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THE INSTITUTIONAL REVIEW BOARD

The Institutional Review Boards (IRB) at Rush-Presbyterian-St. Luke's Medical Center (RPSLMC) are held accountable to the federal agencies that establish guidelines for the use of human subjects in research. The Food and Drug Administration (FDA) and Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP) are the primary regulating agencies for the IRB.

The Rush IRB policies and procedures, in keeping with federal guidelines and regulations requires that all research involving human subjects regardless of sponsorship, be reviewed by the Rush IRBs.

JURISDICTION OF THE RUSH IRB

Prior to beginning any research project, a complete research proposal, all related sponsorship application materials, and all related contracts must be submitted to the Office of Research Affairs (ORA) at the Rush-Presbyterian-St. Luke's Medical Center (RPSLMC) if any of the following four conditions applies:

- (a) The research activities proposed take place on any real property owned or leased by the RPSLMC, including leased professional office space.
- (b) The research activities proposed are to be undertaken by a Principal Investigator employed by the RPSLMC for twenty or more hours per week. Medical Service Plan (MSP) providers are considered employees of the RPSLMC in every case. This category of employees must submit proposals and/or contracts to the ORA, regardless of the location where the research activity takes place.
- (c) the research activities proposed are to be undertaken by a Principal Investigator employed by the RPSLMC less than 20 hours per week throughout the duration of the study, but:
 - (i) the research activity is an explicit component of the part-time employee's job description at the RPSLMC; or
 - (ii) the part-time employee identifies him/herself as a RPSLMC faculty member, staff member, fellow, or employee in publications or presentations of the research work.

The last category of part-time employees must submit proposals and/or contracts to the Office of Research Affairs, regardless of the location where the research activity takes place. The research activities proposed are to be undertaken by a Principal Investigator who is a student of any undergraduate or graduate program of this Medical Center. This category of students must submit proposals and/or contracts to the Office of Research Affairs, regardless of the location where the research activity takes place

THE IRB PROCESS

The Institutional Review Board (IRB) is charged with the protection of human subjects in research, regardless, of whether the research is subject to federal regulation and regardless of the sponsor.

The IRB will review all projects when the research is sponsored by the institution, or; the research is conducted by or under the direction of any employee or agent of this institution in connection with his or her institutional responsibilities, or/ the research is conducted by or under the direction of any employee or agent of this institution using any property or facility of this

institution, or; the research involves the use of this institution's non-public information to identify or contact human subjects.

Rush has established two IRBs to perform the review of human subjects research. Each IRB will review human subjects research projects to determine approval criteria are met. The following will be considered prior to approval of any human subjects project before the IRB or IRB reviewer:

- 1) The risks to research subjects are minimized to the extent possible.
- 2) The risks to research subjects are reasonable in relation to anticipated benefits.
- 3) The risks to research subjects are reasonable in relation to the importance of the knowledge that may reasonably be expected to result.
- 4) The selection of research subjects is equitable.
- 5) Informed consent will be sought from each prospective research subject or the subject's legally authorized representative, in accordance with, and to the extent required by the federal regulations.
- 6) Informed consent will be appropriately documented, in accordance with, and to the extent required by the federal regulations.
- 7) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- 8) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- 9) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

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

Possible IRB actions

When the IRB does take action on a protocol, four different actions are possible. A protocol may receive a vote of approval, disapproval, provisional approval or a vote of no decision.

A vote of approval means that no additional information is required nor are any changes to the consent document required. The date of approval and the cycle for continuing review will be based on the date of the meeting at which approval was granted.

A vote to disapprove means that the IRB has found enough cause, and will document this cause, to prevent this project from beginning. This information will be sent to the principal investigator. The principal investigator will have the opportunity to respond to the committee's concerns either in person or in writing.

A vote of provisional approval means that upon receipt of the required changes/revisions and additional information, the protocol will be approved. Either the chair or a designated member of the IRB will review the material to assure that all issues were addressed. The date of approval and the cycle for continuing review will be based on the date of the meeting at which provisional approval was granted.

A vote of no decision means that the information requested is of a magnitude and importance such that the IRB wants to re-review the project after the changes have been incorporated or the questions answered.

The IRB will include a motion for the period of continuing review. Continuing review will take place at less than one year whenever they find the potential for harm to subjects is increased. The reason for more frequent review will be noted in the minutes.

SUBMISSION AND SCREENING

All applications are screened for complete documentation before being sent to the IRB for review. If the application is incomplete or otherwise not prepared for review, it is returned to the investigator to make the necessary changes, or to provide additional information.

There are three types of review possible: full review, expedited review, and exempt from further review.

EXEMPT STATUS

Federal regulations define research as exempt from committee review when the research involves no risk to the subject. Exempt from IRB review does not mean exempt from application. Exempt research is exempt only from continuing/annual IRB review. Therefore, an application requesting exempt status must still be filed and approved. All of the rights and protection afforded to human subjects in research are required in exempt status projects.

The Senior IRB Administrator will review the application and determine the applicability of exempt status to the project. The exempt status will be confirmed in writing to the Principal Investigator. Any research that is not within the exempt status range will be referred back to the investigator with other appropriate application materials.

See the attached regulations at the back of this booklet for a list of the criteria for exemption.

EXPEDITED REVIEW

The staff of the Office of Research Affairs (ORA) will review and assure that all of the essential elements for review, including consent forms and supporting documents are in place. ORA staff will give the project to the Chair of one of the IRBs or a member designated to review such projects. The IRB Chair or member will review the application, determine the applicability of expedited review to the project. The IRB reviewer may ask for additional information or request revisions to the consent document. Upon completion of this review and approval by the IRB reviewer the approval is then processed and released.

Federal regulations permit expedited review procedures for certain kinds of research that involve no more than minimal. See the list at the back of this booklet that documents the criteria for expedited review.

GUIDE TO CREATING AND SUBMITTING ADVERTISEMENTS

The IRB must review the methods and material that investigators propose to use to recruit subjects.

Direct advertising for study subjects is considered to be the start of the informed consent and subject selection process.

The following types of advertising for research subjects, must be reviewed and approved by the IRB: newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects.

The following types of advertising are not included:

- 1) communications intended to be seen or heard by health professionals, such as "dear doctor" letters and doctor-to-doctor letters (even when soliciting for study subjects),
- 2) news stories and;
- 3) publicity intended for other audiences, such as financial page advertisements directed toward prospective investors.

IRB review and approval of listings of clinical trials on the Internet is not required when the system format limits the information to the following:

- 1) the title
- 2) purpose of the study
- 3) protocol summary
- 4) basic eligibility criteria
- 5) study site location(s)
- 6) how to contact the site for further information

Examples of clinical trial listing services that do not require prospective IRB approval are:

- 1) National Cancer Institute's cancer clinical trial listing (PDQ)
- 2) Government-sponsored AIDS Clinical Trials Information Service (ACTIS).

The IRB will review the information contained in the advertisement and the mode of its communication. You must inform the IRB of every mode of communication you will be using the text of the ad for. If you change modes, you must receive IRB approval.

The IRB will consider the following points:

- 1) Advertisements cannot state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
- 2) The final draft of printed advertisements to evaluate the relative size of type used and other visual effects.
- 3) The audio/video tape and word choices used.
- 4) No claims should be made, either explicitly or implicitly, that the drug or device is safe or effective for the purposes under investigation.
- 5) No claims should be made either explicitly or implicitly that the test article is known to be equivalent or superior to any other drug, biologic or device.
- 6) Advertising for recruitment into investigational drug, biologic or device studies should not use terms such as "new treatment," "new medication" or "new drug". A phrase such as "receive new treatments" leads study subjects to believe they will be receiving newly improved products of proven worth.
- 7) Advertisements should not promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation.
- 8) Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid, by such means as larger or bold type.

- 9) Advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest.

The following items may be included in advertisements:

- 1) the name and address of the clinical investigator and/or research facility
- 2) the condition under study and/or the purpose of the research;
- 3) the criteria that will be used to determine eligibility for the study;
- 4) a brief list of participation benefits, if any (e.g., a no-cost health examination);
- 5) the time or other commitment required of the subjects; and
- 6) the location of the research and the person or office to contact for further information.

When submitting any type of recruitment materials for IRB review and approval:

- 1) Submit **TWO** copies of the flyer, booklet, brochure, letter or other copy.
- 2) Submit one copy of the audio/video tape.

Once approved, your advertisement will receive either a letter of approval or a stamp of approval or both. If you have submitted a flyer for advertisement and this flyer is to be posted on Rush property, the flyer must bear the approval stamp of the Rush IRB. If your flyer requires that you print each one separately due to using colored ink, you may then maintain the approved copy on file for verification. All other types of advertisement require that you have the approved copy on file.

FULL COMMITTEE REVIEW

Research requiring full committee review is research that has been deemed more than minimal risk. This may include research with minors and other populations designated by the federal regulations as vulnerable (prisoners, pregnant women and fetuses), research that involves experimental drugs or devices; or invasive procedures.

After the full committee review, the application may be 1) approved as submitted, 2) provisionally approved with a request for revisions and/or clarification; 3) no decision and a request for further information, revisions or documentation; 4) disapproved. The IRB's action will be communicated to the principal investigator through the ORA

All human subjects research projects are subject to a re-review that takes place at least annually. High-risk projects may require more frequent review or reports. The terms for these special cases will be written in the original approval.

Possible IRB actions

When the IRB does take action on a protocol, four different actions are possible. A protocol may receive a vote of approval, disapproval, provisional approval or a vote of no decision.

A vote of approval means that no additional information is required nor are any changes to the consent document required. The date of approval and the cycle for continuing review will be based on the date of the meeting at which approval was granted.

A vote to disapprove means that the IRB has found enough cause, and will document this cause, to prevent this project from beginning. This information will be sent to the principal investigator.

The principal investigator will have the opportunity to respond to the committee's concerns either in person or in writing.

A vote of provisional approval means that upon receipt of the required changes/revisions and additional information, the protocol will be approved. Either the chair or a designated member of the IRB will review the material to assure that all issues were addressed. The date of approval and the cycle for continuing review will be based on the date of the meeting at which provisional approval was granted.

A vote of no decision means that the information requested is of a magnitude and importance such that the IRB wants to re-review the project after the changes have been incorporated or the questions answered.

The IRB will include a motion for the period of continuing review. Continuing review will take place at less than one year whenever they find the potential for harm to subjects is increased. The reason for more frequent review will be noted in the minutes.

RESPONSE TIME TO IRB REQUEST FOR REVISIONS

After IRB review, the principal investigator will receive approval or a request for more information or further revisions. The investigator has **10 workdays** to respond to any request for revisions, suggestions, etc., as set forth in the letter. If the investigator does not respond within that 10 day time period, the IRB will de-activate the application and in the case of new studies, all materials will be returned to the investigator. The study will then have to be re-submitted as a new application if the investigator subsequently wishes to obtain IRB approval.

PILOT STUDIES, PHASE I STUDIES AND FEASIBILITY STUDIES

Pilot studies and feasibility studies require the same scrutiny as full-scale research projects. The involvement of any human subject requires the independent review and determination of subject protection provided by the IRB. It is the charge of the IRB to assess the balance of risks and benefits to participation in a given research project. The protection of pilot study subjects is no less essential than in any other type of study.

Applications for pilot studies should be identified as such so that the IRB is aware of the true nature of the study.

Study subjects should be told, in the consent form, that the study is a "pilot" or "phase I" study and that the subject may be one of the first human subjects to receive the test article, treatment, or intervention.

Part of making an informed choice is deciding if the risks of the research project are risks that the subject is willing to assume. Some subjects may be willing to participate in a study that has a track record, but are not willing to participate in a pilot or early phase trial; while other subjects are comfortable with participating. To withhold this information could be considered a violation of the subject's rights.

SURVEY RESEARCH

Not all survey research is exempt from IRB review, nor can all survey research qualify for expedited review. Any survey or interview that is likely to cause stress in the subject population or place respondents at something more than minimal risk may require full committee review.

Surveys on, or interviews with, minors or adults of diminished mental capacity will very likely require full committee review.

SUBMISSION OF NEW PROTOCOLS

The new project application must be completed and submitted to the ORA. This application must be signed and have all appropriate support documentation attached. The cover page for the application gives complete instructions. The project will be logged into the ORA database; given a unique identifying number and processed further to determine the appropriate type of review. All submissions must be typewritten or word-processed. The submission of each new project should consist of the following:

The IRB application form signed by the Principal Investigator and the Department Chair. This must be accompanied by, 1) one copy of the consent form, 2) one copy of any protocol or grant. All protocols should include copies of any research tools that will be used; e.g., diaries, questionnaires, telephone scripts and letters of introduction, and 3) any advertisements that will be used to recruit subjects.

THE USE OF INVESTIGATIONAL NEW DRUGS, DEVICES AND BIOLOGICS

The FDA regulates the use of test articles (drugs and devices). The FDA assigns a number to every Investigational New Drug (IND), and Investigational Device Exemption (IDE); that number must be filed with the IRB. The investigator must also supply the IRB with a copy of the Investigator's brochure or device literature. In cases where the investigator holds the IND or IDE, he or she must also forward copies of all correspondence between him/herself and the FDA regarding this investigational drug, device or biologic.

IRB REVIEW OF CONSENT DOCUMENTS AND PROCEDURES

No investigator may involve a human being as a subject in research unless the investigator has obtained the informed consent of the subject or the subject's legally authorized representative.

The only exceptions to the informed consent process requirement are:

- 1) individual studies which have been certified as "Exempt" from IRB review by the Rush ORA; and
- 2) individual studies where the Rush IRB has waived the requirement to obtain all or elements of informed consent or the documentation of consent, and documented in the IRB files with written confirmation to the Principal Investigator.

An investigator shall seek informed consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative.

No informed consent, whether oral or written, may include any language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

REQUIRED ELEMENTS OF INFORMED CONSENT:

- 1) a statement that the study involves research,

- 2) an explanation of the purposes of the research,
- 3) the expected duration of the subject's participation,
- 4) a description of the procedures to be followed,
- 5) identification of any procedures which are experimental (i.e., procedures involving manipulation of the subject physically or psychologically, combination of drugs, new drugs, new devices, etc.)
- 6) a description of any reasonably foreseeable risks or discomforts to the subject,
- 7) a description of any benefits to the subject or to others which may reasonably be expected from the research,
- 8) a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained,
- 9) an explanation of whom to contact for answers to pertinent questions about the research [the Principal Investigator], research subjects' rights [Director, Rush ORA], and whom to contact in the event of a research-related injury to the subject [Principal Investigator], and;
- 10) a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

For specific types of studies upon recommendation by the IRB:

- 1) for research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained,
- 2) for treatment studies, a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject, and

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

- 1) any additional costs to the subject that may result from participation in the research,
- 2) the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject,
- 3) anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent,
- 4) a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable, and
- 5) a statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.

The Rush IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents these findings:

- 1) the research could not practicably be carried out without the waiver or alteration.
- 2) the research involves no more than minimal risk to the subjects;

- 3) the waiver or alteration will not adversely affect the rights and welfare of the subjects;
- 4) whenever appropriate, the subjects will be provided with additional pertinent information after participation.

The informed consent requirements in this policy do not preempt any applicable Federal, State, or local laws that require additional information to be disclosed in order for informed consent to be legally effective.

DOCUMENTATION OF INFORMED CONSENT

The consent form must consist of a written consent document that embodies the elements of informed consent required above. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed. In cases where the consent document is read to the subject or the subject's legally authorized representative, a disinterested third party must be present to witness the consent process. Unless otherwise instructed by the IRB, the witness must document that he or she was present and observed the signing of the consent.

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

- (1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
- (2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

REQUIREMENTS FOR PERMISSION BY PARENTS OR GUARDIANS AND FOR ASSENT BY CHILDREN

The Rush IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived.

In addition to the provisions for waiver of informed consent, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements, provided an appropriate

mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

DOCUMENTING INFORMED CONSENT WITH ILLITERATE SUBJECTS

For the purposes of this document, illiterate will be defined as anyone who did not finish elementary school (6th grade) or anyone who cannot read or write.

When the investigator plans to target illiterate subjects for a study due to their lack of education or ability to read and/or write, a very simple, very basic document will be constructed for the subject to keep in his/her records. This document will outline, in the simplest manner possible, the basic information regarding the study he or she is being asked to participate in.

When recruiting an illiterate subject for study participation, the Principal Investigator or other staff person must make every effort to:

1. Ascertain that the study description is clear and simple enough for the potential subject to understand; and
2. Read the entire informed consent document to the potential subject, along with all other similar documentation;
3. Provide the potential subject with ample opportunity to ask questions and request clarification in an unhurried manner.

The Principal Investigator or other staff person must attach a typed memo to the informed consent document, noting that the subject is considered illiterate and all three of the above conditions have been fulfilled. The subject may sign the consent document in the appropriate place with his/her name or sign (i.e., an "X" is sufficient). The date, identity(ies), and signatures of all study personnel involved in this informed consent process should also be recorded. When a family member of the subject is available and has participated in the informed consent process, that family member should also be noted and asked to sign as a witness to the process. In cases where the consent document is read to the subject or the subject's legally authorized representative, a disinterested third party must be present to witness the consent process. This witness must document that the consent document was reviewed, whether questions were asked and answered and whether or not the subject consented to participate in the research project.

TRANSLATING INFORMED CONSENT DOCUMENTS INTO FOREIGN LANGUAGES

Investigators must use the copy of the informed consent document reviewed, approved, stamped, and dated by the Rush IRB. Unstamped equivalents and altered versions, no matter how small the alteration, may not be used.

All translated consent documents must have prior IRB review and approval. These translated consent documents will receive the IRB approval stamp. For each consent document submitted in a language other than English, the Principal Investigator is required to submit the following documentation:

- (a) a description of the medical translation qualifications of the translator, usually in the form of a curriculum vitae or resume; and
- (b) a letter from the translator, testifying to the completeness of the translation.

The IRB will reserve the right to request that a translation be submitted to a translator of the IRB's choosing for a second opinion about the completeness of the translation, or to request translation by a translation with credentials more readily acceptable to the IRB.

ILLINOIS HEALTH CARE SURROGATE ACT AND CONSENT TO PARTICIPATE IN RESEARCH

Illinois law makes provisions for consenting adults who are not capable of consenting themselves. In cases where an individual is found to lack decisional capacity and the principal investigator wants to enroll the subject into a research project, the following must be documented:

- a) Document that the individual lacks decisional capacity which is defined as the ability to understand and appreciate the nature and consequences of a decision regarding participation in research.
- b) Document that the attending physician concurs that this individual lacks decisional capacity.
- c) Document that a Surrogate Decision-Maker was located and is willing to consent to allow the individual in question participate in the research study.

The Illinois Health Care Surrogate Act defines surrogate decision-maker as one of the following (in order of priority):

- 1) the patients' guardian of the person;
- 2) the patient's spouse;
- 3) any adult son or daughter of the patient;
- 4) any 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.

Upon regaining consciousness or decisional capacity, the subject must be reconsented. This must be documented by a signed consent document and in the subject's research and medical records.

RESEARCH ACTIVITY OUTSIDE RUSH OR THE UNITED STATES

Whenever a Principal Investigator proposes to undertake research outside Rush, the investigator must submit copies of IRB approval or acceptance of Rush IRB approval by the outside agency, campus, etc.

Whenever a Principal Investigator proposes to undertake any research activity outside the United States, the investigator is required to determine whether policies and procedures to protect human subjects in the foreign country differ from those set forth in this policy. If so, the investigator must provide a statement of those different research policies or procedures. If the proposed research will take place in association with any university or medical center in a foreign country, the investigator is required to provide correspondence from the appropriate institutional official, documenting an IRB or ethics board review with appropriate approval. Whenever possible, the results of the human subjects review process at the foreign institution will be provided to the Rush IRB prior to their own review. If the research activity involves any federal funding, the Rush ORA will contact the Office for Protection from Research Risk (OPRR) prior to IRB review for guidance.

MODIFICATION/AMENDMENT OF AN ONGOING PROTOCOLS

Except in cases where subject safety is an issue, investigators must report planned changes in the conduct of a study and receive approval from the IRB prior to implementing these changes. Minor changes, (i.e., title changes, changes in personnel, funding) may be reviewed using the expedited review procedure.

Some changes may require revision of the consent documents. If so, the IRB will not approve the change until the revised documents are submitted for review and approval.

When submitting a modification that requires changes in the consenting documents investigators must submit,

- 1) the current consenting documents,
- 2) a copy of the proposed new document with highlighted changes, and
- 3) a “clean” non-highlighted copy of the new document that the ORA can stamp and date as approved.

The ORA will provide the investigator with documentation showing the date of the amendment and the reason for the amendment, for example, Amendment #1.

REVIEW OF SERIOUS AND UNEXPECTED EVENTS

Investigators are required to submit reports of serious and unexpected events (SAEs) to the Rush IRB. Investigators are informed of this requirement each time that they receive an approval for a new study. All such SAEs must be reported to the Rush IRB regardless of whether they involved Rush subjects or not.

When an investigator submits a report of a serious and unexpected event to the Rush IRB, this report is forwarded to the Human Research Safety Committee (HRSC). This committee of health professionals will review each report and recommend one of the following actions:

- 1) Reviewed and signed, send to file, no further action recommended at this time
- 2) Return to PI for additional information
- 3) Requires review by full IRB due to the following concerns

Reports of fatalities will be sent directly to the IRB for review and consideration.

EMERGENCY USE OF INVESTIGATIONAL DRUGS/DEVICES/BIOLOGICS

FDA regulations allow for use of a test article [i.e., investigational drug or device] in emergency situations without prior IRB approval.

An “emergency situation” is defined as:

- (a) life-threatening;
- (b) no standard acceptable treatment is available; and
- (c) insufficient time to obtain IRB approval.

If the investigator intends subsequent use of the test article at the institution, every effort should be made either to sign on to the sponsor’s protocol or to develop a protocol for future emergency use of the article at the institution, all with prior IRB approval.

Emergency use must be reported to the IRB in writing within five working days of its use. The emergency use description must include a concurrence from a disinterested second-party physician. All subsequent use of the test article must be reviewed by the IRB prior to its use. The IRB Chairman will acknowledge receipt of the emergency use notification and return a letter to the investigator. The IRB will be notified of all emergency uses the next IRB meeting. A copy of all emergency uses will be kept on file in the ORA-HSD.

HUMANITARIAN USE DEVICES AND HUMANITARIAN DEVICE EXEMPTIONS (HUD/HDE)

A Humanitarian Use Device (HUD) is one that has been designated by the FDA for use in populations of individuals of less than 4,000 annually who suffer from a given diagnosis or problem. The FDA requires review, approval and continuing review of the use of HUDs, even when such use has been designated for purely clinical use. If, however, a physician in an emergency situation determines that approval from an IRB cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be administered without prior approval by the IRB located at the facility or by a similarly constituted IRB that has agreed to oversee such use. In such an emergency situation, the physician shall, within 5 days after the use of the device, provide written notification to the chairman of the IRB of such use. Such written notification shall include the identification of the patient involved, the date on which the device was used, and the reason for the use.

The IRBs at Rush reserve the right to review all HUD protocols through their full review system.

SPECIAL POPULATIONS IN RESEARCH

Federal guidelines and Rush policy with regard to research involving human subjects include specific regulations regarding minors, pregnant women, and prisoners.

MINORS

Permission for research with minors, as with any subject population, must be free from coercion, exploitation, and/or unrealistic promises. Careful and thoughtful discussion of the project with the minor is strongly encouraged. Assent by minors does not replace the requirement of parental/guardian consent.

Research involving minors falls into one of four categories:

- 1) Research involving minimal risk;
- 2) Research involving greater than minimal risk, but presenting the prospect of direct benefit;
- 3) Research involving greater than minimal risk with little or no prospect of direct benefit;
- 4) Research that is not otherwise approvable without the review and approval of the DHHS Secretary.

The IRB may require that either an IRB member or an advocate for the minor be present during the assent and permission procedures to verify the minor's understanding and to support the minor's preferences. The IRB may also require that the parents, guardians or a close family member be present during the research, especially if a young child will be exposed to significant discomfort or inconvenience, or if the minor will be required to spend time in an unfamiliar place.

RESEARCH ON FETUSES AND PREGNANT WOMEN

In preparing protocols for this special group of subjects; the investigator should consider and reassure the committee that appropriate studies on animals and non-pregnant individuals have been completed. The investigator should be certain that the risk to the fetus is minimal and except where the purpose of the activity is to meet the health needs of the particular fetus, is the least possible risk for achieving the objectives of the activity. The investigator should be certain that the individuals engaged in the activity will have no part in any decisions to the timing, method and procedures used to terminate the pregnancy; and/or determining the viability of the fetus at the termination of the pregnancy.

The following is a list of research that may involve pregnant women and/or fetuses as subjects:

- 1) Research directed toward pregnant women as subjects.
- 2) Activities directed toward fetuses in utero as subjects.
- 3) Activities directed toward fetuses ex utero, including nonviable fetuses, as subjects.
- 4) Activities involving the dead fetus, fetal material, or the placenta.

Please see 45 CFR 46.201 through 211 for details regarding these regulations.

PRISONERS

Only limited categories of research involving prisoners are permitted under federal regulations. Whenever the IRB reviews a project involving prisoners, a special member of the IRB, known as the prisoner advocate must be present. The types of research allowed include:

- 1) studies of the possible causes effects, and processes of incarceration and of criminal behavior, provided there is no more than minimal risk to the subjects;
- 2) minimal risk studies of prisons as institutional structures or of prisoner as incarcerated persons;
- 3) research on conditions particularly affecting prisoners as a class, research on social or psychological problems; and
- 4) research on practices, both innovative and accepted, which have the intent of improving the health or well-being of the subject.

HUMAN GENETIC RESEARCH

New developments in medical genetic knowledge and technology are already influencing all aspects of medical practice. Investigators need to be knowledgeable about the risks, benefits and limitations of genetic research. Pedigree studies, positional cloning studies, and DNA diagnostic studies may represent risks of social, financial and psychological harm for subjects. Therefore, subject recruitment plans must minimize the possibility of coercion or undue influence by the investigator, family members, family physicians, or others, or by a misunderstanding about therapy. Physician-researchers should keep genetic research records separate from medical records. Identifiable genetic research data should be released with caution only to the subject or the subject's legally authorized representative.

The purposes of the research and the risks and benefits must be clearly explained. The information given to potential subjects should include the benefits of testing to the subject and to others, and the risks. Subjects should be informed if results will be given to them before, or only after the validity of the test is established, or never. Subjects should be given the option of not receiving their results, particularly if no safe and effective treatment is available. The consent of family members may need to be obtained.

The following should be considered and addressed as appropriate:

- 1) Subjects must be told who else might gain access to the results and what could happen as a consequence (e.g., discrimination by insurance companies).
- 2) The subject's written consent is required before findings are released to other parties.
- 3) To protect information on test results from subpoena, certificates of confidentiality can be obtained from the Assistant Secretary for Health, USDHHS.
- 4) The disclosure statement for informed consent must make clear the magnitude of the benefits and the risks, permitting those considering testing to decide for themselves whether they want to participate.
- 5) Subjects should also be told what kind of information (if any) they will receive from their participation.
- 6) It should be made very clear to subjects that there may be tremendous psychological stress involved in knowing or not knowing the results of participation in these studies.
- 7) Potential participants must be told about the rights they retain and the rights they must give up regarding control over what can be done with tissue they donate.
- 8) It should be made very clear what, if any, the consequences will be due to early withdrawal from the study.

TISSUE/DATA REPOSITORIES

There will be situations when investigators will want to collect tissue, serum or data to keep for later use. When this is done at Rush, by Rush investigators, a repository must be created. The Investigator will submit a repository application and consent document. The investigator may then share gathered materials from the repository with other investigators who have received IRB review and approval for their projects.

When considering an application that is solely to create and maintain a repository, the IRB will consider the following issues:

- 1) Faculty/staff/employee status of the Tissue/Data Manager;
- 2) Location of the Repository;
- 3) Scope of the Repository (the complete range of specimens and clinical information for this Repository);
- 4) Where new "donations" to the Repository will come from;
- 5) How the informed consent of Repository donors will be documented within the Repository;
- 6) How inventory of donations and records will be maintained;
- 7) How the Database Manager will document ORA or IRB approvals for use material or information from the repository.

CONTINUING REVIEW

As a courtesy, investigators will be reminded by the ORA-HDS when projects are due for continuing review. However, it is the investigator's responsibility to track when IRB approvals lapse.

When projects are scheduled for continuing review, they will be screened by ORA-HSD staff for completeness and then to determine whether the projects meet the criteria for expedited review.

IRB members will meet at least twice monthly to review all projects that will be scheduled for continuing review. During these review meetings, members from both IRBs will meet and review the complete IRB file, the report from the investigator, the consent document and any additional pertinent information. The IRB members can make recommendations for the disposition of these continuing reviews. Studies that meet the criteria for expedited review will be reviewed and approved at the meeting. Those projects that require full review will be scheduled for the next available agenda. Members at the fully convened meeting will receive, a copy of the continuing review application, a copy of the approved consent document, a copy of the consent document to be used in the coming year, and any other pertinent information. The original file will be available at the meeting for any member to review.

The review will review the risks, benefits, consent document, process, safety issues, and whether there appear to have been any changes made by the investigator without IRB approval. The reviewer will also comment on whether or not the consent documents still adequately reflects the study. This entire process can take 4-6 weeks. The investigator will want to take this into account when planning for continuing review.

INVESTIGATOR RESPONSIBILITIES

The principal investigator, in whose name the certification of review will be issued, must sign the investigator agreement form indicating compliance with all federal, state and University policies as they apply to this study. The principal investigator must attend a human subjects protection workshop yearly. The principal investigator is responsible for every aspect of the study under his/her name regardless of any delegation of specific duties.

By signing his/her name to the human subjects application form, the principal investigator is agreeing to the following:

- 1) to conduct the study(ies) in accordance with the relevant, current protocol(s) and only make changes in a protocol after notifying the IRB, except when necessary to protect the safety, rights, or welfare of subjects;
- 2) to personally conduct or supervise the described investigations;
- 3) to report to the IRB any serious and unexpected adverse experiences that occur in the course of the investigation(s)
- 4) in cases of studies involving investigational devices, drugs or biologics, to have read and understand the information in the investigator's brochure, including the potential risks and side effects of the investigational agent;
- 5) to ensure that hall associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments;
- 6) to maintain adequate and accurate records
- 7) and to comply with all regulations that are pertinent to the study(ies) being performed under his/her name.

RECORD KEEPING

Every principal investigator is required by RPSLMC and federal regulations to maintain records of all reviews and correspondence relating to the use of human subjects in research. Copies of the application for approval, continuing review, amendments, adverse events and consent documents must be maintained in the investigator's records. All records of human subject research are subject to inspection by institutional as well as federal authorities. Copies of all research records should be kept for three years after the close of the study. Studies that involve

drugs or devices seeking FDA approval must be kept for an additional 3 years after the FDA has reviewed the application for approval, disapproval or withdrawal.

HUMAN SUBJECTS RESEARCH TRAINING

Investigators and their key personnel are required to attend human subjects research training. This training provides an overview of the rules, regulations, policies and procedures that make up the frame work for human subjects research. The training course also provides a history of the promulgation of these rules.

Upon request, investigators and key personnel will be provided with a certification of attendance. Other specialized training and topics are available upon request.

FUNDED PROJECTS

Prior to beginning any research project, a complete research proposal, all related sponsorship application materials, and all related contracts must be submitted to the Office of Research Affairs (ORA) if any of the following four conditions applies:

- 1) the research activities anticipated by the proposals and/or contracts are to take place on any real property owned or leased by the RPSLMC, including leased professional office space.
- 2) the research activities are to be undertaken by a Principal Investigator employed by the Medical Center for twenty or more hours per week (at any point in the duration of the study). This standard of twenty hours per week may be defined by a single position, or by a collection of several different positions. Medical Service Plan (MSP) providers are considered employees of the Medical Center in every case. This category of employees must submit proposals and/or contracts to the ORA, regardless of the location where the research activity takes place.

the research activities are to be undertaken by a Principal Investigator is employed by the Medical Center less than 20 hours per week throughout the duration of the study

All grant awards, contract funds, and communications thereto should be directed to Director of Finance/Contracts, Rush Office of Research Affairs. Payments received for all research grants, contracts, and awards should be made out to and directed as follows:

Rush investigators submitting research proposals to federal agencies are required to submit a complete application for IRB review at the same time that the proposal is proffered for institutional signature. In cases where the application for IRB review is not ready for submission, the Rush ORA will allow the investigator a five-business-day grace period beyond the signature date. If the complete application for IRB review has not been submitted at the end of the five-day grace period, the ORA will withdraw the proposal. The Rush ORA reserves the right to decide when an IRB application is “complete” or not.

THE OFFICE OF RESEARCH AFFAIRS – HUMAN SUBJECTS DIVISION

The Office of Research Affairs – Human Subjects Division (ORA-HSD), will be headed by a Senior IRB Administrator who is experienced and knowledgeable regarding human subjects research regulations, the IRB process and human subjects research. The ORA-HSD will manage the logistics regarding scheduling meetings, setting agendas, creating and archiving minutes, as well as creating letters to investigators regarding any revisions or additional information requested by the IRB during its meeting. The ORA-HSD will take responsibility for maintaining

the IRB files, providing educational opportunities for IRB Chairs, members, investigators and research staff. The ORA-HSD will be responsible for providing information to investigators notifying them that when their human subjects research projects that will be due for continuing review, overdue and terminated.

REPORTS OF INVESTIGATOR NON COMPLIANCE

The IRB will receive reports of investigator noncompliance either directly or through the Quality Improvement Subcommittee (QIS). The QIS receives and reviews concerns related to all aspects of research at Rush. Questions or concerns about human subjects compliance will be reviewed and then forwarded to the IRB for a determination of subject harm.