Section 9
Informed Consent

9.1 Informed Consent of Human Subjects of Research (Reviewed 7/1/10)

Respect for persons requires that research subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. The informed consent process is the instrument to provide this opportunity. Except where a waiver is granted, the IRB requires that the investigators of a research project obtain informed consent from human subjects or their legally authorized representative at the time of consent. A legally authorized representative is defined as parent(s) of a minor child; court appointed guardian; or Durable Power of Attorney (DPA) with specific instruction for research. In obtaining informed consent, the investigators shall do the following:

- Determine if the subject has the capacity to understand the protocol and make an informed choice;

- Give the subject (or representative) sufficient information about the study and how the study may affect the subject, and sufficient time to read and consider the informed consent document;

- Deliver the information in a comprehensible manner, using a language readily understandable by the subject, and emphasizing the required and the most important information;

- Assure that participation is voluntary, by providing sufficient opportunity to consider whether or not to participate, and minimizing the possibility of coercion, undue influence, or harassment.

Informed consent is not valid unless the subject or the subject’s legally authorized representative is fully informed about all the information in the consent document. Signatures on consent forms do not absolve the investigator of the responsibility to make sure that the subject or the subject’s legally authorized representative is fully informed about the research. Signatures on the consent form should be the culmination of the initial consent process.

Once a subject agrees to participate, the subject or the subject’s legally authorized representative must initial, sign and date the consent form in the appropriate places. The person obtaining consent must also sign the form and, in so doing, affirm that the subject has been fully informed about all aspects of the study, alternatives to participation have been discussed, and the subject willingly gives their consent to participate in the study. The person obtaining consent should sign the consent form on the date that he/she has actually performed the consent process.

9.2 Obtaining Informed Consent (Reviewed 7/1/10)
The process of obtaining informed consent has two components:

- Providing the information necessary to give informed consent to the person who is being recruited to become a subject of research, or that person's authorized representative, and obtaining the consent to participate in the research as a subject;

- Documentation that informed consent has been obtained to include consent to release Protected Health Information (PHI) as may be necessary.

In accordance with Federal guidelines, under certain circumstances, the IRB has the authority to waive the requirement for obtaining informed consent, or for documenting that the consent has been obtained.

Informed consent must also be obtained prior to invasive procedures that are performed solely to determine eligibility for research.

Consent is an ongoing process that requires the investigator to keep subjects apprised of issues that arise which may affect their willingness to continue participation. The subject’s continued willingness should be documented periodically in the subject’s medical record and/or research record, and in some cases a revised consent form or addendum may be appropriate. There are certain circumstances where a subject may be asked to re-consent to participation in the research study (See Reconsenting Subjects).

9.3 Elements of Informed Consent (Reviewed 7/1/10)

The basic elements of informed consent are reflected in the Pre-submission Quality Assurance Checklist. See the Consent for Research Template for required and suggested language assistance when preparing the informed consent within Tallahassee Memorial HealthCare. It is recommended that Principle Investigators provide research volunteers with the Office of Human Research Protections brochure Becoming a Research Volunteer.

9.4 Informational Component of Informed Consent (Reviewed 7/1/10)

The IRB requires that the information necessary to give informed consent by the research subject is given to that person or the person's authorized representative in writing and orally.

- The written document shall include the title of the study, the names of the investigators, and how the investigators may be reached;

- The name of the Administrative Liaison/IRB and how he/she may be reached;
• The content shall include at least the basic elements of informed consent; the use of a template or checklist prepared by the IRB is strongly recommended. In most instances, a single document shall be employed, encompassing all aspects of the research; the information shall not be fragmented;

• The content shall be easily understandable by a layperson with modest education;

• The investigator shall present the written document to the subject or the subject’s authorized representative, and provide an opportunity and sufficient time for them to study the document and ask questions;

• At the time of obtaining the consent, the investigator shall provide additional verbal information, as needed, so that the nature and anticipated consequences of the study are sufficiently clear;

• 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, an authorized representative of the subject, or if such a representative is not reasonably available, a family member. This information will include the subject’s participation in the clinical investigation, the details of the investigation 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, an authorized representative of the subject, or if such a representative is not reasonably available, a family member that s/he may discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If an authorized representative or family member is told about the clinical investigation and the subject’s condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before an authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject’s authorized representative or family member, if feasible.

• In addition to the information given to the subject or the subject’s authorized representative, the written document shall indicate that informed consent has been obtained prior to initiation of any study procedure. A third person must witness the consent interview only in the unusual situation that the subject or subject’s representative is not given the opportunity to read the consent document before it is signed. The witness will attest to the accuracy of the presentation and the apparent understanding of the subject.

• Investigators will obtain the permission of one or both of the parents or guardian (as appropriate) and the assent of children or decisionally impaired individuals who possess the intellectual and emotional ability to comprehend the concepts involved.

Before the study may start, the text of the informed consent document must be approved by the IRB. Each copy of the document to be presented to the subject of research shall contain a "Date of Approval" corresponding to the date of the initial approval of the project by the IRB or the date that the informed consent was modified and approved by the IRB. (*Exhibit A-TMH IRB Approval Stamp*)
9.5 Documentation of Obtaining Informed Consent (Revised 7/1/10)

In most instances, the act of obtaining consent is validated when the subject or the subject’s authorized representative and the investigator or authorized designee sign the written informed consent. In the case of a child/decisionally impaired individual able to comprehend the nature, risks and benefits of the research study a signature assenting to participate in the study is required in addition to the signature of the authorized representative.

One copy of the signed consent form must be given to the person signing the consent form (subject or representative) and a second copy should be placed in the subject’s medical chart when the study patient is receiving study treatment in the hospital or TMH outpatient setting. The original, signed consent form must be retained in the PI’s research records. Consent forms must be retained for all subjects enrolled in the study, regardless of whether they withdraw or are withdrawn. Subjects are considered enrolled at the moment they sign the consent form, whether or not they actually participate in the research or any of the procedures involved.

The following information should be documented in the subject’s record:

- a statement in the progress note for the professional domain of the investigator/study coordinator obtaining the informed consent that the subject met all inclusion/exclusion criteria;
- the consent was discussed explaining procedures and requirements, viable alternatives and material risks, if any;
- the subject was given an opportunity to ask questions and receive answers;
- the consent was obtained prior to any study procedures;
- the subject was enrolled in study “Title” and given a copy of the consent; and
- the note concludes a signature, date and time.

9.6 Research with Decisionally Impaired Adults/Minors (Revised 7/1/10)

Federal recommendations include the requirement to obtain assent from individuals who do not have the capacity to provide consent for themselves. This may be due to a condition that renders them permanently incapable of consenting, or a temporary condition that makes it impossible to obtain their informed consent at the time that enrollment must occur.

Sample Adult Assent Form

Sample Minor Assent Form

If a protocol includes the recruitment of subjects whose capacity is questionable, it is recommended that a series of review questions be administered following the informed consent process in order to assess individual understanding. In addition to the suggested questions on the review sheet, it may be appropriate to add a few protocol-specific questions in order to assess a subject’s understanding of an unusual or complex aspect of the research.
Sample Research Review Questionnaire

Assent is not just a form, it is a process involving a discussion between the investigator and the decisionally impaired adult. While the assent form example may be used verbatim, investigators should consider whether certain sensitive information, such as requirements for pregnancy or drug testing, should be conveyed in writing. In addition, investigators should list any study requirements the decisionally impaired adult must perform on her/his own, such as keeping a diary, monitoring activity levels, etc.

If a subject regains his/her ability to make healthcare decisions, s/he should be given the opportunity to provide consent. (See Section 9.13 Re-consenting Subjects)

9.7 Waiver of Informed Consent Requirements (Reviewed 7/1/10)

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent in instances where the IRB finds and documents that certain criteria (as listed below) are met. Any waiver that is requested will be considered by the IRB on a case-by-case basis within the framework of the following criteria. IRB Form 4b must be completed when requesting a waiver of the informed consent requirement. The IRB may decide not to grant a waiver, and to require all of the elements of consent, for protocols which appear to meet these criteria if it determines that doing so is in the best interest of the subjects.

A complete waiver of informed consent can only be granted if one of the two following sets of criteria is met:

1. The research or demonstration project is to be conducted by or is 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 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.

Or all of the following must be met:

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.

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
AND the criteria are met for a waiver of HIPAA authorization to use or disclose PHI in the conduct of research. These informed consent requirements are not intended to preempt any applicable Federal, State or local laws which require additional information to be disclosed in order for informed consent to be legally effective. Nothing in this guideline is intended to limit the authority of a physician to provide emergency medical care, to the extent that the physician is permitted to do so under applicable Federal, State or local law.

The IRB will use the criteria above in determining whether or not the consent requirement can be waived. The Principal Investigator must include a request for such a waiver (IRB Form 4b) with the IRB application and must provide justification for the request.

FDA regulations permit a limited class of research in emergency settings without consent. See 9.15 Projects Eligible for Waiver or Alteration of the Informed Consent Process in Emergency Situations.

9.8 Waiver of Documentation of Informed Consent (Revised 7/1/10)

The IRB shall use the criteria in 45 CFR 46.117(c) when considering a request for waiver of documentation of informed consent. The FDA only recognizes a waiver of informed consent for emergency research governed by 21 CFR 50.24, and 21 CFR Parts 56, 312, 314, 601, 812, and 814.

In cases where the documentation requirement is waived, the IRB may require that a written statement summarizing certain elements be provided to the subject. A waiver of signed consent does not exempt an investigator from obtaining verbal informed consent.

9.9 Persons Authorized to Obtain Informed Consent from Research Participants
(Reviewed 7/1/10)

Informed consent for research shall be obtained by the principal investigator or designee who is who familiar with all aspects of the research protocol and is listed on the Application for Approval of Research Involving Human Subjects as a research investigator or co-investigator.

The person obtaining consent must sign the form. By so doing, he/she attests that the subject has been fully informed about all aspects of the study, alternatives to participation have been discussed, and the subject willingly gives her/his consent to participate in the study.

9.10 Persons Authorized to Give Permission for a Subject (other than themselves) to Participate in Research (Revised 7/1/10)
Consent, or agreement to participate in a research study, shall be given by the individual who will be the research subject or a person who is permitted to act on behalf of that individual (a legally authorized representative). Persons consenting on their own behalf must be an adult over the age of 18 years whose clinical condition does not preclude them from making a sound judgment regarding the risks/benefits of participation. For adult subjects incapable of consenting to participation due to their clinical or mental condition, the IRB may approve a process whereby permission may be obtained from the subject’s legally authorized representative or, in limited cases, next of kin.

For children, the parent or legal guardian shall be permitted to act on behalf of the child and give permission for their participation. However, the assent of the child shall be obtained from any child considered mature enough to understand (usually in the range of 7-9 years of age), unless the IRB determines that the assent requirement can be waived (see Waiver of the Assent Requirement).

All research involving children as subjects shall be placed into one of the four categories of risk as outlined at 45 CFR 46.404, 405, 406, 407. The categories are as follows:

- Research not involving more than minimal risk. 46.404
- Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. 46.405
- Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition. 46.406
- Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. (Approval of research included under this category is very rare). 46.407. Research in this category needs approval of the Secretary – DHHS in addition to IRB approval.

9.11 Parental Consent Requirement (Reviewed 7/1/10)

When research is covered under the first or second bullet above (45 CFR 46.404 or 45 CFR 46.405), the permission of one parent shall be considered adequate unless the IRB indicates otherwise in its approval letter.

Where research is covered under the third or fourth bullet above (45 CFR 46.406 or 45 CFR 46.407, and when permission is to be obtained from parents, both parents shall give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. In this case, when only one parent is giving permission, the justification for not requiring the other parent’s signature shall be documented in the research record and on the consent form.
9.12 Waiver of the Assent Requirement  (Reviewed 7/1/10)

The IRB may grant a waiver for the assent requirement when it is determined that there is a prospect of direct benefit, no standard approved therapy exists which is equally effective, and/or the child may not have the ability to understand the ramifications of not participating.

9.13 Re-consenting Subjects  (Revised 7/1/10)

Subjects may need to be re-consented due to changes in their status (i.e., previously enrolled by proxy and are now able to consent on their own behalf) or due to changes in the protocol and/or consent form as follows:

- The protocol and/or consent form has been modified since the subject enrolled and the changes are more than administrative (i.e., the information which has been added/deleted may have an impact on risk to subjects and their willingness to participate).
- The subject was initially enrolled in a study by parents, a legally authorized representative or a research proxy because:
  - The subject was a minor at the time of entry into a study and has since reached the age of 18 and can now consent on his/her own behalf, or
  - The subject was incapacitated at the time of enrollment and has regained capacity to consent on his/her own behalf.

Regarding subjects asked to re-consent due to modifications to the consent form and/or protocol:

- If the modifications are minor (see Modifications) it may be appropriate to provide the subject with an addendum to the original consent form that provides the new information, or to verbally inform subjects of an administrative or other minor change with documentation in the medical record that such notification took place.

- If an addendum is used, it must clearly state that the information in the original consent form is still current and valid, and that the information is the addendum is supplementary.

If the modifications are major, subjects must be given a completely revised consent form to sign.

9.14 Expiration of Consent  (7/1/10)

The process of informed consent shall take place no more than 30 days prior to the initiation of the research. If more than 30 days has elapsed since the subject provided
consent, the process shall be repeated. The same requirements for signatures and obtaining consent apply when re-consenting or presenting an addendum to a study subject.

9.15 Projects Eligible for Waiver or Alteration of the Informed Consent Process in Non-Emergency Situations (Revised 7/1/10)

The FDA does not recognize the waiver of informed consent in non-emergent situations (21 CFR 50.24, and 21 CFR Parts 56, 312, 314, 601, 812, and 814). Consistent with 45 CFR 46.117(c), the IRB may waive the requirement for the investigator to obtain a signed consent form from some or all subjects of research, if the nature of the research meets all of the following:

- Is not violative and not invasive;
- Does not involve risks to the subjects that are more than minimal; minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests;
- Does not reveal subjects' identity, placing them at risk of criminal or civil liability, or damaging their financial standing, employability or reputation;
- Does not involve the collection or study of existing data, documents, records, pathologic specimens, or diagnostic specimens, in such a way that the subjects can be identified directly or through identifiers linked to the subjects;
- The Waiver of HIPAA Authorization Notification Request (see Section 10; IRB Form 4c) was approved.
- 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 the subject wants documentation linking the subject with the research, and the subject’s wishes will govern;

9.16 Waiver of Informed Consent in Emergency Research (Reviewed 7/1/10)

The IRB may considering granting an exception to the requirement for obtaining and documenting informed consent from a person or his/her authorized representative, as a condition of becoming a subject in a research project, in the following circumstances:

- The person being considered as a research subject is facing a life-threatening condition that requires emergent action to save life; and
• The person facing the life threatening, emergent condition is not capable of giving informed consent as a result of the condition; and

• An authorized representative, who could give informed consent in behalf of the person facing the life-threatening condition, is not accompanying the person and is not readily accessible within a therapeutic window of time;

• There is not time enough to locate an authorized representative to obtain consent.

When FDA regulated products are involved (drugs, biological products, and medical devices), the Federal Regulations 21 CFR 50.24, and 21 CFR Parts 56, 312, 314, 601, 812, and 814 are those used by the IRB to determine if a waiver is applicable to grant an exception to the requirement for an informed consent for the individual subject or the subject’s representative for emergency research. In such cases the following apply:

• requires an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE),

• involves human subjects who have a life-threatening medical condition (for which available treatments are unproven or unsatisfactory),

• involves subjects who, because of their condition (e.g., unconsciousness) cannot give informed consent, and

• administration of the intervention must occur before the informed consent from the subjects’ legally authorized representative may feasibly be obtained. Studies involving an exception from the informed consent requirements may proceed only after a sponsor has received prior written authorization from FDA, and the IRB has found and documented that specific conditions have been met.

9.17 Additional Protection of Subjects Rights and Welfare (Reviewed 7/1/10)

Additional protection of the rights and welfare of the subjects will be provided, including, at least:

9.17.1 Community Consultation Requirement (Revised 7/1/10)
• Prospective consultation with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn.

• Community consultation means providing the opportunity for discussions with, and soliciting opinions from the community(ies) in which the study will take place and from which the study subjects will be drawn.

• Consultation provides the initial opportunity for the IRB and clinical investigator(s) to inform community representatives:
  
  o that informed consent will not be obtained for most research subjects;
  
  o about the risks and potential benefits of the research;
• about an individual’s right to refuse to participate in research and ways in which individuals wish to be excluded may indicate this preference.

• The community representatives are expected to provide input to the IRB on community support for, or concerns about, the research activity

9.17.2 Public Disclosure Requirements (Reviewed 7/1/10)

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

• Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results. Based on this community consultation, the IRB should consider the response in reviewing the proposed investigation;

• Study protocols may describe situations in which emergency care personnel could reasonably infer that some incapacitated individuals would not agree to participate in a research study, even if the individuals meet the inclusion criteria. Clinical investigators should examine easily accessible sources of information, such as an individual’s driver’s license or medical jewelry, for evidence related to that individual’s willingness to participate in research;

• Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

• If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator will attempt to contact within the therapeutic window, one or more of the subject’s family members who are not legally authorized representatives. Phone consent will not be accepted. The family member will be asked whether s/he objects to the subject’s participation in the clinical investigation. The investigator will summarize efforts made to contact family members in the appropriate sequence (Durable Power of Attorney, spouse, adult children, parents, and siblings) and make this information available to the IRB at the time of continuing review;

• The investigator will provide a procedure to inform the subject, or if the subject remains incapacitated, an authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject’s inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document, and that s/he may discontinue the subject’s participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If an authorized representative or family member is told about the clinical investigation and the subject’s condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before an authorized
representative or family member can be contacted, information about the clinical investigation is to be provided to the subject’s authorized representative or family member;

- The above documentation is to be retained by the IRB for at least ten years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA.

### 9.18 Requirements to Waive Emergency Research Informed Consent (Reviewed 7/1/10)

The IRB may waive the requirement of informed consent if the IRB determines that all of the following conditions exist:

- Treatment available for the life-threatening condition is unproved or unsatisfactory (there is no alternative accepted method to reverse the life-threatening condition);

- There are sufficient data from animal or other studies to support the likelihood that the investigational intervention may reverse the life-threatening condition;

- There is a reasonable likelihood of direct benefit to the subject;

- The risks of harm to the subject, which may result from the investigational intervention, are reasonable;

- The benefits of the investigational intervention outweigh the risks to the subject;

- The research cannot be practically carried out without the waiver of informed consent requirement;

- The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence and within that window of time; the investigator will attempt to contact an authorized representative for consent. The investigator will summarize efforts made to contact authorized representatives and make this information available to the IRB at the time of continuing review;

- The IRB has reviewed and approved informed consent procedures and an informed consent document. These procedures and the informed consent document are to be used with subjects or those authorized representatives in situations where use of such procedures and documents is feasible.

### 9.19 Projects Eligible for Waiver of the Requirement for Documentation of the Informed Consent (Reviewed 7/1/10)

Provided the Waiver of HIPAA Authorization Notification Request (Section 10; IRB Form 4c) was approved, the IRB may waive the requirement for documentation of the
informed consent (a signed informed consent document), but not that of obtaining informed consent, under one of the following circumstances:

- The principal research risk is potential harm resulting from a breach of confidentiality, and the only record linking the subject and the research is the consent document;

- The research presents no more than minimal risk of harm to subjects, and does not include any procedure for which written consent would be required, if it were to be performed for clinical management. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

In cases where the IRB waives the requirement for documentation of informed consent, the investigators shall still provide the subject with a written informational document, as appropriate, the text of which shall be reviewed and approved by the IRB. Based on this information, the investigator shall obtain oral or implied, i.e., when subjects complete a questionnaire, consent to participate, but the granting of the consent will not be documented in writing.