

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

**OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS**

**SOP Number: 12**

**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 Standard Operating Procedure (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 12.10, 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. Before any research procedures are initiated, NIH requires written informed consent from research subjects, or their legally authorized representatives (LAR) for an adult (see 14E - Research Involving Adults Who Are or May be Unable to Consent), or the permission of parent(s) or guardian(s) for a minor (see 14D - Research Involving Children). Written informed consent is required unless informed consent and/or the written consent document is waived by an Institutional Review Board (IRB), consistent with requirements in this SOP (see 12.10, 12.11, 12.12 and 12.13 below). For more information about FDA requirements, see 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 U.S. Department of Health and Human Services (DHHS) 45 CFR 46 and the FDA 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 (CC), 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 (e.g., NIEHS Research Triangle Park, NIDA/NIA Biomedical Research Center, NIDDK Arizona and NIAID Rocky Mountain Laboratories) applicable local, or state law is followed in the absence of applicable U.S. Federal law. Note: For the purposes of this SOP, use of the term "subjects" will also refer to LARs.

- 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).
- D. Legally Effective Informed Consent: Informed consent is legally effective if it is both obtained from the subject or the subject's legally authorized representative and documented in a manner that is consistent with the HHS protection of human subjects regulations and with applicable laws of the jurisdiction in which the research is conducted. In general terms, the regulations stipulate that an investigator should seek consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to consider whether to participate and that minimize the possibility of coercion or undue influence. The information provided should be in language that is understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language (see 12.4.1 below).
- E. 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 DHHS REGULATORY REQUIREMENTS FOR 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. For more information about what constitutes exculpatory language see the link to the OHRP Guidance in References below.
- D. Except as provided elsewhere in this SOP (see Sections 12.10, 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 Principal Investigator (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)).

## **12.5 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) and 21 CFR 56.109(b) and (c). Generally, FDA requirements for obtaining and documenting informed consent are similar to those required by the Common Rule (45 CFR 46). Some distinctions include exceptions of general requirements for informed consent provided in 21 CFR 50.23 and exception from informed consent requirements for emergency research per 21 CFR 50.24 (see Sections 12.12 and 12.13 below), and that an IRB will require documentation of informed consent except as provided in 21 CFR 56.109(c). For information about FDA requirements for informed consent, see SOP 15 - Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications and SOP 15A - Research Regulated by the Food and Drug Administration (FDA) Information and Policies Specific to Research Involving Investigational New Drugs (Including Biological Products).

## **12.6 RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR**

It is the responsibility of the 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 conflict of interest clearance,

as applicable, from their Institute's ethics office consistent with the requirements of SOP 21 - Conflict of Interest Requirements for Researchers and Research Staff.

## **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 and, as applicable, 21 CFR 50), 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 12.10, 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 (see Section 12.16 below).
- 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 more information, 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).
- G. 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. The consent form will include elements required by Section 12.4 above (see Appendix A - Required Elements of Informed Consent as well as necessary elements from Appendix B - Additional Elements of Informed Consent).
- D. Upon approval, an informed consent form will include the date of IRB approval and the date through which the approval is valid.
- E. At the NIH CC, the NIH Consent templates (Form 2514-1), "Adult 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
- F. Any changes in the standard boilerplate language provided on the NIH consent/ assent templates (Forms 2514-1 and 2514-2, or templates in use at non-CC NIH sites) may be made only when recommended by the NIH IRB and approved by the NIH Office of the General Counsel (OGC). The Office of Human Subjects Research Protections (OHSRP) and the CC Office of Protocol Services (OPS) shall be informed by the IRB of any such changes.
- G. Additional applicable U.S. Federal, state, local, or foreign laws or NIH policies (e.g., privacy or genetic information) affecting consent documents should be considered.
- H. For research reviewed by an NIH IRB and conducted in the NIH CC:
  - 1. Other NIH CC policies address additional consent requirements; for more information, see the link to the Medical Administrative Series (MAS) Policies in References below.
  - 2. Additional approvals of consent documents (such as research radiation use) will be conducted by relevant NIH committees. (See Section 12.7.B above)
- I. In addition to 12.7.1, for research reviewed by an NIH IRB not conducted at the NIH CC:
  - 1. Additional approvals of consent documents (such as research radiation use) will be conducted by committees at other sites, if appropriate.

2. Local context, including site-specific requirements should be addressed, for example policies regarding research injury, privacy or confidentiality, or compensation. For more information, see SOP 20B - NIH IRB Responsibilities When Reviewing Local Context Considerations for Offsite Research.
  3. The approving IRB office will format the IRB-approved consent on the template approved for the non-CC NIH site's use (including the NIH-approved boilerplate language) and provide a copy to the CC OPS for posting on the CC Consent/Assent website.
- J. For research reviewed by a non-NIH IRB but conducted at a NIH site:
1. At the NIH CC: The NIH Consent Document templates (Form 2514-1), "Consent to Participate in a Clinical Research Study" and the "NIH Minor Patient's Assent to Participate in a Clinical Research Study" (Form 2514-2) will be used.
  2. Non-NIH IRBs may not make any changes to the standard boilerplate language within the NIH consent/assent templates.

## **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 OF PRELIMINARY INFORMATION TO PROSPECTIVE SUBJECTS**

In order to provide preliminary study information to prospective subjects, investigators, or others on the research team, may discuss the proposed research with them 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 Office for Human Research Protections (OHRP) guidance. See the link to the OHRP “Guidance on Engagement of Institutions in Human Subjects Research” (section B, Part 4) in References below.

## **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 PI 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.
  - 1. At the CC, IRB-approved consents/assents must be downloaded from the CC active consent website (see References below).
- B. Required signatures on informed consent documents are specified below:
  - 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.

Note: For research conducted at the NIH CC a witness is also required to sign the document. For the long-form consent process, 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.
- 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.
- d. When the short form document is used to obtain informed consent from a non-English speaking subject, the PI or individual authorized to obtain consent or an NIH staff member, must complete the Administrative section of the short form consent. The Administrative section documents whether a staff member who provides interpretation support for consent administration also served as a witness and includes a means to identify the interpreter or other individual providing interpretation support if he or she did not sign as a witness. A telephone interpreter may not serve as a witness. A witness must be present at the location of the individual obtaining consent. If interpretation support is used at the Clinical Center, the PI or authorized person must also complete the fields in the consent progress note within the Clinical Research Informatics System (CRIS) to document that interpretation support was utilized and name or identify the individual providing interpretation support.
- e. If the short form is used for an FDA-regulated study, please be aware of the following excerpt from FDA guidance "A Guide to Informed Consent - Information Sheet: Guidance for Institutional Review Boards and Clinical Investigators": A witness is required to attest to the adequacy of the consent process and to the subject's voluntary consent. (For more information, see <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm>, last updated 01/25/2016)

3. See 12.9.2 and References for more information about alternative, acceptable methods for documenting subject consent.

C. After signatures are obtained:

1. Long form: A copy of the signed and dated consent form must be given to the person signing the form.
2. Short form: 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 at the NIH 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. For research not conducted at the NIH CC: 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, B and C 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 12.9.1.A and 12.9.1.B.2 below, and, as necessary, an interpreter must be used during the consent process. To assure the consent form translation is accurate; the IRB may require a certified translation of the consent language without additional back-translation. If no certified translation is available, a non-certified translation may be used, and an independent back-translation must also be obtained

#### **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). See item 4 below for more information about the use of IRB-approved translations of short-form consents on the CC Consent/Assent website. The IRB must approve the written 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.3 and 12.8.4.C.2 above, once the IRB has approved the use of the short form process and the summary statement (12.9.B.2). All NIH IRBs have approved the translated short forms on the CC website.
    - b. 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 the oral informed consent process, 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 long form informed consent document have already been approved by the IRB.
  6. The witness to a short form consent process is frequently, but not always, conversant in the language of the participant. (The NIH subject population is extremely diverse and researchers cannot always obtain a witness fluent in the participant's language.)
- 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. Generally, the interpreter's role is to accurately convey the information exchange between the individual authorized to obtain consent and the potential subject (such as translating information or questions) and to facilitate an interactive discussion between the potential subject and the person authorized to obtain consent. 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. If interpretation support is used at the Clinical Center: The PI or authorized person must also complete the fields in the consent progress note within the Clinical Research

Informatics System (CRIS) to document that interpretation support was utilized and name or identify the individual providing interpretation support.

### **12.9.2 BLIND, ILLITERATE OR DISABLED SUBJECTS**

An investigator must document the method used for communication with the prospective subject in the subject's research record (and, if at the CC, in the subject's medical record) and must document the specific means by which the prospective subject communicated agreement to participate in the study.

- A. For blind subjects, the IRB may approve a consent document prepared in Braille for blind subjects who read 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. The printed text should be filed in the record with the Braille consent. 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.2 above.
- B. In the case of where disability prevents subjects from being able to physically sign his/her name, or in the case of illiterate subjects, the subjects can be enrolled in a study by "making their mark" on the consent document (long or short-form as applicable), and as applicable, when consistent with state law.
- C. The PI must seek, and the IRB may approve, the use of assistive technology (e.g., audiotape) to aid subjects (e.g., those that are illiterate or blind) to review the consent form content.
- D. A subject who is physically unable to make their mark and unable to speak can be entered into a study if they are competent and able to indicate approval or disapproval by other means approved by the IRB.
- E. IRBs may consider approving the short form consent process in situations where the subject is unable to read the consent form due to illiteracy or blindness.
- F. Waiver of documentation of informed consent must have IRB approval consistent with 45 CFR 46.117 and Section 12.11 below.

### **12.9.3 SUBJECT WITHDRAWAL FROM AN FDA REGULATED CLINICAL INVESTIGATION**

Please see SOP 15 - Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications for guidance on issues related to withdrawal of subjects from the interventional portion of an FDA regulated clinical investigation (e.g., the need for obtaining additional informed consent if the subject is willing to engage in continued limited study participation and such a situation was not described in the original informed consent form).

## **12.10 WAIVING OR ALTERING ELEMENTS OF INFORMED CONSENT UNDER 45 CFR 46**

- A. Circumstances in which the IRB may waive or alter elements of the informed consent procedure or waive the requirements to obtain informed consent: 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 (see 45 CFR 46.116(d), link also in References below).
  
- B. An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent or waive the requirement to obtain informed consent provided the IRB finds and documents that:
  - 1. The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and
  - 2. The research could not practicably be carried out without the waiver or alteration (see 45 CFR 46.116(c)).

## **12.11 WAIVER OF THE REQUIREMENT TO DOCUMENT INFORMED CONSENT IN WRITING UNDER 45 CFR 46**

- A. The IRB may waive the requirement for the investigator to obtain a signed consent form from some or all subjects provided the IRB finds and documents that either:

1. 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. 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. When the IRB considers waiving the requirement to obtain written documentation of the consent process, the IRB reviews a written description of the information that will be provided either verbally or in writing to participants. This may be a script or a statement about what information will be conveyed.
- C. Waiver of Parental or Guardian Consent: In addition to the provisions for waiver contained in §46.116 of subpart A, if the IRB determines and documents 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 in Subpart A and 45 CFR 46.408(b), provided that 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 applicable 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 (45 CFR 46.408(c)).

## **12.12 WAIVER OF THE REQUIREMENT TO DOCUMENT INFORMED CONSENT IN WRITING UNDER 21 CFR 56 (AS APPLICABLE)**

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)). The IRB must document the waiver in the IRB Minutes. When the IRB considers waiving the requirement to obtain written documentation of the consent process, the IRB reviews a written description of the information that will be provided either verbally or in writing to participants. This may be a script or a statement about what information will be conveyed.

## **12.13 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). Please see SOP 15A - Research Regulated by the Food and Drug Administration (FDA): Information and Policies Specific to Research Involving Investigational New Drugs (Including Biological Products) for FDA regulations related to exception from informed consent for emergency research (21 CFR 50.24.) This research must also comply with the requirements of 45 CFR 46, if applicable. The DHHS 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 LARs 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. Please see Appendix D (the OHRP Dear Colleague Letter, on "Informed Consent Requirements in Emergency Research" (October 31, 1996).

## **12.14 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)).

## **12.15 OBTAINING CONSENT BY TELEPHONE**

Generally, informed consent should be obtained in person. For research protocols or any procedures performed for research purposes in which the investigator intends to obtain consent from a subject who is not in the same location as the investigator, for example, for specimen collection or interview, consent may be obtained via telephone and/or another electronic process, rather than in person. A witness to the consent process must be present at the location of the individual obtaining consent. 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. 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 (see 12.10 and 12.11, above, waiving or altering elements of informed consent.

If telephone consent is used and the subject is seen subsequently at an NIH site, it is recommended to re-confirm the subject's understanding of the study and willingness to participate through an additional, brief consent process conducted at the NIH site as required by the IRB.

## **12.16 CONSENT MONITORING**

### **12.16.1 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 capable of 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. At the NIH CC, the Department of Bioethics consult service is available for consent monitoring (i.e. CC Department of Bioethics Ability to Consent Assessment Team (ACAT))

3. NIMH Human Subject Protection Unit (HSPU) also provides consent monitoring as well as other monitoring or consultative services and consent training for investigators and research staff. For more information, see References below
4. 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

## **12.16.2 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. Consent Monitoring Reporting:
  1. The Consent Monitor will document the informed consent process in the medical and/or research record as required by the IRB
  2. A report of the Consent Monitor's observations of the consent process may 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 (FDA) 21 CFR 50: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=50&showFR=1&subpartNode=21:1.0.1.1.19.2>
- D. Food and Drug Administration (FDA) 21 CFR 56.109: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=56.109>
- E. FDA Guidance on Consent of Illiterate Subjects: <http://www.fda.gov/regulatoryinformation/guidances/ucm126431.htm#illiterate>
- F. Clinical Center Active Consent/Assent website: [http://clinicalstudies.info.nih.gov/protocol\\_consent/](http://clinicalstudies.info.nih.gov/protocol_consent/)
- G. 61 Federal Register pp. 51531-51533 October 2, 1996: <http://www.gpo.gov/fdsys/pkg/FR-1996-10-02/html/96-24968.htm>
- H. OHRP Dear Colleague Letter, on “Informed Consent Requirements in Emergency Research” (October 31, 1996): <http://www.hhs.gov/ohrp/policy/hcdc97-01.html>
- I. Medical Administrative Series (MAS) Policies: [http://www.fda.gov/Safety/Recalls/ucm515610.htm?source=govdelivery&utm\\_medium=email&utm\\_source=govdelivery](http://www.fda.gov/Safety/Recalls/ucm515610.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery)
- J. Clinicaltrials.gov: <http://www.Clinicaltrials.gov>
- K. Ability to Consent Assessment Team (ACAT): May be reached at (301-496-9675 or 301-496-2429) at the NIH Clinical Center. For consult at non-CC sites see item M below for the Bioethics Consult Service.
- L. NIMH Human Subject Protection Unit (HSPU): <http://www.nimh.nih.gov/labs-at-nimh/scientific-director/office-of-clinical-director/office-of-the-clinical-director-hspu-mcru.shtml>
- M. Clinical Center Department of Bioethics Consult Service: <http://www.bioethics.nih.gov/clinical/consultation.shtml>
- N. OHRP Guidance: Exculpatory Language in Informed Consent: <http://www.hhs.gov/ohrp/regulations-and-policy/guidance/exculpatory-language-in-informed-consent-documents/index.html>

## LIST OF APPENDICES

Appendix A: Required Elements of Informed Consent

Appendix B: Additional Elements of Informed Consent

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

Appendix D: OHRP Dear Colleague Letter on informed consent requirements in emergency research (October 31, 1996)

## 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)):

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.

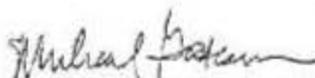
A subcommittee of the Human Subjects Research Advisory Committee (HSRAC), which included the NIH Legal Advisor, has developed the following suggested informed consent language for use in such cases. The first paragraph offers various options (italicized in brackets) for informing subjects that their 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.

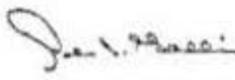
**"The investigators conducting this study do not plan to provide you with the results of any medical tests or evaluations or other information pertaining to you, or other research data or results because *[the results will be preliminary] [the results will require further analysis] [the results may 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

## **APPENDIX D: OHRP DEAR COLLEAGUE LETTER ON INFORMED CONSENT REQUIREMENTS IN EMERGENCY RESEARCH (OCTOBER 31, 1996)**

### **Informed Consent Requirements in Emergency Research**

Number 97-01

Human Subjects Protections

**Revised** (p. 2)

**OPRR Reports**

October 31, 1996

Subject: Informed Consent Requirements in Emergency Research

Dear Colleague:

This letter advises Institutional Officials and Institutional Review Board (IRB) Chairs of responsibilities related to informed consent when research subjects are enrolled in emergent circumstances.

As in the past, the regulations for protection of human subjects of the Department of Health and Human Services (HHS) at 45 CFR Part 46 stipulate requirements for obtaining (Section 46.116) and documenting (Section 46.117) informed consent. And, the regulations give IRBs authority to alter or waive the required consent in certain circumstances (Sections 46.116(c)-(d))<sup>1</sup>. These provisions of HHS regulations remain unchanged and in full force.

On October 2, 1996 (**Federal Register**, Vol. 61, pp. 51531-51533), the Secretary, HHS, announced, under Section 46.101(i), a waiver of the applicability of the 45 CFR Part 46 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, which provides a third route through which IRBs may approve research in this class, takes effect November 1, 1996.

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<sup>1</sup> A previous "Dear Colleague" letter (OPRR Reports 93-3, August 12, 1993) describes this authority of IRBs to alter or waive the requirement for informed consent

This waiver applies to the Basic HHS Policy for Protection of Human Research Subjects (Subpart A of 45 CFR Part 46) and to research involving children (Subpart D of 45 CFR Part 46). However, because of special regulatory limitations relating to research involving fetuses, pregnant women, and human in vitro fertilization (Subpart B of 45 CFR 46), and research involving prisoners (Subpart C of 45 CFR Part 46), this waiver is inapplicable to these categories of research.

### **Emergency Research Consent Waiver**

Pursuant to Section 46.101(i), the Secretary, HHS, has waived the general requirements for informed consent at 45 CFR 46.116(a) and (b) and 46.408, to be referred to as the "Emergency Research Consent Waiver" for a class of research consisting of activities, each of which have met the following strictly limited conditions detailed under either (a) or (b) below:

#### **a. Research subject to FDA regulations**

The IRB responsible for the review, approval, and continuing review of the research activity has approved both the activity and a waiver of informed consent and found and documented:

1. that the research activity is subject to regulations codified by the Food and Drug Administration (FDA) (see **Federal Register**, Vol. 61, pp. 51498-51531) at Title 21 CFR Part 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE), the application for which has clearly identified the protocols that would include subjects who are unable to consent, and
2. that the requirements for exception from informed consent for emergency research detailed in **21 CFR Section 50.24** have been met relative to those protocols, **or**

#### **b. Research not subject to FDA regulations**

The IRB responsible for the review, approval, and continuing review of the research has approved both the research and a waiver of informed consent and has (i) found and documented that the research is not subject to regulations codified by the FDA at 21 CFR Part 50, and (ii) found and documented and reported to the OPRR that the following conditions have been met relative to the research:

1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
2. Obtaining informed consent is not feasible because:
  - i. the subjects will not be able to give their informed consent as a result of their medical condition;
  - ii. the intervention involved in the research must be administered before consent from the subjects' legally authorized representatives is feasible; and
  - iii. there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
3. Participation in the research holds out the prospect of direct benefit to the subjects because:
  - i. subjects are facing a life-threatening situation that necessitates intervention;
  - ii. appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
  - iii. risks associated with the research 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.
4. The research could not practicably be carried out without the waiver.
5. The proposed research protocol 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 representatives and make this information available to the IRB at the time of continuing review.

6. The IRB has reviewed and approved informed consent procedures and an informed consent document in accord with Sections 46.116 and 46.117 of 45 CFR Part 46. 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 research consistent with paragraph (b)(7)(v) of this waiver.
7. 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 research will be conducted and from which the subjects will be drawn;
  - ii. public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits;
  - iii. public disclosure of sufficient information following completion of the research 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 data monitoring committee to exercise oversight of the research; 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 research. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

In addition, the IRB is responsible for ensuring that procedures are in place to inform, 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, of the subject's inclusion in the research, the details of the research and other information contained in the informed consent document. The IRB shall also 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 research and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into research with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the research is to be provided to the subject's legally authorized representative or family member, if feasible.

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

On October 2, 1996 (**Federal Register**, Vol. 61, pp. 51498-51531), the FDA published a final rule which amends FDA regulations to authorize a waiver of informed consent in research which is regulated by FDA. The joint publication of these actions permit harmonization of the HHS and FDA regulations regarding research in emergency circumstances. The HHS waiver, just as the FDA regulatory change, provides a narrow exception to the requirement for obtaining and documenting informed consent from each human subject or his or her legally authorized representative prior to initiation of research if the waiver of informed consent is approved by an IRB. The waiver authorization applies to a limited class of research activities involving human subjects who are in need of emergency medical intervention but who cannot give informed consent because of their life-threatening medical condition, and who do not have available a legally authorized person to represent them. The Secretary, HHS, is authorizing this waiver in response to growing concerns that current regulations, absent this waiver, are making high quality research in emergency circumstances difficult or impossible to carry out at a time when the need for such research is increasingly recognized.

Sincerely,

/s/

/s/

Gary B. Ellis, Ph.D.  
Director  
Office for Protection from Research Risks

Melody H. Lin, Ph.D.  
Deputy Director  
Office for Protection from Research Risks