SOP: SC 502 Version No: Effective Date: 01/01/07	CATEGORIES OF RESEARCH	Supercedes Document Dated:

1. POLICY

The categories of research defined in these policies involve either methodologies that might require additional considerations or for which there are federally mandated determinations that IRBs are required to make and document. These categories of research include, but are not limited to:

- Clinical research involving devices
- Genetic research
- Prospective research in emergency settings
- Emergency use of an investigational article
- Medical records and chart review
- Residual body fluids, tissues and recognizable body parts
- Protocols lacking plans for human involvement
- Other

Specific Policies

1.1 Clinical Research Involving Devices

In addition to the previous policy guidelines, the IRB (or Chairperson if the review is expedited) will determine whether, in the context of the study or by the nature of the investigational medical device (see significant risk devices list), the study presents a significant risk (SR) or a non-significant risk (NSR) of harm to study subjects. This assessment will be based on the information provided by the Investigator and/or the Sponsor. The IRB's device risk determination must be documented in the IRB meeting minutes. [See also RR 402 – Initial Review – Criteria for IRB Approval; RR 402-B and RR 402-C]

If an Investigator submits an NSR device research protocol that is determined by the IRB to be a significant risk device study, the Investigator and FDA will be notified in writing. No further action will be taken by the IRB on the research until the Sponsor or Investigator has met the requirements for an SR study described in 21 CFR 812 (Investigational Device Exemption regulations).

1.2 Genetic Research

Genetic research may require special considerations.

1.4.1 Subjects of Genetic Research:

At first consideration, much genetic research may appear to meet the criteria for expedited review. These include:

- Pedigree studies, which look for a pattern of inheritance of a gene;
- Positional cloning studies, which are conducted to identify particular genes;
- Diagnostic studies, which gather samples to develop techniques to determine the presence of specific DNA mutations.

However, these studies may create a vulnerable population in that subjects' autonomy may be compromised. Therefore in most cases the full IRB must review these studies to answer the following questions:

- Will the samples be made anonymous to maintain confidentiality? If not, to what extent will the results remain confidential; and who will have access to them?
- Will the samples be used for any additional studies not made explicit at the time of donation, or will the samples be destroyed after specified, one-time use?
- Will the donor be informed of any and all results obtained from his or her DNA?
- Will the donor be informed of the results of the entire study?
- Will family members be implicated in the studies without consent?

Gene therapy research (administration of recombinant vectors), which is carried out to develop treatments for genetic diseases at the DNA level, presents obvious and not so obvious questions, including – considerations of delivery methods, target population, required follow-up. Such protocols require use of external consultants to provide independent guidance to the IRB. If the project involves gene therapy to human subjects for other than clinical purposes, the study must be reviewed and approved by the National Institutes of Health Recombinant DNA Advisory Committee prior to IRB approval. Monitoring must be adequate, and a DSMB will be required.

Because there is still little regulatory guidance and relatively few ethical precedents, genetic research will require close scrutiny, and the input of experts in this area.

1.3 Prospective Research in Emergency Settings (Prospective Review)

The IRB, with the concurrence of a licensed physician who is either a member of the IRB or a consultant and who is not participating in the research being reviewed, may waive the requirement for informed consent in certain emergency research if it finds and documents the following:

A. 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.

B. Obtaining informed consent is not feasible because:

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

C. Participation in the research holds out the prospect of direct benefit to the subjects because:

- Subjects are facing a life-threatening situation that necessitates intervention;
- Appropriate animal and other pre-clinical 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
- 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.

D. The clinical investigation could not practicably be carried out without the waiver.

E. The proposed investigational or research plan:

- Defines the length of the potential therapeutic window based on scientific evidence, and
- The Investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and,
- If feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.

The Investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

F. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with applicable regulations.

G. Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent DSMB to exercise oversight of the clinical investigation; and

(v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the Investigator has committed, if feasible, to attempting to contact, within the therapeutic window, the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The study plan must ensure that, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member is informed of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

The study plan must ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided above or because of other relevant ethical concerns, the IRB will document its findings and provide these findings promptly in writing to the Investigator and to the Sponsor of the clinical investigation.

1.4 Emergency Use of Investigational Articles (Retrospective Review)

According to federal regulations (21 CFR 56.102.d and .l), the terms “Emergency Use” and “Test Article” (or investigational article) are defined as:

- Emergency Use means 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.
- Test Article means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive,

electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.

If time permits, the IRB has set forth the following procedures for which Emergency use of an investigational produce, drug or procedure may be granted by the Chairperson of the IRB and may be considered exempt from Committee review:

1) Investigator is to contact the IRB Chairperson or the IRB Administrator, and explain the situation for which the investigator is requesting exemption. If the IRB Chairperson is not available, the request for exemption shall be made to the Vice-President of Medical Affairs (Institutional Official) of Sparrow Health System. The IRB Chairperson (or VP of Medical Affairs, if applicable) shall have absolute discretion to grant or deny a request for exempt status for emergency use of a test article.

2) If an exemption is granted, the IRB Chairperson will immediately send the investigator an acknowledgement letter along with a copy of the policy and FDA Information Sheets.

3) In emergency situation, it may not be feasible to obtain informed consent prior to using the test article. Special procedures for documenting the infeasibility of obtaining consent are described below.

4) Investigator must submit IRB approval documentation to all departments effected by the Emergency Use of the test article.

Furthermore, the federal definition (21 CFR 56.104.c) allowing for exemption from IRB requirements is as follows:

- Emergency Use of a test article, provided that such emergency use is reported to the IRB within five (5) working days. Any subsequent use of the test article at the institution is subject to IRB review. ["Emergency Use" is to be interpreted as the initial treatment course. "Subsequent Use" means any use of the test article that occurs after its initial emergency use.]

If time is not available to obtain permission from the IRB Chairperson for Emergency Use of a test article, the Investigator must send the IRB Chairperson the following information (21 CFR 56.104.c) within five (5) days of the first emergency use of the test article:

- Patient name
- Date of Event
- Diagnosis
- Summary of Event
- Investigational treatment used
- Outcome

In emergent situations it is not always feasible to obtain informed consent. In order to save the patient's life, an exemption from informed consent can be

documented as follow (21 CFR 50.23(a)(1-4). In review of the documentation, the IRB will ensure that the Investigator and a physician not otherwise participating in the clinical investigation have adequately certified the following in writing prior to use of the test article:

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

If immediate use of the test article is, in the Investigator's opinion, required to preserve the life of the subject, and time is not sufficient, prior to administering the test article, to obtain an independent physician's opinion, the determinations of the Investigator must be reviewed in writing within five (5) days after the use of the test article by a physician not otherwise participating in the clinical investigation. In this event, a copy of the independent review must be submitted to the IRB within seven (7) working days after the use of the test article.

1.4.1 Use of data generated prior to IRB approval: Whenever emergency care is initiated without prior IRB review and approval, the patient may *not* be considered to be a research subject. HHS regulations do not permit research activities to be started, even in an emergency, without prior IRB review and approval.

For DHHS-supported or conducted research, the physician may, without prior IRB approval, treat the patient/subject using a test article (if the situation meets the FDA requirements), but the subject may not be considered a research subject and data derived from use of the test article may not be used in the study.

Nothing in this SOP is intended to limit the authority of the physician to provide emergency medical care to the extent the physician is permitted to do so under applicable law.

1.5 Medical Records and Chart Review

Studies involving the use of existing public or privately held records only may qualify for exempt status or expedited review. However, if the nature of the research could put subjects' confidentiality at risk, the study will be reviewed by the full IRB. Studies that involve only chart and record review can sometimes pose significant risk to patients. [Also see WA 1000, SHS Policy HP-53 - HIPAA Use and Disclosure of Protected Health Information for Purposes of Research]

The most common breach of confidentiality is exposure of possible embarrassing information without the knowledge or consent of the patient. Such studies may also lead to recruitment of patients into future non-therapeutic studies in a manner, which may provoke the patient to ask how his/her record was revealed to

someone not part of his/her therapeutic team. The present policy is to require IRB review of studies involving chart review or data collection and analysis.

If identifiers were to be recorded, the research would require IRB review to ensure that, among other things, procedures for protecting privacy and confidentiality are adequate. Furthermore, the Investigator studying cancer risk factors may propose to go on to contact the subjects (if still living) or family members (if the subject is deceased) to gather additional information, which may or may not be subject to the federal regulations.

1.6 Residual Body Fluids, Tissues and Recognizable Body Parts

Body Fluids & Tissues: Research on existing specimens ("on the shelf" or frozen) without identifying information (e.g., no names, initials, hospital number, etc.) may be submitted to the IRB for expedited review, to include a short description of the research and where the tissue is coming from.

1.7 Protocols Lacking Definite Plans for Human Involvement

Certain types of activities are planned and written with the knowledge that human subjects may be involved, but without definite plans for such involvement. Examples of such proposed activities are:

- Training programs in which individual training projects remain to be selected or designed.
- Research, pilot or developmental studies in which the involvement of human subjects depends on such things as the completion of survey instruments or prior animal studies.
- Institutional Support Programs where the selection of the project is the responsibility of the institution or program administrator. When supporting agencies requires review and certification for such programs, protocols are to be submitted to IRB with as much information as is available. The protocols must include assurances that additional information will be submitted when developed and, in the case of training grants, that all trainees will submit individual protocols if human subjects are to be used.

The IRB can give "General Expedited Approval" to programs like those mentioned above with the understanding that the specific research protocol will be submitted to them once it has been developed. "General Expedited Approval" is not appropriate for individual projects or to meet grant deadlines.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The OROC Staff is responsible for maintaining up-to-date review tools for review of research pertaining to these categories based on new and evolving applicable regulations and guidelines.

IRB Chairperson (or designee) is responsible for ensuring the IRB members are well versed in new and evolving regulations and guidelines pertaining to these categories, for selecting primary reviewers with appropriate expertise to conduct the reviews of such

research, and for securing appropriate consulting expertise as needed for selected reviews.

IRB Reviewer is responsible for conducting appropriate review of research planned for these categories in consultation with any appropriate experts and resources.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 812.66

21 CFR 50.23, 50.24, 50.25, 56.104

45 CFR 46.101, 46.103, 46.118, 46.119

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

RR 402-B	Risk Assessment Checklist for Research Studies
RR 402-C	Significant and Non-Signification Risk Checklist (Medical Devices)
SC 502-A	Reporting Emergency Use of Test Article
SC 502-B	Notice of IRB Approval/Acceptance of Emergency Use
SC 502-C	Reporting Emergency Use – Investigator Template
SC 502-D	Checklist- Emergency Research Conducted Under 21 CFR 50.24

7. PROCESS OVERVIEW

All non-emergent protocols will be submitted using the regular submission process. The process for emergent protocols or studies is outlined in this SOP and will be followed by physicians, OROC Staff, and the IRB Chairperson.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

A. Clinical Research Involving Devices

Who	Task	Tool
IRB Coordinator	Include the checklist in the primary reviewer's packet when a medical device is the study article.	RR 402-C - Risk Determination – Devices Refer to SOP RR 202
IRB Member (Reviewer)	Perform the device risk determination to verify that the Sponsor’s determination is accepted.	
IRB Administrator	Notify the appropriate entities if the IRB rejects the Sponsor’s NSR device determination.	Refer to SOP CO 602
IRB Members	Conduct review of NSR device or await Sponsor’s submission of an IDE for SR devices before proceeding with device study review.	

B. Genetic Research

Who	Task	Tool
IRB Administrator and Chairperson	Identify and invite appropriate consultant(s) who may assist the IRB in its deliberations. Ascertain deliberations of other relevant research review groups (e.g., NIH RAC, Institutional Biosafety Committee).	

C. Prospective Research in Emergency Settings

Who	Task	Tool
IRB Coordinator	Provide Investigators with appropriate guidelines regarding research in emergency settings.	SC 502-A - Reporting Emergency Use of a Test Article
IRB Coordinator	Include Checklist in the primary reviewer's packet when a prospective emergency research study is submitted.	SC 502-D - Checklist-Emergency Research Conducted Under 21 CFR 50.24
IRB Member (Reviewer)	Complete checklist during review of research and present recommendations at convened meeting.	

D. Emergency Use of Investigational Articles (Retrospective Review)

Who	Task	Tool
IRB Chairperson (or designee)	Review submitted report(s) and present to the IRB. Determine whether an emergency conference call meeting of IRB is indicated to discuss the use.	SC 502-C - Report of Emergency Use of A Test Article

E. Medical Records and Chart Review

Who	Task	Tool
IRB Administrator	Determine whether the research is exempt from IRB review, eligible for expedited review, or subject to full IRB review.	Refer to SOP FO 302 and RR 401
IRB Coordinator	If subject to full or expedited IRB review, include the Checklist in the primary reviewer's packet.	

F. Residual Body Fluids, Tissues and Recognizable Body Parts

Who	Task	Tool
IRB Administrator	Determine whether the research is exempt from IRB review, eligible for expedited review, or subject to full IRB review.	Refer to SOP FO 302 and RR 401
IRB Coordinator	If subject to full or expedited IRB review, include the Checklist in the primary reviewer's packet.	

G. Protocols Lacking Definite Plans for Human Involvement

Who	Task	Tool
IRB Administrator	Determine whether the research is exempt from IRB review, eligible for expedited review, or subject to full IRB review.	Refer to SOP FO 302 and RR 401
IRB Coordinator	If subject to full or expedited IRB review, include the Checklist in the primary reviewer's packet.	