be

authored by the PI. The IRB may also request to meet with the investigator to have major issues clarified. If a response to the deferral has not been submitted within 60 days of notice of deferral, the protocol may be considered withdrawn, unless extensions have been granted as determined by the IRB office. If withdrawn, any future submissions related to the original protocol will then be considered new submissions and given a new protocol number.

Again, no research may be started until all conditions have been met and formal approval has been obtained from the IRB.

4. REJECTED

Protocols may be rejected by the IRB. This may occur if a protocol has been deferred several times and the IRB feels that the problems with the proposed research have not been adequately addressed, or if the protocol design is not justified or poses severe or unnecessary risk to the subjects. The IRB will not accept any further revisions to a rejected submission. Investigators who wish to modify a submission such that it may be reconsidered by the IRB should submit a new request with substantial modifications incorporated. The decision to reject a protocol cannot be reversed nor overruled by any other University or outside Committee or entity.

5. TABLED

Protocols for which the Committee cannot reach a consensus of opinion in order to determine a status of approval, pending-conditional, pending-deferral, or rejection may be tabled until the next meeting for further discussion. Protocols may also be tabled if quorum is lost or if the Committee does not agree that appropriate expertise is present to review the submission.

C. MINOR CHANGES TO PREVIOUSLY APPROVED RESEARCH: PENDING CONDITIONAL RESPONSES

A status of pending conditional means that the IRB has approved a study pending certain defined changes. If those changes are made as requested, the study can be approved outright. However, if the study team submits changes in response to a pending conditional letter beyond those stated in the pending conditional determination letter, the pending-conditional response may require re-review by the convened IRB or may require additional review by an IRB member. In addition, if the study team cannot comply each all requested pending conditional items, the pending-conditional response may require re-review by the convened IRB or may require additional review by an IRB member.

In this case, the investigator may submit a memo in response to the pending-conditional letter to describe additional changes being made or why a change or changes is not being made, along with a modified submission form, consent form, and/or other supplemental information as requested by the IRB. Changes to previously submitted documents should be highlighted or otherwise noted.

45CFR46.110(b)(1)(ii) allows for non-Committee review of minor changes in previously approved research. If the additional changes or lack of requested change(s) submitted with the pending conditional response are determined by the IRB reviewer to be minor and do not substantially alter previously made determinations of the Committee as per 45CFR46.111, then a reviewer may review these additional changes without full Committee review. The IRB expedited reviewer may grant approval of the protocol but may not disapprove the protocol. If the reviewer has concerns with the pending conditional response and/or the additional changes made with the response, the reviewer may recommend that the response return for full Committee review.

It is the policy of the IRB that revisions to the overall study design and/or other changes to the protocol document will not be considered with a pending-conditional response. If the study team wishes to submit a revised protocol, it should be submitted with an amendment after the current protocol is approved or the current submission should be withdrawn and a new submission completed.

D. REQUESTS FOR EXPEDITED APPROVAL OF NEW PROTOCOLS

Federal guidance as required by regulations specify categories of research that may be reviewed on an expedited basis. The IRB staff provides the initial screening of whether a request for expedited review of a new protocol qualifies for expedited review; the Chair of the IRB or a designee is responsible for making the final determination as to whether a protocol is eligible for expedited review.

In order to determine whether a research project qualifies for expedited review, requirements at 45 CFR 46.111/21 CFR 56.111 as described above must be met. In addition, the details of the protocol must indicate that the research activities fulfill requirements A and B and one of the categories under C as outlined below (see 45 CFR 46.110/21 CFR 56.110 and 1998 OHRP guidance on *"Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure"*):

A. The research activity poses no greater than minimal risk to the subjects; AND

B. The identification of the subjects and/or their responses would not reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's 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 no greater than minimal; AND

C. The project falls under one of the expedited categories listed below.

(1) "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."

Collection of data on routine use of a drug or medical device will generally fall under this category. Administering an approved drug or medical device as part of an interventional research study may or may not fall under this category.

(2) "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."

(3) "Prospective collection of biological specimens for research purposes by noninvasive means. *Examples: (a) hair and nail clippings in a nondisfiguring 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) "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) "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.)"

Research involving materials that "have been collected," i.e. existing materials, should specify the timeline from which data and/or materials originate. For IRB review purposes, to qualify as a purely retrospective study all data including outcomes and follow-up information must be dated prior to the IRB approval date.

Expedite category 5 requires that data to be used in the research must be collected solely for clinical purposes OR that all of the data is retrospective (including outcomes and follow-up data). Therefore, use of data from another research study is only allowed under this category if all data are existing as of the date of IRB submission.

If prospective collection of data from medical records is planned, the IRB Committee asks that written consent be obtained. Under the HIPAA regulations, written authorization is required for the use of private, identifiable information from medical records for purposes other than treatment, payment, or health care operations.

If a waiver of consent is being requested for the retrospective review of records, both waiver of consent and waiver of HIPAA authorization must be justified. This includes providing a justification as to why it is impracticable (i.e. impossible) to conduct the research without a waiver. The investigator should

provide a compelling argument as to why the research could not be done if a waiver of consent was not granted. The investigator must also document why the PHI is necessary for the research as well as how it will be protected from improper use and disclosure. In most cases, requests for waiver of consent/authorization for the prospective collection of data from medical records will be assigned for full review at an IRB meeting in order to consider whether the justification provided by the researchers for waiving consent is sufficient.

(6) "Collection of data from voice, video, digital, or image recordings made for research purposes."

Under Illinois state law, written consent is required for recordings. Every person being recorded must provide written consent for recording as part of the research consent/authorization.

(7) "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."

If investigators believe that a study qualifies for expedited review, they should: (1) complete an entire submission form as required for every protocol and (2) complete the "request for expedited review" section of the submission form. The applicable expedite category on this list should be selected by the investigator. The investigator should also provide any applicable documentation to justify expediting the protocol under this category.

Expedited reviews take place independently of the scheduled meetings. As soon as investigators receive notice of expedited approval, research may be initiated. IRB staff will either inform PIs in writing that the protocol has been expedited or notify PIs that the protocol requires full IRB review at a convened meeting.

The IRB expedited reviewer may grant approval of an expedited protocol but may not disapprove the protocol. Any vote to reject the protocol must come from the convened IRB Committee after full Committee review.

1. LIMITED IRB REVIEW

Under the Common Rule, certain categories of research that are considered exempt from IRB review still require that a limited IRB review be conducted in order to make required findings about the research. Limited IRB review will be

performed by an IRB reviewer who has been designated by the Chair to conduct expedited reviews.

Research that requires limited IRB review should not be initiated until the IRB reviewer has indicated that research has met all requirements.

D. EMERGENCY RESEARCH AND EXCEPTION FROM INFORMED CONSENT

The IRB may approve an investigator to conduct research without requiring informed consent of all research subjects, if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) determines and documents each of the following:

1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
2) Participation in the research holds out the prospect of direct benefit to the subjects because:
   a) Subjects are facing a life-threatening situation that necessitates intervention;
   b) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
   c) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
3) The clinical investigation could not practicably be carried out without the exception to the informed consent requirements.
4) An independent data monitoring committee will exercise oversight of the clinical investigation.
5) For research not subject to FDA regulations, IRB will find and document that the research was not subject to regulations codified by the FDA at 21 CFR 50 and that the criteria were applied in accordance with DHHS criteria.

Exception from informed consent is not allowed when the research involves protected populations as defined by 45CFR46 Subparts B-C.

1. INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for providing all study documents, the community consultation plan, and any additional materials requested by the IRB for review and approval. The investigator is responsible for conducting community consultation and public disclosure of the proposed research.

When the Investigator is unable to locate a legally authorized representative prior to enrolling a subject, the Investigator will attempt to contact, within the therapeutic window, a family member to ask whether that family member objects to the individual's participation. A summary of efforts to contact the legally authorized representative and family members is made available to the IRB at the time of continuing review.

For purposes of this policy, "family member" means any one of the following legally competent persons: spouses; parents; children (including adopted children); siblings and spouses of siblings; and any individual related by blood or affinity whose close association with the participant is the equivalent of a family relationship.

Investigator should provide scientific evidence for length of the potential therapeutic window; and then provide a plan to contact a legally authorized representative for each subject within that window of time. If feasible, the investigator should ask the legally authorized representative for consent. The investigator should summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review, if applicable.

The investigator should provide an informed consent document and procedure for obtaining informed consent from the subject or legally authorized representative consistent with policy and procedure on Informed Consent. These procedures and the informed consent document are to be used where feasible.

If a subject dies before a legally authorized representative can be contacted, information about participation in the research study should still be provided to the legally authorized representative.

2. COMMUNITY CONSULTATION

For research involving emergency exception from informed consent, the IRB requires that the investigator conduct community consultations that include:

a) Consultation with representatives of the communities in which the research study will be conducted and from which the subjects will be drawn;

b) Public disclosure to the communities in which the research study will be conducted and from which the subjects will be drawn, prior to initiation of the research study, of plans for the investigation and its risks and expected benefits; and
c) Public disclosure of sufficient information following completion of the research study to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.

3. IRB RESPONSIBILITIES

IRB staff will determine the investigational new drug (IND) or investigational device exemption (IDE) application allows inclusion of subjects who are unable to consent. Research proposals requesting for emergency exception from informed consent requirements require review at a full board meeting. Research proposals with the inclusion of subjects who are unable to consent are submitted in a separate IND/IDE even if an IND/IDE for the same drug or device already exists.

IRB will document that obtaining informed consent is not feasible because:

a) The subjects will not be able to give their informed consent as a result of their medical condition;
b) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
c) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

IRB will ensure that procedures are in place to inform, at the earliest opportunity, each subject or legally authorized representative, that the subject was enrolled in a research study. The investigator should discuss the informed consent document with the subject or legally authorized representative.

IRB will also ensure that there is a procedure to inform the subject or legally authorized representative that participation may be discontinued at any time without penalty or loss of benefits to which the subject is otherwise entitled. IRB will ensure that procedures are in place to inform the subject, or if the subject remains incapacitated, a legally authorized representative, or if such a representative was not reasonably available, a family member, that they might discontinue the subject's participation at any time without penalty or loss of benefits to which the subject was otherwise entitled.

In addition to the criteria for approval in policy and procedure on initial review, IRB will review and approve the community consultation plan provided by the investigator. Following completion of the consultation as per the proposed plan, based on the response from these consultations, IRB will make a determination whether the study can be approved or if additional consultations are needed.

If IRB determines that it cannot approve a research study because it does not meet the criteria for exception from informed consent requirements for emergency research or because of other relevant ethical concerns, IRB shall provide these findings promptly in writing to the investigator. IRB will require the investigator to notify the sponsor to disclose this information to:

a) FDA*;
b) Other investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor;
c) Other IRBs that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

*When research is not subject to FDA regulations, but follows DHHS regulations, the IRB finds, documents, and reports to DHHS that the conditions of this policy have been met relative to the research.

The IRB will instruct investigators to provide the sponsor with a copy of the information that has been publicly disclosed if they haven't already done so.

If another IRB reviewing this or a substantially equivalent investigation by the sponsor determine that it cannot approve a clinical investigation because the investigation does not meet the criteria for exception from informed consent requirements for emergency research or because of other ethical concerns, the sponsor must notify the IRB.

IX. IRB PROCEDURES FOR THE REVIEW OF AMENDMENTS

When **any** revision to an approved research protocol is desired, including a change in written consent form, co-investigators, research design, and/or advertisement for subject recruitment, the investigator must submit an amendment to the IRB.

Amendments to approved protocols may not be initiated until IRB approval has been obtained, except where necessary to eliminate apparent immediate hazards to the subject.

If the IRB has previously been notified that a study is permanently closed to enrollment and study procedures are limited to data analysis or collecting data from clinical follow up only, amendments for that study should be limited to administrative or informational changes. Enrolling additional subjects on such a study would typically require a new protocol submission rather than an amendment.

A. AMENDMENT SUBMISSION

The amendment should explain what changes are desired as well as provide a rationale for those changes. A revised copy of the pertinent original documents (e.g. protocol, consent form, questionnaire, or advertisement) should also be submitted with the changes identified. A cover letter or additional information may be attached as necessary.

A required element of informed consent is that subjects are provided with "a description of any reasonably foreseeable risks or discomforts" [45CFR46.116(b)(2) and 21CFR50.25]. Therefore, if physical risks of study participation are being altered with the amendment, including risks described in a new or revised investigator brochure, and the protocol is open to enrollment and/or the revised risk information could affect subjects already on study, it is expected that a revised consent form describing the revised risks will be submitted with the amendment. If a revised consent form is not submitted, the research team is expected to a) indicate how current subjects will be informed promptly of the new risk information and b) indicate that enrollment is halted voluntarily until a revised consent form has been approved by the IRB.

Amendments often require full Board review at a scheduled meeting; researchers should consult the IRB website for submission deadlines. At the discretion of the IRB expedited reviewers and senior IRB staff, amendments that reflect simple and/or minor administrative changes and which do not increase the risk to the subject may be reviewed by an expedited process.

Notification of approval of an amendment is handled like the procedure for notification of approval of new protocols. See Section VIII.

B. AMENDMENT POST REVIEW STATUS

As part of its review of an amendment, the Committee will assign a status. It is the policy of the IRB to reflect the comments of the Committee and the primary reviewer(s) in the letters provided to PIs from the review process and to ensure that any conditions given are fully met by investigators prior to study approval. The IRB will not approve an amendment for which conditions and/or reviewer comments have not been fully addressed.

The IRB staff will communicate that status to the investigators following the IRB meetings. The status will be one of the following:

1. APPROVED or APPROVED WITH STIPULATION(S)

If full approval is granted, the investigator may initiate the changes requested in the amendment.

If approval with stipulation(s) is granted, the changes to the research may be initiated to the extent allowed by the stipulation(s).

2. PENDING-CONDITIONAL

"Pending-Conditional" status requires modifications to the proposed changes prior to approval. Pending-conditional status may only be given when the required changes or responses are non-substantive. Pending-conditional responses should involve only a simple concurrence from the investigator.

As with new submissions, investigators have 60 days from the date of the pending-conditional letter to respond to the IRB. If these conditions have not been met within 60 days, the protocol submission may be considered withdrawn, unless extensions have been granted as determined by the IRB office. If withdrawn, any future amendments will be given a new amendment number.

No changes in research should be initiated until all conditions have been met and formal approval has been obtained from the IRB.

3. PENDING-DEFERRAL

A deferred amendment must be revised and resubmitted to the IRB. Revisions generally entail substantial modifications to the amendment, such as providing greater justification for the proposed change or making extensive revisions to submitted documents. Revised deferrals require further discussion and review

by the Committee. In certain cases, deferred amendments may be reviewed by a Committee to which they were not originally assigned. This will be determined on a case-by-case basis.

To respond to IRB concerns, an investigator should submit a letter with the revised amendment in order to clarify discussion points. The response should be authored by the PI. The IRB may also request to meet with the investigator to have major issues clarified. If the IRB has not heard from the investigator within 60 days of notice of deferral, the amendment may be considered withdrawn.

Again, no changes in research should be initiated until all conditions have been met and formal approval has been obtained from the IRB.

4. REJECTED

Amendments may be rejected by the IRB. This may occur if the changes to the protocol design pose severe or unnecessary risk to the subjects or proposed changes are not in accord with policies or practices at this site. The IRB will not accept any further revisions to a rejected amendment.

5. TABLED

Amendments may be tabled if quorum is lost, if the Committee agrees that further information is required in order to review the submission, or if the Committee agrees that appropriate expertise is not present.

C. EXPEDITED AMENDMENTS

Amendments may be given expedited approval if the modification is minor, does not increase the risk to subjects, and does not involve a safety concern. Examples of "minor administrative" changes that may be expedited include:

- adding or removing an institution
- changes in the PI or other research personnel
- adding a standardized (validated) questionnaire
- modification of a previously approved advertisement (such as a change in mode or verbiage)
- changing or adding a location where samples or data will be sent
- modification of investigational brochures that do not affect risks to subjects
- minor editorial modifications to the protocol and/or consent form which do not alter the meaning or procedures or
- removal of a questionnaire and its reference in the consent form.

This list is not exhaustive. IRB members and alternate members designated as expedited

reviewers are responsible for making the final determination as to whether an amendment is eligible for expedited review and whether or not a change is considered minor, administrative, and minimal risk.

The following changes are considered major changes that are not eligible for expedited review:

- report of safety concerns
- extension of study duration
- multiple changes in study design
- additional arm and/or population added to the study
- increase in drug dose or infusion rate
- additional radiation exposure
- new software in devices

At the discretion of the IRB reviewer, amendments to protocols of minimal risk that do not alter the risk level may also be expedited if the protocol was originally expedited.

X. IRB PROCEDURES FOR THE CONTINUED MONITORING OF APPROVED PROTOCOLS

A. CONTINUING REVIEW AND RENEWAL

In accordance with federal regulations at 21 CFR 56.109(f), the IRB is required to ensure that all FDA-regulated active protocols receive "not less than annual review." In addition, certain research activities regulated by 45CFR46 require "review by the convened IRB at intervals appropriate to the degree of risk, not less than once per year." This process is known as continuing review.

Research that has been approved without a requirement for continuing review not less than annually will still be required to submit notification to the IRB of any protocol changes (see Section VIII) and of any unanticipated problems (see Section II).

1. CONTINUING REVIEW SUBMISSION AND TIMELINE

Due to the large numbers of studies applying for renewal each month, the IRB requires adequate review time prior to study expiration to ensure that all submitted renewals are reviewed appropriately. Therefore, approximately three months prior to the study's expiration, investigators are notified of any protocols that require continuing review that are due to expire in that certain month. The PI should then fill out and submit a continuing review form for these protocols due to expire. The form must be completed in full and electronically signed by the principal investigator.

Investigators are asked to provide with the continuing review form (if not already available to the IRB) updated consent documents in the current format, advertisements used to recruit subjects, non-validated surveys and/or questionnaires, approval letters from outside sites supported by U of C funds or at which research is conducted by the U of C investigator, grant progress reports, DSMB reports, reportable and non-reportable event summaries, and updated information relating to known or potential conflict of interest, as appropriate, depending on the status and nature of their protocols. The IRB staff conducts an administrative preliminary review of the renewal application and may request any information that has not been provided with the continuing review form.

The IRB initiates the renewal process to the best of its abilities. However, **it is the responsibility of the principal investigator to ensure that continuing review is completed and approved by the IRB prior to the protocol expiration date**. Continuing Review submissions must be completed in full and received by the IRB office by the IRB submission deadline in order to be reviewed. As a courtesy, the IRB may send a follow-up delinquent notice for inadequate, incomplete, or

otherwise delinquent responses, including submissions containing insufficient information relating to the consent form or continuing review form as requested by the IRB staff or reviewers. Delinquent forms must be reviewed by the IRB prior to the protocol's expiration date.

Failure to provide an adequate and timely response to the IRB will result in an AUTOMATIC EXPIRATION of the protocol. The IRB will consequently send a notice of expiration to the principal investigator. In this case, if future use of the protocol is requested, new submission and approval of the protocol is required.

If a protocol expires, it may no longer accrue subjects and protocol activities must cease, unless these activities are required to ensure the rights and welfare of enrolled study subjects. In addition, if a protocol is subject to FDA regulations due to the use of an investigational drug or device and the protocol expires, all research activity must cease, no additional subjects may be accrued, and enrolled subjects must be notified that the study has expired. Moreover, if the research project is externally funded, sponsor requirements, including those of the NIH, may preclude the investigator from using award funds for human subject-related activities during the period between the protocol expiration date and the date of approval of a resubmitted protocol.

If continuing review is required, the protocol will be renewed for a period no longer than one year. The approval period may be shorter than one year at the discretion of the IRB.

2. REVIEW AT MEETING

During the Committee's review of the protocol for continuing review, the IRB may find that additional information or revisions are needed, in which case the renewal may receive a status of "deferral" or "pending-conditional." A "deferral" or "pending-conditional" vote does not extend the approval period of the protocol; the PI must still respond prior to the expiration date as previously given. Therefore, it is again necessary that the principal investigator respond quickly so that the protocol is renewed prior to expiration.

If the Committee is not able to review a continuing review due to loss of quorum or lack of appropriate expertise, the submission may be tabled. If the submission is tabled, again, the expiration date does not change and the submission must still be reviewed by the IRB prior to the expiration date.

As with new protocols and amendments, it is the policy of the IRB to reflect the comments of the committee and the primary reviewer(s) in the letters provided to PIs from the review process and to ensure that any conditions given are fully

met by investigators prior to study approval. The IRB will not renew a study for which conditions and/or reviewer comments have not been fully addressed.

If approval with stipulation(s) is granted, no immediate response to the IRB is needed and the research may continue to the extent allowed by the stipulation(s).

3. EXPEDITED CONTINUING REVIEWS

In some cases, the IRB may expedite renewals per 45 CFR 46.110 and 21 CFR 56.110 (see OHRP guidance on "Categories of Research that May be Reviewed by the Institutional Review Board (IRB) Through an Expedited Review Procedure"). The research must fall under at least one of the following five categories.

(1) The research was originally reviewed and approved under expedited procedure and continues to fall into one of the expedited review categories (as outlined in Section VIII.C, above).

OR

Continuing review of research previously approved by the convened IRB as follows:

(2) 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
(3) where no subjects have been enrolled and no additional risks have been identified; or
(4) where the remaining research activities are limited to data analysis; or
(5) where the research was not conducted under an investigational new drug application or investigational device exemption and where the original expedite categories 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.

Investigators requesting expedited review of continuing review materials should ensure that the research does indeed fall into an expedited category to avoid delay should the protocol, upon review by the IRB, not qualify for expedited review and require review at a convened meeting.

B. MONITORING OF APPROVED PROTOCOLS

1. CONTINUING REVIEW

Protocols requiring continuing review are granted approval for no longer than one year. Many protocols thus have an approval period of one day less than one year. However, if the IRB has concerns about an approved research protocol, an investigator may be asked to submit a progress report within a shorter time frame than one year for re-review by the full Board. Reminders will be sent to the investigator to provide a report of study progress. Occasionally, investigators may be asked to present a verbal report of their research progress at an IRB meeting.

If the IRB Committee reviews a study and finds that because of safety concerns or other factors, the protocol will not be renewed, this termination of the protocol by the Committee will be reported to OHRP. This termination of approval by the Committee may occur during the renewal process, review of an amendment, or during any other review of protocol events or reports. The PI will be notified by formal letter should this termination occur. As with any other termination, the PI should notify the sponsor or funding agency of the new study status.

Finally, if the IRB receives information that suggests that an approved protocol for which continuing review was not previously required requires a status update and/or additional monitoring, the IRB may require that a continuing review be submitted to the IRB.

2. OUTSIDE MONITORING

As necessary and appropriate, subcommittees of the IRB may be utilized to conduct mandated random surveillance of protocols. In addition, due to a high-risk element or the particular nature of a specific protocol, the IRB may feel the need for further monitoring and may request the Department Chair or Section Head to provide closer surveillance and to report to the Board on a routine basis concerning that protocol.

Any reports from agencies, groups, or Committees external to the University which regularly audit or otherwise monitor the research, including DSMBs and outside groups such as the CALGB or GOG, should be forwarded to the IRB as they become available.

3. SURVEILLANCE COMMITTEE

All clinical Department Chairs comprise the Surveillance Committee. The IRB may call upon them collectively or individually, as appropriate, to assist in the enforcement of research guidelines. In addition, it is expected that all IRB Committee members and Department Chairs will notify the IRB Chair, Dean of the Division, Director of Regulatory Compliance, or the Associate Vice President

for Research Administration if they are aware of circumstances which may be of concern to the IRB. It is the responsibility of the IRB at their discretion to report any serious or continuing noncompliance by investigators or unanticipated problems involving risks to subjects or others to the institutional official or FDA, as appropriate. (See Section II for more information on reporting noncompliance.)

4. SUSPENSION OF A PROTOCOL

In unusual circumstances, if it appears to the IRB that the apparent risk to human subjects has increased significantly in an approved ongoing protocol or new knowledge concerning risk becomes known, the IRB may suspend its approval of a protocol. In this situation, upon written notification, the investigator must immediately stop all research involving the indicated protocol. In most cases, modifications are possible, and research can be resumed when the IRB has reviewed the situation and is satisfied that the protocol meets all regulations and complies with ethical concerns for the protection of human subjects. More rarely, the IRB may request that a protocol be halted permanently.

The IRB has the right to suspend and/or terminate approval of research that is not being conducted in accordance with any stated requirements or that has been associated with unexpected serious harm to subjects.

5. IRB AUDITING

The Office of Clinical Research has designed an auditing program in order to better monitor approved protocols. An OCR staff member may be assigned to audit a particular protocol or PI to ensure that the approved procedures are being followed, including the use of the approved version of the consent form and other documents, and to ensure that human subjects and their data are being protected in the research setting. Submissions will be audited to ensure compliance with the determinations of the reviewing IRB. The audit program is not designed to penalize or reprimand investigators, but rather to encourage and educate investigators on regulatory and ethical guidelines for the proper conduct of a research study.

Per 45CFR46.109(g), the IRB has the authority to observe or have a third party observe the consent process and the research.

Investigators will be informed prior to an audit of the intention to perform an audit. Audit results will be made available to the investigator.

C. INVESTIGATING NONCOMPLIANCE

As previously stated, the IRB is responsible for reporting any serious or continuing noncompliance by investigators to the Institutional Official and the FDA, as appropriate. Although audits are not intended to uncover noncompliance, an audit may reveal a serious problem that requires reporting.

Every noncompliance report or complaint about human research protections is taken seriously by the University. Any allegation or complaint received by the University will be referred to the appropriate IRB for initial assessment and follow up.

Reports of potential noncompliance that are received by Principal Investigators must be disclosed to the IRB. This report should be made using the Unanticipated Problem report form. Each report disclosed to or received directly by the IRB is initially documented and evaluated by the appropriate IRB Chair or designee and IRB administrative staff; follow up will also be documented. The IRB is responsible for assuring that the report of noncompliance is investigated appropriately relative to its level of seriousness, taking special steps to assure that problems involving risks to health and wellbeing of subjects have first priority. The IRB shall move quickly to suspend or terminate approval of research that is suspected of causing serious harm to subjects at the University of Chicago. A PI may also voluntarily elect to suspend subject accrual to a protocol on which an allegation of noncompliance is being investigated.

The BSD/UCMC IRB is responsible for carrying out initial inquiries and reporting the outcomes as follows.

1. STUDY SUSPENSION

The IRB will determine if immediate suspension of enrollment is required for the protocol in question as well as for other protocols with the same PI. This initial decision, including the duration of the suspension, will be made by the IRB Chair or designee in consultation with IRB Administrators and other institutional officials as may be appropriate.

The initial inquiry will examine information such as the nature of the study and whether or not the consent form contained inappropriate information. A report of the factors considered will be prepared and the IRB Chair or designee, in consultation with the IRB Director, will determine whether the report must be brought before the full IRB Committee prior to forwarding to the PI. The Report must include the date and signature(s) of the IRB officials who made the determination, with a statement of the conclusion and the subsequent action(s) to be taken. All communication and ultimate resolution of the situation will be documented and maintained in the IRB protocol file.

If the IRB Chair or Board, in consultation with the IRB Director, determine the situation does not merit suspension, a letter stating this will be sent to the PI and a copy of all communication and ultimate resolution of the situation will be documented and maintained in the relevant IRB protocol file(s).

If the report indicates that suspension of the research study is merited, further steps are required:

a) Notice of suspension effective immediately will be sent to the PI, department Chair, institutional official, and IRB Chair. The notification includes the requirement to halt further participant enrollment and the timeline for doing so. When the PI voluntarily elects to suspend a study while an investigation of noncompliance is undertaken, the IRB must notify the Institutional Official that a voluntary suspension is in place, identifying the PI, the protocol, and a preliminary indication of the situation.

b) Within two working days, the IRB Chair, Vice Chair(s), IRB Administrator, PI, and other parties as may be appropriate given the circumstances, shall discuss the nature of the situation and determine if the situation merits a designation of serious or continuing noncompliance.

c) Further study of the situation, including an examination of consent forms, all data related to the study, IRB protocol documentation, and other data or documents may be necessary to determine whether a designation of serious or continuing noncompliance is warranted. The PI is required to produce whatever records are called for by the IRB and University. The IRB may take what steps are considered appropriate and necessary to carry out its initial investigation, including the use of outside experts. Any involvement of investigation where outside expertise is solicited will not be undertaken without the knowledge and concurrence of the Institutional Official.

The results of the review of protocol and study records and discussions with the PI will determine whether the situation is of nonserious and noncontinuing nature.

2. NONSERIOUS AND NONCONTINUING

If the incident appears to be isolated and of a nonserious and noncontinuing nature, the incident will remain internal to the University and the documentation will remain with the IRB. A letter from the IRB office to the PI summarizing the investigation of the allegation will be written. A response from the PI describing corrective actions is also required. IRB Chair/Vice Chair acceptance of the PI

response and corrective action will constitute closure to the incident. Suspension of subject enrollment will be lifted.

3. SERIOUS OR CONTINUING

If the IRB determines that the situation should be considered serious or continuing, the IRB must notify the University Institutional Official, including a copy of the investigative report, no later than 48 hours after the determination of serious and/or continuing is made, no matter whether the project is externally funded or not. Reports of serious and/or continuing noncompliance must be brought before the full IRB for review. If the research is not federally funded, the IRB may make a recommendation as to whether the noncompliance should be reported to OHRP, recognizing that the University's FWA requires federally-funded serious and continuing noncompliance to the reported to OHRP and other federal agencies as may be necessary.

The institutional official coordinates review of the IRB's investigation of a situation determined to be serious or continuing with appropriate institutional officials, including the Office of General Counsel and the Office of the Provost. It is the responsibility of the institutional official, when the University is required to make a disclosure, to notify OHRP, FDA, or other required sponsor when or if it elects to self-report. The institutional official will notify OHRP (or FDA or other appropriate agency as may be required) of the incident of serious, continuing noncompliance. The notification letter will briefly describe the incident, the preliminary corrective steps, and the time frame for full audit and full report to follow, including corrective actions for this specific incident and for the research program in order to ensure that such incident(s) will not occur again.

The institutional official and the IRB Chair and IRB Director will assure that all documentation supporting the audit of the incident, any additional audits of other research conducted by the investigator in question, and all communication with internal offices and other regulatory bodies at the University of Chicago as may be required are completed. It is the responsibility of the IRB to maintain all audit records of the investigation and to assure that all corrective action requirements made by the IRB and/or the University are implemented.

4. CORRECTIVE ACTION STEPS

In the course of investigation of allegations of noncompliance, corrective actions plans may be stipulated to assure that the situations giving rise to the investigation do not occur again. Examples of corrective action plans that may be initiated by the PI or imposed by the IRB and/or the University include, but are not limited to:

- Suspend the research until certain conditions are met
- Terminate the research
- Require additional training for research staff
- Impose other sanctions, such as limiting the number of subjects to be enrolled
- Require modifications/amendments to the protocol

XI. OTHER RESEARCH OVERSIGHT COMMITTEES

Occasionally, other committees at the University of Chicago may be required to review human subjects research in conjunction with the IRB. Investigators should ascertain whether submission to any other committee is necessary, and if so, that approval from that committee is sought prior to or concurrent with IRB review, as required.

A. RADIOACTIVE DRUG RESEARCH ADVISORY COMMITTEE (RADRAC)

The University and University Medical Center Combined Human Use of Radioactive Drug Research Advisory Committee is charged with the responsibility for review, approval and surveillance of the purchase and use of radioisotopes in humans (including research and routine) at the University of Chicago and University of Chicago Medical Center. All research protocols submitted to the RADRAC are also required to be submitted to the IRB for approval. A copy of the RADRAC's approval must be referenced in the IRB's files and approval of the IRB Committee is contingent upon RADRAC approval. Coordination of review by these committees will be done through the IRB staff.

The IRB requests that for any protocol proposal involving radiation in human subjects, the investigator complete the applicable section of the IRB submission so that the IRB Committee may assess whether submission to the RADRAC is also necessary.

B. NURSING RESEARCH COMMITTEE (NRC)/NURSING EVIDENCE-BASED RESEARCH COUNCIL (NERC)

The purposes of the Nursing Research Committee (NRC) are to facilitate the implementation of clinical research involving nursing staff and/or nursing care and to support evidence-based nursing practice. Nurse investigators wishing to implement clinical research involving nursing staff and/or nursing care are required to obtain approval from the NRC as well as from the IRB before proceeding with their study. Nurses who are hired to do research and collect data for physicians' research or those hired as Clinical Research Associates are exempt from bringing their proposals to the NRC. Nurses who are doing independent research are required to submit their proposal to the NRC prior to submitting their proposal to the IRB.

A copy of the NRC/NERC approval must accompany the IRB submission. Investigators should contact the head of the Nursing Research Committee in the University of Chicago Medical Center for more information.

C. INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)

The Institutional Biosafety Committee is charged with the responsibility for review, approval, and surveillance of all research protocols at the University of Chicago involving the use of biohazardous materials. Biohazardous materials include recombinant DNA, agents infectious to humans, animals, or plants (e.g. parasites, viruses, bacteria, fungi), and other genetically altered organisms and agents. Most commonly, these would include gene therapy protocols.

A copy of each Committee's approval must be cross-referenced in the other Committee's files and approval of one Committee will be contingent upon the other. Coordination of review by these committees will be done through the IRB staff.

D. PROTOCOL REVIEW AND MONITORING COMMITTEE (PRMC)

All institutional clinical research protocols involving cancer patients must be reviewed by the Protocol Review and Monitoring Committee (PRMC) of the University of Chicago Comprehensive Cancer Center (UCCCC) in addition to the IRB. The PRMC was formerly known as the Clinical Trials Review Committee (CTRC). The PRMC is responsible for conducting scientific peer-review of institutional clinical research protocols including protocols that have not been reviewed and approved by the Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute (NCI) and all pharmaceutical company supported protocols. Cooperative group protocols (CALGB, GOG, CCG) and protocols reviewed and approved as part of a NIH (R01, P01, etc.) or national ACS grant are exempted from in-house review.

Clinical trials whose primary objective is to develop a new technology, procedure, or clinical tool and that enroll a broad spectrum of patients, only some of whom carry a cancer diagnosis, will not require PRMC review. On the other hand, protocols whose primary objective is to test the validity or limitations of a cancer diagnostic procedure or that enroll a cohort of patients with a defined cancer or cancer-prone syndrome will be subject to PRMC review.

PRMC review is required **prior** to IRB review.

Continuing reviews of studies originally requiring CTRC/PRMC review will be conducted by the PRMC of the UCCCC to ensure compliance with initially approved data and safety monitoring plans. Please contact the UCCCC for further information.

E. PATHOLOGY BIOSPECIMEN UTILIZATION COMMITTEE (PBUC)

Protocols in which the only objectives are to evaluate or study archival diagnostic specimens do not require PRMC review if they undergo review by the Pathology Biospecimen Utilization Committee (PBUC). Tissue evaluation protocols focused on cancer tissue that are not reviewed by this pathology committee will require full PRMC

review. In addition, protocols requiring prospective tissue collection and/or prospective clinical data collection will require PRMC review.

The IRB will require evidence of PBUC approval or PRMC approval prior to approving a study involving cancer patients or tissues.

PBUC approval is also required for all other studies that propose the use of non-cancerous archival tissue blocks from the Human Tissue Resource Center (HTRC).

F. CLINICAL RESEARCH CENTER (CRC)

The purpose of the Clinical Research Center (CRC) at the University of Chicago is to enable faculty to conduct clinical research protocols of high scientific merit. The CRC supports bed costs and/or ancillary services for inpatient and outpatient research. The CRC resources may be used alone or in combination with the investigator's other research support. The CRC makes space and support services available for faculty to conduct research initiated and sponsored by pharmaceutical or other biomedical industries. The terms of the CRC's grant require that it recover all costs of supporting such research and that the industrial concerns cover all hospitalization and ancillary expenses through contracts with the faculty investigators. If a faculty member wishes to do research in the CRC, specific CRC guidelines apply. While the CRC submission forms are different from the IRB forms, the CRC format for the scientific narrative is acceptable to the IRB. Please note that CRC approval is contingent upon IRB approval.

Please also consult any guidance provided by the Institute for Translational Medicine (ITM).