

NIH HRPP SOP 12 v1

**HRPP STANDARD OPERATING PROCEDURE/POLICY APPROVAL &
IMPLEMENTATION**

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

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SOP Title: REQUIREMENTS FOR INFORMED CONSENT

**Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB
Chairs, IRB Administrators, Protocol Navigators**

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SOP 12 REQUIREMENTS FOR INFORMED CONSENT

12.1 PURPOSE

This SOP describes NIH Human Research Protection Program (HRPP) requirements for obtaining and documenting legally effective informed consent for research participation.

12.2 POLICY

Except as provided elsewhere in this SOP (see Sections 12.11, 12.12 and 12.13 below) no investigator may involve a human as a subject in research covered by this policy unless the investigator has obtained the subject's legally effective informed consent. NIH requires research subjects' written informed consent, or that of their legally authorized representatives, before any research procedures are initiated, unless informed consent or the written consent document is waived by an NIH IRB consistent with requirements in this SOP (see Sections 12.11 and 12.12 below), and for applicable FDA-regulated research, those of SOP 15 "Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications". For specific requirements about obtaining consent or assent from vulnerable populations, see SOPs 14B, "Research Involving Pregnant Women, Human Fetuses and Neonates", 14C, "Research Involving Prisoners", 14D, "Research Involving Children", 14E "Research Involving Adults Who Are or May be Unable to Consent" and 14F "Research Involving NIH Staff as Subjects".

This policy is consistent with the ethical principles of The Belmont Report and the regulatory requirements of the Department of Health and Human Services 45 CFR 46 and the Food and Drug Administration 21 CFR 50 (as applicable), (see References below for links to these regulations and guidance).

12.3 DEFINITIONS

- A. **Adult:** For the purpose of consent at the NIH Clinical Center, an adult is anyone 18 years or older or an emancipated minor (such as a minor who is married or a parent). At non-CC NIH sites, applicable local, state or foreign law is followed in the absence of applicable U.S. Federal law.

- B. **Consent Monitor:** An impartial observer who ensures that the approved consent process is being followed properly.

- C. **Legally Authorized Representative (LAR):** A legally authorized representative is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to the participation in the procedure(s) involved in the research (see 45 CFR 46.102(c) and 21 CFR 50.3(l) (see References below for links).

Note: For the purposes of this SOP, use of “subjects” will refer also to LARs.

- D. **Witness:** An individual who is present when the informed consent document is signed and attests to the validity of the research subject’s signature or mark and/or an individual who is present and attests to an oral consent presentation made to a research subject.

12.4 RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR

It is the responsibility of the Principal Investigator (PI) to ensure that informed consent is obtained consistent with the requirements of this SOP and, as appropriate, SOP 15 “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications”.

The PI may designate other qualified persons to obtain consent from prospective subjects (see SOP 19, “Investigator Responsibilities”). Those designated must be identified in the protocol application or in subsequent protocol amendments. The PI is responsible for assuring that these persons (1) have thorough knowledge of the protocol, enabling them to answer questions from potential subjects; (2) receive appropriate training in obtaining proper informed consent related to the protocol; (3) have appropriate training in human subjects research protections (see SOP 25 “Training Requirements for the NIH HRPP”), and (4) have appropriate conflict of interest clearance, for NIH Employees this is from their Institute’s ethics office (see SOP 21 “Conflict of Interest Requirements for Researchers and Research Staff”).

12.5 DHHS REGULATORY REQUIREMENTS FOR INFORMED CONSENT

12.5.1 ELEMENTS OF INFORMED CONSENT

- A. An investigator shall seek consent only in circumstances that provide the prospective subject sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.
- B. The information that is given to the subject shall be in language understandable to the subject.
- C. No informed consent, whether oral or written, may include any exculpatory language through which the subject 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.
- D. Except as provided elsewhere in this SOP (see 12.11, 12.12 and 12.13), in seeking informed consent, the required basic elements of informed consent listed in Appendix A "Required Elements of Informed Consent" shall be provided to each subject. (45 CFR 46.116(a)).
- E. When deemed appropriate by the PI and an NIH IRB, one or more of the additional elements of informed consent listed in Appendix B "Additional Elements of Informed Consent" shall also be provided to each subject. (45 CFR 46.116(b)).
- F. The IRB may require that additional information be given to the subjects when, in the IRB's judgment, the information would meaningfully add to the protection of the rights and welfare of subjects. (45 CFR 46.109(b)).

12.6 FOOD AND DRUG ADMINISTRATION (FDA) REGULATORY REQUIREMENTS FOR INFORMED CONSENT

FDA Regulations regarding informed consent are listed at 21 CFR 50, Subpart B (Informed Consent of Human Subjects). For NIH HRPP requirements regarding informed consent related to FDA-regulated research, see SOP 15 "Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications".

12.7 APPROVAL OF INFORMED CONSENT

- A. Written consent documents shall be approved by the IRB at the same time as the written research protocols. Amendments or other changes in the approved protocol that may affect informed consent shall be incorporated into a revised consent document and approved by the IRB prior to use. Minor changes may sometimes be approved by expedited review. The consent document shall be reviewed and approved by the IRB at least once a year.
- B. Consent documents and protocols involving the research use of ionizing radiation shall also be reviewed by the Radiation Safety Committee and, if indicated, by the Radioactive Drug Research Committee. Protocols may also require additional review, depending on the type of research, by other committees such as the Recombinant DNA Advisory Committee or the Institutional Biosafety Committee.
- C. In certain circumstances prescribed by the Federal regulations (45 CFR 46), an IRB may waive the requirement to obtain informed consent, or may approve a consent process which alters or does not include some of the required elements (see Sections 12.11, 12.12 and 12.13, below)
- D. The IRB has the authority to have IRB members observe or monitor the consent process or to require an impartial third party observe or monitor the consent process.
- E. The informed consent process is an ongoing discussion about the study, and continues after the informed consent form is signed. For instance, when new risk information relevant to a subject's ongoing participation is discovered, notification to the subject may be required by the IRB (for example, see SOP 16 "Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations").
- F. Except when the IRB waives the requirement (45 CFR 46.117(c), see Section 12.11 below), the informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject (45 CFR 46.117). Sample or draft consent documents may be developed by a sponsor or cooperative study group for review by IRBs in participating organizations. However, NIH IRBs have the final authority for the content of consent documents to be used in protocols in which NIH IRBs are responsible for reviewing the research.

12.7.1 THE INFORMED CONSENT DOCUMENT

- A. The consent form is intended, in part, to provide information for the potential subject's current and future reference and to document the interaction between the subject and the investigator.
- B. To the extent possible, the language shall be understandable by a person who is educated to 8th grade level and layman's terms shall be used in the description of the research.
- C. For research reviewed by an NIH IRB and conducted in the NIH CC:
 - 1. The NIH Consent Document Form 2514-1, "Consent to Participate in a Clinical Research Study" will be used. For discussion of the use of the NIH Minor Patient's Assent to Participate in a Clinical Research Study (Form 2514-2), see SOP 14D "Research Involving Children".
 - 2. Medical Administrative Series (MAS) 77-2, "Informed Consent", contains additional requirements for consent forms used in research. It also provides additional information about consent for clinical procedures. Other CC policies address additional consent requirements as well.
 - 3. The consent form will include elements required by Appendix A "Required Elements of Informed Consent" as well as necessary elements from Appendix B "Additional Elements of Informed Consent", and any other additional information determined by the IRB, so an individual may be fully informed about study participation.
 - 4. Any changes in the standard boilerplate language provided on the NIH form 2514-1 may be made only when recommended by the NIH IRB and approved by the NIH Office of the General Counsel (OGC). OHSRP and the CC Office of Protocol Services (OPS) shall be informed by the IRB of any such changes.
 - 5. Additional approvals of consent documents (such as research radiation use) will be conducted by relevant NIH committees. (See 12.7B, above)

D. For research reviewed by an NIH IRB and conducted at non-CC NIH sites:

1. The IRB-approved consent form must include the regulatory elements listed in Section 12.5 above (see Appendix A “Required Elements of Informed Consent”).
2. Additional approvals of consent documents (such as research radiation use) will be conducted by committees at other sites, if appropriate.
3. Additional applicable U.S. Federal, state, local, or foreign laws (e.g., privacy or genetic information) affecting consent documents should be considered.
4. Local context, including site-specific requirements should be addressed, for example policies regarding research injury, privacy or confidentiality, or compensation.

E. Upon approval, an informed consent form will include the date of IRB approval and the date through which the approval is valid

12.7.2 TYPES OF WRITTEN RESEARCH CONSENT DOCUMENTS

A. An NIH IRB may approve the following written consent documents (45 CFR 46.117(b) and 21 CFR 50.27(b)):

1. A written consent document (long form) that embodies the elements of informed consent found in 45 CFR 46.116 (see 12.5.1). The consent form may be read to the subject, but the subject must be given adequate opportunity to read it before it is signed; or
2. A short form written consent document stating that the required elements of informed consent from 45 CFR 46.116 have been presented orally to the subject. (Use of a short form may be appropriate for unexpected enrollment of non-English speaking (see 12.9.1.B) or blind (see 12.9.2) subjects as approved by the IRB).

B. When the short form document is used:

1. The IRB must approve the short-form document and a written summary of what is to be said to the subject.

2. There must be a witness to the oral presentation.

12.8 INFORMED CONSENT PROCESS

12.8.1 BASIC CONSIDERATIONS

The consent process includes:

- A. Determination of the subject's capacity to provide informed consent. If the individual(s) authorized to obtain consent, or others, think the subject does not have appropriate decision-making capacity to consent to the research, additional evaluation of the subject's capacity may be warranted. (See SOP 14E "Research Involving Subjects Who Are or May be Unable to Consent" regarding the permissibility and assessment of surrogate decision makers in the event a subject cannot provide consent.)
- B. Disclosure of relevant information necessary to make an informed decision to the prospective subject about the research.
- C. Facilitating the understanding of what has been discussed.
- D. Promoting the voluntariness of the decision by the subject, including minimizing the possibility of coercion and undue influence.

12.8.2 PROVISION TO PROSPECTIVE SUBJECTS OF PRELIMINARY INFORMATION

In order to provide preliminary study information to prospective subjects, investigators, or others on the research team, may communicate with prospective subjects about the prospective research before consent is obtained and formally documented so long as such communication is prospectively approved by the IRB. Such communications may include face-to-face conversations, postal mail, e-mail, telephone, facsimile, or other methods of communication. NIH allows interaction with prospective subjects without IRB approval if the interaction is not considered engagement in human subjects research per OHRP guidance¹.

¹ See the OHRP Guidance on Engagement of Institutions in Human Subjects research (section B, Part 4)

12.8.3 INFORMED CONSENT DISCUSSIONS

- A. Informed consent begins with the initial approach of an investigator to a potential subject (e.g., through a flyer, brochure or any advertisement regarding the research study) and continues until the completion of the research study, or until the individual completes study participation, withdraws consent, or is withdrawn from the study.
- B. The process of informed decision-making by research subjects includes discussion about the research study with the Principal Investigator and/or his/her designee in language understandable to the subject, sufficient time and opportunity to discuss the research, minimizing or eliminating coercion or undue influence, and signing the current IRB-approved informed consent document, when required.

12.8.4 INFORMED CONSENT DOCUMENTATION

- A. Informed consent shall be documented using the current IRB-approved consent form, except where this written requirement is waived by the IRB. At the CC, this must be downloaded from the CC active consent website (see References below).
- B. Required signatures on informed consent documents:
 - 1. English or translated long form consent: When consent is obtained, the consent document(s) must be signed and dated by the subject, and the person obtaining consent. In the case of illiterate subjects, “making their mark” is acceptable.

Note: For research conducted at the NIH Clinical Center a witness is also required to sign the document. The witness attests only to the validity of the signature or mark (i.e., that the research subject signed the consent document), not to the validity or quality of the consent. Any adult other than the person obtaining or providing consent may serve as a witness. If the subject does not speak English, the interpreter may serve as the witness, sign the consent document as the witness, and should note “Interpreter” under the signature line.

2. Short form consent:

- a. The short form document is signed by the subject. In the case of illiterate subjects, “making their mark” is acceptable.
- b. The witness to the oral presentation must sign both the short form and a copy of the written summary.
- c. The PI or individual authorized to obtain consent must sign the written summary.

C. After signatures are obtained:

1. A copy of the signed and dated consent (long) form must be given to the person signing the form.
2. If applicable, a copy of the signed written summary and a copy of the signed short form must be given to the person signing the form.
3. For research conducted in the Clinical Center (CC), the original signed consent documents (including short form consents and the written summary) are transmitted to the Medical Records Department for placement in the subject's permanent CC medical record. If an interpreter was used, the progress notes should reflect this, including the name of the interpreter.
4. In cases where subject accrual for NIH protocols occurs outside the CC and there is a non-NIH medical record, the PI is responsible for maintaining a copy of the informed consent in the research record if the original consent is added to the medical record. If accrual of NIH subjects occurs outside the CC and there is no related medical record, the PI is responsible for maintaining the original informed consent in the research record.

12.9 SPECIAL CONSENT CIRCUMSTANCES

12.9.1 NON-ENGLISH SPEAKING SUBJECTS

No-one should be excluded from the consent process on the basis of language alone. For non-English speaking subjects, the consent process should occur as provided in 12.9.1 A and B below. The consent document (long or short form) should be written in a language that the subject can understand (e.g., in Spanish for a Spanish-speaking subject), as provided at 12.9.A.1 and 12.9.1.B.2 below, and, if necessary, a translator should be provided.

A. Expected enrollment of non-English speaking subjects:

1. In studies where the PI expects non-English speaking subjects to be screened or enrolled, translation and IRB approval of the long form consent document is required.

B. Unexpected enrollment of non-English speaking subjects:

1. If a non-English speaking subject is unexpectedly enrolled in a study, there may not be an existing IRB-approved written translation of the consent document.
2. The IRB must approve the use of the short form process and the translated short form. The IRB must receive all foreign language versions of the short form document as a condition of approval under the provisions of 45 CFR 46.117(b)(2). The IRB must approve the summary statement provided to the subject, which may be the long form consent document.
3. When a short form and oral presentation are used with subjects who do not speak English, (i) the oral presentation and the short form written document should be in a language understandable to the subject; and (ii) the IRB-approved English language informed consent document may serve as the summary.
4. For subjects at the CC:
 - a. If a short-form consent in the subject's language is available and posted on the CC website (see References

below) follow the procedures for a short form written consent as described in 12.8.4.B.2 and 12.8.4.C above, once the IRB has approved the use of the short form process and the summary statement (12.9.B.1). All NIH IRBs have approved these translated short forms.

- b. When a short form is not available on the CC website, a translation must be obtained, as follows:
 - i. To assure the translation is accurate; the IRB requires a certified translation of the standard short form language without additional back translation. If no certified translation is available, a non-certified translation may be used, if an independent back translation is obtained.
 - c. For non-English speaking subjects for whom no written language exists, the English short form consent may be used with an interpreter and the IRB-approved English consent as the basis of oral translation, unless the IRB waives this requirement and provides an alternate plan for informed consent.
- 5. Expedited review of the short form consent process may be used if the protocol and the full informed consent document have already been approved by the IRB.

C. Use of interpreters in the consent process: Unless the person obtaining consent is fluent in the prospective subject's language, an interpreter will be necessary to deliver information in the IRB-approved oral consent process. It is preferable that someone who is independent of the subject (e.g., not a close family member, significant other, partner, etc.) be the interpreter.

12.9.2 BLIND SUBJECTS

The IRB may approve the use of an audiotaped consent for blind subjects. For blind subjects who read Braille, the IRB may approve a consent document prepared in Braille. In order to assure itself that a Braille consent document is accurate, the IRB may require a transcription into print text or a certified review of

the document by an IRB member or other person who reads Braille. If possible, the subject will sign the Braille consent; otherwise oral short-form consent will be obtained consistent with 12.8.4.B.2 and 12.8.4.C above. The printed text should be filed in the record with the Braille consent.

12.10 WAIVING OR ALTERING ELEMENTS OF INFORMED CONSENT

A. Circumstances in which the IRB may waive or alter elements of the informed consent procedure or waive the requirements to obtain informed consent (see 45 CFR 46.116(d) link in References below): An NIH IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent set forth in 45 CFR 46.116(a-b), or waive the requirements to obtain informed consent, provided the IRB finds and documents in the IRB meeting minutes:

1. The research involves no more than minimal risk to the subjects.
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
3. The research could not practicably be carried out without the waiver or alteration, and
4. Whenever appropriate, the subjects must be provided with additional pertinent information after participation.

B. IRBs may also waive or alter the elements of informed consent related to projects conducted or requiring approval of state or local government officials, (see 45 CFR 46.116(c)(1)).

12.11 WAIVER OF THE REQUIREMENT TO DOCUMENT INFORMED CONSENT IN WRITING

A. The IRB may waive the requirement for the investigator to obtain a signed consent form from 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 he/she wants documentation linking the subject with the research, and the subject's wishes will govern (45 CFR 46.117(c)(1)) (for example: domestic violence research where the primary risk is discovery by the abuser that the subject is talking to researchers); 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 the research context (45 CFR 46.117(c)(2)). (Examples include drawing a blood sample, or asking shoppers in a mall about the ambient lighting or temperature).
- B. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.
- C. FDA-regulated research, when applicable: The IRB may waive documentation of informed consent as described in SOP 15A "Research Regulated by the Food and Drug Administration (FDA): Information and Policies Specific to Research Involving Investigational New Drugs (Including Biological Products)", (21 CFR 56.109(c)).

12.12 WAIVER OF INFORMED CONSENT FOR PLANNED EMERGENCY RESEARCH

In limited circumstances, FDA and DHHS regulations allow for exception from informed consent requirements for some emergency research. For FDA these circumstances are described at 21 CFR 50.24 and 61 Federal Register pp. 51531-51533 October 2, 1996, (see References below). The HHS regulations provide a waiver of the applicability of the requirement for obtaining and documenting informed consent for a strictly limited class of research, involving research activities that may be carried out in human subjects who are in need of emergency therapy and for whom, because of the subjects' medical condition and the unavailability of legally authorized representatives of the subjects, no legally effective informed consent can be obtained. This waiver applies to Subpart A and Subpart D of the regulations (research involving children), but is inapplicable to Subparts B and C. See OHRP Dear Colleague Letter, on "Informed Consent Requirements in Emergency Research" (October 31, 1996) (see References below).

12.13 EMERGENCY MEDICAL CARE

This SOP does not limit the authority of a physician to provide emergency medical care, to the extent permitted to do so under applicable federal, state or local law (45 CFR 46 116(f)).

12.14 OBTAINING CONSENT BY TELEPHONE

For research protocols or any procedures performed for research purposes in which the authorized individual intends to obtain consent from a subject is not in the same location as the subject, for example, for specimen collection or interview, consent may be obtained via telephone and/or another electronic process, rather than in person. The procedures for obtaining consent, including how the consent document and/or other information will be transmitted and documented and by whom, shall be described in the written protocol (see 12.10 and 12.11, above, waiving or altering elements of informed consent). Prospective IRB review and approval is required. If eligible, the IRB may choose to review such requests through the expedited review procedure. A written signed consent must be faxed and/or mailed and made part of the record unless the IRB waives written consent.

Except in the examples above or in extraordinary circumstances, research consent should normally be obtained in person. For research conducted at the CC, the CC has additional policies regarding telephone consent that must be followed, Medical Administrative Series (MAS) 77-2, "Informed Consent" (see References below).

12.15 CONSENT MONITORING

12.15.1 CONSENT MONITORING BY AN IRB OR AUTHORIZED THIRD PARTY

DHHS Federal regulations allow an IRB, or an authorized third party, to observe the consent process and the research (45 CFR 46.109(e)).

- A. An NIH IRB may determine that monitoring of the consent process by an impartial observer (consent monitor) is required. For example, such monitoring may be warranted for:

- 1. High risk studies.

2. Studies that involve particularly complicated procedures or interventions.
3. Studies involving vulnerable populations.
4. Other situations when the IRB has concerns that the consent process may not be conducted appropriately, for example, to reduce the possibility of coercion and undue influence, to ensure that the approved consent process is being followed, or to ensure that subjects are truly giving informed consent.
5. As a corrective action where the IRB has identified problems associated with a particular investigator or a research project (see SOP 16A “Allegations of Non-compliance with Requirements of the NIH Human Research Protection Program (HRPP)”).

B. Development of a consent monitoring plan:

1. If the IRB determines that consent monitoring is required, the PI will develop a consent monitoring plan for review and approval by the IRB. The consent monitoring may be conducted by qualified persons including IRB members or others, either affiliated or unaffiliated with the NIH.
2. In the NIH CC, the Department of Bioethics consult service is available for consent monitoring.
3. When the IRB determines that consent monitoring is appropriate, the PI will be notified in writing including the reasons for the determination. The determination will also be noted in the IRB minutes/record.

12.15.2 MONITOR RESPONSIBILITIES

A. Monitor(s) may be asked to evaluate some or all of the following:

1. Whether the informed consent process was documented appropriately.

2. Whether the consent process minimized coercion or undue influence to the extent possible.
 3. Whether subjects were provided with adequate time to consider participation and have their questions answered.
 4. Whether the person obtaining consent appeared to be knowledgeable about the study and was able to answer questions.
 5. Whether the information was accurate and conveyed in understandable language, and
 6. Whether subjects demonstrated understanding of the information presented and gave their voluntary consent.
- B. If required by the IRB, a report of the findings during the observation of the consent process will be submitted to the IRB.

REFERENCES

- A. The Belmont Report: <http://www.hhs.gov/ohrp/policy/belmont.html>
- B. Department of Health and Human Services 45 CFR 46:
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>
- C. Food and Drug Administration 21 CFR 50:
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50&showFR=1&subpartNode=21:1.0.1.1.19.2>
- D. CC active consent
website: http://clinicalstudies.info.nih.gov/protocol_consents/
- E. 61 Federal Register pp. 51531-51533 October 2, 1996:
<http://www.gpo.gov/fdsys/pkg/FR-1996-10-02/html/96-24968.htm>
- F. OHRP Dear Colleague Letter, on “Informed Consent Requirements in Emergency Research” (October 31, 1996):
<http://www.hhs.gov/ohrp/policy/hcdc97-01.html>

G. Medical Administrative Series (MAS) 77-2, "Informed Consent": <http://cc-internal.cc.nih.gov/policies/PDF/M77-2.pdf>

H. Clinicaltrials.gov: <http://www.Clinicaltrials.gov>

LIST OF APPENDICES

A. Appendix A: Required Elements of Informed Consent

B. Appendix B: Additional Elements of Informed Consent

C. Appendix C: DDIR memorandum dated March 16, 1999 regarding NIH Policy on Reporting Clinical Research Results to Subjects

APPENDIX A: REQUIRED ELEMENTS OF INFORMED CONSENT

Except as provided elsewhere in this SOP (see 12.11), in seeking informed consent, the information listed below, at minimum, shall be provided to each subject as required by regulation:

- A. A statement that:
 - 1. 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, and
 - 5. Identification of any procedures which are experimental
- B. A description of any reasonably foreseeable risks or discomforts to the subject
- C. A description of any benefits to the subject or to others which may reasonably be expected from the research
- D. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
- E. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
- F. For research involving more than minimal risk, an explanation as to whether any compensation is offered, 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
- G. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

- H. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled (see 45 CFR 46.116(a)(1)-(8)). NIH Policy further requires the following information when seeking informed consent:
1. Contact information for the subjects to obtain answers to questions about the research or to voice concerns or complaints about the research and to obtain answers to questions about their rights as a research subject; in the event the research staff could not be reached or in the event the subject wishes to talk to someone other than the research staff.
- I. When the research is under the regulatory authority of the FDA, include:
1. A statement that there is the possibility that the Food and Drug Administration may inspect all research related records (21 CFR 50.25(a)(5)) – see SOP 15 “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications” and
 2. The following language for all applicable clinical trials approved by IRBs on or after March 7, 2012 (21 CFR50.25(c)):
 3. 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.”

APPENDIX B: ADDITIONAL ELEMENTS OF INFORMED CONSENT

When appropriate one or more of the following elements of information shall be provided to each subject (See 45 CFR 46.116(b)(1)-(6)).

- A. 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) that are currently unforeseeable. (For example: Include when the research involves investigational test articles or other procedures in which the risks to subjects are not well known.)
- B. Anticipated circumstances in which the subject's participation may be terminated by the investigator without regard to the subject's consent. (For example: Include when there are anticipated circumstances under which the investigator may terminate participation of a subject.)
- C. Any additional costs to the subject that may result from participation in the research.
- D. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- E. 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. (For example: Include when the research is long term and interim information is likely to be developed during the conduct of the research.)
- F. The approximate number of subjects involved in the study. (For example: Include when the research involves more than minimal risk to allow for an assessment of cumulative risk.)

NIH policy also requires consideration of inclusion of language about investigators' financial interests in the research, or other conflict of interest issues, and funding of the research by pharmaceutical companies or other organizations. Also, if the PI and IRB agree that certain research information ought not to be shared with subjects, the NIH requires inclusion of language that explains this limitation but recognizing that this limitation does not require the subject to waive any existing rights regarding access to information in the medical record. (See Appendix C)

APPENDIX C: DDIR MEMORANDUM DATED MARCH 16, 1999 REGARDING NIH POLICY ON REPORTING CLINICAL RESEARCH RESULTS TO SUBJECTS



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

Date: March 16, 1999

From: Deputy Director for Intramural Research, NIH
Director, Clinical Center and NIH Associate Director
for Clinical Research

Subject: NIH Policy on Reporting Clinical Research Results to Subjects

To: IC Scientific Directors
IC Clinical Directors
IRB Chairs
Laboratory, Branch and Section Chiefs
Clinical Investigators

In general, one of the expectations human subjects have when they participate in research is that they will learn something from their involvement. Principal Investigators (PIs) usually share appropriate research information with the subjects of their studies, either during the course of participation or after the study has been completed. However, the sharing of information with research subjects is not always explicitly addressed in informed consent documents.

In some cases, PIs and IRBs agree that, for various reasons, certain research information, particularly genetic research information, ought not to be shared with research subjects, and occasionally, NIH informed consent documents contain IRB-approved language which states that certain information will not be provided to research subjects. However, the Federal Privacy Act applies to the records of research conducted at the NIH when such records are retrievable by an individual identifier (see attached Summary of the Privacy Act). This means that any language in a consent form that waives an individual's right to obtain access to his/her records is inconsistent with the Privacy Act as well as with the Federal Regulations for the Protection of Human Subjects (45 CFR.46). These regulations prohibit the use of language in informed consent documents that would waive or appear to waive the rights of the subject (45 CFR 46.116).

In order to ensure compliance with the Privacy Act and the Federal regulations, effective immediately, for new protocols where the IRB and the PI agree that it is in research subjects' best interests not to have research information provided to the subjects, informed consent documents must explain the reason for this limitation and not remain silent about it. Also, the consent documents must state explicitly that subjects do not waive any rights they may have regarding access

to research information. Current consent documents that restrict subjects' access to research information should be carefully checked by the IRB and PI at the time of continuing review and revised appropriately.

A subcommittee of the Human Subjects Research Advisory Committee (HSRAC), which included the NIH Legal Advisor, has developed the following suggested informed consent language for use in such cases. The first paragraph offers various options (italicized in brackets) for informing subjects that their access to information may be limited. This paragraph may be altered or expanded by the PI and the IRB as necessary to fit the protocol, but the language of the second paragraph **must not be changed**, although where it is placed in the informed consent document should be as judged appropriate by the PI and the IRB. Furthermore, it is only necessary to include these two paragraphs in consents where subjects' access to research information is to be limited; they are not required if PIs plan to allow subjects unlimited access to information.

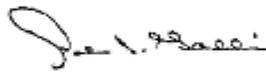
"The investigators conducting this study do not plan to provide you with the results of any medical tests or evaluations or other information pertaining to you, or other research data or results because [the results will be preliminary] [the results will require further analysis] [the results may reveal unwanted information about family relationships] [further research may be necessary before these results are meaningful]. [If meaningful information is developed from this study that may be important for your health, you will be informed when it becomes available.]

"By agreeing to participate in this study, you do not waive any rights that you may have regarding access to and disclosure of your records. For further information on those rights, please contact Dr. _____ (PI)."

It is important for PIs to know that if a subject requests medical/research information about himself or herself, the Federal Privacy Act requires the PI to give that information either to the subject or to a third party designated by the subject (such as a family physician) whether or not the subject has signed a consent form that contains language similar to that above. The Privacy Act regulations' special access provision applies to medical records, and although there is no definition of "medical", the NIH Legal Advisor considers the term broad enough to encompass records of experimental tests and treatment provided in clinical research. PIs are strongly urged to familiarize themselves with the provisions of the Privacy Act in order to make sure they understand how this act applies to their research.

If you have questions about the use of the suggested informed consent document language, please contact Dr. Alan Sandler, Director, Office of Human Subjects Research, at 2-3445.


Michael M. Gottesman, M.D.


John I. Gallin, M.D.

Attachment

cc: Mr. Lanman
Dr. Sandler