INFORMED CONSENT

General requirements for informed consent, whether written or oral, are set forth as follows and apply to consent obtained in accordance with Federal regulations. Broad consent may be obtained in lieu of informed consent with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens, and may be used as described below. General waiver or alteration of informed consent is also described below.

In general, before involving a human subject in research covered by this policy, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the legally authorized representative shall be in language understandable to the subject or the legally authorized representative and they must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.

Except for broad consent, informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participated in the research. Informed consent as a whole must present information in sufficient detail relating the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

No informed consent may include any exculpatory language through which the subject or the legally authorized 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(a))

THE CONSENT FORM

The basic elements of a consent form are listed below. Since several of the items (numbers 4, 5, 6, 7, 8) can be worded in the same manner for most protocols, for your convenience an example last page of a consent form containing these elements is presented on page 23. If subjects under 19 years of age are involved in the project, please note additional instructions following this list.

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

   For studies involving FDA regulated products, the consent form must contain a statement that the purpose of the study also includes evaluation of the safety as well as the effectiveness of the test article.

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

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

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

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.

   For studies involving FDA regulated products, the consent form should inform subjects that the FDA may review the research records without prior clearance or permission by the clinical investigator, the subject, or the IRB.

6. A section advising the subject who to contact for <u>each</u> of the three instances (a)-(c) as well as the statement of (d) verbatim below:

   A. Name and phone number of person and location to contact regarding questions about the research.
   B. Name and phone number of person and location to contact regarding the research subjects' rights.
   C. Name and phone number of person and location to contact in the event of research related injury to the subject.
   D. 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.

7. An instruction that the person is free to withdraw his consent and discontinue participation in the project or activity at any time without prejudice.

8. An injury compensation clause stating where applicable that EAMC has made no provision for monetary compensation in the event of physical injury resulting from the research and in the event of such injury, medical treatment is provided, but is not provided free of charge.

9. If the consent form has more than one page, a line for the patients' initials should be included on all pages prior to the last page.

10. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject if otherwise entitled, and that the subjects may discontinue participation at any time without penalty or loss of same.

11. The consent form must contain one of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
   A. A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

B. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

12. One or more of the following elements of information, when appropriate, shall also be provided to each subject or the legally authorized representative:

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.

B. A statement of anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent.

C. A statement of any additional costs to the subject that may result from participation in the research.

D. A statement revealing 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 that may relate to the subject's willingness to continue participation will be provided to the subject.

F. The approximate number of subjects involved in the study

G. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.

H. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.

I. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

13. Each consent form should provide place for:

A. The signature of the subject or legally authorized representative
B. The signature of a witness
C. The dates of receipt of these signatures
D. The initials of the subject or legally authorized representative on each page

14. The last page should contain an IRB expiration date for the Consent Form and cannot be used beyond this date until renewal approval has been obtained.

15. A copy of the consent form must be provided for the subject to keep.

BROAD CONSENT

Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) is permitted as an alternative to the informed consent requirements. (45 CFR 46.116(d))

If the subject or the legally authorized representative is asked to provide broad consent, the following shall be provided to each subject or the subject's legally authorized representative:

1. The basic elements of the consent contained in items 2, 3, 5, and 10; and when appropriate elements 12(G) and 12(I) listed above under THE CONSENT FORM.

2. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted.

3. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens.

4. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite).

5. Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies.

6. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject.

7. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens and whom to contact in the event of a research-related harm.

Alteration or Waiver of Individual Authorization for Disclosure of Protected Health Information

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 in regulation, or waive the requirements to obtain informed consent provided the IRB finds and documents that (45 CFR 46.116(e)):

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. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format; and
5. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

In order to perform research using this Alteration or Waiver, the principal investigator must complete the form in Appendix B)

For access or use of an individual's protected health information in the conduct of research without the express authorization of the individual, the principal investigator must provide certain information related to the health information requested using the questionnaire for Waiver of Individual Authorization for Disclosure of Protected Health Information.

RESEARCH INVOLVING CHILDREN AS THE SUBJECTS

It is the policy of the IRB that research will include additional safeguards to protect the rights and welfare of children and that the regulatory criteria allowing approval under 21 CFR Part 50 subpart D have been met. As such, investigator must classify and satisfy the criteria for parts 50.51-50.54 as requested in the Project Review Panel report (page30).

For research involving children, the following conditions must be met:

ASSENT OF CHILD

Assent means the potential subjects' affirmative agreement to participate in the research. Mere failure to object should not, in the absence of affirmative agreement, be construed as assent. The following list indicates how assent of children should be handled for children of different ages.

For the purpose of research involving children, a child is defined as a person under the age of 19 years.

1. For children under 7 years of age, the child is assumed to be incapable of giving assent (see "Parental Consent" below).

2. For children 7-19 years of age, the assent of the child or documentation of the reason for waiver of the assent is required. Assent of the child may be waived if the capability of the child to give assent is judged limited to by age, maturity, or psychological state. On page 24 is an example signature page of a consent form for research involving children.

PARENTAL CONSENT

1. If the proposed research involves no more than minimal risk, or is of possible direct benefit to the child, the consent of one parent is required.

2. If the research involves greater than minimal risk without direct individual benefit, permission must be obtained from both parents unless there is only one reasonably available parent. Guardian consent should be substituted for parental under appropriate legal constraints.

3. The investigator may request a waiver of parent or guardian consent if the research design does not require such consent to protect the subjects (for example, neglected or abused children), provided an appropriate mechanism is substituted.

4. Special provisions must be made for children who are wards of the state or any other agency, institution, or entity to be included in research involving greater than minimal risk without direct individual benefit.

EXAMPLE LAST PAGE OF INFORMED CONSENT

If you have any questions concerning the procedures, the responsible investigators will be glad to answer them for you. At the bottom of this page is a list of the names and numbers you may call for answers to your questions.

You are free to withdraw your consent and to discontinue participation in this project at any time without prejudice against future medical care you may receive at this institution. If the study is discontinued, standard treatment will be available.

The confidentiality of any information obtained from this study will be protected.

You understand that EAMC has made no provision for monetary compensation in the event of physical injury resulting from the research and in the event of such injury, medical treatment is provided but is not provided free of charge.

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.

(List here the names and numbers of persons who may be contacted for questions, see item 6, page 21 for requirements. This list must contain at a minimum the contact of the EAMC IRB Chairperson at 334-528-1326.)

_____ _____

Signature of Subject Date

_____ _____

Signature of Physician Date

_____ _____

Signature of Witness Date

_____

IRB Expiration Date

EXAMPLE SIGNATURE PAGE OF CONSENT FORM
FOR RESEARCH INVOLVING CHILDREN

You are making a decision whether or not to have your child participate in this study. Your signature indicates that you have decided to allow your child to participate, that you have read (or been read) the information provided above and that you have received a copy of this consent form.

_____ _____
Signature of Patient, Parent or Person responsible Date

_____ _____
Signature of Physician Date

_____ _____
Signature of Witness Date

ASSENT OF CHILD

_____ (name of child) has agreed to participate in research
_____ (title of project).

_____ _____
Signature of Parent, Guardian, or Child Date

WAIVER OF ASSENT

The assent of _____(name of child) was waived because of:

____ Age
____ Maturity
____ Psychological state of the child

_____ _____
Signature of Parent or Guardian Date

AUTHORIZATION OR WAIVER OF INFORMED CONSENT FORM

ALTERATION OR WAIVER OF INDIVIDUAL AUTHORIZATION FOR DISCLOSURE

OF PROTECTED HEALTH INFORMATION (Not applicable if Informed Consent is used)

I. Title of Project:

II. Principal investigator:

III. Date of Review:

IV. Describe the Protected Health Information ("PHI") for which use and access is necessary for this research project. Protected Health Information" shall have the meaning set forth in 45 CFR 164.501, including, without limitation, any information, whether oral or recorded in any form or medium: (i) that relates to the past, present or future physical or mental condition of an individual; or (ii) the provision of health care to an individual; or (iii) the past, present or future payment for the provision of health care to an individual; and (iv) that identifies the individual or with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

V. Criteria. The following criteria must be explained in detail:

A. Explain how the use or disclosure of the PHI involves no more than a minimal risk to the privacy of individuals, based on elements (1), (2) and (3) below:

(1) Describe the plan to protect the identifiers from improper use and disclosure.

(2) Describe the plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research. If there is a health or research justification for retaining the identifiers or such retention is otherwise required by law, please explain in detail.

(3) Attach a written statement setting forth adequate assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use of disclosure of PHI would be permitted by law.

B. Explain why the research could not practicably be conducted without the alteration or waiver.

C. Explain why the research could not practicably be conducted without access to and use of the PHI.

D. Explain why if the research involves using PHI or identifiable biiospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

VI. Explain how waiver of consent will not adversely affect the privacy rights and the welfare of the individuals.

VII. Explain how the privacy risks to individuals whose PHI is to be used or disclosed are reasonable in relation to the anticipated benefits, if any, to the individuals, and the importance of the knowledge that may reasonably be expected to result from the research.

NOW, THEREFORE, the Institutional Review Board of the East Alabama Healthcare Authority d/b/a East Alabama Medical Center after reviewing the information required by the Institutional Review Board as provided to use by the Principal Investigator for the Research Project titled _____ and determining that the Research Project meets the criteria established hereby approves the request for an alteration or waiver of individual authorization for disclosure of PHI and that said research be, and is hereby, authorized and empowered to alter or waive the individual authorization for disclosure of PHI as requested.

Alteration or Waiver of Authorization:

_____Approved on this _____ day of _____, 20___.

_____L.S.

Chairperson, Institutional Review Board
(or his/her designee)