SECTION 2

Authority, Duties, and Responsibilities of the IRB

2.1 Institutional Authority (Reviewed 7/1/10)

The responsibility for compliance with federal, state and Tallahassee Memorial Health Care, Inc. (TMH) regulations concerning activities involving human subjects and for assuring the protection of human subjects rests with the TMH Board of Directors. The Board of Directors have delegated this authority to the President/Chief Executive Officer (CEO) of TMH, who is legally authorized to act for the institution and to assume, on behalf of the institution ("Signatory Official"), the obligations under TMH’s Federal Wide Assurance (FWA) with the Department of Health and Human Services (DHHS).

TMH has designated an internal Institutional Review Board (IRB) to provide oversight for all research conducted under its FWA with DHHS. The IRB acts under the authority of the President/CEO. Additional Boards may be established as necessary.

TMH bears full responsibility of the performance of all research involving human subjects and for the protection of the rights and welfare of human subjects under its Assurance with DHHS, including complying with federal, state, or local laws as they may relate to such research and protections.

2.2 IRB Duties, Responsibilities, and Subcommittees (Reviewed 7/1/10)

IRB approval is required whenever human subjects are involved in the following:

- Research is to take place on the premises of any TMH facility;
- Research is to take place elsewhere, and involves an employee of TMH or related facilities as an investigator;
- Research is to take place elsewhere, utilizing data collected on current patients, research subjects or staff of TMH or related facilities, including those data stored in any form, off the premises of TMH or related facilities.

At its discretion, the IRB may accept for review and approval research projects that are to take place elsewhere on or off the premises of TMH or related facilities, with or without the involvement of members of the staff of TMH.

2.2.1 Duties (Reviewed 7/1/10)

The duties of the IRB include the following:

- Review all research protocols involving human subjects before the involvement of human subjects;
• Require revisions in research protocols and informed consent documents as a condition for initial or continuation approval;
• Approve, modify or disapprove new research projects and continuation of previously approved projects;
• Review and approve the methods that investigators propose to use to recruit participants;
• Monitor the activities in approved projects, in any way deemed necessary, including regularly scheduled progress reports at least every twelve months, to verify compliance with approved research protocols and informed consent procedures;
• Ensure prompt reporting to the IRB of any planned changes in approved projects so that no material changes occur without prior approval by the IRB;
• Ensure prompt reporting to the IRB of any severe adverse events occurring in approved projects or in other projects related in context to the approved projects;
• Suspend or terminate an approved project that is not being conducted in accordance with IRB’s requirements or that has been associated with unexpected serious harm to subjects;
• Review and monitor the use of test articles (investigational drugs and devices) for the purpose of treatment of serious or life-threatening illnesses.

The IRB will employ a review process which conforms to the Federal Policy for Protection of Human Subjects, the regulatory codes 45 CFR 46 of the HHS and 21 CFR 50, 56, 312 & 412 of the FDA, and the current Federalwide Assurance (FWA). The review process will be the same for all research involving human subjects conducted at TMH.

The IRB will notify the investigator of the project and TMH administration through the designated Institutional Official of its decisions to approve, disapprove, suspend or terminate research projects. In the case of disapproval, suspension or termination, the notification statement will include clearly defined reasons for the decision.

2.2.2 Responsibilities (Revised 7/1/10)

During initial protocol reviews, the IRB will attempt to identify:

• The potential for or existence of unfair or inappropriate billing of patients, Medicare, and other third party payors for medical items and services provided solely as part of experimental trials;
• Potential, unreasonable economic burdens imposed on research subjects;
• Improper or coercive financial incentives offered to subjects, or unethical recruitment methods;
• Inadequate budget support for promised activities;
• Grants awarded to investigators for little or no effort, or for studies of insufficient scientific value;
• Financial conflicts of interest that might bias an investigator.
2.2.3 Subcommittees (Reviewed 7/1/10)

Subcommittees will not be used to supplement the IRB’s initial review, continuing review, review of protocol changes, and/or review of reports of unanticipated problems involving risks to subjects or others or of serious or continuing noncompliance.

2.3 Investigator Conflicts of Interest (Reviewed 7/1/10)

The Institutional Review Board at Tallahassee Memorial HealthCare considers that the most important step in managing potential conflicts of interest lies in appropriate disclosure, and this begins with the investigator disclosure to a sponsor and the IRB of financial holdings, relationships, and other interests which might constitute a conflict of interest for the researcher as an investigator.

In order to comply with the Department of Health and Human Services (DHHS) guidance entitled "Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection (FDA)," TMH has established a policy for reviewing financial conflicts of interest of investigators and research staff. A Conflict of Interest Disclosure Questionnaire IRB Form 3 is completed with each new study application and each progress report renewal application.

The investigator or study staff will be considered to have a financial conflict of interest if they or their immediate family have material interests over $10,000 in the sponsoring entity, including speaking fees, consultation fees, stock ownership or other equity interests, patents, trademarks, copyrights, or licensing agreements. Interests under $10,000 are not considered to present a financial conflict, unless such interests represent over 5% ownership in the sponsoring entity.

A financial conflict of interest is not intrinsically wrong. Rather, the purpose in analyzing a financial conflict of interest is in trying to determine when the interest offers incentive to the investigators or other party to breach a duty to subjects or to society, and how to address the conflict of interest. As individuals vary in their personal integrity, and as the TMH IRB generally does not know investigators and other parties intimately enough to judge their integrity, the IRB at TMH uses two reasonable-person standards for analysis:

- First, the Board considers whether the financial conflict of interest could challenge the integrity of a reasonable individual.
- Second, the Board considers whether the financial conflict of interest would appear to a reasonable member of the general public to be a conflict that could challenge the integrity of the conflicted party.

Using these reasonable-person standards, the Board considers the following factors in its analysis of the reported conflict of interest:

- Amount of Risk
The degree of risk and discomfort faced by subjects in research varies greatly. In high-risk studies, such as those involving the use of a medical device in invasive surgery, a conflict of interest could greatly affect the risks faced by subjects. In a study involving the analysis of human tissue studies, the risks to the subjects are generally limited to confidentiality issues.

- **Effect of the Conflict of Interest on Subjective Decision-Making**

The participation of the party with the conflict of interest could affect subjective decision-making, both consciously and subconsciously, and thus influence the conflicted party's judgment and behavior. Subjective decisions that could be influenced by a conflict include the design of the research, choosing which subjects to enroll, clinical care provided to the subjects, use of subjects' confidential medical information, data collection and analysis, adverse event reporting, and the presentation of research findings.

- **Amount of Interaction Between the Conflicted Party and the Subjects**

Many of the concerns about the conflicted party's decisions will be lessened if the conflicted party does not interact directly with subjects. For example, in many tissue studies the conflicted investigator simply receives waste samples from a surgery facility, and has no contact with the subjects. On the other hand, in a similar study the investigator may also perform the surgery, in which case the concerns over the effect of the conflict are greater.

### 2.4 Other Parties Involved in Overseeing the Conflict of Interest (Reviewed 7/1/10)

- For FDA-regulated studies, the FDA will be providing a scientific review of the research results.

- NIH does detailed reviews of research proposals in advance, and inquires about conflicts of interest at certain procedural steps.

- An assigned subject advocate may sit in on the consent process.

The Board will consider the role and oversight of these and other such parties.

### 2.5 Training in Conflict of Interest (Reviewed 7/1/10)

The investigator or other conflicted party may have participated in training on the ethical analysis of conflict of interest and, therefore, may be more aware of the ethical issues and in need of less oversight.
2.6 Nature of the Interest, and Relationship to the Research (Reviewed 7/1/10)

The interest may be one in which large change is possible based on the outcomes of the study under review. An equity interest in a start-up company could be drastically affected by the research results, whereas stock in a large pharmaceutical company is not as likely to be affected. Is it a single site study or a multi-center study? The ability of the investigator or other conflicted party to affect the financial interest varies greatly in these different situations.

2.7 Unique Investigator or Institution Qualifications to Conduct the Research (Reviewed 7/1/10)

Occasionally, the investigator or institution is uniquely qualified to conduct the research. For instance, the investigational article may be a surgical device that has been developed by a surgeon who specializes in a surgical technique that only he or she performs.

2.8 Compensation to Investigators for the Conduct of Research (Reviewed 7/1/10)

Financial compensation to investigators should be at fair market value for the procedures and services provided. The IRB will review "bonus payments" and other compensation to investigators that is not directly tied to payment for study procedures or services on a case-by-case basis. (AMA Code of Medical Ethics Policy #E-8.0315)

2.9 Evaluating Conflicts of Interest (Reviewed 7/1/10)

Each conflict of interest shall be disclosed by the investigator. The disclosed or otherwise identified conflict of interest shall be presented to the Full Institutional Review Board. Completing and/or updating the Conflict of Interest Disclosure Questionnaire IRB Form 3 shall fulfill this requirement.

2.10 Managing Investigator Conflicts of Interest (Reviewed 7/1/10)

The following are actions the Board may take regarding Investigator conflicts of interest:

- A finding that the conflict of interest is not likely to jeopardize subject safety or bias the investigator's decision-making and does not require further action.

- A finding that disclosure of the conflict to subjects or others is necessary.
• A finding that controls on the conflict need to be put into place, such as limiting the role of the investigator with a conflict of interest.

• A finding that the conflict is unacceptable, and must be eliminated in order for the research to proceed.

2.11 IRB Member Conflicts of Interest (Reviewed 7/1/10)

IRB Members must recuse themselves from reviewing a research protocol whenever they self-identify themselves as possessing a Conflict of Interest in relation to that protocol. Recusal must occur before the discussion of, and vote on, the research protocol in relation to which the IRB Member has a Conflict of Interest. Nevertheless, the IRB Member may remain in the room prior to the discussion or vote in order to provide information relating to the protocol, and may, if he or she is an inventor and/or serves as an Investigator/Co-Investigator on that protocol, present or assist in presenting the protocol to the IRB Members.

2.12 Monitoring Research Accounting Practices (Reviewed 7/1/10)

The IRB relies on the Tallahassee Memorial HealthCare Compliance Program to monitor research accounting practices for:

• Inappropriate billing;
• Improper use of grant monies received by TMH or its employees;
• Compensation to TMH from sponsors in amounts greater than fair market value for services provided.

The IRB will notify the investigator of the project and TMH administration through the designated Institutional Official of its decisions to approve, disapprove, suspend or terminate research projects. In the case of disapproval, suspension or termination, the notification statement will include clearly defined reasons for the decision.

The Office of Research/IRB reviews Conflict of Interest Disclosure Questionnaire IRB Form 3 submitted with initial and continuing review applications. The Board will review any disclosed conflict of interest information at the Board meeting when the study is reviewed. The Chair or designee will be provided with any documentation of conflict of interest information submitted with the review packet at the time of expedited review. If the individual disclosing the conflict of interest has not presented an adequate plan to address the conflict of interest, the Board reserves the right to take the steps deemed prudent to ensure the conflict is managed in an effort to protect the rights of the study participants.