Michigan State University
Human Research Protection Program

Subject: Informed Consent

Section: 6-4

This policy and procedure supersedes those previously drafted.

Approved by: Vice President of Research and Graduate Studies, 4-21-2005. Revision 1 approved by the Vice President of Research and Graduate Studies on 2-1-2006. Revision 2 approved by VP Research & Graduate Studies on 3-9-2008. Revision 3 approved by VP Research & Graduate Studies on 8-22-2011.

Related Sections: 2-2-A, 2-2-C, 2-4, 6-4-A, 6-4-B, 6-4-C, 6-5, 6-8, 7-4, 9-7, 12-4

1. “Except as provided elsewhere in this policy, §§50.23 and 50.24, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.

2. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

3. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative.

4. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.” 45 CFR 46.116, 21 CFR 50.20 [FDA]

Obtaining informed consent is typically a fundamental ethical requirement for research involving human subjects; it reflects the basic principle of respect for persons. Respect for persons requires that subjects, to the degree they are capable, be given the opportunity to choose what shall or shall not happen to them. Informed consent assures that prospective human subjects will be informed of the nature of the research and can knowledgeably and voluntarily decide whether or not to participate. Informed consent must be obtained voluntarily, without undue influence or coercion, especially when vulnerable populations are involved, such as children, mentally handicapped persons, prisoners, and institutionalized persons. See the Human Research Protection Program (HRPP) Manual 6-8 “Special Categories of Subjects” for policies and procedures regarding vulnerable populations. See HRPP Manual 6-4-C “Parental Consent and Child Assent” for policies and procedures relevant to research involving children. However, in some cases, informed consent can be waived. See HRPP Manual 6-4-B “Waiver or Alteration of Informed Consent” for policies and procedures on waiver of informed consent. See HRPP Manual 12-4 “Consent Form Guidelines” for further guidelines regarding the consent form.
When evaluating the consent process, the Institutional Review Board (IRB) will consider the general regulatory requirements for informed consent.

IRB members should also evaluate the consent form(s) using the basic and additional elements of consent.

**Basic Elements of Informed Consent**

"Basic elements of informed consent. [Except as provided in paragraph (c) or (d) of this section,] in seeking informed consent the following information shall be provided to each subject:" [HHS] 45 CFR 46.116(a), 21 CFR 50.25(a)

1. **A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.**

   An estimate of the total amount of time required on the part of the subject (e.g., number of sessions, frequency of testing) should be included.

2. **A description of any reasonably foreseeable risks or discomforts to the subject.**

   If there is a risk of injury to the subject(s) one of the following statements must appear on the consent form. The principal investigator (PI) is responsible for assuring that appropriate financial arrangements have been met, if appropriate, and providing documentation (e.g., contract).

   1. **No costs will be paid**

      "If you are injured as a result of your participation in this research project, Michigan State University will assist you in obtaining emergency care, if necessary, for your research related injuries. If you have insurance for medical care, your insurance carrier will be billed in the ordinary manner. As with any medical insurance, any costs that are not covered or are in excess of what are paid by your insurance, including deductibles, will be your responsibility. The University’s policy is not to provide financial compensation for lost wages, disability, pain or discomfort, unless required by law to do so. This does not mean that you are giving up any legal rights you may have. You may contact [insert principal investigator’s name and phone number] with any questions or to report an injury."

   2. **Third party will pay**

      "If you are injured as a result of your participation in this research project, Michigan State University will assist you in obtaining emergency care, if necessary, for your research related injuries. If you have insurance for medical care, your insurance carrier will be billed in the ordinary manner. Any costs that are not covered or are in excess of what are paid by your insurance, including deductibles, shall be paid by [insert name of payee]. The University’s policy is not
to provide financial compensation for lost wages, disability, pain or discomfort, unless required by law to do so. This does not mean that you are giving up any legal rights you may have. You may contact [insert principal investigator’s name and phone number] with any questions or to report an injury.”

3. For research studies that are funded

If the sponsor has requirements different or in addition to the statements above (i.e., U.S. Army), language will be negotiated with the IRB and other appropriate individuals (e.g., PI, department, sponsor, legal counsel). In any case, “no informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.” 45 CFR 46.116, 21 CFR 50.20.

(3) “A description of any benefits to the subject or to others which may reasonably be expected from the research.”

If treatment is involved, include a statement that beneficial effects cannot be guaranteed.

(4) “A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.”

When a treatment is involved, alternative treatments/therapies, including standard therapy, should be described before the description of the research protocol. The alternative treatment description should include a record of the alternative treatment’s successes.

(5) “A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained [and that notes the possibility that the Food and Drug Administration may inspect the records].” [FDA]

Statements concerning confidentiality should include language equivalent to the following: “Your privacy and / or confidentiality will be protected to the maximum extent allowable by law.” Since there are situations in which a researcher may be compelled to break the confidentiality of subjects (e.g., in response to a subpoena or at the request of an MSU IRB), no absolute guarantees of confidentiality are possible.

For research studies to which U.S. Food and Drug Administration (FDA) policies and procedures apply, a statement must be included that notes the possibility that the FDA may inspect the records.
(6) “For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.”

See required element (2) for risk of injury language.

(7) “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.”

All consent forms should include the researcher's contact information and MSU’s IRB contact information. Subjects should be invited to contact the researcher to discuss any questions about the research or research related injuries or to lodge a complaint. Additionally, the consent form should plainly state that if subjects have questions regarding their role and rights as subjects of research, they may contact the IRB separate from the PI. See HRPP Manual 12-4 “Consent Form Guidelines” for recommended language.

IRB contact information should be incorporated into the body of the consent form(s). It is not acceptable as a footnote or in a smaller typeface than the regular text.

(8) “A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.”

Explanation should include that the subjects may refuse to participate in certain procedures or answer certain questions.

Additional Elements of Informed Consent

“When appropriate, one or more of the following elements of information shall also be provided to each subject” 45 CFR 46.116(b), 21 CFR 50.25(b)

(1) “A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.”

Medical consent forms should include a phrase explaining the possibility of unforeseeable risks.

(2) “Anticipated circumstances under which the subject’s participation may be terminated without regard to the subject’s consent.”

(3) “Any additional costs to the subject that may result from participation in the research.”

Such a statement should be included when subjects are paying some kind of fee for service. Investigators should distinguish between fees from ordinary care or service and fees that might result from the subject’s participation in research. See HRPP Manual 7-4 “Charging for Investigational Drugs” for policies and procedures.
For medical research studies, investigators must incorporate one of the following three paragraphs in their consent form(s):

1. “Your participation in this research project will not involve any additional costs to you or your health care insurer.”

2. “Your participation in this research will necessitate additional procedures [indicate procedures, e.g., obtaining medical tests and examinations] which will be discussed with you. The cost may be covered by your insurance. Those costs not covered by the insurance will be provided by research funds. However, you will still remain responsible for the insurance deductibles and co-pays.”

3. “Your participation in this research project may involve additional costs to you for [indicate source of cost, e.g., drugs, device, diagnostic procedure, therapeutic procedure]. Your health care insurance probably will not pay for all of these additional costs. We [or your health care provider] estimate that the additional, unreimbursed costs to you will not exceed ($     ). If actual costs exceed this estimate, you are still responsible for them.”

(4) “The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.”

See HRPP Manual 9-7 “Subject Withdrawal from Research” for guidance on subject withdrawal.

(5) “A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.”

(6) “The approximate number of subjects involved in the study.”

**FDA Requirement for Clinical Trials**

(c) When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act.

The statement is: “A description of this clinical trial will be available on [http://www.ClinicalTrials.gov](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.” 21 CFR 50.25, Federal Register Vol. 76, No. 2 (January 4, 2011)

Published in the Federal Register Vol. 76, No. 2 (January 4, 2011), the FDA amended its “current informed consent regulations to require that informed consent documents and
processes for applicable drugs (including biological products) and device clinical trials include a specific statement that clinical trial information will be entered into a databank.” The rule is effective March 7, 2011 and the compliance date is March 7, 2012, for clinical trials that are initiated on or after the compliance date. The “FDA intends to enforce this final rule, new 50.25(c), only for informed consent documents and processes that are initiated on or after the compliance date. . . . Re-consent, based solely on the new requirement, of clinical trials participants in clinical investigations that were initiated before the compliance date will not be required. If a clinical investigation is ongoing as of the final rule compliance date, the new requirement will not be applicable.” Federal Register Vol. 76, No. 2 (January 4, 2011).

**Informed Consent Process**

The IRB must determine that in seeking consent, the required disclosures will be provided to each subject or a legally authorized representative in accordance with legal and regulatory requirements and consider whether additional disclosures are required for inclusion in the consent process and that the appropriate elements of disclosure are included.

Informed consent should be thought of as an educational process that takes place between the researcher and the prospective subject rather than simply a form that must be signed. In the process of obtaining informed consent, each element of consent should be carefully, patiently, and simply explained to the prospective subject in terms he/she can understand. Therefore, informed consent language and its documentation should be written in "lay language" (i.e. understandable to the people being asked to participate). Use of scientific terms and legalese is not appropriate. Simple declarative sentences are most appropriate for explaining the research study’s purpose, duration, experimental procedures, alternative treatments (if applicable), risks, and benefits. To ensure that the subject will be able to make an informed decision about whether to participate (particularly in instances where research involves significant risk or prospective subjects are likely to have difficulty understanding the procedures that will involve them), investigators may want to use audiovisual aids, enlist the help of lay people in explaining informed consent, utilize comprehension tools, or periodically assess the prospective subject’s understanding of informed consent by asking questions. The consent process will be documented according to legal and regulatory requirements. See HRPP Manual 6-4-A “Documentation of Informed Consent.”

The IRB will review the nature and circumstances of the consent process, such as who will conduct the consent interview, the timing of obtaining consent, and any waiting period between informing the subject and obtaining consent, and based on this information, determine whether the criteria for approval of research are met. The IRB will evaluate the information that will be communicated to the subject during the consent process, and determine which information will be disclosed.

**Foreign Language Consent**

If subjects are not fluent in English, translations of the consent form into the subject’s primary language(s) must be submitted to the IRB before these subjects can be
enrolled. It is solely the responsibility of the investigator to ensure that any translation is error free. An English version of the consent must be submitted, reviewed, and approved by the IRB with the translated consent. In some cases a short form can be used. See HRPP Manual 6-4-A “Documentation of Informed Consent” for details regarding use of a short form.

**Observation of Informed Consent**
The IRB has the authority to observe, or have a third party observe, the consent process and, when necessary, the IRB may require such observation as part of the consent process. 45 CFR 46.109(e), 21 CFR 56.109(f). The observation might be done by the IRB, IRB staff, other individuals within the organization, by a third party hired by the organization, investigator, sponsor, or other appropriate individuals as requested by the IRB.

IRB observation of consent may be required in situations in which the competence of the subject to provide informed consent is questionable, e.g., research subjects with diminished capacity.

Other situations where observation of informed consent may be requested include:
- Concerns raised during the initial review due to the sensitive nature of the research study (e.g., if the investigator described safeguards to assure the protection of research subjects, verification that safeguards are in place)
- High risk research studies (e.g. Phase I)
- Clinical investigations where the investigator is also the sponsor
- Previous noncompliance
- Complaints
- Others as the IRB sees fit

**Subject Withdrawal of Consent**
A decision by any subject to withdraw his/her consent and to discontinue participation in the investigation shall be honored promptly and unconditionally. Investigators may not withhold benefits to subjects that they would be otherwise entitled to (e.g., other extra credit opportunities for students or medical/psychological care for patients that would be normally available). See HRPP Manual 9-7 “Subject Withdrawal from Research” for additional requirements for subject withdrawal.

**Passive Consent**
Passive consent is a practice of providing the subjects with information and informing them that they will be included in the research unless they explicitly object to their inclusion. This does not meet the regulatory criteria for obtaining legally effective informed consent in accordance with 45 CFR 46.116. Passive consent may only occur if the IRB approves a waiver or alteration of informed consent. See HRPP Manual 6-4-C “Waiver or Alteration of Informed Consent” for requirements.
Waivers
If the investigator would like to waive or alter the consent procedure or waive the documentation requirement, specific criteria must be met. See HRPP Manual 6-4-C “Waiver or Alteration of Informed Consent” and 6-4-D “Waiver of Documentation” for policies and procedures.

Incentives
Incentives should be described in consent form. See HRPP Manual 6-5 “Selection of Subjects and Recruitment” for policies and procedures.

Placebo Control Studies
The IRB recommends that the following paragraph be placed in the consent form of placebo-controlled studies. It may be modified as necessary for the terms of the research study.

“This is a placebo-controlled study. There will be two (or more) groups of patients; one or more groups will receive the active drug which is being studied; the other(s) will receive a placebo. A placebo is an inactive substance which will have no direct effect on your illness. The patients in the study will be assigned at random, that is, by a method of chance, to one of the groups. You will have a chance of being in a placebo group or an active drug group. Neither you nor your physician will know which group you are in.”

Exculpatory Language
The consent form cannot include any language whereby the subject waives, or appears to waive, any of his/her legal rights. Further, it cannot include any exculpatory language releasing the institution or its agents from their responsibility to subjects.

Use of IRB Approved Consent Form
Investigators must use the consent form approved by the IRB. Investigators should typically use the consent form with the actual IRB approval/expiration footer language included in the form by the IRB. Investigators should contact the IRB staff if they are unable to use the consent form with the IRB approval / expiration footer language (e.g., mail merge).

Copy of Consent Form Provided to Subjects
Subjects must be provided with a copy of the consent form. In some instances, the subject must be provided with a copy of the signed consent form. When oral consent is used, subjects may be provided a written copy of the consent script including PI and IRB contact information. For online research (e.g., online surveys), the investigator should include an option for the subject to print the consent information for their records.

Consent Form Record Retention
By federal regulation, investigators must retain copies of signed consent forms or oral consent records (e.g., logs) for at least three years past the completion of research activities. For audit purposes, it is recommended that copies of all documents submitted to the IRB also be kept for three years following study completion. Investigators should
not retain only the signature page, but the entire consent form so that they retain the entire consent form as signed.

**Consent Form Guidance**
See the HRPP Manual 12-4 “Consent Form Guidelines” for guidance on consent form requirements. Consent form templates for biomedical and social science research are also available on the [HRPP website](http://hrpp.org).

**Additional Considerations**
For research studies subject to the requirements of the U.S. Department of Defense, the Department of Justice, or the International Conference on Harmonization Good Clinical Practice (E6), see the following sections of the HRPP Manual:
- 2-2-A U.S. Department of Defense
- 2-2-C U.S. Department of Justice
- 2-4 International Conference on Harmonization Good Clinical Practice (E6)