1. INTRODUCTION

The ethical principle of respect for persons requires that subjects be given the opportunity to choose what shall and shall not happen to them. Valid informed consent requires: (1) **Disclosure** of relevant information to prospective subjects about the research; (2) their **comprehension** of the information, and (3) their **voluntary agreement**, free of coercion and undue influence, to research participation.

The process of informed decision-making by research subjects generally includes discussion of the research study with the Principal Investigator (PI), and others as appropriate, and signing the written informed consent document. Depending on the nature, type and duration of the research, ongoing discussion with and education of subjects about the study may continue long after the informed consent document is signed.

A goal of the NIH is to assure that all written informed consent documents are complete and clearly written so as to promote informed decision-making by subjects participating in its research activities. This information sheet provides guidance to NIH clinical researchers and IRBs on the procedures and requirements for informed consent to research participation and the content and format of written consent documents.

2. REQUIREMENTS FOR INFORMED CONSENT

(a) General Procedures

Unless otherwise waived by the IRB, NIH research investigators should obtain valid informed consent from all research subjects (or their legally authorized representatives) who participate in their research studies. Generally, after the Principal Investigator has explained the research study to the subject, the subject's informed consent is documented by signing the protocol's written consent document, which an IRB must have previously reviewed and approved. The NIH consent document form **NIH-2514-1** (Consent to Participate in a Clinical Research Study), obtainable from IRB Protocol Administrators, is used for all subjects enrolled in research conducted at the Clinical Center. Form **NIH-2514-1** is also available from the Clinical Center's Protocol Coordination Service Center (301-496-0744).

The subject is given a copy of the signed document, and, when the research is conducted in the Clinical Center, the Principal Investigator ensures that the original signed consent document is filed in the subject's permanent medical record maintained by the Clinical Center's Medical Record Department. In cases where subject accrual occurs elsewhere, signed consent documents are retained according to the policies of the institution where the research is conducted.

(b) General Principles

Unless otherwise authorized by an IRB, research investigators are responsible for ensuring that informed consent shall:

- be obtained in writing from the subject or the subject's legally authorized representative;
- be understandable to the subject or her/his representative. Suggestions for writing consent documents are provided in 3., below.
- be obtained in circumstances that are not coercive and that offer the subject (or her/his representative) sufficient opportunity to decide whether she/he should participate. The consent document should not contain language that implies or suggests that the subject (or her/his

- representative) gives up any legal rights or releases research investigators or the NIH from liability for negligence.

(c) Basic Elements for Written Informed Consent Documents

Unless otherwise authorized by an IRB, research investigators must provide the following information to each subject in writing:

The basic elements which have an asterisk (*) are incorporated in existing language printed on form NIH-2514-1 (Consent to Participate in a Clinical Research Study). Nevertheless, to enhance comprehension and readability, investigators are strongly urged to use a format in the body of the consent form that presents information in sections, introduced by headings, and that clearly and simply identifies and describes each of the elements to be discussed, even if the sections repeat information that appears on the printed form. For an example of an effective way to use headings, see 4. below.

- A statement that the study involves research;*
- An explanation of the purpose 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 that are experimental;
- A description of any foreseeable risks or discomforts to the subject, an estimate of their likelihood, and a description of what steps will be taken to prevent or minimize them;
- A description of any benefits to the subject or to others that may reasonably be expected from the research. Monetary compensation is not a benefit. If compensation is to be provided to research subjects or healthy volunteers, the amount should be stated in the consent document;
- A disclosure of any appropriate alternative procedures or courses of treatment that might be advantageous to the subject;
- A statement describing to what extent records will be kept confidential, including a description of who may have access to research records;*
- For research involving more than minimal risk, an explanation and description of any compensation and any medical treatments that are available if research subjects are injured; where further information may be obtained, and whom to contact in the event of a research-related injury;*
- An explanation of whom to contact for answers to pertinent questions about the research and the research subject's rights (include the Clinical Center's Patient Representative and telephone number);* and
- A statement that participation is voluntary and that refusal to participate or discontinuing participation at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled.*

(d) Additional Elements

When appropriate, and required by the IRB, one or more of the following elements of information will also be provided to each research subject:

- If the subject is or may become pregnant, a statement that the particular treatment or procedure may involve risks, which are currently unforeseeable, to the subject or to the embryo or fetus;

- A description of circumstances in which the subject's participation may be terminated by the investigator without the subject's consent;

- Any costs to the subject that may result from participation in the research;

- What will happen if the subject decides to withdraw from the research and how withdrawal will be handled;

- A statement that the Principal Investigator will notify subjects of any significant new findings developed during the course of the study that may affect them and influence their willingness to continue participation;

- The approximate number of subjects involved in the study;

- The amount of remuneration/compensation, if any, that will be provided to subjects. See Information Sheet #20 "Information on Remuneration of Research Subjects in the Intramural Research Program."

- When appropriate, a statement concerning an investigator's potential financial or other conflict of interest in the conduct of the study.

(e) Waiver or Alteration of the Required Elements of Informed Consent

In certain circumstances prescribed by the Federal Regulations (45 CFR 46.116(d)), an IRB may waive the requirement to obtain informed consent, or may approve a consent process which does not include or alters some or all of the elements in (c) above. For more information, see the NIH Standard Operating Procedures for IRBs.

3. SUGGESTIONS FOR WRITING INFORMED CONSENT DOCUMENTS

When an investigator writes or reviews a research consent document, she/he should ask the following questions:

Question 1: Is it written at a reading level understandable to research subjects?

- A general rule of thumb is that consent documents should be written so that they are understandable to people who have not graduated from high school. The reading level of a document is more difficult if it contains long sentences, words with more than two syllables, and continuous run-on text.

- Therefore, if possible use words with fewer than three syllables; use non-scientific/non-medical words; use short sentences, and break the text up into short sections.

Question 2: Is the document formatted well? Does it have headings which break the text into short sections?

Question 3: Does the document contain the basic elements for informed consent and are they presented in a clear, easy-to-understand way? Even though the printed NIH consent form incorporates some of the elements of consent, depending on the particular research study, it may be useful to include the information a second time but in a simpler form.

Question 4: Can the document be shortened without compromising clarity or other requirements? Usually, before a person agrees to take part in a research study, he/she not only reads a written consent document but also discusses the study with a researcher. A suggestion when writing consent documents is to assume that prospective subjects will not talk to a researcher (or research nurse) at all about the study, and that all their information will come entirely from the consent document. If this approach is used the document is more likely to be clear, complete, devoid of medical/scientific terminology and able to "stand
alone."

4. THE USE OF HEADINGS TO FORMAT INFORMED CONSENT DOUMENTS

The use of headings in informed consent documents helps to ensure that all the basic elements of informed consent are conveyed to the prospective research subject in a simple, efficient way. Headings promote comprehension and readability. The number, order, and language of headings are left to the author of the informed consent document with the approval of the IRB. The following headings are included in the Clinical Center consent writing module of Prototype.

(1) Introduction. ***Use the CC standard language which is part of the consent form template***; starting with " We invite you . . . " and ending with " . . . personal physician or other health professional."

(2) Why is this research being done?

(3) Why are you being invited to participate?

(4) How many people will take part in this research study?

(5) How long will you take part in this research study?

(6) What do we do to decide if you are eligible for this research study?

(7) What procedures, drugs or other treatments are involved in this research study?

(8) What are the risks and discomforts of this research study?

(9) Are there any benefits to you if you take part in this research study?

(10) What other choices do you have?

(11) Are there reasons that your research participation may end early?

(12) What will happen when the research study is over?

(13) Will your clinical and other test results be shared with you?

(14) Will the results of this research study be shared with you?

(15) Will any of your blood, tissue or other samples be stored and used for research in the future?

(16) Will you receive any compensation (money or other) for taking part in this Research study?

The following CC minimum language is part of the consent template and must be used: "In general, patients are not paid for taking part in research studies at the NIH. The amount paid to research volunteers is guided by National Institutes of Health policies."

Add appropriate language if compensation is to be paid, including the amount of compensation.

(17) Do any of the researchers or the NIH have a financial interest related to this research study?

(18) What privacy and confidentiality procedures apply to the information gathered about you in this study?

The following CC standard minimum language is part of the consent template and must be used: "When results of an NIH research study are reported in medical journals or at scientific meetings , the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical records. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance. The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical records without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or other authorized people."

(19) What is the NIH's policy regarding research-related injuries?

The following standard CC minimum language is part of the consent template and must be used: "The Clinical Center of the NIH will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action."

(20) Who can answer your questions about the research and your rights as a research subject?

The following standard CC minimum language is part of the consent template and must be used: "If you have any problems or questions about this study, about your rights as a research participant, or about any research-related injury, contact the Principal Investigator of this study **INSERT** at telephone number **INSERT**. His/her address is **INSERT**. Another researcher you may call is: **INSERT**., telephone **INSERT**.

You may also call the Clinical Center Patient Representative at 301-496-2626.